Clinical Practice Module

Quality Assurance

in

Collection of Donor Eyes

&

Corneal Grafting

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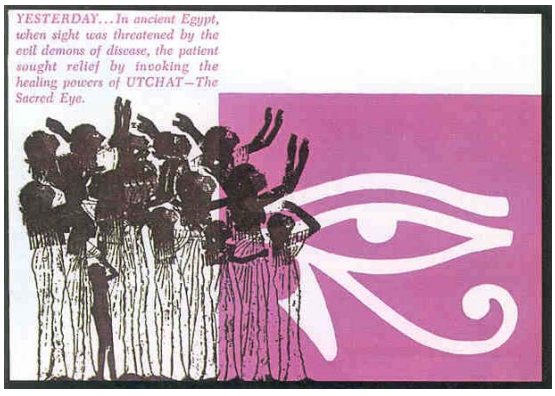

THE EYE IN MYTHOLOGY

The symbol of the Eye of Horus

In Egyptian religion, Horus was a falcon-headed solar diety.

The symbol was portrayed in Egyptian iconography as an "R" with an eye inside the top circle. It became a symbol of healing called Utchat. It is also believed to be the original form of "Rx". Amulets representing the Eye of Horus - The Sacred Eye - were used as protection against eye diseases and the evil eye.

Collection of Donor Eyes

Legal aspects of eye donation

The transplantation of Human Organs Bill, 1994, passed as Act No.42 of 1994 as the transplantation of Human Organs Act 1994.

This provides for the regulation of removal, storage and transplantation of Human Organs for therapeutic purposes and for the prevention of commercial dealings in human organs.

All the eye banking and collection of eyes has to be done as per this act.

- Eyes should be retrieved within **6 hours** after death.
- Donation can occur only after death.
- The legal ownership of the deceased belongs to the next of kin, and hence proper consent is required prior to enucleation. A prior pledge is invalid, unless proper consent is available from kith and kin.
- The enucleation can be done only by registered medical practitioners.
- There should not be any commercial benefit out of the entire process.
- The tissue can only be utilised by qualified ophthalmologist.
- The donor's identity is not disclosed.
- The identity of the recipient is not disclosed to the donor's next of kin.
- Tissue has to be distributed without discrimination; irrespective of race, creed, caste, color and nationality.

The following are the conditions in which the eyeballs should not be harvested from the donor:

1. Death due to AIDS
2. Death due to unknown cause
3. Death due to slow virus disease
4. Death due to Septicemia, cholera, tetanus
5. Malignancy with secondaries, ocular malignancy
6. Death due to Rabies
7. Hepatitis B and C and any type of infective hepatitis.

How to begin?

When the "donor call" is received, be sure to get as much information as possible from the caller, such as Donor's name, age, location, time of death, and cause of death. Also remember to get the caller's name, hospital or residence with telephone number. Possible landmarks for quicker approach & to avoid delay.

Some basic instruction can be given over the telephone such as, to close the lids immediately after death, head can be placed in an elevated position; ice packs can be placed on the closed eyelids, if available. Close relatives could be identified for signing the consent form.

Upon arriving on the scene one has to be sure to seek the eye donation pledge card if any, death certificate; if not confirm the death, look into medical history from donor's medical report, as there are few diseases which would preclude removing the tissue from the body.

Before starting enucleation, a word of sympathy could ease the tense, grim situation. One should also be appreciative of the generosity of the eye donation. The consent form should be filled up and duly signed by the next of the kin. The date, time and cause of death should be ascertained. The actual procedure of enucleation should preferably be conducted in a secluded place and never in open places. The sterilised drum/tray should be kept upon a clear surface close to the donor's head. As far as possible, the enucleation should not be done in the presence of family members, unless they are keen in watching the process. The procedure of enucleation should be carried out within 6-8 hours after death.

Enucleation Preparation

Donor's head is immobilised to prevent it from moving during the procedure. The surgeon should wear sterile gloves after scrubbing with soap and water. Try to avoid borrowing anything from the donor family. The surgical field (clean the area around the eyes and closed lids) should be painted by antiseptic lotion (spirit / 5% betadine). The area to be covered includes the eyebrows, nose and lower cheeks. It is essential that none of the antiseptic lotion come in contact with an exposed eye. One drop of 5% betadine is instilled into the conjunctival sac and irrigated with 20-cc saline. Antibiotic drops (gentamycin or chloramphenicol) are instilled.

Enucleation Procedure

The majority of corneas are retrieved from deaths occurring at home. The incidence of hospital retrieval is low in our country. The domestic retrieval is disadvantageous because of following reasons: (1) Atmosphere inside the house is somber and emotionally charged. (2) The enucleation has often to be conducted in the squatting posture as the bodies are placed on the floor; hence the enucleation becomes uncomfortable. (3) It is not sterile for several reasons. Corneal excision is not recommended for the following three reasons: i. Trained doctors or technicians are not available in all eye donation centres. ii. Storage medium is supplied to only selective eye banks in India. iii. STRICT asepsis is mandatory and one can not achieve it at home. The whole globe can be enucleated from the body or only the cornea with a 2-mm scleral rim can be excised in situ. The whole globe enucleation is more frequently done in our country.

Advantage of in situ corneo-scleral button excision

The viability of the endothelial cells are better preserved since the excised button is immediately transferred to a culture media. Cosmetically it looks better once the shell is placed over the globe.

Disadvantages of in situ excision

The person who excises the cornea should have sufficient training in assessing the donor cornea. Enucleation should be carried out only by registered practitioners in India. Technicians are not legally permitted to retrieve the tissue from the donor in our country. The medical personnel are expected to have good knowledge about the evaluation of donor eye and the significance of viable endothelium. There are chances to graft sub optimal tissue unless they notice and document aphakia, pseudophakia, diffuse folds etc.

Enucleation should be carried out by doctors trained for this job. This is particularly important in our country since eye donation is still very few in numbers.

Check List for Retrieval of Eyes after Death

1. Eye is draped.
2. The lid speculum is inserted to hold the eyelids apart. Antibiotics are applied liberally.
3. With the tissue forceps and conjunctival scissors, a cut is made in the conjunctiva about 3 mm from the limbus in each quadrant. After each cut of the scissors the blades are inserted to undermine the conjunctiva from the sclera. Conjunctiva is cut all around. (About 3 mm from the limbus).
4. With the muscle hook, the superior rectus is hooked. The muscles are cut with strabismus scissors close to the globe. The muscles should not be cut too close to the globe as this may lead to perforation.
5. The same procedure is adopted for inferior rectus and to cut all the recti muscles.

6. Enucleation spoon is introduced from the temporal side and the optic nerve is engaged in the slot of the spoon.
7. Now the enucleation scissors is inserted with blades closed either from the temporal side or from the nasal side. The tips of the scissors can be used as probe to find the optic nerve. Once the nerve is located, the scissors are opened and the nerve is cut. It may require several snips before the nerve is completely cut.
8. Care is taken not to loosen the speculum. A gentle upward traction is applied on the globe via the hemostat until it pops out. The globe will usually have some tissue attachment to the orbit – which should be cut to make the globe free.
9. Then the globe is transferred carefully under aseptic condition to appropriate eye collection chamber. The eyeball rests on cotton roll or preferably in eye holding metal stand. The eyeball rests in the chamber with cornea facing upwards. The cotton roll should be sterile and moist, with no excess solution in the container.
10. The second eye is then draped. The same procedure is repeated for the second eye.
11. The empty orbit is filled up with cotton balls or artificial eyes – after ensuring hemostasis. The eyelids are closed with black silk in case of whole eye retrieval.
12. The enucleated eyes are refrigerated as soon as possible at 4^0 C or placed in thermocol boxes containing ice cubes to maintain the temperature at about 4^0 C.
13. After the enucleation about 10 cc of blood is collected from the jugular vein or heart for routine serological investigations as recommended by Eye Bank Association of India (HIV, Hepatitis B, HCV and syphilis).
14. NEVER place the jars containing eyes in the FREEZER.
15. NEVER use DRY ICE.

Corneal Excision Procedure

This procedure needs more technical skill and requires great care under strict aseptic conditions. The excised corneoscleral button is then transferred to bottles containing M.K. Medium or any other recommended storage medium. The procedure of the excision is discussed in the section of corneal preservation.

Processing of Donor Eyes and storage in Eye Bank

Eyes are received from donors in wide mouthed eye collection sterile bottles containing eye stands to hold eyes. Moist cotton is placed at the bottom of the eye collection bottle.

Microbiological Investigation

1. In the Eye Bank, before processing the eyes, a swab is taken for bacterial and fungal culture from the donor eye.
2. The eyes are washed with 20 ml of sterile normal saline. Any extraneous matter should be removed. The eyes are cleaned of excess orbital tissue etc.
3. Treatment with antibiotics:

   After culture specimens have been taken, eyes are immersed in freshly prepared solution of 5% betadine for 2 minutes and then gentamycin solution for 5 minutes.
4. Eyes are then evaluated under focal illumination and slit lamp regarding epithelial status, corneal edema, folds, and total corneal thickness.
5. The eyes are treated with antibiotics again and transferred to preservation bottles.
6. Preservation.

   A. Moist Chamber: Could be used up to 48 hours. Surgery should be performed as an emergency on waiting recipients at hospital or within the city. So surgeon faces a lot of practical problems in getting the surgical team without a proper schedule.

B. M.K. Medium: For short-term preservation (up to 4 days), corneas with 2 – 3 mm scleral rim is preserved in McCarey Kaufman medium. For this, first with 2 – 3 mm of scleral rim is removed from the rest of the globe. The procedure is carried in laminar flow hood, under strict aseptic conditions. The blade tip enters beneath the sclera in the suprachoroidal space and incision is completed with corneal scissors. Precaution is taken not to loose AC at any time and iris or lenticular touch with the cornea is avoided. Scleral rim is then finally grasped and underlying iris as well as ciliary body is pushed away from the sclera by spatula. The corneal button with endothelial side up is placed in M.K. Medium. If budget permits the Eye Bank can use optisol for storage up to 2 weeks. M.K. Medium is prepared in India and supplied to recognised Eye Banks.

C. Glycerine Preservation: For non-viable long-term preservation, cornea with scleral rim is removed as above and placed in 100% Glycerine – Glycerine acts in deturgescing the cornea. Such corneas can be used for lamellar keratoplasty and emergency procedures like tectonic or therapeutic grafts.

D. Cryo Preservation: This involves the process of slow cooling to -196^0 C and rapid thawing. It is an expensive and cumbersome procedure, and hence is not practiced anywhere.

Various other procedures like organ culture method and other solution for intermediate preservation are being used by various eye banks.

Evaluation of donor tissue and its distribution.

The acceptability of all corneas and/or eyes received is subject to several criterias.

Age limits: Those under one year of age or over 70 years of age are not used for optical grafts. But the decision is made by the surgeon.

Time between death and enucleation should not be more than six hours and the preservation time should be within 18 hours.

Following assessments are made in slit lamp microscope:

Epithelial erosion, defects:

Extent of folds – Central, peripheral, diffuse

- Aphakia or Pseudophakia
- Guttate changes
- Haziness of cornea
- Arcus senilis
- Dense KP or a cloudy anterior chamber

In general, the eye bank personnel will perform the screening of acceptability of donor tissue that is to look for any systemic conditions obtained from donor's medical history. But the final responsibility for evaluation lies with the surgeon. AIDS screening is an important parameter in the present scenario.

* Serological tests to rule out HIV, Hepatitis – B & C, $HTLV_1$ and $HTLV_2$, Syphilis are routinely performed in all Eye Banks in developed countries. These tests are being carried out in few Eye Banks in India with technical assistance from International Federation of Eye Banks. It is ideal to perform these tests before passing the tissue as suitable for corneal grafting.

Equipments to run Modern Eye Bank

1. Frost free refrigerator with temperature monitoring device.
2. Autoclaves.
3. Slit lamp biomicroscope.
4. 4 – 6 sets of instruments for enucleation / excision.
5. Biohazard laminar flowhood.
6. Serology kits and equipments.
7. Kerato-analyzer (Optional).
8. Computers for data entry.
9. Audio-visual equipment for motivation and training the doctors, technicians and paramedical staff.

References

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2. *Eye Bank Association of America, Medical Standard Manual 1993.*

Corneal Grafting

Definition

Corneal grafting is the surgical procedure in which the abnormal recipient corneal tissue, either of full thickness or partial thickness, is replaced by donor corneal tissue of the same species.

a. Penetrating graft

Here the donor tissue replaces the full thickness of the recipient diseased cornea including endothelium.

b. Partial thickness or lamellar grafts

In this procedure only the superficial pathological portion of the recipient tissue is replaced leaving deeper layers intact.

Historical considerations and evolution

The first corneal transplant was performed by Reisinger in 1824. Over the past 50 years there has been a remarkable turn about in the success of corneal grafting through the work of many pioneering surgeons.

Epidemiology and Magnitude of Blindness

We have 12 million blind in our country i.e. a prevalence of 1.49 %. Among these 12 million blind, 2 million are blind in both eyes due to corneal disease. If we include patients who are blind in one eye the figure of corneal blinds in our country goes beyond 2 million. Every year 25,000 children go blind due to Vitamin A deficiency. 50% of 8 lakhs patients estimated with corneal ulcer in India, end up in mono-ocular blindness or visual impairment.

It has been reported[3] that 100 eye banks will have to collect 2,700 eyes each to clear the backlog of corneal blindness. Currently about 15,000 eyes are collected annually in India. Only 30-40% of donor eyes could pass the quality control and be released for corneal grafts.

General Indications for Corneal Grafting

1. Optical
2. Tectonic
3. Therapeutic
4. Cosmetic

Common Indications among Indians

1. Corneal Scar following keratitis, trauma, trachoma
2. Keratoconus
3. Pseudophakic or Aphakic corneal edema
4. Corneal dystrophy
5. Regrafts
6. Herpetic keratitis
7. Fuch's dystrophy

Indications in Paediatric Age Group

1. Congenital
   - Peter's anomaly
   - Sclerocornea
   - Glaucoma with corneal edema
2. Acquired
   - Corneal Scar, Ectasia
   - Corneal Edema
   - Regraft

Prognosis for Graft Clarity	Diagnosis
Group 1 Excellent prognosis 90% or more	Keratoconus Central Inactive Scar Granular or Lattice dystrophy Central Fuch's dystrophy Autografts
Group 2 Very good prognosis 80% - 90%	Advanced Fuch's dystrophy Pseudophakic or Aphakic Bullous keratopathy without vitreous disturbance and glaucoma Herpetic Scar, Interstitial keratitis Macular corneal dystrophy Regrafts in phakic eyes
Group 3 Fair prognosis 50% - 80%	Mild chemical burns Congenital Hereditary Endothelial Dystrophy Moderate keratitis sicca Regrafts in pseudophakic or aphakic eyes
Group 4 Poor prognosis 0 - 50%	Severe chemical injury Stevens Johnson Syndrome Associated severe glaucoma Multiple graft failure Therapeutic keratoplasty for active microbial keratitis

The above table gives a rough idea about the prognosis in various groups. Prognosis also depends on quality of donor tissue, surgical skill and postoperative follow-up.

Pre-operative evaluation and patient selection

Aim

To assess suitability for transplantation and establish prognosis for successful anatomical and functional result.

Methods

Detailed History

Complete Ophthalmic Examination

Systemic Examination to identify risk factors

Investigations

- Duration
- Predisposing factor
- Previous medical treatment
- Previous surgery
- Social history helps predict patient compliance, ophthalmic examination and diagnostic tests
- Pupillary reaction (consensual in other eye if opacity is dense)
- Associated squint, cataract
- Fixation of light
- Nystagmus
- Color recognition
- Slit lamp evaluation
- Ocular surface problem
  - Corneal Anaesthesia
  - Dry eye
  - Trichiasis
  - Exposure
  - Blepharitis
  - Rosacea
- IOP (pre-existing glaucoma)
- Ocular inflammation
- Calculation of IOL power in triple procedure and exchange of IOL
- Corneal vascularisation – superficial or deep and in how many quadrants
- Extent / Area of opacity, depth and density
- Fundus evaluation if possible
- Fluorescein Angiography to exclude CME and ARMD (optional)

Opaque media

- USG – If posterior segment pathology is suspected in children with congenital lesions
- Potential visual acuity meter
- Laser interferometer
- Blue field entoptic phenomenon testing
- VEP

Optional

Treatment

With the meagre supply of corneal tissue at one hand and the unusually high demand for corneal grafting on the other, a stringent balance is required to maintain uniform tissue distribution. Blindness due to bilateral corneal diseases, children with unilateral corneal pathology under six years in order to reverse or prevent amblyopia; symptomatic individuals such as painful bullous keratopathy should be given top priority. Also importance is given to cases with good prognosis; and deferred for cases like cosmetic correction and patients likely to have deep amblyopia usually seen in blind school. Patient education and counselling is done to make them realize the importance of follow up especially in children. Paediatrician and paediatric anaesthetist also take part in this process.

Choice of Anaesthesia

Local anaesthesia (retrobulbar or peribulbar and supplementary facial block) is adequate for most cases. General anaesthesia is preferred for children, likely in a prolonged surgery, and cases where the surgeon will not be able to communicate with the patients due to mental retardation, language barriers, deafness, epilepsy.

Surgery Step by Step

1. Making the recipient bed

This size of the pathological portion of recipient cornea is determined by calipers which is usually of size between 7.0 to 8.0 mm. Larger size grafts can develop peripheral anterior synechiae and postoperative glaucoma. Smaller grafts (less than 6.5 mm) will have suture tracks infringing on to the central cornea.

Disposable trephines are economical and used conveniently. A gentle groove is made for proper centration and then firm pressure with a rotatory motion is applied to cut the cornea with trephine blade. A sensation of giving way and leakage of aqueous with shallowing of anterior chamber indicates AC has been entered. Visco elastic substance is injected and AC is deepened. The cut is completed with care to achieve a vertical edge.

2. Excising the donor tissue

This method of donor excision is similar to the recipient trephination. The disadvantage of this technique is that significant endothelial cell loss could occur due to shear force exerted by the scissors blades during completion of the cut.

3. Punching from the endothelial aspect

The sclero-corneal button is placed on a teflon block with epithelial side over the block. A trephine is vertically placed to avoid irregular punching and slanting cut. One can use IOWA punch or other disposable trephines. Always have oversize of about 0.25 mm – 0.5 mm.

4. Suturing the Graft

The donor button is placed carefully over the recipient bed, with adequate visco buffer in anterior chamber taking care not to allow any unusual sliding of the donor tissue over conjunctiva. The first suture is passed through the donor button at 90% depth at 12 o'clock and through the host cornea at the same depth. The second suture is placed at 6 o'clock ensuring equal tissue distribution on both sides. The third and fourth sutures are placed at 3 0'clock and 9 o'clock position. The four cardinal sutures result in a diamond shaped contour. AC is deepened further and interrupted sutures are then placed sequentially in each quadrant. Sutures are then placed radially and centrally between two adjacent sutures and symmetrically at diagonal opposite ends. A total of 16 interrupted sutures are generally required; but more sutures may be applied if required. The visco elastic substance has to be replaced with balanced salt solution at the end of 8 interrupted sutures. The graft can be secured in several ways. Interrupted sutures are most commonly used, but many surgeons prefer continuous sutures or a combination of interrupted and continuous sutures. It is always safe to use interrupted sutures in cases of vascularised recipient corneas and corneas with variable thickness. Interrupted sutures facilitate selective suture removal.

Corneal Grafting Suturing

Suture material

10.0 Nylon suture ideal.

10.0 Mersilene suture (used by few surgeons when healing is delayed).

10.0 Nylon as interrupted sutures, combined with a single continuous (11.0 nylon) suture.

The four cardinal sutures could be removed or left after completing the surgery when continuous sutures are used. Bites are always from donor side towards the recipient cornea.

At the end of the surgery all suture knots should be buried on the donor side or recipients side and the donor edge should be tucked underneath the recipient edge to promote epithelial growth from host to donor postoperatively. In large sized grafts it is better to bury the knots in donor cornea to prevent vascularisation of suture tract.

Subconjunctival gentamycin (20 mg) is injected at the end of the procedure. In regrafts one can inject 2 mg dexamethasone also.

Routine postoperative medications

- Antibiotic (broad-spectrum) eye drops four times daily.
- Topical steroid four times daily (Prednisolone acetate 1% or Dexamethasone 0.1%).
- Topical beta blockers, tab acetazolamide if there is an elevated intraocular pressure especially in aphakic eyes.
- All systemic medications are continued (diabetics, cardiac, asthmatic, hypertensives).

The recipient should be examined at slit lamp microscope during each visit. They should usually be treated as inpatients for 5 – 7 days, if they have to travel long distance.

Postoperative Follow-up Visit

Patient is either treated as inpatient or outpatient depending on practical considerations. There is no text book follow-up schedule, which depends on nature of disease and type of patient.

- Weekly till one month, if the recipient lives near the facility or high risk recipient like children and therapeutic grafts
- Every month for 3 months
- Every 3 months for 1 year
- Annual follow-up

Note: Regrafts, bilateral grafts and patients with glaucoma and diabetic retinopathy should be followed up frequently. During each visit, the drugs are checked for compliance and the dosage adjusted.

Suture Removal

Sutures could be removed at slit lamp or under operating microscope under topical anaesthesia except in children.

Continuous sutures:

Can be left indefinitely unless it is broken, vascularised or result in high astigmatism.

Interrupted sutures:

1. The duration is unpredictable and variable according to the recipient pathology. In vascularised corneas, sutures can be removed even within 2-4 weeks after grafting.
2. In eyes with Keratoconus it is always better to wait until 6-12 months.
3. In children healing seems to be faster and early suture removal may be recommended.

In late postoperative period, all loose sutures should be removed and steroids should be restarted atleast for a week in order to prevent graft rejection. Loose sutures always promote infection and rejection.

Regrafts:

When will you do? It depends on blindness level and availability of better tissue. A bilaterally blind patient cannot wait to a theoretical possibility of reducing antigen load and suppression of inflammation. Ideally one has to wait for one year. The size of graft could be same or smaller.

Tissue Matching:

Available data doesn't conclusively prove the role of tissue matching in high risk patient. Moreover it is expensive and requires skilled manpower that may not be possible in developing countries.

For the detailed description of corneal grafting in children, triple procedures, exchange of implants, vitrectomy, silicone oil removal, the reader is recommended to read standard textbooks on corneal grafting.

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