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The Basics of Corneal Transplantation: From Donor to Recipient

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Introduction

While many people are aware of the possibility for transplantation, few are aware of the details surrounding the process. The technical skill and tissue preparation required for transplant are extensive. The graciousness of the donating patients and families makes the process possible. This is a brief overview of the process, from donor's death to the recipient's long-term outcome.

Table 1. Corneal Transplant Recipient Diagnoses in 2007

Indications for PKP	
Keratoconus	19.6%
Post-cataract surgery edema	15.7%
Repeat corneal transplant	15.7%
Fuchs Dystrophy	9.1%
Mechanical or chemical trauma	2.9%
Microbial changes	2.8%
Congenital Opacities	1.7%
Post-Refractive surgery	0.2%
Other causes of corneal opacification or distortion	19.3%
Other degenerations or dystrophies	12.8%
Indications for LKP	
Unspecified Anterior Stromal Scarring	32.7%
Keratoconus	27.6%
Ulcerative Keratitis or Perforation	16.2%
Corneal Degenerations	14.3%
Pterygium	4.3%
Trauma	3.2%
Post-Keratectomy	1.4%
Reis-Buckler's Dystrophy	0.3%

Source: Eye Bank Association of America, Year 2007 Statistical Report (EBAA, 1015 18th Street, NW, Suite 1010, Washington, DC, 20036).

History

Corneal transplantation is reported to have been first conceptualized in the late 1700's, beginning with the idea of using a glass disc.[1] It wasn't until later, with the advancement of anesthetic and antiseptic techniques that operations could be expected to take place with success. Several decades passed with experiments using xenograft and allograft methods with variable, but generally poor results. The first successful transplant occurred in December of 1905 by Eduard Zirm, MD.[7] In the 1920's and 30's, Professor Anton Elschnig refined what was a crude procedure into a reliably successful one.[1] Today, the process is widely available and occurs with much greater success. In 2007, over 50,000 transplants occurred in the United States, an 11% increase over 2006's 45,035.[2] Table 1 shows the most prevalent indications for both full-thickness, or penetrating keratoplasty (PKP), and partial-thickness, or lamellar keratoplasty (LKP). These indications change over time. For example, the closed-loop anterior chamber intra-ocular lens (ACIOL) used in the 1970's and 1980's ultimately generated the need for corneal transplants secondary to corneal edema.[1] With improvement of the intraocular lens (IOL), the rate of corneal edema secondary to bullous keratopathy declined. However, with the longer life expectancies of patients after cataract surgery, the incidence of post-cataract - corneal edema may be on the rise again.[1]

Table 2. Contraindications to being a Corneal Donor
Unknown Cause of Death
Dementia of Unknown Cause
Leukemia or Lymphoma
Sepsis
HIV Infection
Active Viral Hepatitis
Congenital Rubella
Rabies
Ocular Tumors
Active Ocular Inflammation
Congenital or Acquired Corneal Disease/Damage
Non-medical IV Drug Use in Last 5 Years
Male-to-Male Sexual Contact in Last 5 Years
Imprisonment for 72 Hours in Last 12 Months
Inadequate Donor Blood Sample
Many Others
Source: EBAA Medical Standards, 2007 (EBAA, 1015 18th Street, NW, Suite 1010, Washington, DC, 20036).

The Donor

With every death there is potential for that person to become an organ or tissue donor. The way in which different states or hospitals go about this process may vary depending on hospital policy or state laws. Typically, a centralized referral service fields the initial calls and sends a page to the eye technician when they are informed of a person's death. Several medical conditions in the patient may preclude the referral service from contacting the eye bank, but others are decided upon by the eye bank technician on a case-by-case basis. For example, a potential donor must fall between specified age limits before the referral service contacts the eye bank. Table 2 lists a few of the other most prominent reasons for which a potential donor may be ruled out. When a patient is found to meet the initial requirements for corneal donation, the eye bank technician makes the decision to approach the family concerning donation. The family is approached while the eye technician awaits the resulting paperwork.

Once consent has been verified by the eye bank and the medical and social questionnaires are reviewed for any contraindications to corneal donation, the technician then begins to work out the details of obtaining the tissue. The eye bank must retrieve the globes or corneas (in the case of in-situ retrieval) from the donor within the bank's time limit from cardiac death, and the corneoscleral button must by preserved usually no longer than twenty four hours after cardiac death. Prior to enucleation or in-situ corneal removal, the body is inspected for signs of trauma, therapeutic and non-therapeutic IV sites, scars, and tattoos. Blood is drawn for serology tests (see Table 3). While many eye banks do not currently test for West Nile Virus it will be mandatory by the end of the year. The eyes are inspected with a pen light for any diseases or debris. During a whole globe enucleation, the skin of each eyelid and around the eyes is cleansed with Betadine or something comparable. A sterile field is set up as best as conditions allow (considering recoveries often occur in morgues or funeral homes).

Table 3. Donor Blood Screening
HIV I &II Antibody
HIV NAT (nucleic acid amplification testing)
Hepatitis C Antibodies
HCV NAT
Hepatitis B surface antigen
Syphillis (RPR, FTA-ABS if RPR positive)
West Nile Virus

The eyelids are held open with a Barraquer or comparable speculum. The conjunctiva is grasped at the limbus and cut with Stevens Tenotomy scissors. The scissors are used to separate the conjunctiva from the sclera. A muscle hook is used to hook the muscles to bring them into view to be cut. The lateral rectus muscle is grasped with the forceps and the globe is gently lifted a few centimeters to allow greater visibility within the socket. The enucleation scissors are then used to cut the optic nerve, freeing the globe from the socket, and any remaining tissue is removed from the globe. The globes are secured in metal cages via the optic nerve stump and placed in moist chamber jars with antibiotics for transport back to the eye lab (see Figure 1). The globes are put on ice (but not dry ice) during transport to improve tissue viability.

Figure 1

Once the globes are in the lab, they are soaked in 5% Betadine followed by a sterile saline rinse, and placed in the flow hood to begin the excision (Figure 2). The excision is when the cornea and a 2-4mm rim of sclera is removed from the rest of the eye, forming the corneosleral button. The globe is stabilized with a thin piece of sterile gauze, and manipulated without touching the globe with one's gloves. Any remaining conjunctival debris is scraped away from the limbus and sclera with a scalpel blade. A second scalpel blade is used to make a small incision in the sclera a few millimeters from the

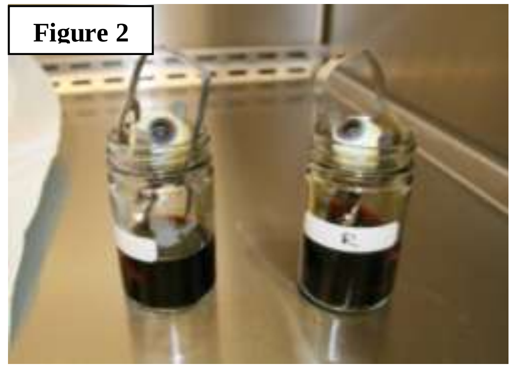


Figure 2

limbus. Using tenotomy scissors, the incision is extended around the circumference of the globe while attempting to prevent vitreous leakage. Once the incision is complete, two pairs of forceps are used to grasp the corneoscleral button and separate it from the underlying iris. This button is then placed in a viewing chamber filled with Optisol GS, the most commonly used storage media. Optisol GS is a mixture of dextran, antibiotics (gentamycin and streptomycin), amino acids, chondroitin, and vitamins which allows storage at 4ºC for up to 14 days.[3] Previous storage media types were less successful for endothelial survival; and while freezing is possible, it is far more technically difficult. While 14 days may be the accepted storage period, most eye banks and surgeons prefer to use the cornea long before this deadline. The chambers are closed, labeled, shrink-wrapped, and placed in the cooler (Figure 3).

Figure 3

Finally, the tissue must be examined by slit lamp biomicroscopy to determine its integrity. The epithelium, stroma, and endothelium must all be examined via this method. The Eye Bank Association of America (EBAA) guidelines suggest examining epithelial integrity, epithelial and stromal opacities, presence of foreign bodies and infectious infiltrates, evidence of prior anterior segment surgery, degree of stromal clarity and thickness, Descemet's membrane folds, and extent of endothelial guttae, snail tracks, and precipitates.[1] The endothelial layer of cells examined by specualr microscopy must meet set morphology and density parameters prior to transplant. Assuming all tests and exams come back acceptable, the cornea is arranged for transplant locally or exported to another eye bank. When tissue demands in a particular area can't be met, eye banks across the nation work as a single network by sending tissue to those centers in need.

The Recipient

The indications for corneal transplant are listed in Table 1. Keratoconus is a disorder in which the cornea undergoes thinning and ectasia resulting in a conically shaped surface causing astigmatism and refractive changes.[1] A rigid, gas-permeable contact lens may correct the patient's vision initially, but when corneal scarring or contact lens intolerance occurs, corneal transplant may be required to improve visual acuity.[4] In Fuchs dystrophy, abnormal drop-like deposits of basement membrane material (guttata) are deposited by the endothelial cells resulting in a loss of these cells.[4] The remaining endothelial cells cannot maintain corneal dehydration and edema develops with subsequent separation of the epithelium from the cornea with

Figure 4. The honey-comb or beaten metal appearance of Fuchs dystrophy. Obtained with permission from www.eyetext.net. May 21, 2008.

formation of bullae (Figure 4).[4] In Reis-Bückler dystrophy, Bowman's membrane develops honeycomb-like deposits resulting in membrane thickening and scarring with separation of the epithelium from the membrane.[5]

When preoperatively evaluating the patient, several factors must be addressed. A good history and physical must be obtained to assess for comorbidities and how these may affect the type of operation or anesthesia used. One must address the future plans and hobbies of the recipient as these lifestyle factors may need to change to increase transplant success and lifespan.[1] The eye exam focuses on finding any infections or other conditions which may require treatment prior to surgery.[1] Similar to other types of organ transplantation, the postoperative period is crucial to the surgical success and visual outcome. Also, the native crystalline or intraocular lens is inspected as cataract removal, intraocular lens readjustment, removal, or exchange can be done at the same time as transplant.[1]

At the time of surgery, the recipient eye and donor cornea must be properly prepared. The recipient must be under the appropriate anesthetic and paralytic agents, and the pupil should be constricted if not manipulating the lens, or dilated if one is to work on the lens at the same surgical episode.[1] The eyelids are held open with a speculum and a single or double Flieringa ring is sutured to the episclera to prevent anterior chamber collapse during the open-sky period.[1] The donor cornea must be cut, or trephined, to match the recipient's corneal defect. The best time to do this is prior to initiating the surgery so that the open-sky period is minimized. There are differing opinions and reasons as to whether to trephine the donor tissue larger than or equal to the recipient corneal defect; however, this is beyond the scope of this paper. The recipient's cornea must also be trephined to mark the intended incision.[1]

To begin the surgery, a pair of curved scissors is used to cut the trephined mark on the recipient's cornea, attempting to use only one, continuous incision to create a smooth cut.[1] One must be careful to ensure Descemet's membrane is removed, especially in cases of Fuchs dystrophy or severe edema where the membrane may be separated from the cornea.[1] A viscoeleastic material is injected into the anterior chamber of the recipient eye to protect the donor epithelium, maintain the anterior chamber depth, slow any anterior uveal bleeding, and improve the accuracy of cornea and suture placement; however, one must be careful to remove all of this material afterwards to prevent postoperative intraocular pressure spikes.[1] Such spikes can lead to leakage or wound dehiscience.

Finally, sutures are placed in one or a combination of ways. First, regardless of the suturing method, four sutures are placed, one in each of the cardinal directions for proper centering of the donor cornea and to help prevent unequal tension.[1] From there, the surgeon may apply interrupted sutures, one or two running sutures, or a combination of both interrupted and running sutures. While interrupted sutures are technically easier to place, the task is more grueling because of the multiple knots tied; however, in corneas with peripheral thinning, a continuous suture may unravel initially in one location and subsequently all around the periphery leading to disastrous results.[1] A running suture requires more skill, as it is more technically difficult, but requires less time to place. With a double-running suture, the sutures are placed in opposite directions to counteract each others' torsion (Figure 5).[1] The viscoelastic material is aspirated and replaced with a compound more like the aqueous humor, BSS. The graft is checked for leakage by one of a variety of ways. Antibiotics (avoiding gentamicin due to its potential toxicity to the cornea) with or without being mixed

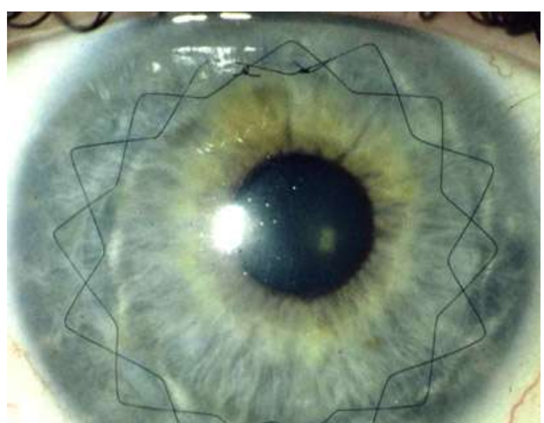


Figure 5. This image highlights the use of a double-running suture. Obtained with permission from www.eyetext.net, on May 23, 2008.

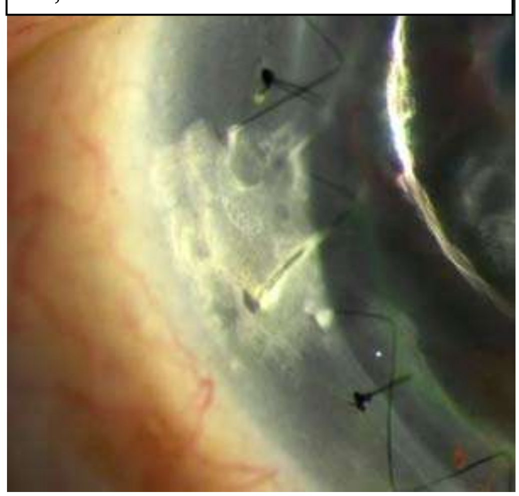
with corticosteroids are injected into the subconjunctival space for added protection while the eye is patched for the next 24 hours.[1]

The above procedure is penetrating keratoplasty (PKP), but there are other procedures which replace only certain layers of the cornea, namely LKP and DSAEK (Descemet's stripping automated endothelial keratoplasty). LKP involves only the anterior layers of the cornea and, as can be seen from Table 1, the indications are those which are more likely to affect only these layers. This procedure is less common in the face of improved PKP, but has its own advantages and disadvantages. The advantages include more laxity in terms of donor tissue quality (since the endothelial layer isn't used), superior wound healing, and a lesser propensity to form cataracts and retinal detachment; however, disadvantages include more haziness secondary to debris or vascularization, potentially decreased vision due to interface aberrations, and its greater technical difficulty.[1] DSAEK is a much newer procedure than either PKP or LKP. It involves replacement of the endothelial layer, Descemet's membrane, and possibly the posterior stroma. Advantages include a smaller incision with quicker healing and a higher predictability of postoperative need for visual correction; disadvantages include more manipulation of the endothelial layer causing the need for repositioning in 25% of cases, and a less well established long-term outcome secondary to its novelty.[6]

Post-Operative Patient Care

Care of the corneal transplant patient requires close follow-up. Typically, a patient is seen the day after surgery, at the end of the first post-operative week, 2 to 4 weeks post-operatively, and then every 2 to 3 months for the next year.[1] The patient is instructed to contact the ophthalmologist if there is any significant pain which may represent post-operative glaucoma, or if they notice any other unexpected changes. At each visit, the eye is carefully inspected by examining intraocular pressure, status of the sutures, anterior chamber problems, retinal adherence, and visual acuity. The cornea must be examined for rejection, infection, precipitates, ulceration, prolonged healing, or leakage.[1] Any problems found must be treated with the appropriate medications or interventions to improve graft survival. As the wound heals, the cornea often undergoes slight changes in shape, requiring the need for correctional eyewear. It may take several months for a patient to achieve their best corrected visual acuity. Periodic suture removal may be necessary based on loosening of the sutures or changes in astigmatism.

Figure 6. Note the white, lacy, crystalline infiltrate in the suture track. Obtained with permission from www.eyetext.net, on May 23, 2008.



A multitude of complications can occur, ranging anywhere from within a day to years after the surgery. Many of them are listed above with the post-operative exams. Leaks may occur requiring watchful waiting, bandage lenses, collagen shields, or additional sutures. As with any other operation requiring violation of normal tissue integrity, a variety of post-operative infections can occur, including infections around the suture sites (Figure 6). As with other types of transplant procedures, the risk of rejection is present. Despite the cornea being avascular, the risk remains significant. Rejection was found in up to 12% of PKP's in one study, but less than 2% resulted in irreversible, rejection-related graft failure.[1] The cell-mediated immune response can involve any of the corneal layers individually or together.

Finally, and arguably just as important as the procedure itself, the donor is remembered. If the family so chooses, a letter is sent to them giving a brief amount of information, without violating the recipient's right to patient privacy, about whether or not the tissue could be used and a little about the recipient. This small act of recognition closes the donor-recipient loop.

A special thanks to all the donors and their families who make this whole process possible.

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