Ophthalmic transplantology: Anterior segment of the eye – Part I

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Summary

Background:
Transplantology is a quickly developing field of ophthalmology. It currently is able to treat many inherited, degenerative, inflammatory, traumatic, and cancerous diseases. This review outlines recent concepts and methods of treating ocular diseases with tissue and cell grafts. Ocular transplants related to the anterior part of the eye, including the conjunctiva and the cornea, are reviewed in Part 1.

Material/Methods:
The scientific literature dated from January 2005 to July 2011 was thoroughly searched using Medline and PubMed. Publications dated 2009, 2010, and 2011 were analyzed in detail. Search terms were as follows: auto-, homo-, heterologous transplantation, eyeball, ocular adnexa, anterior segment of the eye, cornea, lamellar keratoplasty, stem cells, cultured cells. Further data were found at the website of the Eye Bank Association of America.

Results:
Nearly all tissues of the anterior segment of the eye (the conjunctiva, sclera, eye muscles, and cornea) are transplanted. Because of the recent significant progress in the field, cornea transplantation was analyzed in more detail, specifically procedures such as limbus grafts and anterior and posterior lamellar keratoplasty. Indications, advantages, and drawbacks of the transplant techniques were also reviewed.

Conclusions:
Recent progress in the field of cornea transplants allows treatment at the level of the endothelium and the use of cultured limbal epithelial stem cell grafts. However, compared with previous techniques, modern and multilayered transplant techniques of the cornea require much more expertise and longer training of the surgeon, as well as expensive and technologically advanced equipment. The availability of donor tissue is still the main limitation affecting all transplants. Therefore, cell culturing techniques such as stem cells, as well as artificial cornea projects, seem to be very promising.

key words: transplantation • autologous • homologous • heterologous • eye

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BACKGROUND

The oldest and most common form of solid tissue transplantation in humans is the corneal graft, first carried out in 1905 [1]. Since then, transplantology in the field of ophthalmology has developed dynamically. The eye, while representing a part of the central nervous system, is a specific area in terms of transplantology because of its anatomical size, complex structure, and specific optical and metabolic processes. The cornea, anterior chamber, vitreous body, and subretinal space are "immune privileged" [2]. Allosensitization does occur in the cornea, but "immune quiescence," maintained by active processes (specific factors stimulating immune cell apoptosis, the phenomenon of anterior chamber-associated immune deviation) leads to sequestration of antigens and failure of immune-mediated inflammation [1,3].

The aim of this review is to present the latest advances in ophthalmic transplantology.

EYEBALL TRANSPLANTATION

At present, it is impossible to transplant the whole eyeball in humans for several reasons [4]. One is the viability of the donor's eyeball, which is thought to sustain the functions of the photoreceptors shown in electroretinography. Another reason is related to the regeneration of the optic nerve and the reconstruction of its topography. The problem lies in the viability of ganglion retinal cells (GRCs) [4] and in the specific "axon regeneration inhibitors" that accumulate on residual myelin at injury sites [5–7]. GRCs vital for optic nerve regeneration degenerate after nerve II transsection; promising research on animals, however, shows that the full population of GRCs is not required for the regeneration of the optic nerve [4]. A family of 3 protein molecules – myelin-associated glycoprotein, reticulon RTN4, and oligodendrocyte myelin glycoprotein – as well as their axonal receptors (specifically, sialoglycans GD1a and GT1b and receptors of reticulon RTN4) plays a fundamental role in axon-myelin stabilization, but unfortunately inhibits axon regeneration after injury [5–7]. What is required for healthy nervous system functioning is counterproductive after enucleation inhibits axon elongation and regrowth [5–7]. The third important factor is related to enucleated eyeball reperfusion and tissue rejection [4]. Animal studies show that photoreceptors survive enucleation if instant reperfusion of the ocular artery is ensured; further studies on the improvement of the reperfusion technique are required that examine all transplanted arterial and venous anastomoses [4].

OCULAR APPENDAGE GRAFTS

Ocular transplants include the eyelids [8–10], lacrimal canaliculus [11], and eyebrows [12,13]. Autotransplantation of the eyelid skin is performed (rarely allotransplantation), as well as transplantation of the skin with the orbicular muscle, of the tarsus with eyelid conjunctiva, and of full-thickness eyelids, including the skin, muscle, tarsus, and conjunctiva.

TRANSPLANTATION IN THE EYEBALL SPACE

Conjunctiva

Autologous transplantation of the ocular conjunctiva is performed most often to treat primary and recurrent pterygium [14,15]. The limbal conjunctival autograft technique seems to be most effective for reducing recurrent rates after pterygium surgery compared with the bare sclera technique or amniotic membrane graft technique [15]. In the case of recurrent pterygium, some investigators recommend pterygium extended removal followed by extended conjunctival transplant, which depends on the transplantation of a large superior-posterior conjunctival section following an extensive excision of the pathological tissue [16]. Others suggest a small flap technique without autotransplantation [17]. The use of Mitomycin C in disease recurrence is controversial. Mitomycin C and subconjunctival injections of antivascular endothelial growth factor do not reduce disease recurrence after primary and secondary pterygium surgery combined with autologous conjunctival grafts [18,19]. Some surgeons use sutures to attach the grafts, whereas others use tissue glue [20–22].

Sclera

Allogenic transplants of the preserved sclera are used in the treatment of sclera defects after trabeculectomy [23,24] and Ahmed glaucoma valve transplantation [25], as well as for covering ocular implants to prevent their extrusion following eyeball enucleation [26].

Muscles

Transplants and transpositions of the orbicular muscle are performed in paralytic lagophthalmia [27] and a range of strabismus surgical procedures [28,29].

Cornea

The most dynamic and innovative area of transplantation techniques concerns the cornea. The scope of corneal transplants covers the corneal limbus, corneal layers, full-thickness cornea (penetrating keratoplasty [PK]), and combined limbal transplantation with penetrating or lamellar keratoplasty.

LIMBAL EPITHELIAL STEM CELL GRAFTS IN LIMBAL EPITHELIAL STEM CELL DEFICIENCY

A limbal epithelial stem cell (LESC) graft is recommended in partial or total LESC deficiency that has been confirmed by impression cytology [30–32]. LESC deficiency develops when there is stem cell deficiency or when LESCs are destroyed [30–32]. Limbal grafts are transplanted in congenital LESC deficiency (with aniridia), atopic conjunctivitis and keratitis, pemphigoid, and Stevens-Johnson syndrome, as well as for chemical and thermal burns [30–32]. LESCs are a unique population of cells that form healthy corneal epithelium, maintain its homeostasis, and constitute a physical barrier against vessels and conjunctival epithelium [32]. Without progenitors of epithelial cells, the healthy epithelium could not be formed. Their deficiency causes recurrent corneal epithelium deficiency (by definition, lasting more than 2 weeks despite therapy), vessel ingrowth, conjunctivalization, inflammation, ulcers, and scarring of the ocular surface [30,32]. In LESC deficiency, impression cytology shows the presence of goblet cells that are characteristic for the conjunctiva [30,31]. The fact that they appear in the 4 quadrants of the corneal surface shows that the limbal barrier is broken, that there are no stem cells, and that a total LESC deficiency has occurred [30,32].

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Partial LESC deficiency without changes in the central cornea is inoperable [32]. Surgery is performed for partial LESC deficiency with changes in the central cornea because the elimination of conjunctivalization and use of an amniotic membrane graft are necessary [32]. Total LESC deficiency requires a conjunctival-limbal autograft (CLAU) or allograft (CLAL) from a living donor, a keratolimbal or corneoscleral allograft from a cadaver, or a cultured LESC graft [32,32]. A CLAU is harvested from the patient's other healthy eye and a CLAL is harvested from a patient's relative, with the use of the same techniques and based on the same recommendations as in CLAU [30,31]. A "family" graft is performed in monocular patients or when the patient's other eye is in poor condition with no prospects for improvement. The term CLAL is also used in reference to limbal grafts harvested from the patient's other eye [30]. CLAU and CLAL are used in partial or total LESC deficiency treatment. The grafts are harvested from the superior and/or inferior limbus, the areas of the greatest limbal stem cell concentration. The flap has a rhomboid shape and comprises 1 mm of the transparent cornea, the limbus and the conjunctiva stretching 8 mm from the limbus. It is attached to the recipient's bed with interrupted or continuous sutures [31,33]. Originally, in total LESC deficiency treatment, large parts of the limbus were harvested, traditionally 2 sections ranging from 5 to 7 mm, and corresponding to the 12 o'clock and 6 o'clock positions (2×3 h of circumference). Numerous modifications can be made concerning different graft areas; basically, smaller sections are harvested in the treatment of total LESC deficiency (1×6 mm, 1×2 h of circumference) and in the case of combining CLAL with an amniotic membrane graft [31]. Grafts from the patient's other eye do not require immunosuppression, but since healthy tissue is disturbed, it may lead to iatrogenic LESC deficiency despite the fact that the number of complications after limbal transplantation is not as high [31].

A keratolimbal allograft (KLAL) is a ring-shaped graft harvested from a cadaver that is used in total bilateral LESC deficiency treatment. The ring is placed in the recipient's limbus and sutured to the sclera, and subsequently the conjunctiva is placed on the ring and attached [34,35]. KLAL will not provide the desired results in patients with total LESC deficiency and leukoma because it does not improve the transparency of the cornea or the condition of the epithelium. In such patients, KLAL and PK should be combined, or a corneoscleral graft performed [34]. Two sections are harvested from an oversized (15 mm) donor's button comprising the whole cornea, the limbus, and the sclera (2–3 mm); the limbal-scleral ring is used for KLAL and the central cornea (7.5–7.75 mm) for PK. PK is performed first and is finally separated from KLAL by the opaque area of the recipient's cornea, which is a physical barrier against epithelial rejection [31,34]. In some patients with total LESC deficiency and opacity of the outer corneal layers, it is advisable to combine deep anterior lamellar keratoplasty (DALK) with KLAL, rather than PK with KLAL, in order to prevent endothelial rejection [34].

A Corneoscleral allograft can be used after extensive burns and in the treatment of total bilateral LESC deficiency with coincident leukoma [34]. After the removal of the recipient's cornea, a graft of 11–12 mm in diameter is sutured to the sclera and the conjunctiva is placed on it and attached (as well as the amniotic membrane) [34]. The donor's larger graft solves the problem of LESC deficiency and leukoma but involves more allergens, which may lead to epithelium and endothelium rejection. There is no physical barrier (as in PK with KLAL) against vessels, cells, and inflammatory and immune agents [34].

CULTURED LIMBAL STEM CELL GRAFT

Owing to the development of molecular bioengineering, limbal stem cells can be cultured [30,32,36–39]. In some conditions, a very small autologous (from the other eye) or allogenic limbal section produces a large population of cells, which are subsequently grafted to the eye in total LESC deficiency [32]. The section (1×1 mm) harvested at 12 o'clock can be cultured in an explant culture system or a suspension culture system, which is sustained by trypsin [30,32]. The amniotic membrane is usually used to culture grafts [30,32,33,39], but a standard hydrogel contact lens [30,40], plastic compressed collagen [41], and the patient's oral mucous membrane [32] may also be used. The graft is submerged in allo/autoserum and incubated for about 10 days at a certain humidity and CO_2 level [30,32]. If the cultured cells are confluent on the 2×2 mm sheet and a basement membrane is formed, then the cells may be used as a graft. The colonies of cells are airlifted and then transferred to the recipient's cornea [30,32]. The graft is more successful in patients with short-term LESC deficiency. A cultured LESC graft leads to improvement of visual acuity (2 more lines on the European Society of Cataract and Refractive Surgeons charts) and cytochemical condition of the cornea in 60% of the patients with total LESC deficiency [30]. The viability of the graft depends on the environment of the recipient's cornea; therefore, prior to transplantation, it is vital to completely remove conjunctivalization and prevent hemorrhage during surgery [31,34]. If impression cytology has shown conversion, then the graft has been accepted (ie, the conjunctival phenotype has changed into the corneal phenotype). Initially, animal cells were used to culture grafts to produce and stimulate colony growth, and calf's fetal serum was used as a medium – without it, the proliferation process was less effective [32]. A limbal auto/allograft became a xenograft in those conditions with all animal antigens and pathogens. The use of the allogenic amniotic membrane, the autologous mucous membrane, and autologous or allogenic serum, as well as contact lenses, alleviates problems with immunity and solves ethical dilemmas related to experimenting on animals [32]. The development of cell bioengineering for the LESC graft is related to research on alloserum (in some patients autoserum cannot be used for religious or medical reasons (eg, with positive test results for hepatitis B virus, hepatitis C virus, HIV1, HIV2, lymphoma I and II, or lues) and to research on other sources of harvesting stem cells such as the placenta, embryonic progenitor cells, bone marrow, and hair follicles [30]. Cultured LESC grafting represents the optimal solution because a small sample of the autologous tissue is used, the biopsy can be repeated, risk of rejection is mitigated, and no immune suppression is necessary [30,32]. CLAL is a more aggressive surgical technique, as it disturbs healthy tissue and there is a risk of iatrogenic LESC deficiency; whereas in KLAL, immune suppression is required [30,31].

PENETRATING KERATOPLASTY

PK has been considered the gold standard for treating a wide range of corneal diseases related to the epithelium, stroma, and endothelium, although at present, it is not recommended as often as it used to be [42–57]. The diseases treated with PK include the following: keratoconus with scarred Descemet membrane or corneal thickness less than 300 µm; bullous keratopathy secondary to pseudophakia or aphakia and simultaneous opacity or stromal scars, or corneal thickness of over 800-850 µm; mature (or complicated) cataract with swollen Fuchs' dystrophy and simultaneous opacity or stromal scars, or corneal thickness of over 800–850 µm (conventional triple procedure, [ie, simultaneous PK, cataract surgery, and artificial lens implantation]); and opacity comprising the whole thickness of the cornea [42,43,47–50].

CORNEAL LAMELLAR GRAFTS

The use of anterior and posterior lamellar keratoplasty depends on the selective transplantation of certain corneal layers. Technically, it is more difficult and more time-consuming than PK, but in particular cases, better anatomical and functional (visual acuity) results are achieved [47–51,58,59]. Lamellar keratoplasty has become an alternative method to PK as a result of the following factors: it is a causative therapy (selective stroma or endothelium transplantation); it prevents complications resulting from an "open sky" technique and immunization; it optimizes refraction effects; it improves recovery conditions, including healing time; and it uses the donor's tissues economically (1 cornea for the anterior/posterior transplants in 2 recipients) [47,49,51,60].

Anterior lamellar keratoplasty is performed in epithelial/subepithelial dystrophy (gelatinous drop-like corneal dystrophy); Bowman membrane dystrophy (Reis-Bücklers corneal dystrophy); stroma dystrophy that does not include the Descemet membrane (lattice corneal dystrophy, granular corneal dystrophy); opacity and scars after inflammation and burns; LESC deficiency combined with LESC graft; keratoconus (most common); and keratectasia following laser *in-situ* keratomileusis [47,48,51–53,61]. The recipient's bed can be prepared by means of manual lamellar dissection with residual posterior stroma, or the "big bubble" technique, which fully removes stroma and bares the Descemet membrane (DALK) [47,48,51,62]. A new surgical technique – enzymatic DALK – facilitates stromal dissection [63]. The big bubble technique [48] is initiated with a circular incision of the recipient's peripheral cornea, 60–80% thick. The 25(30)-gauge needle is put deeply through this groove into the paracentral stroma, and air is injected into the cornea. As a result of even spreading of the air bubble (after 3–4 injections), the stroma is totally separated from the Descemet membrane and a white, opaque disc surrounded by the circular incision ring is formed. The front of the air bubble is punctured in the area of circular incision, which leads to its collapse and darkening of the separated stromal disc. Next, an Anwar spatula is put into up-growth inter-corneal canal to lift and safely detach the stroma while excising it with a knife. The residual stroma is finally excised with blunt corneal scissors as far as the circular incision. The graft, consisting of the epithelium and stroma only (after stripping the Descemet membrane), is sutured to the recipient's bared bed. The introduction of the big bubble technique improved visual acuity results and reduced the frequency of perforation of the Descemet membrane compared with previous techniques (hydrodelineation is not as effective, and viscoelastic applied under high pressure causes perforation and postoperative complications such as abnormal adhesion of tissues) [48]. The complete removal of the recipient's stroma and the donor's Descemet membrane eliminates postoperative symptoms in the host/donor interface such as folds; second anterior chamber; and opacity, scars, and a haze phenomenon typical of manual lamellar dissection (light dispersion on the recipient/donor interface due to the residual recipient's stroma) [47,48].

Therapeutic DALK (TDALK) is used in active stages of keratitis that are resistant to conventional treatment and caused by herpes, *Pseudomonas aeruginosa*, fungi, or Acanthamoeba (mainly in patients using contact lenses) [47]. The excision of the cornea eliminates the source of the pathogen and is an urgent procedure required to prevent secondary endophthalmitis and perforation. TDALK should be performed early, before corneal neovascularization and before the limbus has been damaged. Late and/or incomplete excision of the pathogen is connected with the recurrence of inflammation in the graft [47]. Good results (86.6% in TDALK) can be compared with the 88% results of therapeutic penetrating keratoplasty (TPK). TDALK rarely causes endothelial rejection (15% after TPK), it increases the viability of the graft after a year (90% after TDALK, 78% after TPK), it does not lead to secondary endophthalmitis (50% after TPK), and it hardly ever causes secondary cataract and glaucoma, as penetration of the anterior chamber is not required [47]. DALK combined with CLAU is recommended in LESC deficiency treatment [36]. PK is not required in some patients with LESC deficiency (if opacity does not comprise the whole cornea, if it does not stretch to the Descemet membrane, and if the defect of the endothelium does not occur); however, in all patients with total LESC deficiency, central corneal transplantation (PK or DALK), without a simultaneous LESC graft, is not sufficient. DALK, compared with PK, causes less immunization, and CLAU is more effective than allogenic limbal grafts [36]. DALK in moderate to advanced stages of keratoconus is an alternative method to PK [48,52–54,64,65], as good visual acuity results are achieved; the risk of endothelial graft rejection is eliminated, and in most patients, it can be performed with the use of the big bubble technique (if intraoperative perforation of the Descemet membrane occurs, then PK transplantation should be performed) [54,64]. According to Anwar and Teichman [48], however, DALK can be dangerous and ineffective in corneas after hydrops (the air comes through the Descemet membrane perforation, the big bubble does not form, the Descemet membrane of the host is not entirely bared, and force separation of the stroma in the area of the scar comprising the Descemet membrane may lead to perforation). After hydrops, it is advisable to retain residual stroma covering the perforation and hence the manual lamellar dissection should be used here [48]. Supporters of PK [55] in the surgery for keratoconus emphasize that the manual lamellar dissection technique causes the haze phenomenon, which worsens visual acuity, has less spectacular results compared with PK, and is not tolerated by younger patients. DALK rarely causes endothelial graft rejection, but may also lead to subepithelial/stromal graft rejection, which occurs in PK [55,66].

Compared with PK, DALK does not significantly disturb the eyeball (important in terms of potential damage in the future, in particular in monocular patients); it does not lead to intraoperative complications (expulsive hemorrhage, intraocular inflammation, and adhesions); it has minimal impact on endothelial cell loss; it does not require long-term corneal sutures; it does not cause severe astigmatism and therefore its results are more predictable and ensure better visual acuity; and finally, it does not require indications that are as strict as for PK [47,51,55]. The drawbacks of DALK include intraoperative Descemet membrane perforation and the risk of subepithelial/stromal rejection. Moreover, this technique is more time-consuming and requires special technical skills [48,55,66].

Posterior lamellar keratoplasty (PLK) depends on the allogenic replacement of the Descemet membrane with endothelium [49]. Primary bullous keratopathy in Fuchs' dystrophy, or corneal edema secondary to pseudophakia, aphakia, or antiglaucoma implant, are usually indications for PLK [49]. PLK cannot be performed in patients with stroma opacity or scarring, or in hypotony; it is sometimes recommended in posterior polymorphic dystrophy, iridocorneal endothelial syndrome, and endothelial defect after acute glaucoma or PK [56,57,67,68]. PLK is performed in adults, as well as in children [69,70]. In the United States, endothelial keratopathy accounts for 1/3 to 1/2 of all transplants [42,44]. Endothelial keratoplasty techniques include deep lamellar endothelial keratoplasty (DLEK), Descemet stripping endothelial keratoplasty (DSEK), Descemet stripping automated endothelial keratoplasty (DSAEK), Descemet membrane endothelial keratoplasty (DMEK), Descemet membrane automated endothelial eratoplasty (DMAEK), and femtosecond laser-assisted corneal endothelial keratoplasty (FLEK; see below). The first posterior grafts turned out to be inferior to PK, but DLEK, introduced by Terry in 2000 and modified by Melles in 2002, initiated the spectacular development of PLK [71]. "Small incision" DLEK depends on the transplantion of a 9 mm folded flap, through a 5 mm deep and inaccessible corneal canal. The donor's flap consists of the posterior stroma and Descemet membrane with endothelium (the anterior stroma is excised with a manual keratome). The recipient's bed (the posterior stroma and Descemet membrane with endothelium) is excised with the trepan through the same corneal canal. The graft is stabilized by the air bubble injected into the anterior chamber. The rough host/donor stromal interface contributes to the viability of the graft [72–74]. Small incision DLEK provides stable central corneal topography [75] and good refraction and visual acuity results in long-term follow-up, and it seems to be a better alternative to PK for the purpose of treating endothelial dysfunction [76,77].

DSEK and DSAEK are 2 innovative techniques that depend on a different manner of preparing the recipient's bed. The Descemet membrane with endothelium is stripped in the anterior chamber; i.e., it is not excised with a trepan as in DLEK [78–82]. Stripping is easier and faster and preparation of the corneal tunnel is not required. Stripping contributes to smooth the host/donor interface, which, compared with DLEK and PK, enhances postoperative results concerning corneal structure and refraction [80,83–88]. However, smooth host/donor interface leads to frequent dislocation and abnormal graft adhesion (in DLEK the interface

is rougher) [80,89–95]. The difference between DSEK and DSAEK is in the preparation of the graft. In DSEK, the donor's anterior stroma is excised with a manual keratome, and in DSAEK it is excised with an automated keratome [78,79]. In DSAEK, the depth of the incision is 300 µm for central corneal thickness that is less than 550 µm, or 350 µm for thickness that is more than 550 µm; the measurement is taken with an ultrasound pachymeter after removal of epithelium [79]. Automated preparation of the graft is faster, more precise, and repeatable. In both techniques, the donor's flap includes residual stroma, less of it in DSAEK (about 10–20%), and Descemet membrane with endothelium, but in DSAEK, the flaps are smoother [80]. In DSEK, large differences in the thickness of flaps occur, which does not significantly affect visual acuity [83]. Recommended flap thickness in DSAEK is 120–180 µm [84]. The 8.5–9.0 mm flap is excised with a trepan and inserted into the recipient's anterior chamber through a 5.0 mm corneal incision, which requires folding it in such a way that the endothelium can be placed in the middle [78,79,96]. After partial unfolding of the flap in the anterior chamber, the air is injected to enable its total unfolding and adhesion to the recipient's bed. After the surgery, the patient must lie flat for an hour [78,79]. Forceps-assisted (standard "taco" technique) and Busin guide-assisted methods, as well as drag techniques (using forceps or suture), are performed to insert a flap during DSAEK [97–99]. Marked loss of the corneal endothelium is the main reason for primary DSAEK graft failure [90,92]. The Busin guide is a derivative of the taco technique; it protects and decreases the endothelium damage of the flap, but best-corrected visual acuity is not significantly different between the forceps-assisted and the Busin guide-assisted groups according to Bahar et al. [97]. The new triple procedure, which combines DSAEK with cataract surgery and intraocular lens implantation, provides rapid visual recovery [100,101]. Technological advancement has led to a new technique, FLEK [102–104]. The femtosecond laser causes regular and smooth posterior stromal ablation. It allows for a precise, deep, horizontal and lamellar incision of the donor's cornea as deep as 400 µm. The graft is 150–200 µm thick, thinner in the central part and thicker on the circumference, and used in a standard DSAEK [102–104]. The flap prepared with the use of a femtosecond laser causes a mild hyperopic shift [103,105], provides good endothelial cell viability [104], and contributes to less extensive astigmatism and easier wound healing [103].

DMEK was introduced by Miller in 2006. It is the only technique that in practice contributes to an endothelial pathological treatment of the cause. The Descemet membrane with the endothelium is transplanted without the donor's posterior residual stroma [106,107]. The innovation lies in the fact that stripping includes both the recipient's and the donor's cornea. The graft is stripped off rather than excised as in DSEK/DSAEK. An 8.5–9.0 mm ultrathin flap (practically 1 layer of cells on the Descemet membrane) is implanted from the injector through a 2.8–3.0 mm corneal incision, and is unfolded in the anterior chamber by means of irrigation fluid and stabilized with air bubble injection. After the procedure, the patient must lie flat [106,107]. After DMEK, the following is smaller – central corneal thickness (average 530 µm; 650 µm after DSAEK), postoperative hyperopia (average 0.5 D; 1.05 D after DSAEK), and the range of spherical equivalent (average 2.5 D; 4–5 D after DSAEK).

DMEK surpasses DSAEK in terms of the percentage of patients with full visual acuity [85,86]. Problems arise in connection with graft preparation and its frequent detachment and surgical – sometimes multiple – repositioning caused by the ultrathin donor's flap and both smooth surfaces of the interface [106].

DMAEK is a hybrid technique. The innovation depends on a sophisticated technique of the donor's flap preparation to improve its viability in the recipient's bed [108,109]. The initial stage of the donor's flap preparation is the same as in DSAEK (the depth of incision is 300 µm for a central corneal thickness of less than 550 µm, or 350 µm for thickness of more than 550 µm). After removing the cornea from the artificial chamber and turning it with the endothelium facing upwards, with the use of the big bubble technique, the posterior residual stroma is separated from the Descemet membrane in the range of the central 6.0–7.0 mm, and the Descemet membrane is dyed with trypan blue. Next, the graft is turned with the endothelium facing downwards, and the separated stroma is excised with scissors in the range of the central 5.0–6.0 mm. The flap is again turned over with the endothelium facing upwards, and the graft with the diameter of 8.5–9.0 mm is excised with a trepan. Finally, the graft has only Descemet membrane with the endothelium in its central part, which is not stripped off as in DMEK but separated by means of air, and it includes a 2.5 mm ring of the posterior rough stroma on its circumference, as in DSAEK. The ultrathin graft is implanted by means of a Busin glide and stabilized by the air bubble. After the procedure, the patient must lie flat [108]. As a hybrid technique, DMAEK combines good DMEK refraction (resulting from an ultrathin graft in the center) with DSAEK stabilization of the graft (greater than in DMEK in connection with preserved circumferential rough stromal ring) [108].

The advantages of PLK compared with PK are as follows: anterior ocular wall integrity, faster rehabilitation (on average within 1.5 weeks, whereas it is within 5 weeks after PK), better visual acuity (corrected/uncorrected), and better contrast sensitivity. PLK do not cause anterior wave defects, or severe astigmatism, or wound leakage. Moreover, they do not require long-term sutures and the risk of severe intra/postoperative complications (expulsive hemorrhage and intraocular inflammation) is reduced [110–116]. PLK requires a high-quality donor cornea (an endothelial cell count of a minimum of 2700/mm²); intraoperative damage and low endothelial cell count are the major drawbacks of PLK. The recurrence of endothelial defects adversely affects the results of PLK, and new surgery is required [117,118]. Complications after PLK are as follows: graft dislocation and/or abnormal adhesion (total or partial detachment), glaucoma pupillary block (caused by air tamponade), endothelial ingrowth, fibrose of the interface, posterior corneal membrane, endothelial rejection or inflammation, keratitis and intraocular inflammation, and Urrets-Zavalia syndrome [87,89–93,119–121]. Advanced PLK techniques require manual dexterity and sophisticated, costly equipment.

Non-immunologic graft failure and allograft endothelial rejection are the main causes of long-term adverse effects of corneal transplantation, as approximately only 70% of corneal transplantations are successful within 5 years [121]. The development of artificial corneas could resolve the immune and the organ supply problems. Tissue-engineered neo-corneas are composed of cultured and human corneal endothelial cells that are expanded *in vitro* and seeded onto thin carriers – a biodegradable gelatinous membrane, an amniotic membrane, a Descemet membrane, and a fibrin-based matrix or a human acellular corneal scaffold [121,123]. The 120 (200) µm-thick, decellularized corneal scaffold is obtained through cutting the stroma into 4 (3) slices and through high-hydrostatic pressurization, which removes native stromal cells, but retains the extracellular matrix and its major protein and biomechanical properties [123,124]. In an animal study, the transplantation of acellular stromal slices covered with human corneal endothelial cells (130 cells/mm²) did not cause an immune reaction [123,124]. The concept of an artificial cornea formed by combining new biomaterials with cells from *in vitro* directed differentiation of adipose-derived stem cells into endothelium is promising [125].

AMNIOTIC MEMBRANE GRAFT

Allogenic amniotic membrane grafts are performed to treat the ocular surface in chronic loss of epithelium, LESC deficiency, bullous keratopathy, and corneal hydrops; after conjunctiva, strabismus, eye socket, and refraction surgery; and after chemical and thermal burns [30]. Amniotic membrane is anti-inflammatory and anti-bacterial, it regenerates epithelium (the source of viable stem cells), and it inhibits angiogenesis and scarring (it stimulates apoptosis of inflammatory cells and obstructs proteases and myofibroblasts) [30]. Grafts are performed with the use of the overlay technique (2 amniotic membranes are sutured to the cornea, the smaller one compensating for epithelium loss and the other covering the whole cornea, both with the epithelium down) or the bandage technique (1 amniotic membrane is sutured to the whole cornea with the epithelium down) [30]. The stroma, which is directed upwards, is a type of scaffolding for the formation of corneal epithelium. In the pterygium, fornix reconstruction and symblepharon surgery is not recommended to go beyond the limit of the limbus and the suture of the amniotic membrane to the cornea [30,126]. An amniotic membrane graft is also controversial in the primary pterygium. According to Ye et al. [127], the temporary (lasting for 5 days) amniotic membrane patch is an effective and safe procedure, but according to others [30,126], it increases pterygium recurrence rates and should be avoided.

ANTERIOR LENS CAPSULE GRAFT

An autologous anterior lens capsule graft in the scleral tunnel is recommended in a hybrid procedure that combines glaucoma and cataract surgery (phacotrabeculectomy with intraocular artificial lens implantation) [128]. In terms of filtration, the results for intraocular pressure and best-corrected visual acuity are similar and comparable to those for mitomycin C. At the same time, an anterior lens capsule graft does not cause complications related to the use of an antimitotic [128].

CONCLUSIONS

Autotransplants and allotransplants of tissues of the anterior segment of the eye allow treatment of many genetic,

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degenerative, post-inflammatory, traumatic, and cancerous eye diseases. Recent progress in the field of cornea transplants has been tremendous, including treatment at the level of the endothelium (DMEK, DMAEK) and cultured LESC grafts. Modern and multilayered transplant techniques of the cornea do, however, require much more expertise and longer training of the surgeon, as well as expensive and technologically advanced equipment. The availability of donor tissue continues to be the main limitation affecting transplantation. Therefore, extensive research on cell culturing techniques, such as stem cells, and artificial corneas, is ongoing.

Abbreviations

CLAL – conjunctival-limbal allograft; CLAU – conjunctival-limbal autograft; DALK – deep anterior lamellar keratoplasty; DLEK – deep lamellar endothelial keratoplasty; DMAEK – Descemet membrane automated endothelial keratoplasty; DMEK – Descemet membrane endothelial keratoplasty; DSAEK – Descemet stripping automated endothelial keratoplasty; DSEK – Descemet stripping endothelial keratoplasty; FLEK – femtosecond laser-assisted corneal endothelial keratoplasty; GRC – ganglion retinal cells; KLAL – kerato-limbal allograft; LESC – limbal epithelial stem cells; PK – penetrating keratoplasty; PLK – posterior lamellar keratoplasty; TDALK – therapeutic deep anterior lamellar keratoplasty; TPK – therapeutic penetrating keratoplasty.

REFERENCES:

1. Chong EM, Dana MR: Graft failure IV. Immunologic mechanisms of corneal transplant rejection. Int Ophthalmol, 2008; 28: 209–22

2. Streilein WR, Streilein JW: Ocular immune privilege: therapeutic opportunities from an experiment of nature. Nat Rev Immunol, 2003; 3: 879–89

3. Cunnusamy K, Paunicka K, Reyes N et al: Two different regulatory T cell populations that promote corneal allograft survival. Invest OphthalmolVis Sci, 2010; 51: 6566–74

4. Ellenberg D, Shi J, Jain S, Chang J-H: Impediments to eye transplantation: Ocular viability following optic-nerve transaction or enucleation. Br J Ophthalmol, 2009; 93: 1134–40

5. Rainer SJ, Lee H, Baldwin KT et al: Oligodendrocyte-myelin glycoprotein and Nogo negatively regulate activity-dependent synaptic plasticity. J Neurosci, 2010; 30(37): 12432–45

6. Nguyen T, Metha NR, Conant K et al: Axonal protective effects of the myelin associated glycoprotein. J Neurosci, 2009; 29(3): 630–37

7. Lee JK, Geoffroy CG, Chan AF et al: Assesing spinal axon regeneration and sprouting in Nogo MAG and OMgp deficient mice. Neuron, 2010; 66(5): 663–70

8. Akdag F, van den Bosch W, Ganteris E, Paridaens D: "Sandwich block" for eyelid reconstruction. Orbit, 2010; 29(2): 110–13

9. Morley AM, deSousa JL, Selva D, Malhotra R: Techniques of upper eyelid reconstruction. Surv Ophthalmol, 2010; 55: 256–71

10. Onoda M, Fujikawa M, Koh K: Full-thickness eyelid reconstruction using orbicularis oculi muculocutaneous flap raised from lateral orbital region. Ann Plast Surg, 2010; 64: 294–97

11. Meltzer MA, Zatezalo CC, Zoltan S: Lacrimal canalicular transplantation with composite eyelid graft. Ophthalmic Plastic & Reconstructive Surgery 2010; 26: 23–25

12. Laorwong K, Pathomvanich D, Bunagan K: Eyebrow transplantation in Asians. Dermatol Surg, 2009; 35: 496–503; discussion 503–4

13. Gho CG, Neumann HA: Improved hair restoration method for burns. Burns, 2011; 37: 427–33

14. Soliman Mahdy MA, Bhatia J: Treatment of primary pterygium: role of limbal stem cells and conjunctival autograft transplantation. Eur J Ophthalmol, 2009; 19: 729–32

15. Ozer A, Yildirim N, Erol N, Yurdakul S: Long-term results of bare sclera, limbal-conjunctival autograft and amniotic membrane graft techniques in primary pterygium xcisions. Ophthalmologica, 2009; 223: 269–73

16. Hirst LW: Recurrent pterygium surgery using pterygium extended removal followed by extended conjunctival transplant: recurrence rate and cosmesis. Ophthalmology, 2009; 116: 1278–86

17. Kim M, Chung SH, Lee JH et al: Comparison of mini-flap technique and conjunctival autograft transplantation without mitomycin C in primary and recurrent pterygium. Ophthalmology, 2009; 116: 1278–86

18. Almeida GC Jr, Frederico FB, Watanabe KP et al: Evaluation of epithelial cell proliferating activity and fibroblast nuclear kariometry in recurrent pterygium treated with mitomycin C. Arq Bras Oftalmol, 2008; 71: 568–75

19. Razeghinejad MR, Hosseini H, Ahmadi F et al: Preliminary results of sub-conjunctival bevacizumab in primary pterygium excision. Ophthalmic Research, 2010; 43: 134–38

20. Hall RC, Logan AJ, Wells AP: Comparison of fibrin glue with sutures for pterygium excision surgery with conjunctival autografts. Clin Experimental Ophthalmol, 2009; 37: 584–89

21. Por YM, Tan DT: Assessment of fibrin glue in pterygium surgery. Cornea, 2010; 29: 1–4

22. Ratnalingam V, Eu AL, Ng GL et al: Fibrin adhesive is better than sutures in pterygium surgery. Cornea, 2010; 29: 485–89

23. Au L, Wechsler D, Spencer F, Fenerty C: Outcome of bleb revision using scleral patch graft and conjunctival advancement. J Glaucoma, 2009; 18: 331–35

24. King AJ, Rotchford AP: The use of a scleral micro-patch graft and fibrin glue to treat scleral flap defects following trabeculectomy. Br J Ophthalmol, 2009; 93: 1269–70

25. Zeppa L, Romano MR, Capasso L et al: Sutureless human sclera donor patch graft for Ahmed glaucoma valve. Eur J Ophthalmol, 2010; 20: 546–51

26. Toteberg-Harms M, Bredehorn-Mayr T: Preparation and use of human sclera grafts in ophthalmic surgery. Dev Ophthalmol, 2009; 43: 105–8

27. d'Alcontres FS, Cuccia G, Lupo F et al: The orbicularis oculi muscle flap: its use for treatment of lagophthalmos and a review of its use for other applications. J Plast Reconstr Aesthet Surg, 2010; 63: 416–22

28. Godeiro KD, Kirsch D, Tabuse MK, Cronemberger M: Yamada's surgery for treatment of myopic strabismus fixus. Int Ophthalmol, 2009; 29: 305–8

29. Yazdian Z, Rajabi MT, Ali Yazdian M et al: Vertical rectus muscle transposition for correcting abduction deficiency in Duane's syndrome type 1 and sixth nerve palsy. J Pediatr Ophthalmol Strabismus, 2010; 47: 96–100

30. Rauz S, Saw VP: Serum eye drops, amniotic membrane and limbal epithelial stem cells-tools in the treatment of ocular surface disease. Cell & Tissue Banking, 2010; 11: 13–27

31. Kheirkhah A, Raju VK, Tseng SC: Minimal conjunctival limbal autograft for total limbal stem cell deficiency. Cornea, 2008; 27: 730–33

32. Kolli S, Ahmad S, Lako M, Figueiredo F: Successful clinical implementation of corneal epithelial stem cell therapy for treatment of unilateral limbal stem cell deficiency. Stem Cells, 2010; 28: 597–610

33. Baradaran-Rafii A, Ebrahimi M, Kanavi MR et al: Midterm outcomes of autologous cultivated limbal stem cell transplantation with or without penetrating keratoplasty. Cornea, 2010; 29: 502–9

34. Shi W, Gao H, Wang T, Xie L: Combined penetrating keratoplasty and keratolimbal allograft transplantation in comparison with corneoscleral transplantation in the treatment of severe eye burns. Clin Experiment Ophthalmol, 2008; 36: 501–7

35. Choi SK, Kim JH, Lee D, Oh SH: A new surgical technique: a femtosecond laser-assisted keratolimbal allograft procedure. Cornea, 2010; 29: 924–29

36. Shimmura S, Tsubota K: Surgical treatment of limbal stem cell deficiency: are we really transplanting stem cells? Am J Ophthalmol, 2008; 146: 154–55

37. Eve D, Fillmore R, Borlongan C, Sanberg P: Stem cells have the potential to rejuvenate regenerative medicine research. Med Sci Monit, 2010; 16(10): RA197–217

38. Park DH, Eve D: Regenerative medicine: Advances in new methods and technologies. Med Sci Monit, 2009; 15(11): RA233–51

39. Pauklin M, Fuchsluger TA, Westekemper H et al: Midterm results of cultivated autologous and allogeneic limbal epithelial transplantation in limbal stem cell deficiency. Dev Ophthalmol, 2010; 45: 57–70

40. Di Girolamo N, Bosch M, Zamora K et al: A contact lens-based technique for expansion and transplantation of autologous epithelial progenitors for ocular surface reconstruction. Transplantation, 2009; 87: 157

41. Levis HJ, Brown RA, Daniels JT: Plastic compressed collagen as a biomimetic substrate for human limbal epithelial cell culture. Biomaterials, 2010; 31: 7726–37

42. Yalniz-Akkaya Z, Nurozler AB, Yildiz EH et al: Repeat penetrating keratoplasty: indications and prognosis, 1995–2005. Eur J Ophthalmol, 2009; 19(3): 362–68

43. Ghosheh FR, Cremona FA, Rapuano CJ et al: Trends in penetrating keratoplasty in the United States 1980–2005. Int Ophthalmol, 2008; 28: 147–53

44. Goins KM: Surgical alternatives to penetrating keratoplasty II: endothelial keratoplasty. Int Ophthalmol, 2008; 28: 233–46

45. Eye Bank Association of America. Eyebanking Statistical Report 2007. Available at: *http://www.restoresight.org*

46. Maeno A, Naor J, Lee HM: Three decades of corneal transplantation: indications and patient characteristics. Cornea, 2000; 19: 7–11

47. Anshu A, Parthasarathy A, Mehta JS et al: Outcomes of Therapeutic Deep Lamellar Keratoplasty and Penetrating Keratoplasty for Advanced Infectious Keratitis. Ophthalmology, 2009; 116: 615–23

48. Anwar M, Teichman KD: Big-bubble technigue to bare Descemet' membrane in anterior lamellar keratoplasty. J Cataract Refract Surg, 2002; 28: 398–403

49. Terry MA, Shamie N, Chen ES et al: Endothelial keratoplasty for Fuchs' dystrophy with cataract: complications and clinical results with the new triple procedure. Ophthalmology, 2009; 116: 631–39

50. Shimazaki J, Shimmura S, Ishioka M: Randomized clinical trial of deep lamellar keratoplasty vs penetrating keratoplasty. Am J Ophthalmol, 2002; 134: 159–65

51. Sugita J, Kondo J: Deep lamellar keratoplasty with complete removal of pathological stroma for vision improvement. Br J Ophthalmol, 1997; 81: 184–88

52. Watson S, Ramsa E, Dart J et al: Comparison of deep lamellar keratoplasty and penetreting keratoplasty in patients with karatoconus. Ophthalmology, 2004; 111: 1676–82

53. Colin J, Velou S: Current surgical options for keratoconus. J Cataract Refract Surg, 2003; 29: 379–86

54. Feizi S, Javadi MA, Jamali H, Mirbabaee F: Deep anterior lamellar keratoplasty in patients with keratoconus: big-bubble technique. Cornea, 2010; 29: 177–82

55. Ardjomand N, Hau S, McAlister JC: Quality of vision and graft thickness in deep anterior lamellar and penetrating corneal allografts. Am J Ophthalmol, 2007; 143: 228–35

56. Duarte MC, Herndon LW, Gupta PK, Afshari NA: DSEK in eyes with double glaucoma tubes. Ophthalmology, 2008; 115: 1435

57. Huang T, Wang Y, Ji J et al: Deep lamellar endothelial keratoplasty for iridocorneal endothelial syndrome in phakic eyes. Arch Ophthalmol, 2009; 127: 33–36

58. Javadi MA, Feizi S, Rastegarpour A: Effect of vitreous length and trephine size disparity on post-DALK refractive status. Cornea, 2011; 30: 419–23

59. Utine CA, Tzu JH, Akpek EK: Lamellar keratoplasty using gamma-irradiated corneal lenticules. Am J Ophthalmol, 2011; 151: 170–74

60. Heindl LM, Riss S, Bachmann BO et al: Split cornea transplantation for 2 recipients: a new strategy to reduce corneal tissue cost and shortage. Ophthalmology, 2011; 118: 294–301

61. Javadi MA, Feizi S: Deep anterior lamellar keratoplasty using the bigbubble technique for keratectasia after laser *in situ* keratomileusis. J Cataract Refract Surg, 2010; 36: 1156–60

62. Buzzonetti L, Laborante A, Petrocelli G: Standardized big-bubble technique in deep anterior lamellar keratoplasty assisted by the femtosecond laser. J Cataract Refract Surg, 2010; 36: 1631–36

63. Bonci P, Bonci P, Della Valle V et al: Enzymatic descemetic lamellar keratoplasty: pilot study. Eur J Ophthalmol, 2010; 20: 879–84

64. Kubaloglu A, Sari ES, Unal M et al: Long-term results of deep anterior lamellar keratoplasty for the treatment of keratoconus. Am J Ophthalmol, 2011; 151: 760–67

65. Reinhart WJ, Musch DC, Jacobs DS et al: Deep anterior lamellar keratoplasty as an alternative to penetrating keratoplasty a report by the American Academy of Ophthalmology. Ophthalmology, 2011; 118: 209–18

66. Spiteri N, Tu KL, Kaye S: Subepithelial infiltrates in deep anterior lamellar keratoplasty in the presence of a corneal rust ring. Cornea, 2011; 30: 460–61

67. Prasher P, Muftuoglu O: Herpetic keratitis after descemet stripping automated endothelial keratoplasty for failed graft. Eye Contact Lens, 2009; 35: 41–42

68. Mittal V, Mittal R, Sangwan VS: Successful Descemet stripping endothelial keratoplasty in congenital hereditary endothelial dystrophy. Cornea, 2011; 30: 354–56

69. Fernandez MM, Buckley EG, Afshari NA: Descemet stripping automated endothelial keratoplasty in a child. JAAPOS, 2008; 12: 314–16

70. Jeng BH, Marcotty A, Traboulsi EI: Descemet stripping automated endothelial keratoplasty in a 2-year-old child. JAAPOS, 2008; 12: 317–18

71. Terry MA: Endothelial keratoplasty: history, current state, and future directions. Cornea, 2006; 25(8): 873–78

72. Melles GR, Lander F, Nieuwendaal C: Sutureless, posterior lamellar keratoplasty: a case report of a modified technique. Cornea, 2002; 21: 325–27

73. Terry MA, Ousley PJ: Small-incision deep lamellar endothelial keratoplasty (DLEK): six-month results in the first prospective clinical study. Cornea, 2005; 24: 59–65

74. Fogla R, Padmanabhan P: Initial results of small incision deep lamellar endothelial keratoplasty (DLEK). Am J Ophthalmol, 2006; 141: 346–51

75. Lombardo M, Lombardo G, Friend DJ et al: Long-term anterior and posterior topographic analysis of the cornea after deep lamellar endothelial keratoplasty. Cornea, 2009; 28(4): 408–15

76. Machor RS, Kaiserman I, Kumar NL et al: Deep Lamellar Endothelial Keratoplasty.Up to 5-Year Follow-up. Ophthalmology, 2010; 117(4): 680–86

77. van Dijk K, Dapena I, Moutsouris K et al: First DLEK series: 10-year follow-up. Ophthalmology. 2011; 118(2): 424.e1–3

78. Price FW, Price MO: Descemet stripping with endothelial keratoplasty in 50 eyes: A refractive neutral corneal transplant. J Refract Surg, 2005; 21: 339–45

79. Gorovoy MS: Descemet- stripping automated endothelial keratoplasty. Cornea, 2006; 25: 886–89

80. Mau K: What DSAEK is going on? An alternative to penetrating keratoplasty for endothelial dysfunction. Optometry, 2009; 80(9): 513–23

81. Straiko MD, Terry MA, Shamie N: Descemet stripping automated endothelial keratoplasty under failed penetrating keratoplasty: a surgical strategy to minimize complications. Am J Ophthalmol, 2011; 151: 233–37

82. Tsui JY, Goins KM, Sutphin JE, Wagoner MD: Phakic descemet stripping automated endothelial keratoplasty: prevalence and prognostic impact of postoperative cataracts. Cornea, 2011; 30: 291–95

83. Nieuwendaal CP, van Velthoven ME, Biallosterski C et al: Thickness measurements of donor posterior disks after descemet stripping endothelial keratoplasty with anterior segment optical coherence tomography. Cornea, 2009; 28: 298–303

84. Thiel MA, Kaufmann C, Dedes W et al: Predictability of microkeratome-dependent flap thickness for DSAEK. Klinische Monatsblatter fur Augenheilkunde, 2009; 226: 230–33

85. Esquenazi S, Rand W: Effect of the shape of the endothelial graft on the refractive results after Descemet's stripping with automated endothelial keratoplasty. Can J Ophthalmol, 2009; 44: 557–61

86. Scorcia V, Matteoni S, Scorcia GB et al: Pentacam assessment of posterior lamellar grafts to explain hyperopization after Descemet's stripping automated endothelial keratoplasty. Ophthalmology, 2009; 116: 1651–55

87. Bahar I, Kaiserman I, McAllum P: Comparison of posterior lamellar keratoplasty techniques to penetrating keratoplasty. Ophthalmology, 2008; 115: 1525–33

88. Price MO, Fairchild KM, Price DA, Price FW Jr: Descemet's stripping endothelial keratoplasty five-year graft survival and endothelial cell loss. Ophthalmology, 2011; 118: 725–29

89. Di Pascuale MA, Prasher P, Schlecte C et al: Corneal deturgescence after Descemet stripping automated endothelial keratoplasty evaluated by Visante anterior segment optical coherence tomography. Am J Ophthalmol, 2009; 148(1): 32–37

90. Oster SF, Ebrahimi KB, Eberhart CG et al: A clinicopathologic series of primary graft failure after Descemet's stripping and automated endothelial keratoplasty. Ophthalmology, 2009; 116: 609–14

RA

91. Shih CY, Ritterband DC, Rubino S et al: Visually significant and non-significant complications arising from Descemet stripping automated endothelial keratoplasty. Am J Ophthalmol, 2009; 148: 837–43

92. Shulman J, Kropinak M, Ritterband DC et al: Failed descemet-stripping automated endothelial keratoplasty grafts: a clinicopathologic analysis. Am J Ophthalmol, 2009; 148: 752–59

93. Suh LH, Dawson DG, Mutapcic L et al: Histopathologic examination of failed grafts in descemet's stripping with automated endothelial keratoplasty. Ophthalmology, 2009; 116: 603–8

94. Peng RM, Hao YS, Chen HJ et al: Endothelial keratoplasty: the use of viscoelastic as an aid in reattaching the dislocated graft in abnormally structured eyes. Ophthalmology, 2009; 116(10): 1897–900

95. Clements JL, Bouchard CS, Lee WB et al: Retrospective review of graft dislocation rate associated with descemet stripping automated endothelial keratoplasty after primary failed penetrating keratoplasty. Cornea, 2011; 30(4): 414–18

96. Bhogal M, Angunawela RI, Allan B: The 2-dot technique: minimalist donor lenticule marking in endothelial keratoplasty. Cornea, 2011; 30: 447–48

97. Bahar I, Kaiserman I, Sansanayudh W et al: Busin Guide vs Forceps for the Insertion of the Donor Lenticule in Descemet Stripping Automated Endothelial Keratoplasty. Am J Ophthalmol, 2009; 147: 220–26

98. Hwang H, Kim M: Endothelial damage of a donor cornea depending on the donor insertion method during Descemet-stripping automated endothelial keratoplasty in porcine eyes. Jpn J Ophthalmol, 2009; 53(5): 523–30

99. Khor WB, Mehta JS, Tan DT: Descemet stripping automated endothelial keratoplasty with a graft insertion device: surgical technique and early clinical results. Am J Ophthalmol, 2011; 151: 223–32

100. Covert DJ, Koenig SB: New Triple Procedure: Descemet's Stripping and Automated Endothelial Keratoplasty Combined with Phacoemulsification and Intraocular Lens Implantation. Ophthalmology, 2007; 114: 1272–77

101. Padmanabhan P, Warade SK, Sejpal K: New endothelial keratoplasty, phacoemulsification, and intraocular lens implantation triple procedure: comparison with conventional triple procedure. J Cataract Refract Surg, 2010; 36: 1142–48

102. Cheng YY, Kang SJ, Grossniklaus HE et al: Histologic evaluation of human posterior lamellar discs for femtosecond laser Descemet's stripping endothelial keratoplasty. Cornea, 2009; 28: 73–79

103. Cheng YY, Schouten JS, Tahzib NG et al: Efficacy and safety of femtosecond laser-assisted corneal endothelial keratoplasty: a randomized multicenter clinical trial. Transplantation, 2009; 88: 1294–302

104. Mootha VV, Heck E, Verity SM et al: Comparative study of descemet stripping automated endothelial keratoplasty donor preparation by Moria CBm microkeratome, horizon microkeratome, and Intralase FS60. Cornea, 2011; 30: 320–24

105. Hwang RY, Gauthier DJ, Wallace D, Afshari NA: Refractive changes after descemet stripping endothelial keratoplasty: a simplified mathematical model. Invest Ophthalmol Vis Sci, 2011; 52: 1043–54

106. Price MO, Giebel AW, Fairchild KM, Price FW Jr: Descemet's membrane endothelial keratoplasty: prospective multicenter study of visual and refractive outcomes and endothelial survival. Ophthalmology, 2009; 116: 2361–68

107. Dapena I, Moutsouris K, Droutsas K et al: Standardized "no-touch" technique for descemet membrane endothelial keratoplasty. Arch Ophthalmol, 2011; 129: 88–94

108. MacCauley MB, Price FW Jr, Price MO: Descemet membrane automated endothelial keratoplasty: hybrid technique combining DSAEK stability with DMEK visual results. J Cataract Refract Surg, 2009; 35: 1659–64

109. McCauley MB, Price MO, Fairchild KM et al: Prospective study of visual outcomes and endothelial survival with Descemet membrane automated endothelial keratoplasty. Cornea, 2011; 30: 315–19

110. Bahar I, Kaiserman I, Levinger E et al: Retrospective contralateral study comparing descemet stripping automated endothelial keratoplasty with penetrating keratoplasty. Cornea, 2009; 28: 485–88

111. Hjortdal J, Ehlers N: Descemet's stripping automated endothelial keratoplasty and penetrating keratoplasty for Fuchs' endothelial dystrophy. Acta Opthalmologica, 2009; 87: 310–14

112. MacLaren JW, Patel SV, Bourne WM, Baratz KH" Corneal wavefront errors 24 months after deep lamellar endothelial keratoplasty and penetrating keratoplasty. Am J Ophthalmol, 2009; 147: 959–65

113. Rose L, Kelliher C, Jun AS: Endothelial keratoplasty: historical perspectives, current techniques, future directions. Can J Ophthalmol, 2009; 44: 401–5

114. Price MO, Fairchild KM, Price DA, Price FW Jr: Descemet's stripping endothelial keratoplasty five-year graft survival and endothelial cell loss. Ophthalmology, 2011; 118: 725–29

115. Neff KD, Biber JM, Holland EJ: Comparison of central corneal graft thickness to visual acuity outcomes in endothelial keratoplasty. Cornea, 2011; 30: 388–91

116. Price FW Jr, Price MO, Arundhati A: Descemet stripping automated endothelial keratoplasty under failed penetrating keratoplasty: how to avoid complications. Am J Ophthalmol, 2011; 151: 187–88

117. Dooren BT, Mulder PG, Nieuwendaal CP: Endothelial cell density after posterior lamellar keratoplasty: five- to seven-year follow up. Am J Ophthalmol, 2007; 144: 471–73

118. Letko E, Price DA, Lindoso EM et al: Secondary graft failure and repeat endothelial keratoplasty after Descemet's stripping automated endothelial keratoplasty. Ophthalmology, 2011; 118: 310–14

119. Anshu A, Chee SP, Mehta JS, Tan DT: Cytomegalovirus endothellitis in Descemet's stripping endothelial keratoplasty. Ophthalmology, 2009; 116: 624–30

120. Bansal R, Ramasubramanian A, Das P et al: Intracorneal epithelial ingrowth after descemet stripping endothelial keratoplasty and stromal puncture. Cornea, 2009; 28: 334–37

121. Russell HC, Srinivasan S: Urrets-Zavalia syndrome following Descemet's stripping endothelial keratoplasty triple procedure. Clin Experiment Ophthalmol, 2011; 39: 85–87

122. Peh GS, Beuerman RW, Colman A et al: Human corneal endothelial cell expansion for corneal endothelium transplantation: an overview. Transplantation, 2011; 91: 811–19

123. Choi JS, Williams JK, Greven M et al: Bioengineering endothelialized neo-corneas using donor-derived corneal endothelial cells and decellularized corneal stroma. Biomaterials, 2010; 31: 6738–45

124. Hashimoto Y, Funamoto S, Sasaki S et al: Preparation and characterization of decellularized cornea using high-hydrostatic pressurization for corneal tissue engineering. Biomaterials, 2010; 31: 3941–48

125. De Miguel MP, Alio JL, Arnalich-Montiel F et al: Cornea and ocular surface treatment. Curr Stem Cell Res Ther, 2010; 5(2): 195–204

126. Snibson GR, Daniell M, Tole DM: Amniotic membrane grafting in the surgical management of primary pterygium. Clin Experiment Ophthalmol, 2004; 32: 501–4

127. Ye J, Kook KH, Yao K: Temporary amniotic membrane patch for the treatment of primary pterygium: mechanisms of reducing the recurrence rate. Graefe's Arch Clin Exp Ophthalmol, 2006; 244: 583–88

128. Lu D, Liu W, Li H, Ji J: The application of human anterior lens capsule autotransplantation in phacotrabeculectomy: a prospective, comparative and randomized clinical study. Eye, 2009; 23: 195–201