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Therapeutic Keratoplasty for Microbial Keratitis

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1. Introduction

Keratitis infections caused by bacteria, fungus or *Acanthamoeba* may be the most important reason for visual loss after trachoma and xerophtalmia in undeveloped and developed countries. Wilhelmus KR. 1998.

Early diagnosis and the availability of the powerful antibiotics give the opportunity of having a better control of the corneal infectious processes, mainly in those of bacteriological etiology.

However, the virulence and resistance of some bacteria Hill JC et al 1986, fungi Polack FM et al 1971 and *Acanthamoeba* Blackman HJ 1984 may progress inexorably despite the maximum therapy applied and in those cases the integrity of the ocular globe will be jeopardized and then, it will be necessary to realize a penetrating keratoplasty, by removing, totally of partially, the infectious area in the cornea in the levels where the antibiotics and defense mechanisms of the guest, might be effective.

The tectonic and therapeutic keratoplasty constitute a significant percentage of corneal transplants held in Asia and in some other under developed cities. In Singapore, it was reported a survey in which 13% of all transplants were with therapeutic or tectonic indication Tan DT, Janardhanan P 2008.

In Mexico, it was reported, in a 10 year-period, from 2001 thru 2010, out of the 3240 transplants carried out in the Hospital for the prevention of Blindness, "Asociación para Evitar la Ceguera en Mexico, IAP" Mexico City had a tectonic or therapeutic indication. If we divide the therapeutic indication from the tectonic, the percentage lows down to 2.06%

2. Indications

The therapeutic keratoplasty is a surgical procedure whose indications include the following circumstances:

a. To solve an infectious keratitis or a maximum conventional refractory inflammatory treatment.
b. To reestablish the integral structure of the ocular globe because of the risk of sclera extension, descematocele or corneal perforation (tectonic keratoplasty). In some cases, both situations occur.

The Therapeutic keratoplasty is an emergency in which the integrity of the ocular globe is at risk, contrary to the optical keratoplasty where the visual rehab is indicated after the process is already controlled.
Infectious keratitis present different clinical characteristics and history, depending on its etiology: therefore, the situations which require a penetrating keratoplasty are different from the bacterial micotic keratitis or for the *Acanthamoeba.*

2.1 Bacterial keratitis

The impact of bacterial keratitis on corneal blindness for scars, or other ocular complications is very important. In undeveloping countries for traumas risk, or in developed coutries in contact lens users, bacterial keratitis is a leading cause of corneal blindness.
Probably, the first indication for therapeutic keratoplasty, within the perforated corneal ulcers whose etiological agent is *Psedomonas aeruginosa*, especially in tropical climates, in contact lens users and in hospitalized or weak patients.
Psedomonas aeruginosa typically present as a rapidly evolving suppurative stromal infiltrate with marked mucopurulent exudate and become to corneal perforation in 24 to 48 hours because P *aeruginosa* due to colagenase production causing an important corneal stroma loss. Therapeutic keratoplasty is required too in corneal ulcers caused by others Gram negative bacteria as *Enterobacter*, *Serratia, klebsiella and Escherichia* that contaminate contact lens and cause a severe corneal desepitelization and ulcers with a great damage of corneal stroma with marked mucopurulent exudate frequently with similar characteristics of progressive suppurative keratitis. Fig 1,2
According to a survey published in 2007 by Ti et al, out of a revision of 92 patients (1991 to 2002) with acute infectious Keratitis in Singapore National Eye Centre, reported the *Pseudomonas aeruginosa* as the main etiological agent, responsible for the keratitis requiring therapeutic keratoplasty.

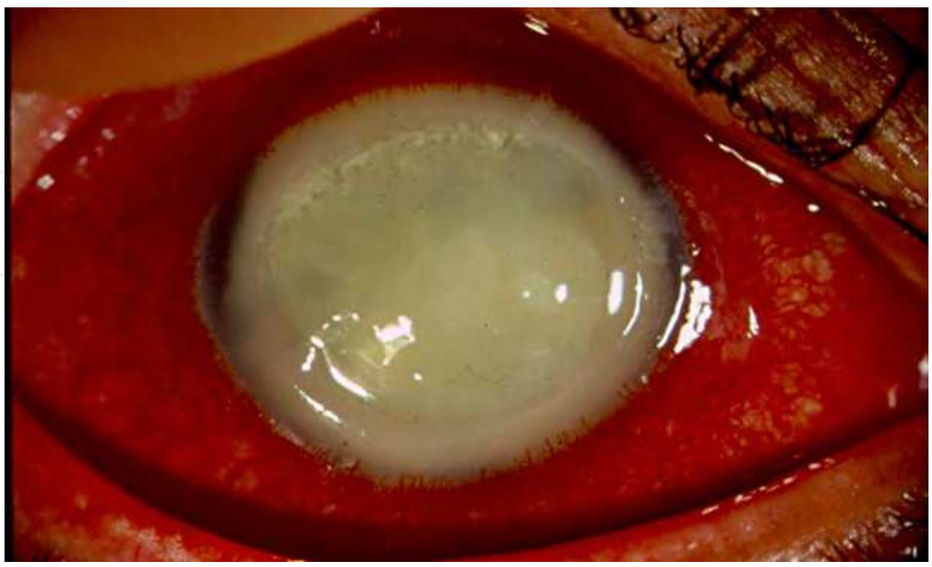


Fig. 1. Corneal ulcer caused by Gram negative, with perforation and poor response to medical treatment.

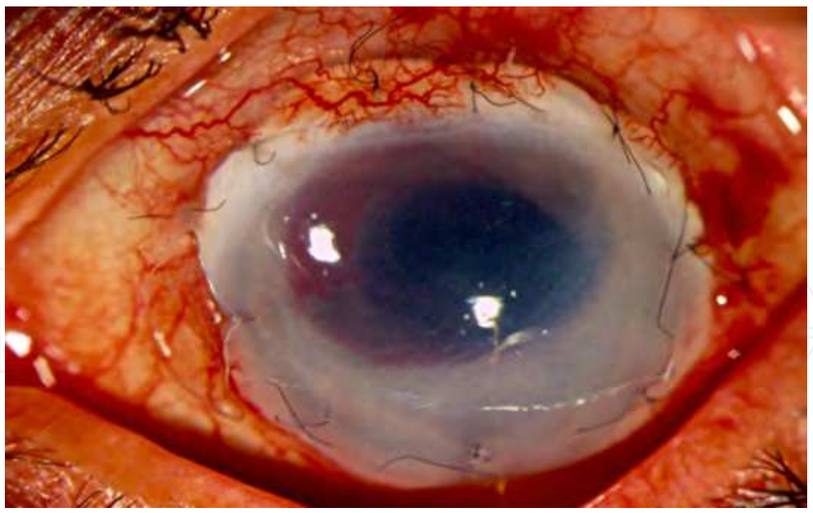


Fig. 2. The same eye 4 weecks after therapeutic sclerokeratoplasty (Courtesy of Alfredo Gomez Leal,MD Phathology Service of "Asociacion para Evitar la Ceguera en Mexico Hospital "Dr. Luis Sanchez Bulnes")

Other bacterial keratitis that might require a therapeutic keratoplasty are those infections that do not reply to a medical treatment, whose etiological agents grow slowly and behave as opportunists and sluggish and that continue to grow despite the aggressive treatment including crystalline keratopathy caused by alphahemolytic *Streptococcus* Stern GA 1993 The concomitant corneal ulcers are a sequence of severe *gonococcal* conjunctivitis Kawashima M et al 2009 and the ulcer caused atypical mycobacterium, an opportunist pathogen that produce lesions in areas where local resistance is compromised by trauma or prior surgery. Clinically, non-tuberculous *Mycobacteria* cause slow-progressing keratitis, which may mimic the indolent course of disease caused by others organism as fungi or anaerobic bacteria and frequently an delayed diagnosis progress to a severe keratitis Perez-Balbuena et al, 2010. Figs. 3, 4, 5

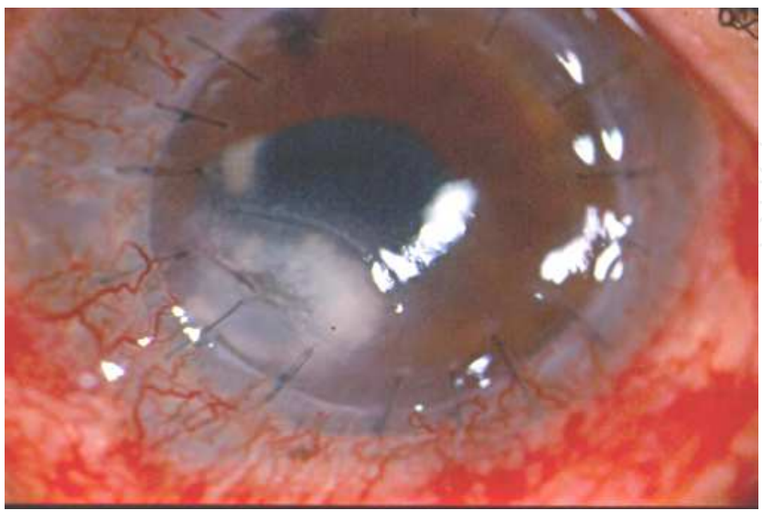


Fig. 3. *Mycobacterium chelonae* Keratitis. At initial examination, 4 weeks after penetrating keratoplasty with corneal infiltrates (3.0 X 2.0 mm) withe –gray with irregular and elevated edges in the donor-receptor interface.

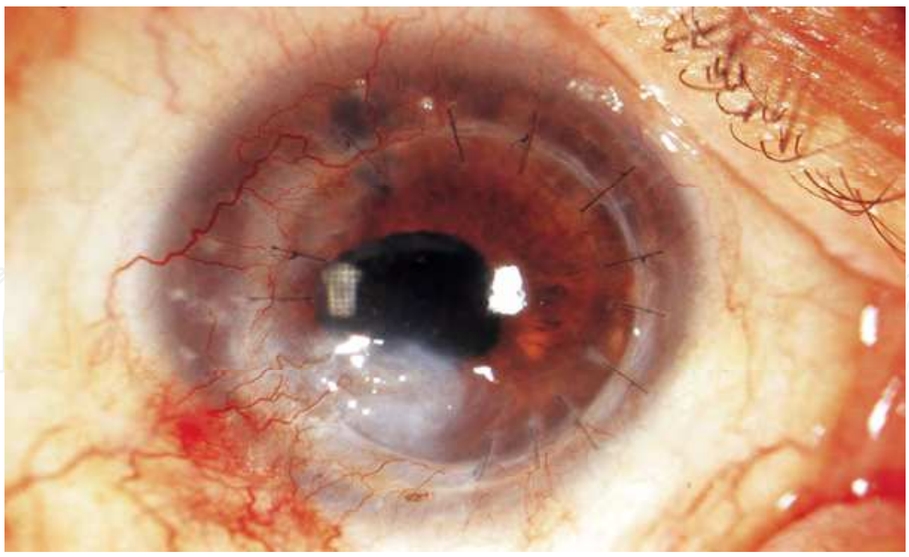


Fig. 4. Successful therapy 2 months with after topical Gatifloxacin 0.3% therapy.

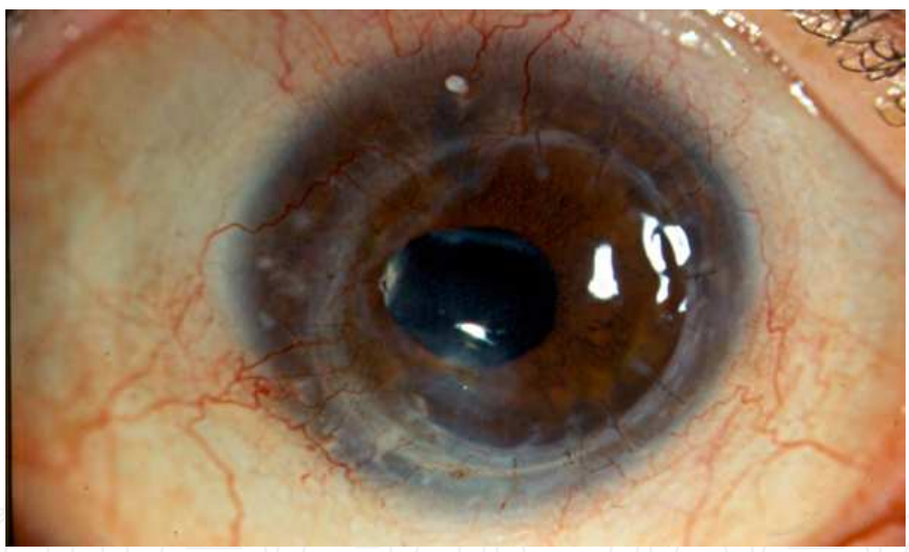


Fig. 5. Eighteen months after therapy discontinuation, corneal graft is infection–free and clear in the visual axis.

Mycobacterium keratitis is frequently present after a surgical procedure like refractive surgery (LASIK) with a slow progression to need a flap amputation or a therapeutic keratoplasty Susiyanti M, et al 2007.

Critical corneal infections occasionally requires conjunctival flap or therapeutic keratoplasty, in USA eye banking statistics identify microbial keratitis as a reason for keratoplasty in 1% of all corneal transplantation and in relation to bacterial keratitis incidence approximately 1% of USA cases of corneal infections become surgical candidates. Wilhelmus KR. 1998

In the experience obtained at the cornea service of "Dr. Luis Sánchez Bulnes" Hospital in Mexico, reported 2025 cases of infectious keratitis (survey carried out by fellow Carlos Johnson Villalobos MD. In a period from 2001 thru 2010, the causative agents were Gram

positive bacteria in 67.2% cases, Gram negative bacteria in 14.91%, and fungal keratitis in 6.81% cases; In my Service, I found in 3240 keratoplasties from 2000-2010, 3.30% patients needed therapeutic keratoplasty. Figs. 6, 7

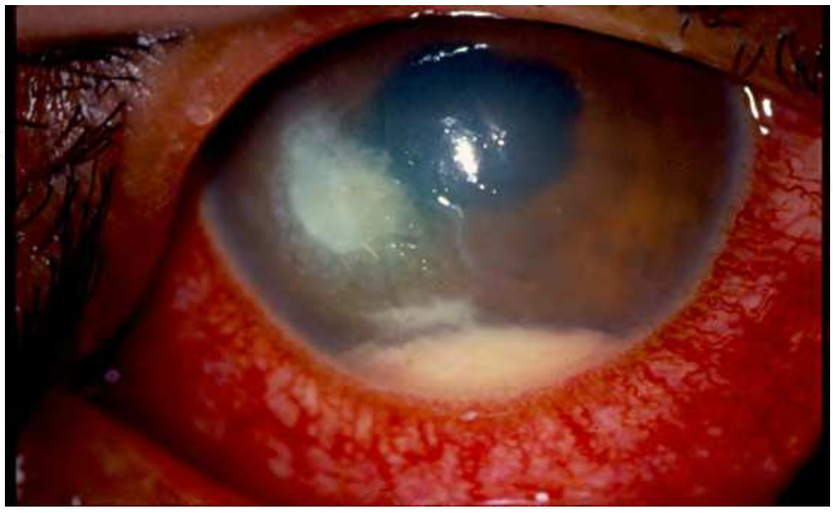


Fig. 6. Fungal keratitis (*fusarium solani*) 4 weeks evolution.

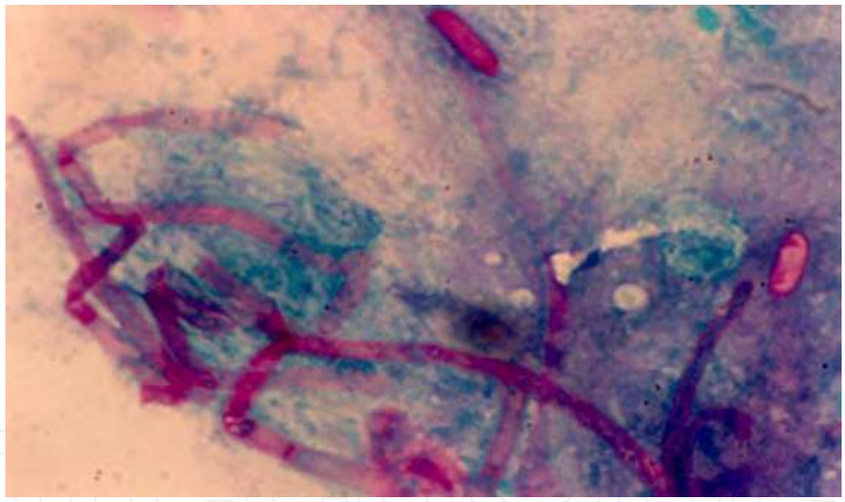


Fig. 7. Septated hyphal cells from *Fusarium solani* (Schiff stain 100X)

With the upcoming of new and more powerful antibiotics (fourth generation quinolones), the therapeutic keratoplasty is less frequently required for keratitis caused by Gram positive bacteria Al-Shehn et al. 2009, highlighted this over a 10-year period (1995-2005). They noted significant improvement in percentage of eyes achieving microbiological cure with medical therapy alone (76.0% in 1995 vs. 92.2% in 2005; p=0.002) or combining with surgical intervention (92.4% in 1995 vs. 100.0% in 2005; p=0.005).

2.2 Fungal keratitis

The therapeutic keratoplasty has an important role in the refractory mycotic ulcers treatment. In a series published by Ibrahim MM et al in 2009 in Brasil, 66 patients with

mycotic ulcer, therapeutic keratoplasty was required in 38% of cases; the most frequent isolated etiological agent was *Fusarium* in 67%, *Aspergillus* 10.5% and *Candida* 10%.
In several studies published by Perez-Balbuena et al. 2009, Vanzzini et al. **2010**, the main fungal pathogens for keratitis in Mexico are *Fusarium solani* and other species, dematiaceous fungus that include a wide group of black colony forming fungus and *Aspegillus* with several species too.

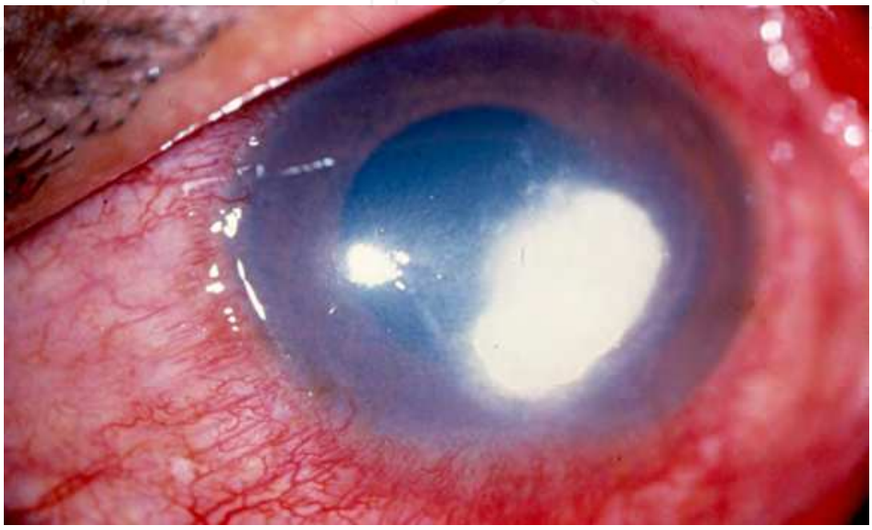


Fig. 8. *Fusarium* large corneal ulcer 10 days after injury with organic material.

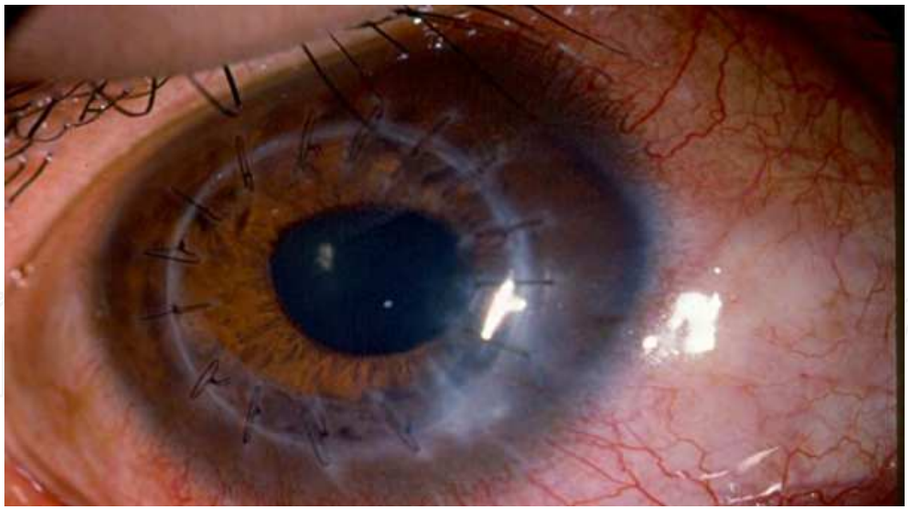


Fig. 9. Successful postoperative the same eye outcome six months after therapeutic keratoplasty loose suture after surgery

In a retrospective survey carried out from 1981 to 2001 in the Cornea Service of "Asociacion para Evitar la Ceguera en Mexico Hospital "Dr. Luis Sanchez Bulnes", we studied 120 cases of mycotic keratitis selecting 61 cases whose etiological agent was *Fusarium solani,* confirmed by the cultures. In total, 78% were male (average, age, 41.5 years) the principal risk factor was ocular trauma contaminated with organic material, dry eye, post corneal surgery in

infections and *Candida albicans* in contact lens user, and the patient came to be examined 2 to 6 weeks after the trauma.
The ulcers observed were indolent, with satellite lessons in 30% patients, irregular edges, dense infiltrate and hypopyon, ciliary injection in conjunctiva, Figs .8, 9, 10, 11 usually treated before with antibacterial drops without clinical healing.

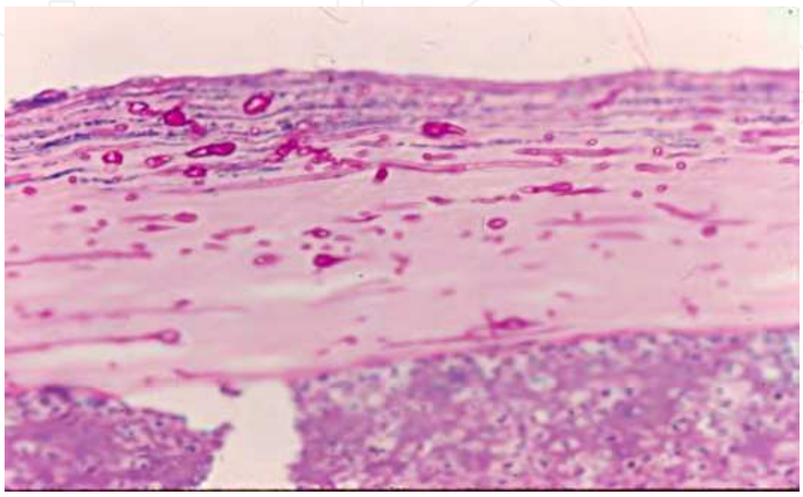


Fig. 10. Hyphal elements visible on pathologic examination of corneal button. Schiff stain (20X magnification).

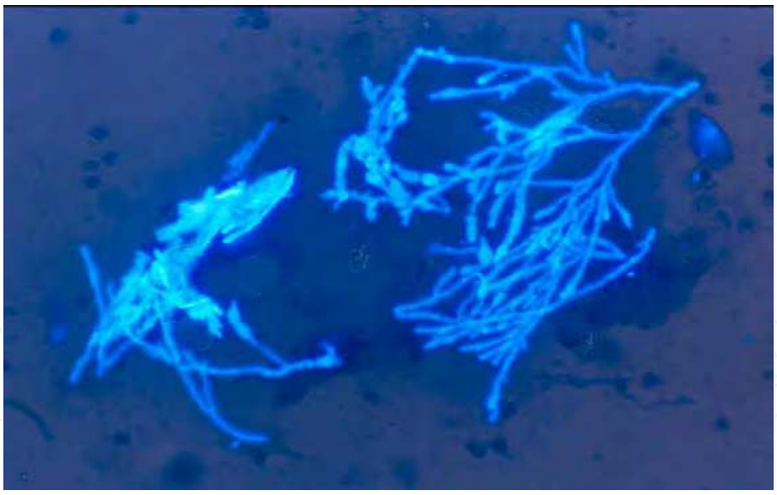


Fig. 11. Septate hyphal fungus cells in the corneal scrap smears of fungal keratitis patients, stained with calcofluor (Cellfluor) and fluorescens microscopy (20X magnification)

The antifungal treatments were started immediately after the diagnosis was confirmed in each case. The total 81% of patients were treated with monotherapy and 18.4% patients with combined antifungal therapy. As antifungal therapy, 2% ketoconazole suspensión was prepared using 200 mg tablets (Nizoral®, Janssen Cilag, Mèxico City), manually crushed to fine poder and suspended in hidroxypropylmethyl-cellulose eye drops. A total of 14 of 27 (51.2%) cases also received oral ketoconazole 200-400 mg every 24 hours. Nine patients were

treated with topical itraconazole 1.0% drops (Sporanox®, Janssen-Cilag, Mèxico City) made in the same way as ketoconazole. Perez-Balbuena et al. 2009
The Fluconazole (2mg/ml Diflucan®, Pfizer) topical drops were made with intravenous solution of 2 mg/mL with <1mg/mL (0.66 mg) in final concentration using hidroxypropylmethyl-cellulose eye drops.
Severe cases were assigned to the medical and surgical treatment, using either monotherapy or combined topical antifungal treatment plus one or more surgeries. Therapeutic keratoplasty was indicated in 14/61 patients 23%. Conjuntival flap was indicated en 4 of 61 patients 6.5%, eviscearation surgeries were practiced in 14 of 61 patients 22.9%.
For medical treatment actually we use Natamycin 5% suspension in ocular droops (Miconacina® Grin laboratorios Mexico City) each 1 hour initially for two days, and after each 4 hours for 8 to 15 days upon the clinical response, we use this last dosage at least for 30 to 40 days, in cases of *Aspergillus* keratitis the medication mentioned before is associated with oral Itraconazole 100 mgs/ 12 hours. For *Candida* keratitis we use topical Voriconazole 1% (V-Fend® Pfizer Germany)) or Fluconazole 1% (Diflucan® Pfizer Germany). The indications for therapeutic keratoplasty included minimun improvement with medical therapy or high perforation risk. Table 1

	Medical / Surgical Therapy group					
Drug	n	Conjuncti-val Flap	Penetrating kerato-plasty	Tectonic kerato-plasty	Eviscera-tions	Tome of Treatment Days
Natamycin	0	0	0	0	0	0
ketoconazole	11	0	4	1	7	20.6
Miconazole	0	0	0	0	0	0
Itraconazole	3	2	2	1	2	26
Fluconazole	1	1	0	0	1	40
Ketoconazole+Natamicycin +Fluconazol	1	0	1	0	0	15
Ketoconazole+Itraconazole	1	0	1	0	0	20
Ketoconazole+Fluconazole	3	0	1	0	2	78.3
Itraconazole+ Fluconazole	2	0	2	0	0	47
Natamycin+ Fluconazole	1	1	1	0	0	170
Ketoconazole+ Miconazole	1	0	0	0	1	20
No treatment and lost follow-up	4	0	3	0	1	0
Total	28	4	15	2	14	

Table 1. Antifungal therapy used in the medical and surgery group

Killingsworth et al. 1993 obtained a 100% recovery in 15 ulcers treated with therapeutic Keratoplasty. We suggested surgical therapy with conjunctive flap or penetrating keratoplasty in advanced cases when there has been a poor response to medical therapy or a very low final visual acuity.

2.3 Acanthamoeba keratitis

The ophthalmic pathology caused by *Acanthamoeba* might produce severe and extensive corneal necrosis that tome times require therapeutic keratoplasty. The evolution of an infection becomes in a severe stromal keratitis of late diagnosis, inadequate treatment and severe consequences.

Patient with acanthamoebic keratitis are tipically young, healthy individuals, males or females are equally affected, almost all are daily contact lens wearer, or using non sterile wather for wash the contact lenses, is most frequently is an unilateral keratitis but bilateral cases have ocurred. The most important clinical sign is a severe pain even with a small epithelial dendritiform ulcer because the recurrent epithelial breakdown like an herpetic ulcer in the early stages of the infection. Some patients have a stage of disease mimicking disciform stromal keratitis and others develop radial neuritis. The occurrence of satellite lesions, stromal abscess, necrotizing inflammation, hypopyon, scleral nodules, diffuse scleritis or posterior scleral inflammation are signals of advanced infection. Figs. 12, 13 The most characteristic stromal antigen-antibody inflammatory reaction is the stromal ring formation that can consist of single, multiple or overlapping rings around the main corneal ulcer. Alizadeh H, et al 1998

The ophthalmic pathology caused by *Acanthamoeba* might produce severe and extensive corneal necrosis that tome times require therapeutic keratoplasty. The evolution of an infection becomes in a severe stromal keratitis of late diagnosis, inadequate treatment and severe consequences. Despite is rare pathology, in the last decade are incremented its frequency, associated to contact Lents user. Ficker LA et al 1993.

Before carrying out a therapeutic keratoplasty it is important to give a medical therapy and many drugs have been tested for *Acanthamoeba* infections as mentioned in the Box No 1, the most used are Chlorexidine 0.01% in aqueous solution not commercially available, Polimethylene biguanide 0.3% in aqueous solution (Brolene® UK). Oral Itraconazole 100 mgs/ 12 hours combined with topical Netilmycin 0.3% (Netira® SCIFI laboratories Italy) are actually used in our acanthamoebic keratitis patient.

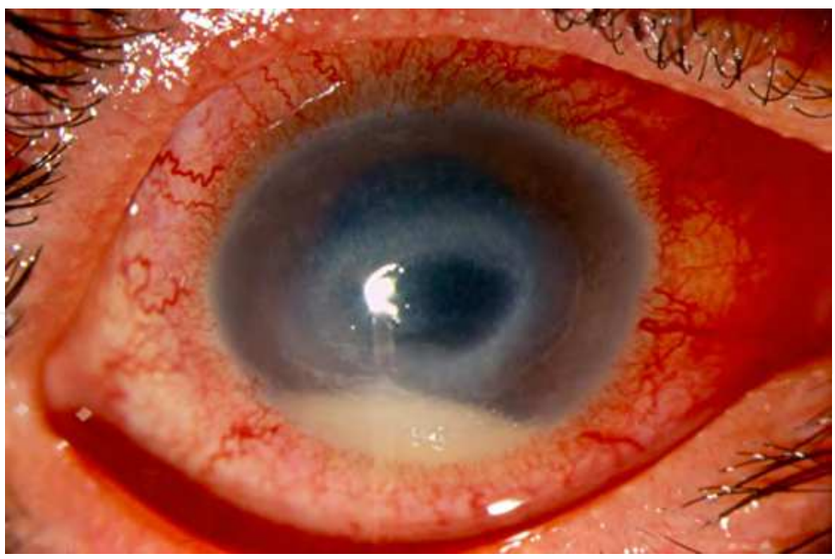


Fig. 12. *Acanthamoeba* keratitis in young and healthy female patient, 6 weeks evolution time, edema, and central ulcer.

Laboratory diagnosis are better done by visualizing cyst cells in the mucous exudate or in corneal biopsies, by stain tecniques like Giemsa Fig. 13 or Calcofluor (Cellfluor) and fluorescence ligth microscopy and by cultures C in non nutrient Pages medium with a layer of inactivated cells of *Enterobacter aerogenes.*

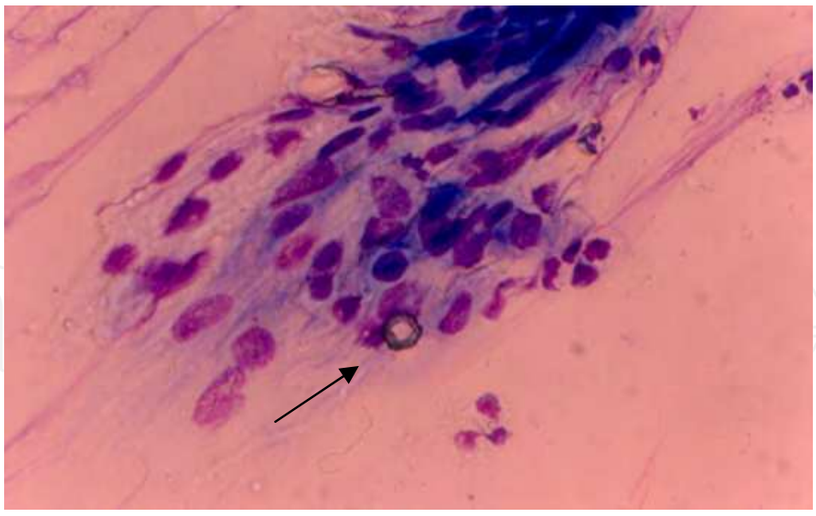


Fig. 13. *Acanthamoeba* cyst Giemsa stein, in light microscope view (20 X magnification)

Before carrying out therapeutic keratoplasty it is important to give a medical therapy and many drugs have been tested for *Acanthamoeba* infections as mentioned in the , the most used are Chlorexidine 0.01% in aqueous solution not commercially available, Polimethylene biguanide 0.3% in aqueous solution (Brolene ®UK) we used in our
Oral Itraconazole 100 mgs/ 12 hours combined with topical Netilmycin 0.3% (Netira® SCIFI laboratories Italy) are actually used in our acanthamoebic keratitis patient. Medical and surgical treatment in Keratitis by *Acanthamoeba* is controversial.
In some cases with early diagnosis these cases have been successfully treated with medical treatment without being necessary to undergo a surgical procedure of therapeutic keratoplasty. Ficker et al 1993, mention that the over life of the graft by Keratitis by *Acanthamoeba* is of poor outcome, reporting more than 50% recurrence incidence of the graft. However, in our personal opinion, the Keratoplasty continues to have a central role in the management of patients who progress or do not respond to medical treatment. The acute management of these active cases is to sterilize the infection as rapidly as posible and to dalay surgical management until the patient receives adequate antiamebic therapy.

3. Pre-surgical evaluation

When the decision has been taken to perform a therapeutic Keratoplasty, a good examination is necessary to value the following points.
To evaluate the size, depth and place of the infiltrate or corneal ulcer, if the limbos is compromised, or if there is imminent or actual perforation.
To evaluate the posterior pole under dilation, if it is possible, specially the vitreo retinal area, and when it is not possible we must realize a B Scan ultrasound and if the integrity of the ocular globe is affected by an imminent perforation it is necessary to make a Trans palpebral ecography to evaluate a probable endophtalmitis. Increased risk for endophthalmitis at the time of therapeutic keratoplasty includes the presence of fungal disease, corneal perforation and patients who have undergone previous cataract extraction.
To evaluate the presence of cataract and to carefully decide the extraction of the crystalline since this is a barrier to avoid the extension of the infectious process toward the posterior pole. It is recommended to try to keep the posterior capsule to diminish the risk of Endophthalmitis. SpeakerMG et al 1991.

Before surgery, intraocular pressure should be evaluated in eyes without a perforation.
Adequate pressure control remains essential. In patients with markedly elevated intraocular pressure or in patients with a corneal perforation in which the lens-iris-diaphragm has moved forward, we give intravenous manitol to control intraocular pressure and to reduce the vitreous volume.
In eyes with a crystalline lens or posterior chamber intraocular lens, and patients with iris incarcerated in a wound, we give Pilocarpina 2% 1 hour prior to surgery, to protect the lens, and maintain a posterior lens-iris diaphragm.
We do not recommend carrying out the surgery with local anesthesia, it is much better to perform it under general anesthesia and in all cases we must maintain the arterial pressure under control to reduce the risk of expulsive choroidal hemorrhage, especially in those patients with perforation.

4. Preoperative treatment

Before therapeutic keratoplasty for infectious keratitis, the patient should be treated with topical and systemic therapy directed towards the offending microbe. This treatment applies to bacterial, fungal and *Acanthamoeba.*
Regardless of the infectious etiologies, we always recommend topical antbiotic therapy to prevent bacterial super infection.
The preoperative antibiotic prophylaxis should be broad spectrum and nontoxic to help promote reepithelization and prefer an antibiotic that penetrates into the cornea, aqueous achieve levels above to MIC_{90} of most pathogenic bacteria.
We currently use a topical fourth –generation fluoroquinolone Gatifloxacin 0.3% (Zymar^{R}; Allergan Inc, Irvine, CA) with a saturating dosage of one drop every 15 minutes for 1 hour before keratoplasty.

5. Donor material

Criteria for the selection of donor corneas are stringent, except in cases of large perforation when access to tissue of optimal quality is not possible. Corneal tissue of excellent grade offers the following advantages:
5.1. Healthy tissue with intact epithelium minimizes the risk of re infection in the graft and use of healthy endothelium is critical for the survival of the graft.
5.2. Compact and clear tissue helps in monitoring anterior chamber reaction during the immediate postoperative period.
Yao et al. 2003. If fresh donor tissue is not available, the use of cryopreserved tissue and donor corneas preserved in pure glycerin or water-free calcium chloride are effective substitutes in therapeutic keratoplasty to control severe fungal corneal infection and preserve the global integrity.

6. Surgical techniques

Although corneal transplantation for infections keratitis follows the basic surgical technique of penetrating keratoplasty, special attention must be given to certain details:

6.1 Preoperative procedures

We recommend general anesthesia .It is important to have a soft eye preoperatively so that problems related to positive vitreous pressure can be prevented.

Intravenous Manitol produces deturgescence of the vitreous and helps to minimize these problems.
At the time of therapeutic keratoplasty by placing the appropriate trephine over the cornea and creating an indentation in the epithelium.

6.2 Exposure

In general, we commonly use lid speculum and suture a Fleringa ring in place to provide scleral support, in cases of large ulcers that reach up to the limbus, peritomy is required and homeostasis is achieved by the use of wet-field cautery.

6.3 Host preparation bed

The goal of surgery is to excise all necrotic or infected tissue during trephination. It possible, a 1 mm rim of healthy corneal tissue should also be removed to leave a stable, no infected recipient bed.
Conjuntival peritomies should be done in cases requiring large or eccentric grafts.
The trephination of the recipient bed can be technically difficult. Careful partial-thickness trephination with a Sharp trephine is done in the absence of any perforation; in eyes with a perforation, support is obtained with cyanocrylate and viscoelastic protection and anterior chamber can be reformed and the host trephination can be performed under a more controlled environment, care should be taken to avoid exerting excessive pressure on the globe to prevent extrusion of the ocular contents a freehand dissection of the host bed may be done.

6.4 Clearing the anterior chamber of exudates

Irrigation of the anterior chamber is done using a balanced salt solution. Elimination of all exudative material from the anterior chamber helps to prevent the recurrence of infection and reduces complications such as glaucoma.
The membranes over iris are dissected gently by the irrigating cannula and are removed with forceps. Any membrane covering the iris surface should be removed very gently, and every effort should be made to arrest bleeding from the iris surface.
Intracameral antibiotics or antifungals can be used whenever they are required.
Two large peripheral iridectomies are recommended .Removal of cataracts should be deferred because the lens forms an effective barrier that prevents the spread of infection into the vitreous. When vitreous involvement is diagnosed, open sky vitrectomy is indicated. The anterior chamber is reformed with a viscoelastic substance, and the margin of the recipient bed is trimmed.

6.5 Preparation of the donor botton

The donor button should be trephined after the size of the recipient opening is measured and preparation of the host bed, because necrotic tissue may require additional trimming which may alter the size of the graft.
The donor button is punched from the endothelial side and usually 0.5-1.0 mm larger than the selected host trephine.

6.6 Suturing

The donor-recipient junction was sewn by 10-0 monofilament Nylon interrupted sutures passing though at least 70% depth of the host cornea is the preferred technique. Full

thickness bites are not taken as they may form a conduit for passage of infection from the cornea into the anterior chamber. It is not uncommon to use greater number of sutures than conventional technique of keratoplasty (16 Sutures).Table 2

Age	50,90 ± 16,298 years old
Sex	68,7 % (♂)
Type penetrating keratoplasty	98.5% QPP vs.1.5% Lamelar
Endophthalmitis	11,9 %
Perforation	50,7 %
Survival graft	10,08 ± 15,97 months
Size of the donor	8,80 ± 0,19 mm.
Size receiver	8,17 ± 0,13 mm.

Table 2. Profile of infectious keratitis 2025 cases, during 10 years (2000-2010) in 14.65% cases with therapeutic keratoplasty in advanced process, dates of "Asociación Para Evitar la Ceguera en México Hospital "Dr. Luis Sanchez Bulnes"

7. Postoperative management

Immediate postoperative treatment focuses on prevention of recurrence of infection and hastening the complete epithelization of the graft.

Bacterial keratitis.
Systemic antimicrobial: Initiate 1 day prior, continue for 2 weeks. **Topical antibiotic:** With most sensitivity, given hourly and topically. Combination therapy or a broad – spectrum antibiotic for which sensitivity is unknown. **Topical corticosteroids**: Every 1 or 2 hours initially. Given judiciously. **Cycloplegics:** Recommended to ciliary spasm and prevent synechiae. **Antiglaucoma medication**: If intraocular pressure is elevated (avoid pilocarpine, prostaglandin analogues). **Tears substitutes**: Frequent instillation is recommended to hasten re-epithelization.
Fungal Keratitis.
Topical antifungals: Every hour initially continue for 8-12 –weeks. **Systemic antifungals**. Oral Itraconazole 200 mg two times daily continues for 2 -6weeks. **Corticosteroids:** Only under extremely special conditions. Given judiciously. **Cyclosporine:** Topical drops 0.5% **Cycloplegics**: Recommended to ciliary spasm and prevent synechiae. **Antiglaucoma medication**: If intraocular pressure is elevated (avoid pilocarpine, prostaglandin analogues). **Tears substitutes:** Frequent instillation is recommended to hasten re-epithelization.
***Acanthamoeba* keratitis.**
Topical amoebicidal: Drugs – every 1 to 2 hours. **Systemic antifungal**: Oral Itraconazole 200 mg two times daily. **Topical Corticosteroids:** Given judiciously. **Cycloplegics.** Recommended to ciliary spasm and prevent synechiae. **Antiglaucoma medication**: If intraocular pressure is elevated (avoid pilocarpine, prostaglandin analogues). **Tears substitutes** frequent instillation is recommended to hasten re-epithelization

Box 1. Guidelines for postoperative management of terapeutic keratoplasty

Appropriate antimicrobial therapy must be continued postoperatively until the corneal epithelium has healed
The general guidelines for postoperative management are shown in (Box 1). Therapy may be guided by histopathological and microbiological evaluation of the excised corneal tissue.

8. Complication

Postoperative complications after therapuetic keratoplasty are virtually the same as in other situations, except the prevalence is greater.
Depending on the time of onset, complications can be divided in early- onset complications (within 2 weeks) and late-onset complications. The early postoperative period may be complicated with wound leak, shallow anterior chamber, hyphema, anterior uveitis, elevated intraocular pressure, persistent epithelial defect and re- infection of the graft. Late postoperative complications include cataract, glaucoma, graft failure secondary to rejection, infection or endothelial decompensation and phthisis bulbi. Table 3

COMPLICATION	%
Corneal Decompesation/ primary failure	37.31
Recidive	31.34
Persistent epithelial defect	23.88
Glaucoma	22.38
Refractory to treatment reyect	7.46
Cataract	7.46
Ptisis bulbi	2.98
Corneal melting	4.47
Seidel	1.49
Retinal detachment or DC	1.49
Cellulitis orbitaria	1.49
Primary failure	26.66
Corneal decompensation Flat anterior chamber	10.44 1.70

Table 3. Therapeutic keratoplasty Complications of infectious keratitis 2025 cases, during 10 years (2000-2010) in 14.65% cases with therapeutic keratoplasty in advanced process, dates of "Asociación Para Evitar la Ceguera en México Hospital "Dr. Luis Sanchez Bulnes", some patient had one or two complications.

8.1 Early-onset complications

8.1.1 Seidel

This is an avoidable complication if the surgical technique is careful and the wound is well constructed The best way to prevent wound leaks is to ensure meticulous wound apposition at the end of the procedure. Promptly resuturing is recommended if non surgical attempts like patching or contact lens bandage fail to seal the leak. Prolonged contact between the donor cornea and the iris, lens, or IOL may result in irreversible complications and sequel. In our experience resuture was needed in 1, 49% of therapeutic keratoplasty.

8.1.2 Shallow or flat anterior chamber

This is a generally avoidable complication with a watertight wound. At the end of the surgery is critical that we ensure the integrity of the wound. Shallow or flat anterior chamber if present, should be managed as soon as possible to avoid synechiae formation which may result in irreversible endothelial cell loss and consequently early graft failure. In our center we needed to reform the anterior chamber either with BSS or with viscoelastic substances in 1, 7 % of the cases.



Fig. 14. Flat anterior chamber in this patient with synechiae formation post therapeutic keratoplasty

8.1.3 Hyphema

Surgical trauma on an eye with vessels on the surface of the iris or in the cornea can cause hyphema. Every effort should be done to prevent bleeding from the iris surface. Slight bleeding usually stops spontaneously with closure of the eye and return of adequate IOP. If the hemorrhage persists in the presence of an adequate IOP, then it may need to be

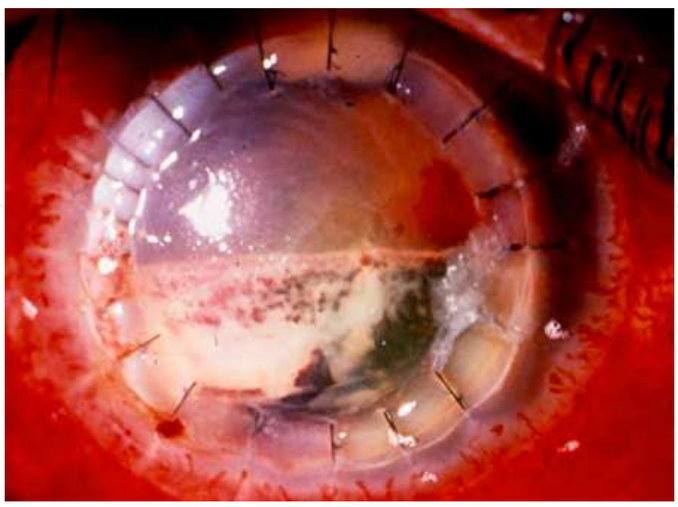


Fig. 15. Fibrine and hyphema 48 hours post keratoplasty in severe fungal ulcer (*Aspergillus flavus)*

Controlled using cautery, compression with viscoelastic, or tamponade with sponges soaked with epinephrine 1:1000. If hyphema is persistent and provokes a rise in intraocular pressure, it should be immediately evacuated. Fig. 15

8.1.4 Anterior uveitis

Infectious keratitis itself explains the great inflammation that is seen after PK in these patients. The risk of severe postoperative inflammation can be diminished by gentle manipulation during surgery and the meticulous removal of all inflammatory material of the anterior chamber. The aggressive control of postoperative inflammation is also essential for the prevention of synechiae formation. Usually the uveitis is solved with the aid of cicloplegic and corticosteroid drugs, but the latter should be used with caution in fungal and *Acanthamoeba* keratitis.

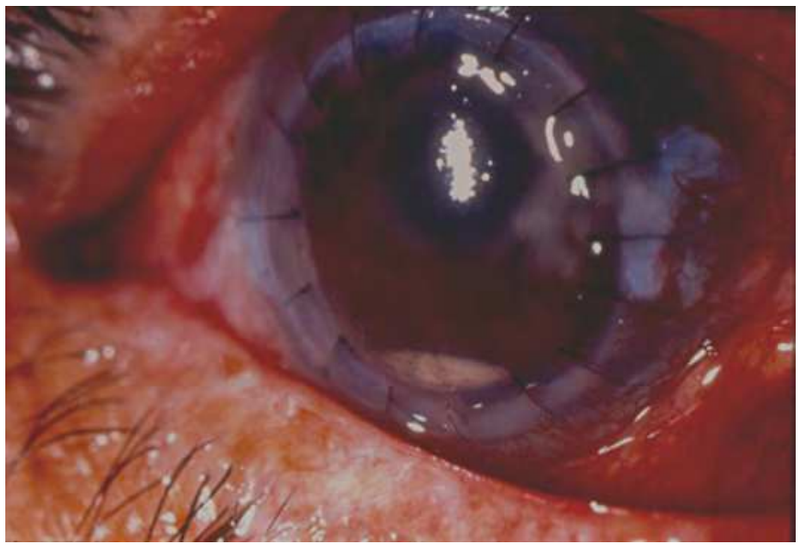


Fig. 16. Corneal ulcer by *Aspergillus flavus* ,three days Post- keratoplasty

8.1.5 Ocular hypertension

Severe inflammation causes trabeculitis and this causes elevation of the intraocular pressure. Besides peripheral anterior synechiae if present and not broken during surgery can impeed aqueous outflow and cause secondary glaucoma. Usually elevation of intraocular pressure can be controlled with beta blockers and systemic acetazolamide while the inflammation diminishes.

8.1.6 Persistent epithelial defect

Careful handling of the donor cornea intraoperatively is imperative to avoid damaging the epithelium. Good wound apposition and prevention of an overriding edge leads to better tear-film distribution and a reduced incidence of epithelial defects. A persistent epithelial defect has the potential to secondary infection thus reepithelialization and the maintenance of an intact epithelium is critical for postoperative wound healing, graft survival, and protection against infection and melting. Initial treatment requires application of topical lubricants and if it persists a permanent or temporary tarsorrhaphy early in the

postoperative period can be performed. Alternatively, botulinum A toxin injected into the elevator muscle to induce a complete ptosis, may help reduce the severity and persistence of an epithelial defect.
The use of preservative-free medication is recommended to reduce the risk of epithelial toxicity and corticosteroids may need to be decreased.

8.1.7 Recurrence

The indiscriminate use of corticosteroids postoperatively can cause recurrence of the infection, especially in micotic keratitis. In our experience we report recurrence in 31, 4%, being the most frequent cause fungal keratitis, as Rao et al 1999 reported. 50% of these recurrences needed a new PK to be free of infection. Time of recurrence varied between 1-42 days.

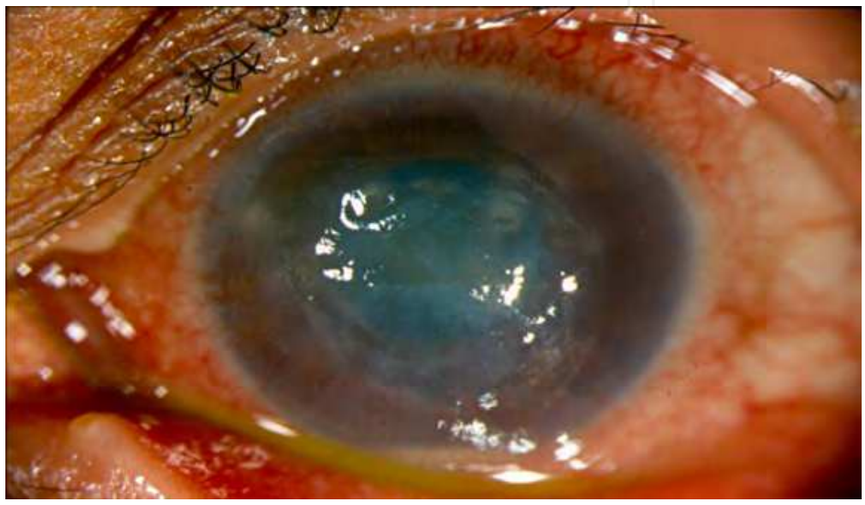


Fig. 17. Therapeutic keratoplasty, *Mycobacterium chelonae* corneal ulceration 30 Days post LASIK

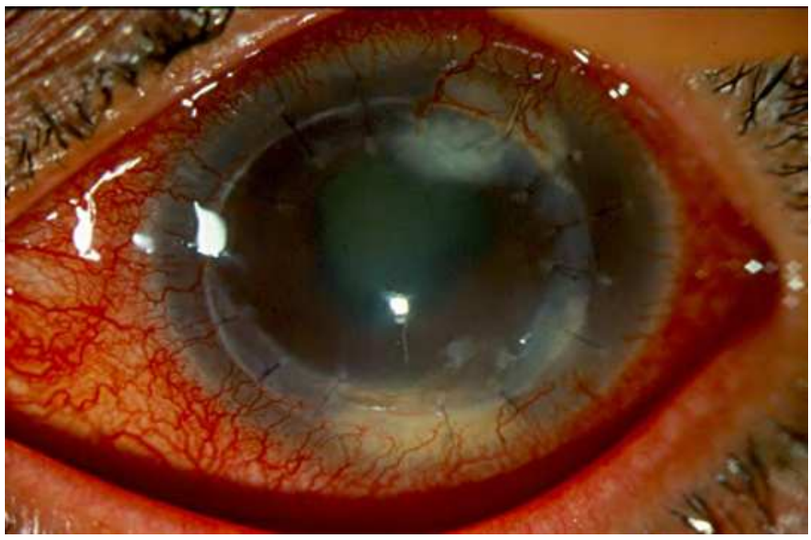


Fig. 18. Same eye showing recurrence of infection (*Mycobacterium chelonae)* Involving the entire graft

Recurrences can be avoided by performing a careful excision of the recipient cornea including all the infected material and with as adequate postoperative antibiotic and corticosteroid management. In our experience in fungal keratitis an Non tuberculous *Mycobacterium* we observed 31.34% recurrences. Fig. 17,18.

8.2 Late-onset complications

8.2.1 Secondary glaucoma

Adequate control of postoperative inflammation and careful liberation of synechiae during surgery lowers the incidence of secondary glaucoma which can endangers keratoplasty success. We found a incidence of secondary glaucoma of 22,4%. Only 4, 47% patients needed a filtering surgery to control intraocular pressure. Fig. 19.

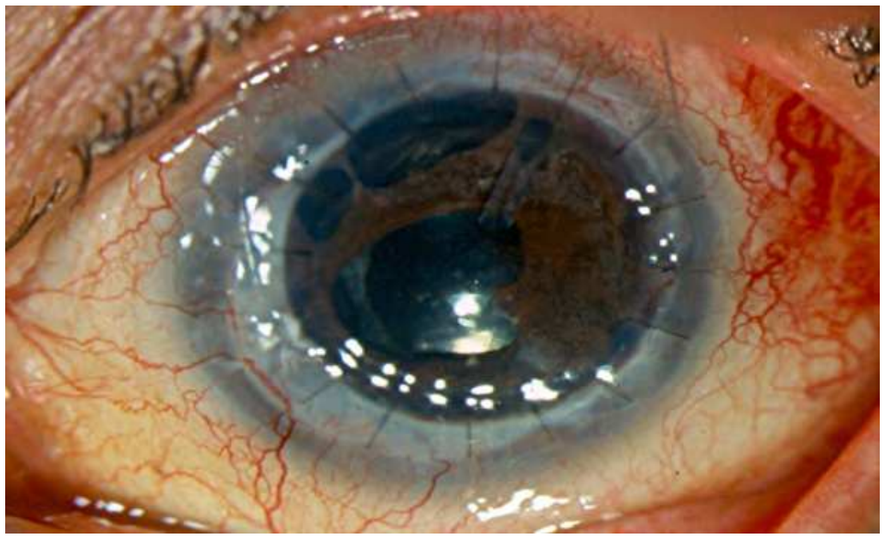


Fig. 19. Some patient needed Ahmed valvule for hypertension control

8.2.2 Cataract

As lens metabolism is dependent on the health of the eye, any ocular disease that affects the supply of oxygen and nutrients, or produces toxic substances will give rise to cataract. Also the incidence of cataract formation is higher because of the intense postoperative steroid treatment. We did find an incidence of 7, 46%.

8.2.3 Graft failure

Graft failure can be secondary to unresponding to treatment graft reject, endothelial descompensation or infection recurrence. It is much more common in therapeutic keratoplasties than in other indications. We report an incidence of 38,8%. In our center is much higher than in other reports because the quality of donor tissue in this type of keratoplasty is not as good as in optical procedures because of the relative paucity of corneal tissue in our country as well as the emergency under which this surgery is performed. Sharma et al. 2010 After the integrity of the globe is preserved and ocular inflammation has subsided, a smaller-diameter optical keratoplasty may be performed electively for visual rehabilitation

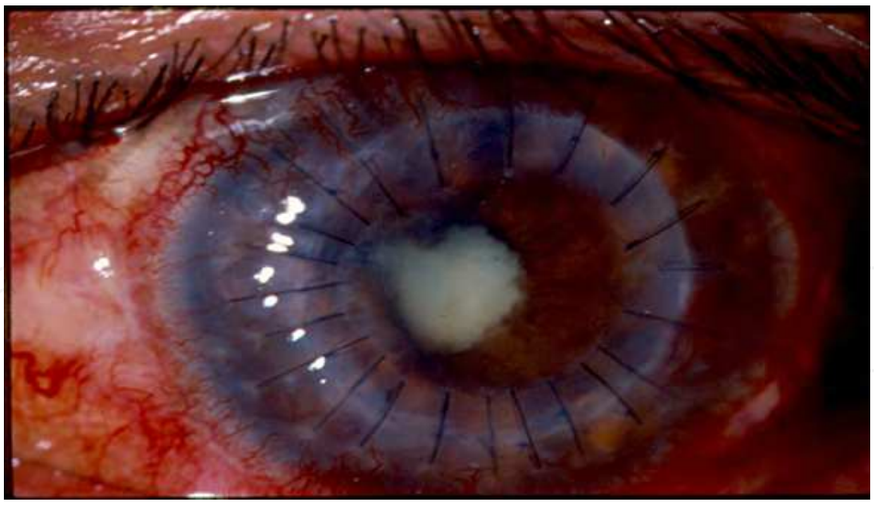


Fig. 20. Post Therapeutic keratoplasty in Candida keratitis, with clear button and cataract.

8.2.4 Phthisis bulbi

Severe inflammation causes if left untreated, can cause great alteration and disorganization of intraocular structures and atrophia. Despite all efforts to maintain globe integrity we still can find phthisis in 2, 98% of the therapeutic keratoplasties.

9. Conclusion

Therapeutic keratoplasty is generally an emergency, high-risk procedure that challenges the surgical and medical skills of the corneal surgeon. It requires meticulous attention to detail and careful postoperative monitoring. Therapeutic keratoplasty play a definitive role in the treatment of microbial keratitis refractory to medical therapy. Advances in microsurgical technique, antimicrobial therapy new and more powerful antibiotics (fourth generation quinolones), and control of inflammation have resulted in an improved prognosis for therapeutic keratoplasty in cure and improved visual outcomes.

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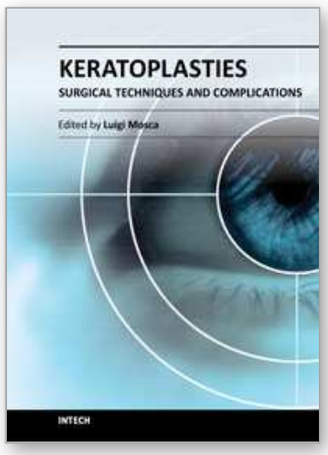
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