

NON TRADITIONAL MANAGEMENT OF FUNGAL KERATITIS

MOHAMED SAAD ,MD
PROF. OF OPHTHALMOLOGY
ASSIUT UNIVERSITY HOSPITAL



FINANCIAL DISCLOSURE:

- No financial interest.

Fungal keratitis is a sight-threatening condition that requires immediate laboratory diagnosis and prompt therapeutic intervention to prevent loss of the eye. (*Klotz, S.A.,2000&Elgazayerly 1997*)

What are the problems of fungal keratitis?

Resistance.

Lytic activity by;

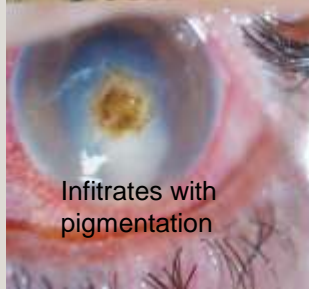
Microbial endotoxins.

PNL enzymes

Penetration.

Perforation. (*Seal and Kirkness 1995*)

CASES OF FUNGAL KERATITIS

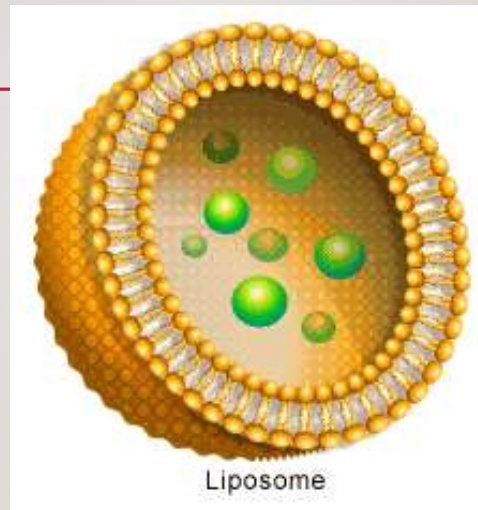


MODALITIES

- New long acting antifungal formula.
- Intrastromal injection of antifungal.
- Therpeutic PPK

LIPOSOMES LOADED WITH ANTI FUNGAL DROPS: (A NEW LONG ACTING ANTIFUNGAL FORMULA)

- Liposomes are artificial vesicles composed of concentric lipid bilayers which are separated by water compartments. *(Fre'zard, F. 1999).*
- Vesicular drug delivery systems :
 - Prolonged and controlled action at the corneal surface
 - Preventing the metabolism of the drug by enzymes present at the tear/corneal surface.
 - Biodegradable and relatively non-toxic. *(Kaur, I.P.et al,2004)*
 - Increasing the probability of ocular drug absorption.





ANIMAL TRIAL

- 40 rabbits
- Induced bil. Candida keratitis.
- 22 ulcers treated with fluconazole loaded liposomes...cure 86%
- 18 ulcers treated with fluconazole sol.....cure 50%

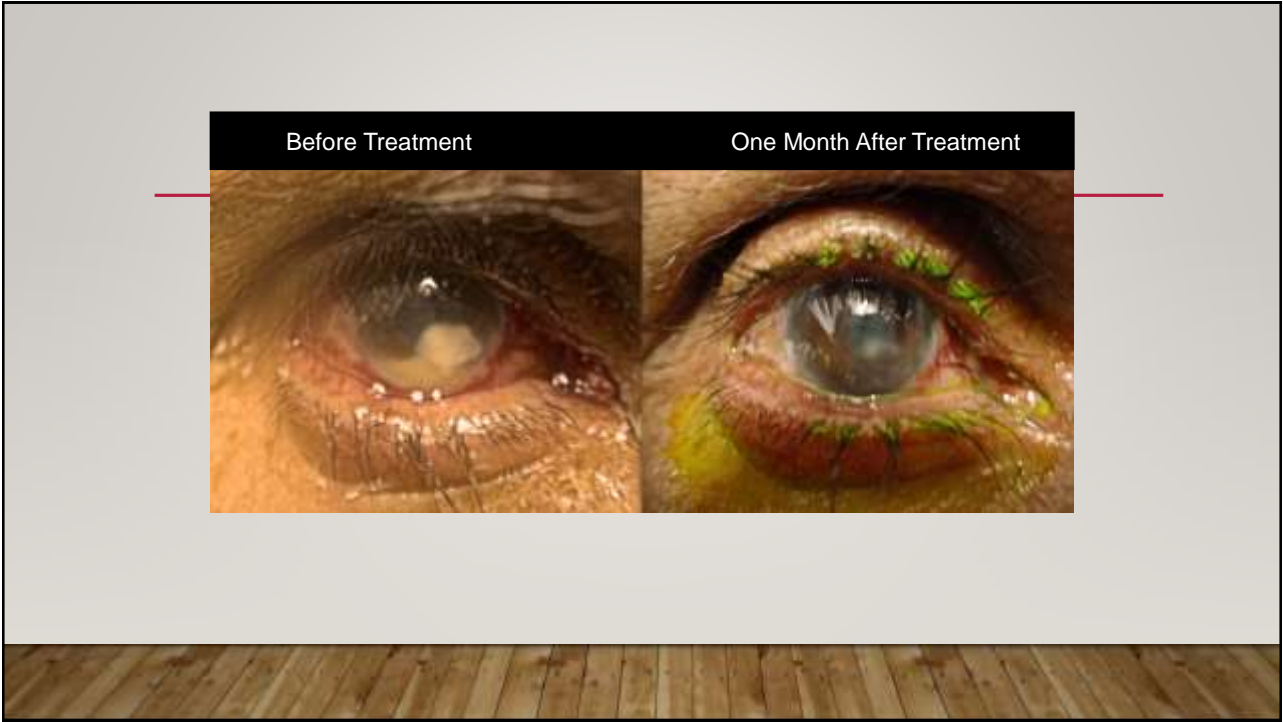


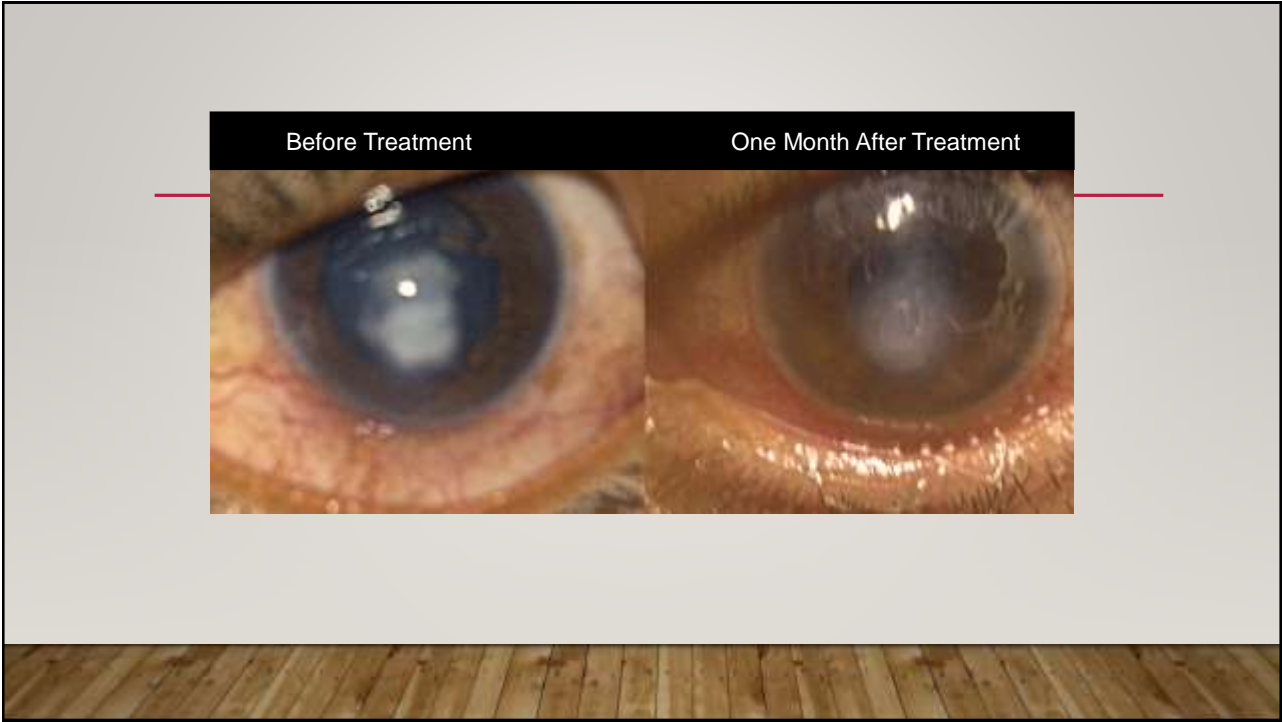
Acta Ophthalmol. 2010 Aug 14. Liposomes as an ocular delivery system of fluconazole: in-vitro studies. Habib FS, Fouad EA, Abdel-Rhman MS, Fathalla D.

HUMAN STUDY

- 11 eyes with candida keratitis were treated with fluconazole loaded liposomes.
- 8 patients had complete cure.
- 1 patient got partial improvement.
- 2 patient did not improve.

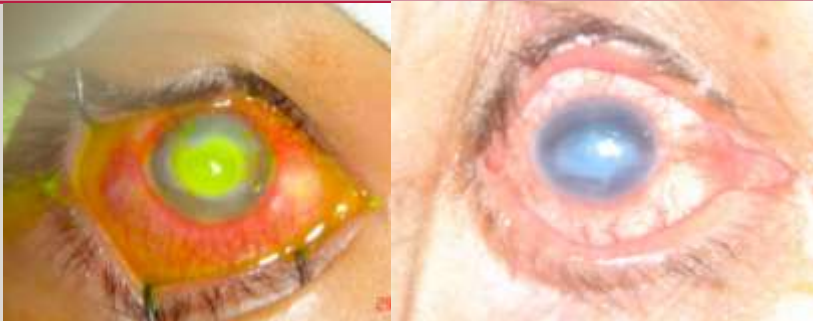
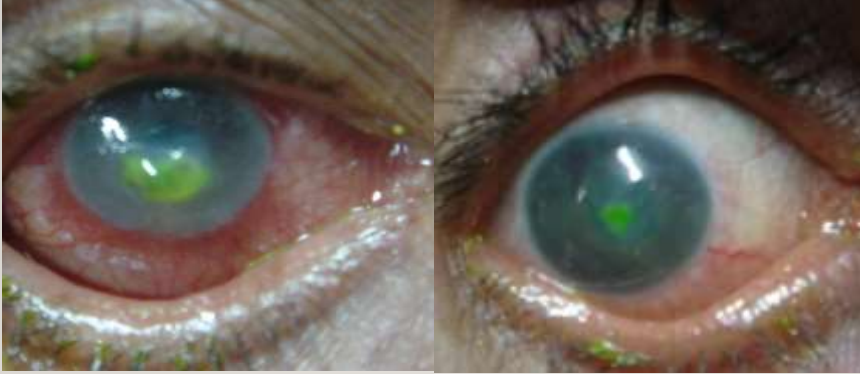
Patient	Sex	Age(years)	Duration of ulcer at presentation (days)	Response to treatment	Diameter of ulcer at presentation (mm)
1	M	65	5	improved	3.5
2	M	47	7	improved	4
3	F	44	14	partial improvement	5
4	M	56	9	improved	4.5
5	M	34	1	improved	5
6	f	54	3	no improvement	5.5
7	m	60	11	no improvement	5
8	m	67	8	improved	6
9	F	39	7	improved	6.5
10	F	50	9	improved	4
11	m	61	4	improved	6





Before Treatment

One Month After Treatment





CONCLUSION

Therapy with topical liposomal fluconazole (2 mg/ml) in treating patients with candida keratitis, carries **high success rate ,prolonged duration of action , higher corneal penetration, better eye tolerability and free of side effects.**

*A New Long-acting Liposomal Topical Antifungal
Formula: Human Clinical Study*

Mohamed S. Abdel-Rhman, MD,* Wael Soliman, MD, PhD,*
Fawzia Habib, PhD,† and Dina Fathalla, PhD†

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INTRASTROMAL INJECTION OF ANTIFUNGAL DRUGS

THE ANTIFUNGAL AGENTS :

- **Polyenes** (eg, natamycin, amphotericin B),
- **Azoles** (eg, ketoconazole, miconazole, fluconazole, itraconazole),
- Fluorinated **pyrimidines** (eg, flucytosine).
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- Amphotericin B yeasts.
 - Natamycin filamentous organisms.
 - Oral fluconazole and ketoconazole deep fungal keratitis.
 - Ketoconazole..... *Fusarium, Aspergillus, Curvularia, and Candida* species.
 - Fluconazole....deep fungal keratitis.
 - Voriconazole....Aspergillus,Fusarium.

MOST COMMON ANTIFUNGAL DRUGS IN OPHTHALMIC USE : DOSES

Drug	Amphotericin B	Fluconazole	Voriconazole
Route			
Topical	0.15%	0.2%	1%
Subconjunctival	Not prepared due to its high toxicity	2 mg/ml	1%
Intrastromal (intracorneal)	5 to 10 µg	2 mg/ml	50 µg/0.1 ml
Intracameral	5 to 10 µg/0.1 ml	Not available in literature	50 µg/0.1 ml
Intravitreal	1 to 10 µg/0.1 ml	25 µg/0.1 ml	50 µg/0.1 ml

PREPARATION OF ANTIFUNGAL:

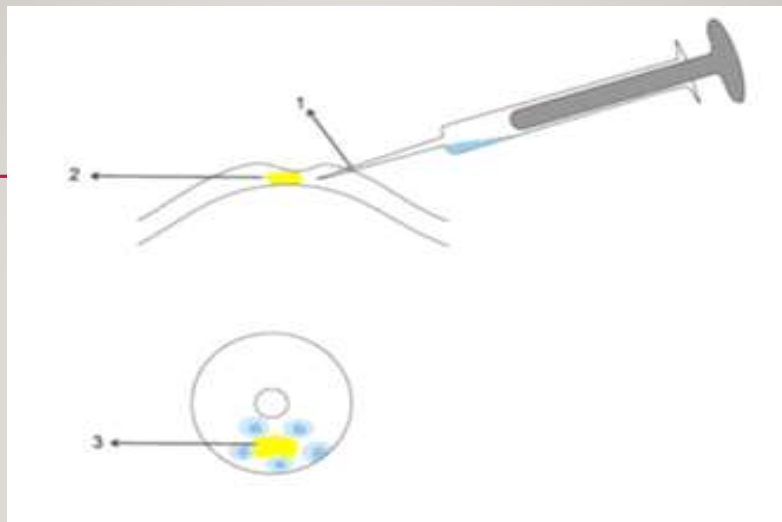
- **Topical Amphotericin B 0.15%:**
- Method: Add 10 ml distilled water to parenteral 50mg of Amphotericin B powder for injection (5 mg/ml). Draw 3 ml of this and add to 7 ml of artificial tears eye drops.
- Storage: Refrigerate in 4°C
- Shelf life: 7 days in refrigerator at 4°C and 4 days in room temperature
- **Amphotericin B 5 to 10 µg/0.1 ml for intracameral, intrastromal and intravitreal injection:**
- To reconstitute 10 µg/0.1 ml
- Method: Prepare 5 mg/ml (as mentioned above) –take 0.2ml solution and add to 0.8ml BSS. Now take 0.1 ml of this solution and add 0.9ml BSS to create 0.1mg/ml equivalent to 10µg/0.1 ml.
- Use Immediately

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- **Fluconazole 0.2% (2mg/ml) for topical, subconjunctival and intrastromal routes:**
 - This concentration is available without the need for preparation. (each 1 ml contains 2mg)
 - **Fluconazole 25 µg/0.1 ml for intravitreal injection:**
 - Method: Draw 1.25ml of 0.2% Fluconazole and add to 8.75ml BSS to make concentration of 2.5mg/10ml equivalent to 25µg/0.1 ml.
 - Storage: Refrigerate in 4°C
 - Shelf life: 7 days in refrigerator at 4°C and 4 days in room temperature
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- **Voriconazole 1% for topical and subconjunctival use:**
 - Method: Mix 20ml ringer lactate to 200 mg Voriconazole lyophilized powder.
 - Shelf life and storage: 30 days at 4°C or room temperature
 - **Voriconazole 50 µg/0.1 ml for intrastromal, intracameral and intravitreal injection:**
 - Method: From 1% solution Voriconazole, take 1 ml, add to 19 ml ringer lactate to make 0.05mg/ml (50 µg/0.1ml).

TECHNIQUE OF INTRASTROMAL INJECTION:

- The preloaded drug should be administered under **operating microscope**.
- 1. The needle (**30 gauge**) is inserted obliquely from the uninvolved clear area to just reach the abscess at mid-stromal level with the **bevel down**.
- 2. The drug is injected to produce **stromal hydration**.
- 3. **Five** divided doses are given around the abscess to form a deposit of the drug around the circumference of the lesion.



(1): DIRECTION OF 30G NEEDLE, (2): DEEP FUNGAL INTRASTROMAL ABSCESS, (3): BARRAGE OF HYDRATION AROUND THE INFILTRATE



RESULTS OF INTRASTROMAL INJECTION OF ANTIFUNGAL DRUGS

- Example of complete cure after single intrastromal injection



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- Example of complete cure after second intrastromal injection



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- **Example of incomplete cure after second intrastromal injection.**



THERAPEUTIC PPK

INDICATIONS IN MYCOTIC ULCER

Prolonged unresponse (how long?)

Progression (stromal ulceration, thinning; increase hypopyon, increase IOP and perforation (*Jones 1990*))

Advantages over medical TTT

Eradication of infection

Vision restoration

Shorter hospitalization

Disadvantages

Recurrence

Graft complications are higher than visual keratoplasty e.g. rejection ,failure, glaucoma, slipped stitch, endophthalmitis.

Criteria for success;

Early interference

Small sized graft (less than 7mm)

Complete inclusion of the pathology.

IMPORTANT SURGICAL NOTES

Excision of **whole infected tissue** + safety margin. (0.25–0.5 mm larger than the infected area of the cornea.)

Hand held trephine is superior to vaccum trephine,

Irrigation with **antimicrobial**. (0.2% fluconazole)

Removal of hypopyon/membranes.

Viscoelastics is a must. (**Bleeding is controlled** by the use of Healon and cautery of vessels).

Graft **diameter**.(8mm)

Trephine size in perforation.

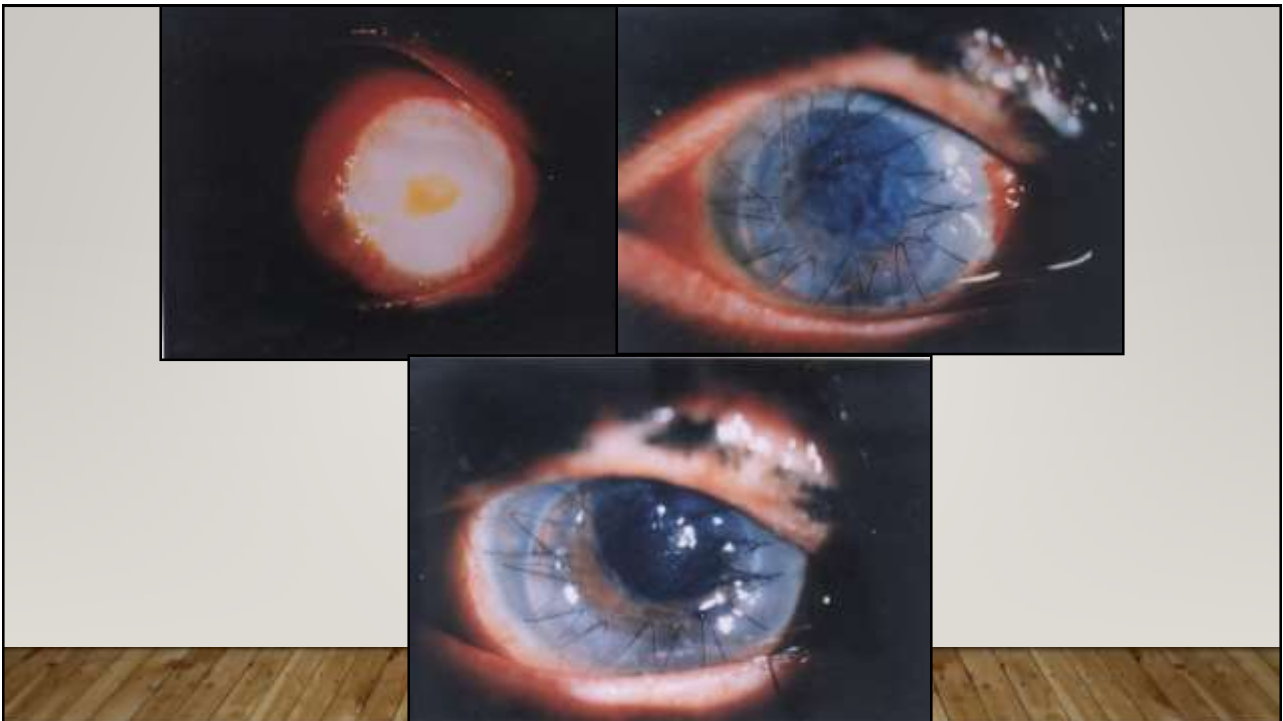
Peripheral iridectomy.(Killingsworth, 1993)

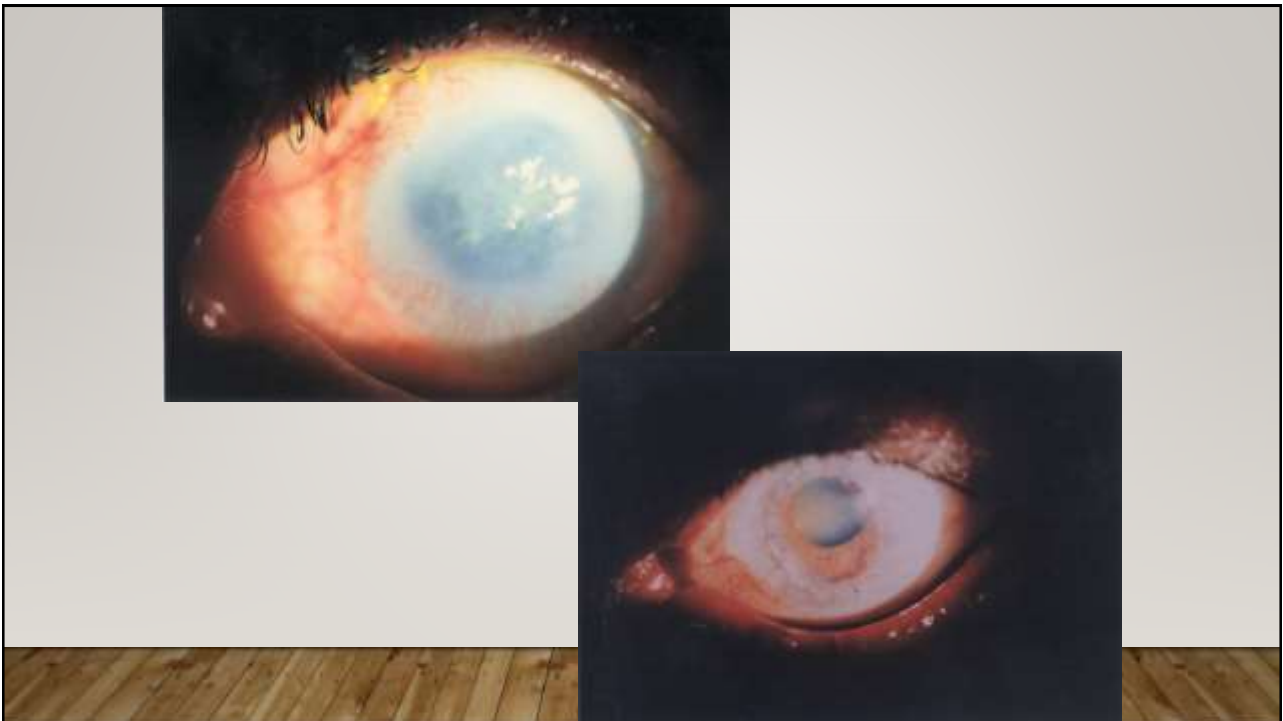
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- Try to keep the graft **as small as possible**, because it's likely that you'll need a secondary optical graft later, and you don't want that area to become vascularized and not allow the secondary graft,"
 - Leave the patient **phakic**, even if he has the beginnings of a cataract, in order to leave a barrier to further fungal penetration or endophthalmitis. .
 - The excised cornea is sent to **lab**.

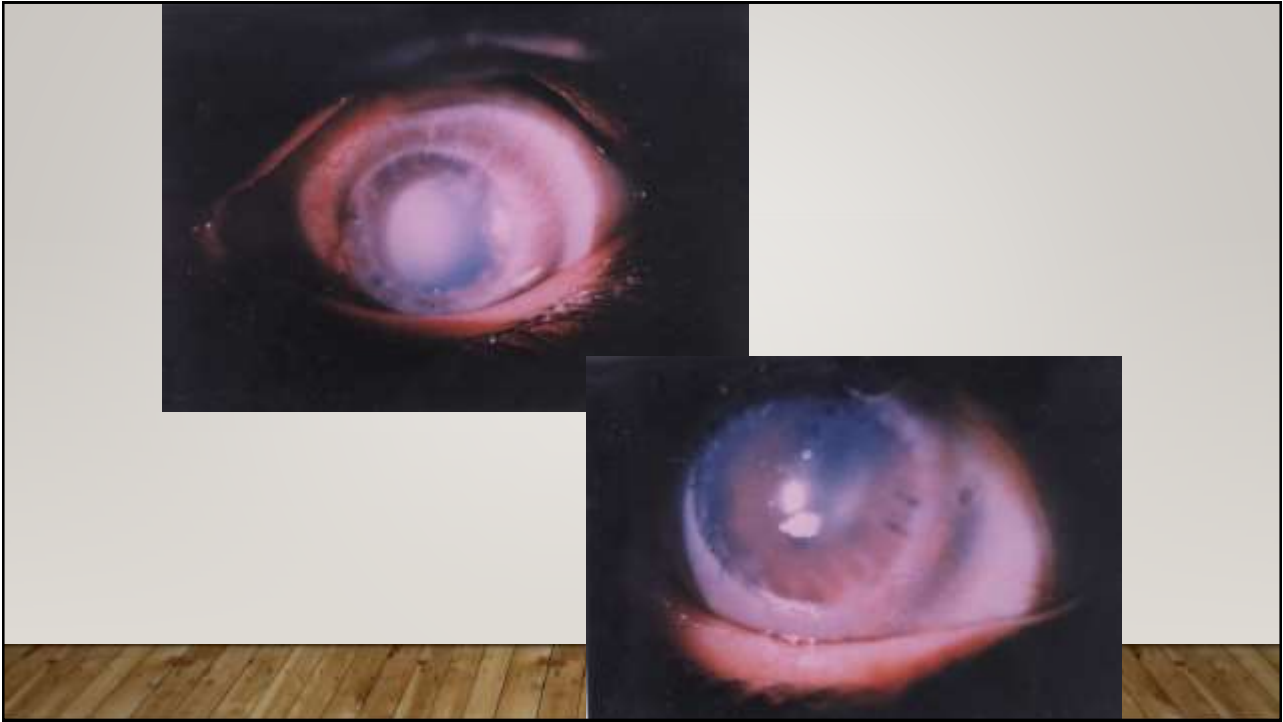
POSTOPERATIVE MANAGEMENT

- Recurrent fungal infection can be particularly difficult to treat.
- Following PKP both systemic and topical **antifungal** agents must be used.
- **Corticosteroids** were **not** used unless significant inflammation was present.(not during first 3 days)
- If by 2 weeks after PKP recurrent fungal infection was not seen systemic antifungal agents were tapered in the following 2 weeks.
- Manage **intraocular pressure** with **medications** in the postop period because fungi have been known to destroy trabecular meshwork tissue. or even require a secondary glaucoma **surgery** postop.”

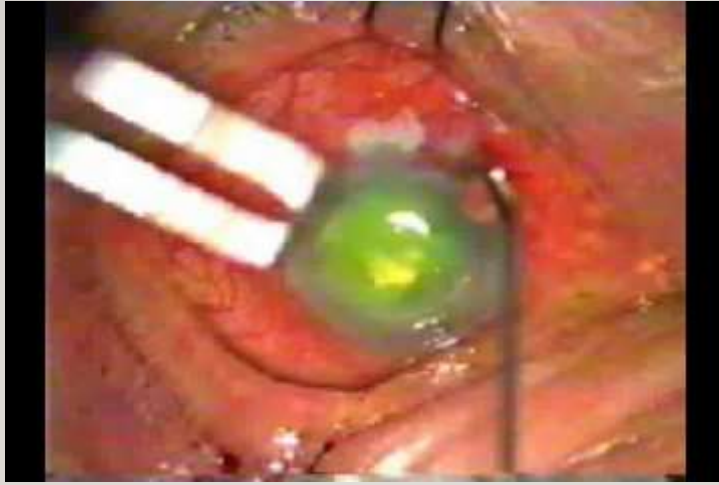














TAKE HOME MESSAGE

- Fungal keratitis is sight threatening condition.
- Decision making in proper time is essential to save infected eyes.
- Surgical intervention with special precautions may be the only choice to save these eyes.

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THANK YOU