



Resistant Keratitis

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Acknowledgement

Prof. Harminder S Dua

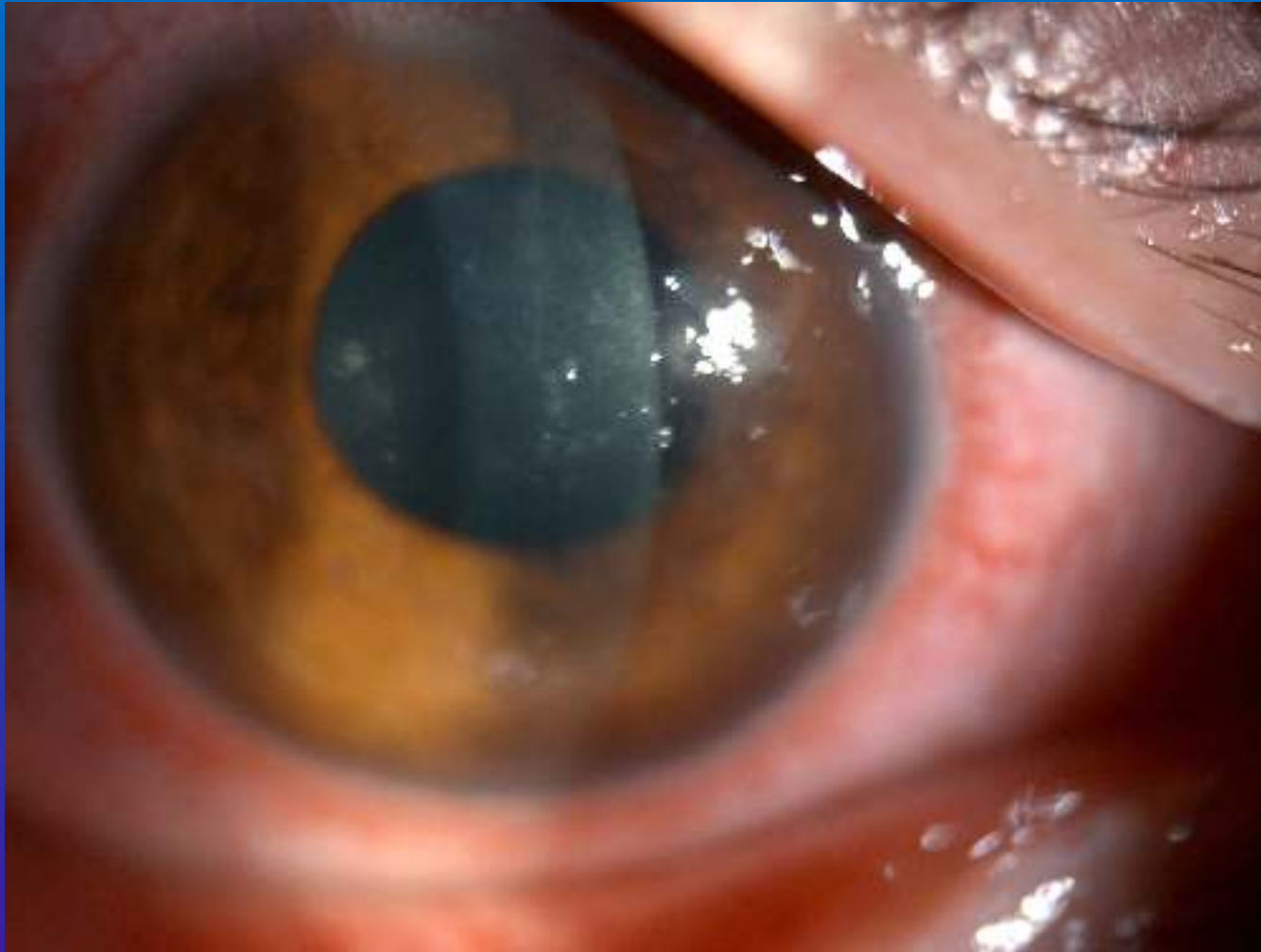


What makes Keratitis Resistant?



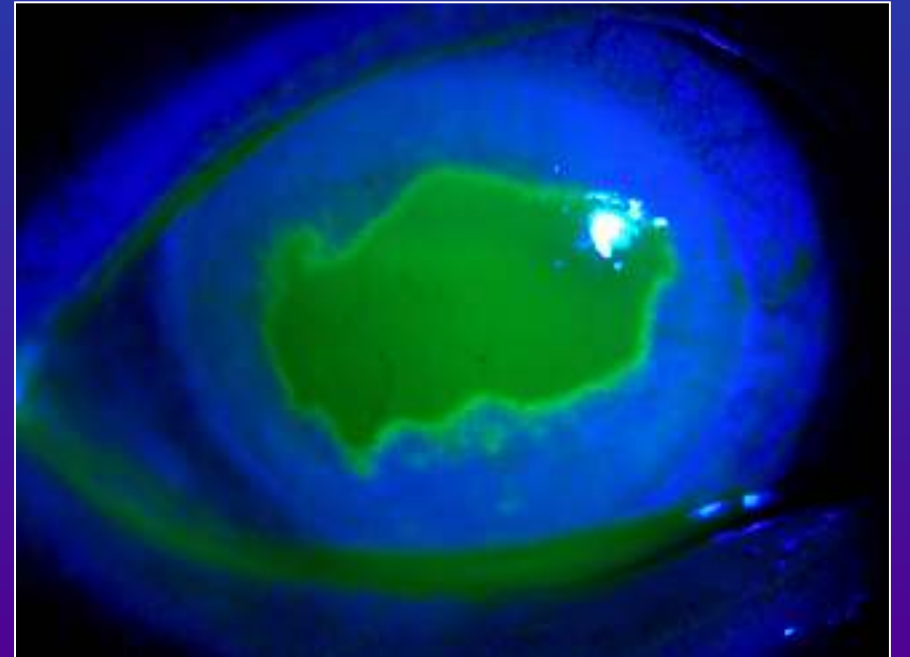
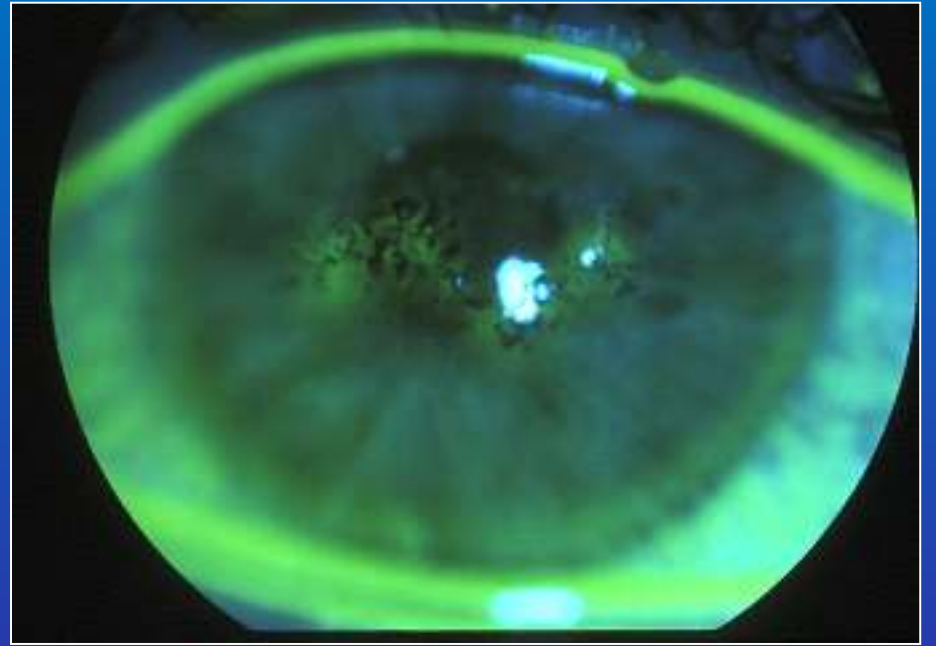
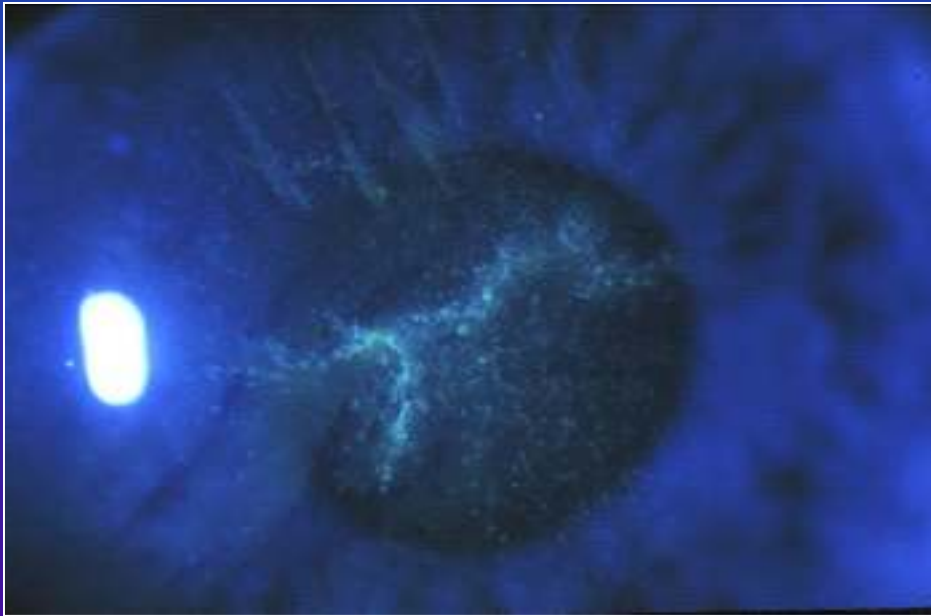
- Challenges in diagnosis and mixed infections
- Problem of resistant strains
- Problem of surgical planes
- Promising but not highly specific therapeutic modalities

Acanthamoeba Keratitis



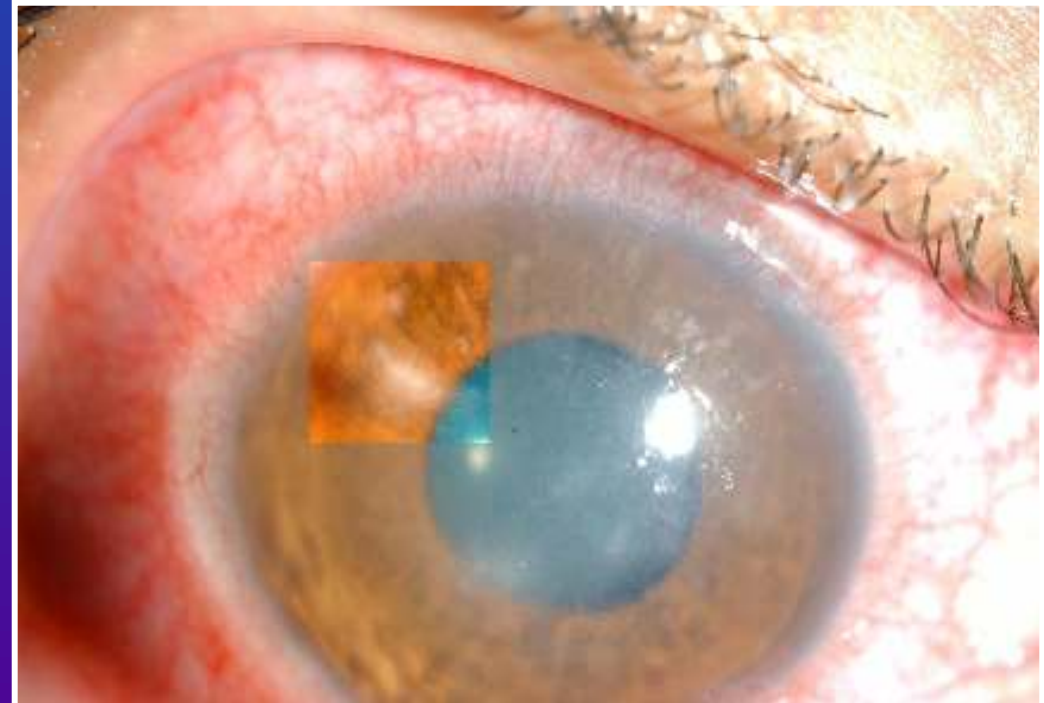
Epitheliopathy, epithelial and subepithelial infiltrate,
pseudodentrite (within first month)

Early stages can mimic viral
Keratitis and can be associated
with concomitant infection



□ Perineuritis
(Pathognomonic)

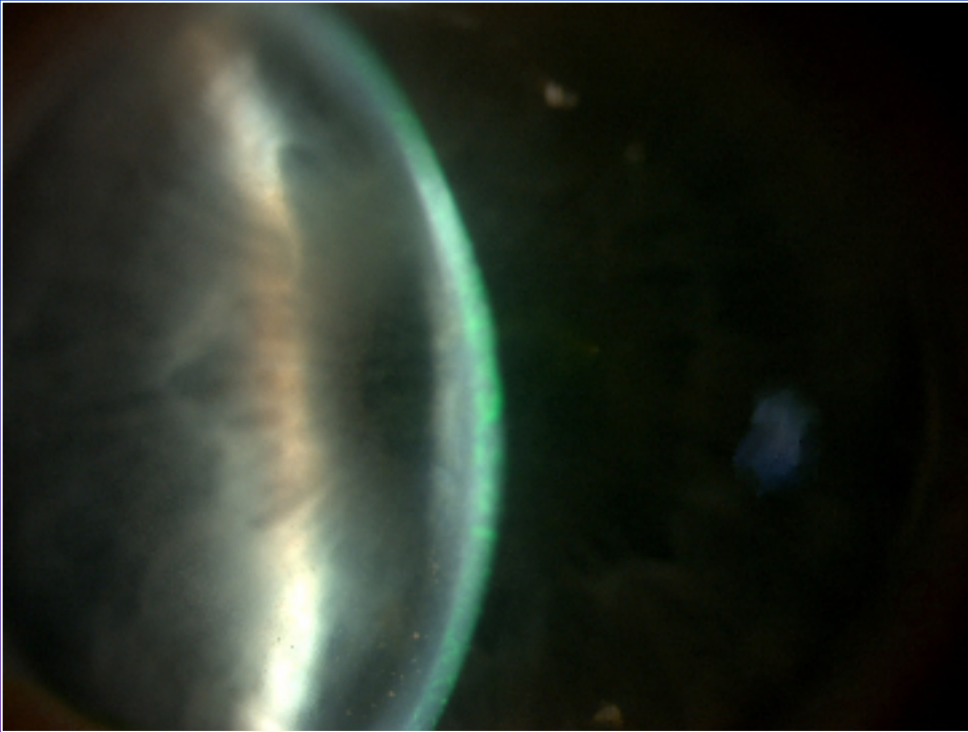
□ 3-4 weeks stage



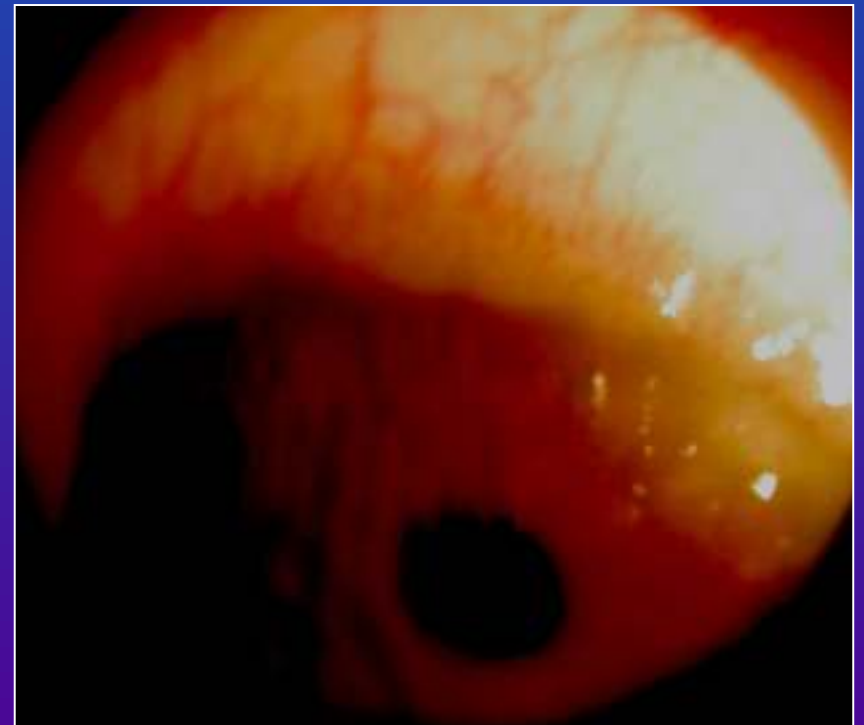
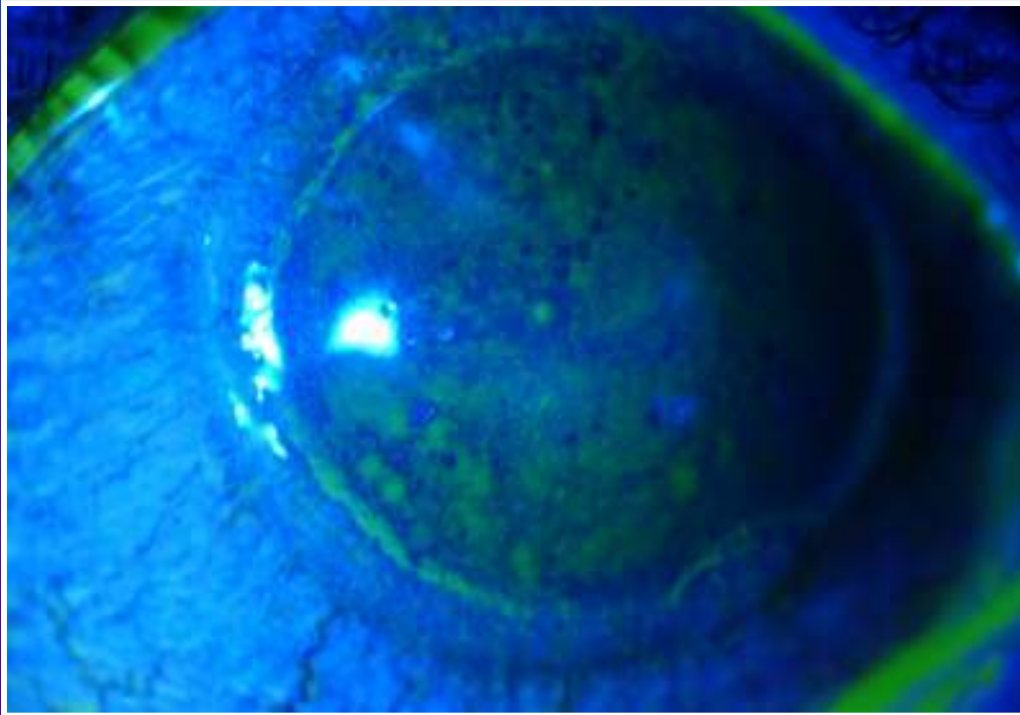
Perineuritis : pathognomonic ”
60% of cases”



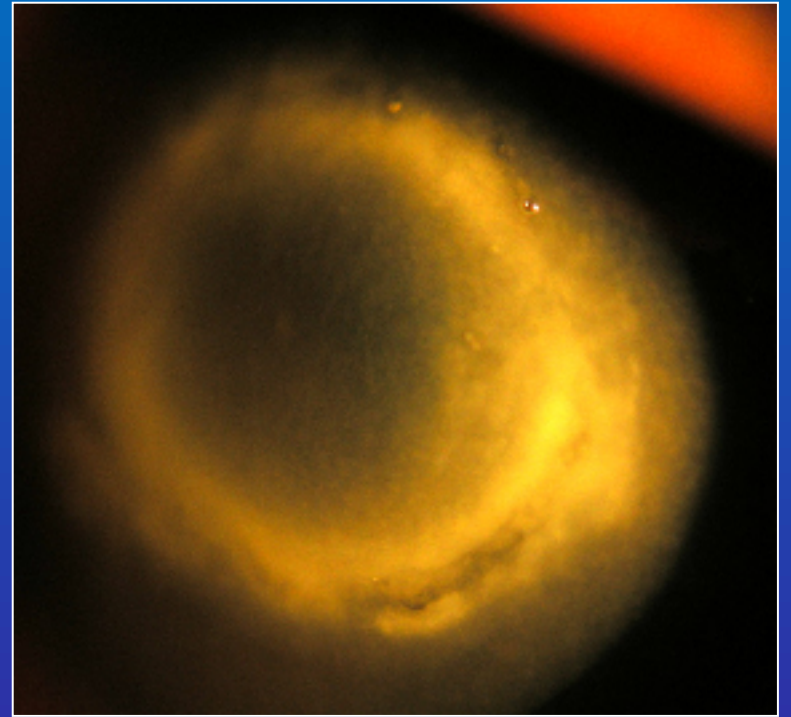
Anterior Uveitis (At presentation or later on)

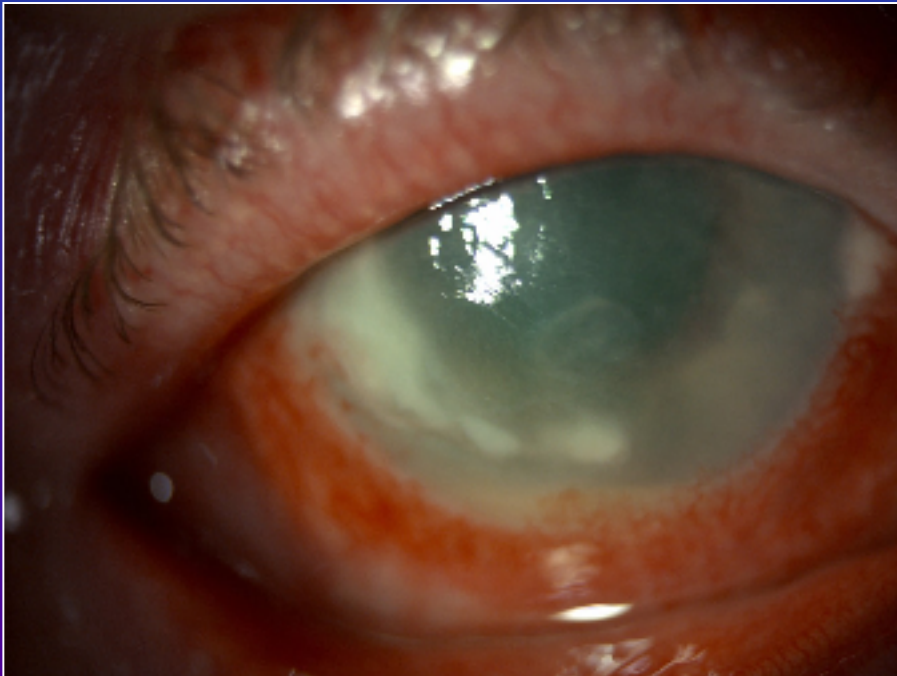
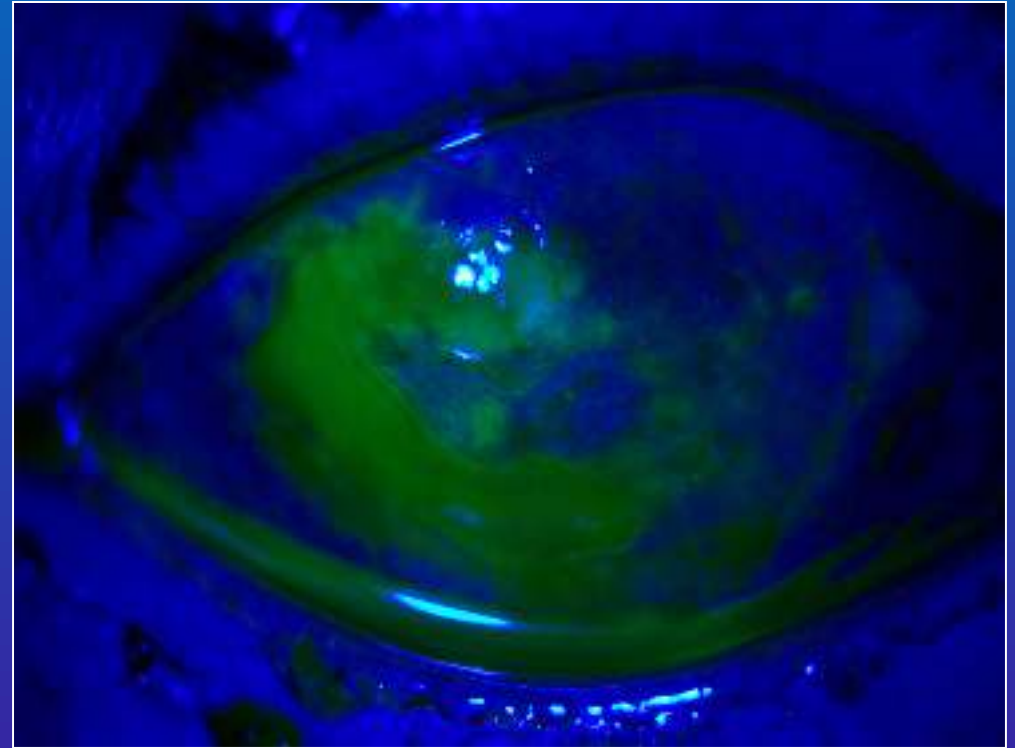


Limbus: Limbitis in *Acanthamoeba* and HSK



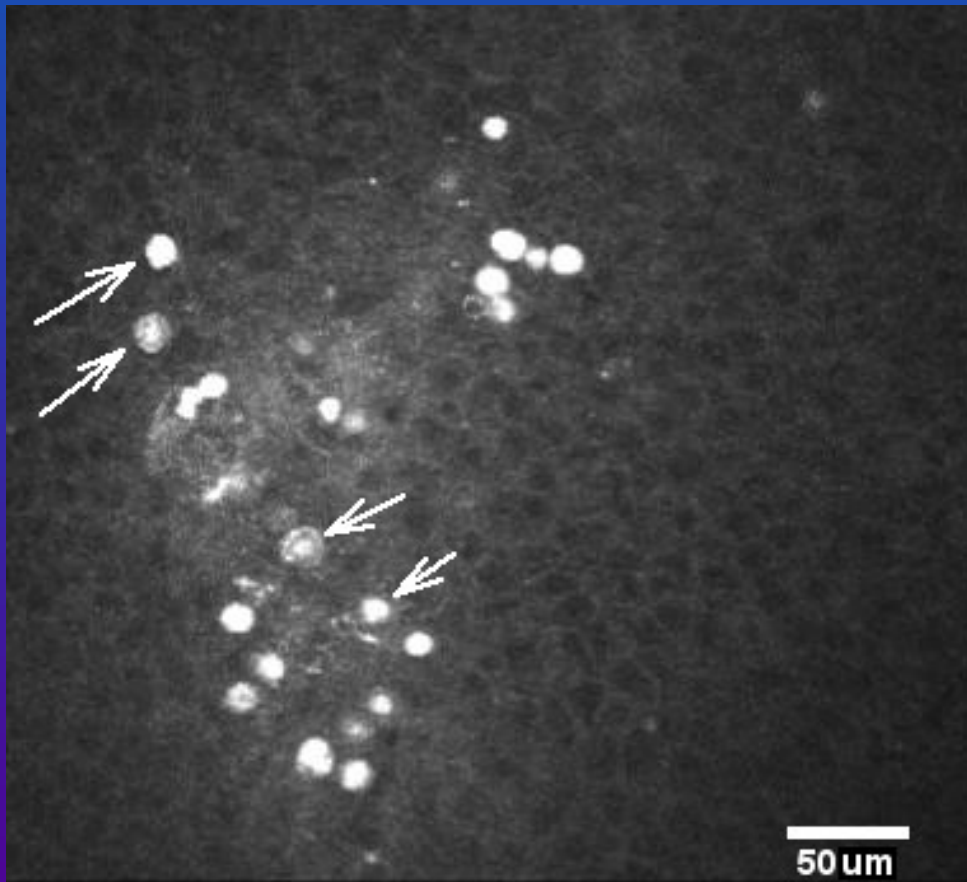
- Ring infiltrate “>1 month”
- Single or double ring abscess
- Ulceration
- Scleritis
- Cataract, Glaucoma
- Iris atrophy





Multifocality and
prolonged infection can
mimic fungal Keratitis

Confocal images: Early Diagnosis

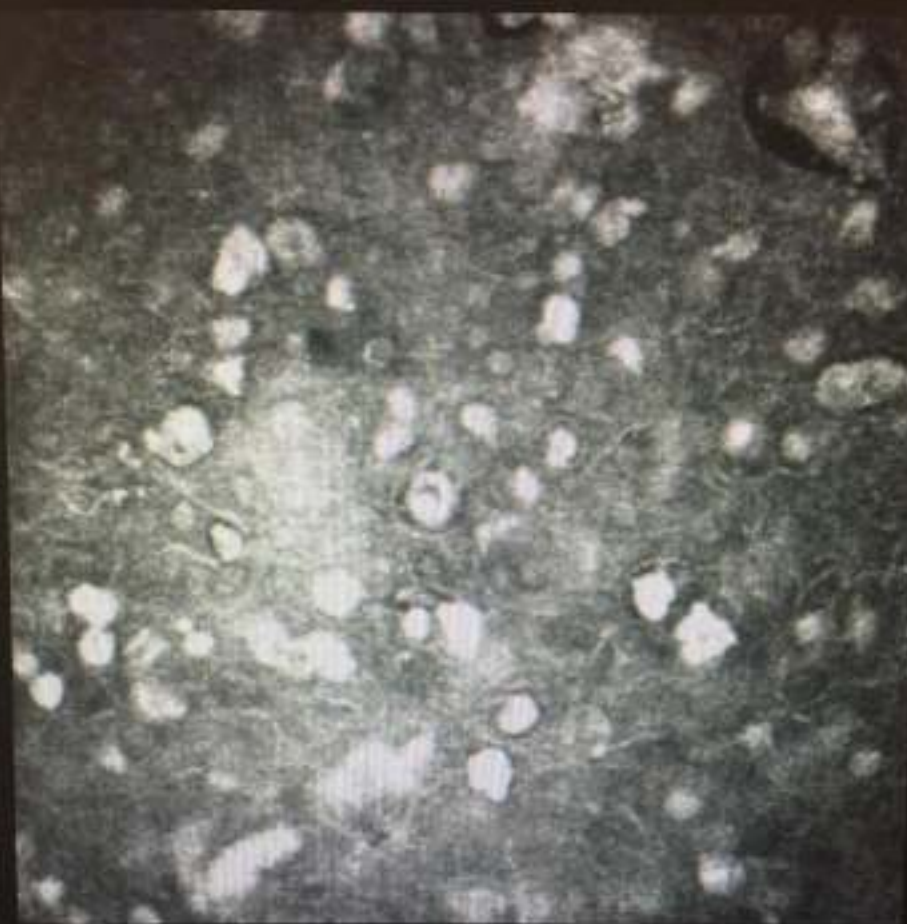


Acanthamoeba

Bright Spots

Double walled cysts

Signet ring cysts

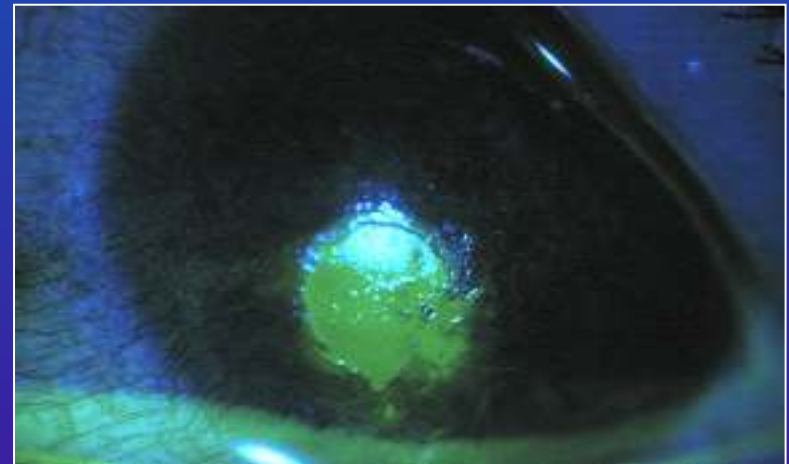
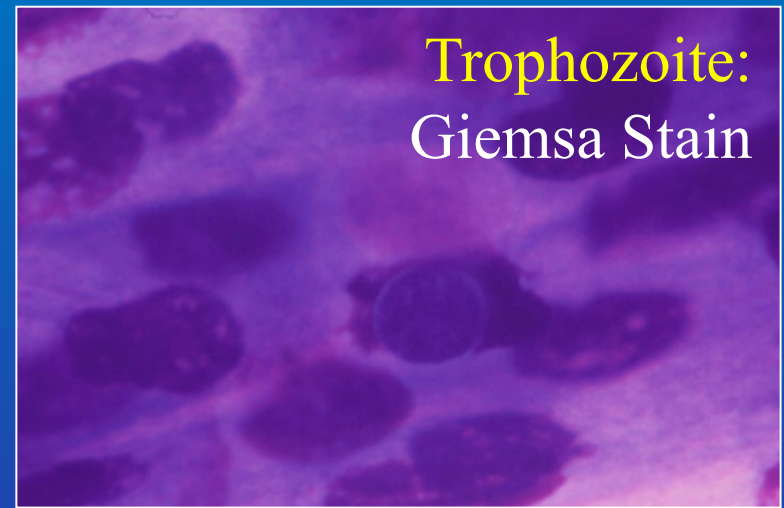
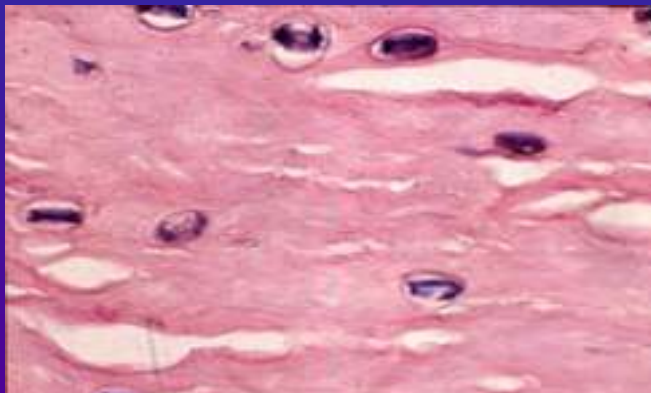


Cornea Section [29], 17/11/2008, OD

1 / 1: — μm

HEIDELBERG
ENGINEERING

- Gram and Giemsa stain
- Culture on Non-Nutrients e coli enriched agar
- PCR
- Corneal biopsy



EPITHELIAL & STROMAL AK

Medical Treatment – Cationic antiseptic agents

- PHMB (Polyhexamethelyne biguanide) 0.02%
- Chlorhexidine 0.02%
 - Have the best anti amoebicidal and cysticidal activity
 - Disrupt cell membranes
 - Minimal cysticidal concentration (MCC) - 2µg/ml
 - Low toxicity, can be used at 100 times MCC (0.02%)

EPITHELIAL & STROMAL AK

Medical Treatment – Aromatic diamidines

- Propamidine isethionate, Pentamidine isethionate, hexamidine diisethionate, dibromopropamidine, diminazene aceturate
 - Inhibitors of S-adenosylmethionine decarboxylase in trophozoites and cysts
 - Interact with nucleic acids
 - Inhibit cytoplasmic enzymes (in neutrophils and possible in acanthamoeba)
 - Well tolerated but have epithelial toxicity

EPITHELIAL & STROMAL AK

Medical Treatment – Imidazoles

- Miconazole (1%) and Clotrimazole (1%)
 - Amoebistatic rather than amoebicidal
 - Miconazole is quite toxic
 - Ketaconazole and Itraconazole – systemic administration

EPITHELIAL & STROMAL AK

Medical Treatment

- Additive effect between chlorhexidine & propamidine; PHMB & neomycin and neomycin & diamines
- Synergistic effect between chlorhexidine and PHMB

Clinical Trial > Ophthalmology. 2024 Mar;131(3):277-287. doi: 10.1016/j.opththa.2023.09.031.

Epub 2023 Oct 5.

The Orphan Drug for Acanthamoeba Keratitis (ODAK) Trial: PHMB 0.08% (Polihexanide) and Placebo versus PHMB 0.02% and Propamidine 0.1

John K G Dart ¹, Vincenzo Papa ², Paolo Rama ³, Karl Anders Knutsson ³, Saj Ahmad ¹, Scott Hau ¹, Sara Sanchez ⁴, Antonella Franch ⁵, Federica Birattari ⁵, Pia Leon ⁵, Adriano Fasolo ⁶, Ewa Mrukwa Kominek ⁷, Katarzyna Jadczyk-Sorek ⁷, Fiona Carley ⁸, Parwez Hossain ⁹, Darwin C Minassian ¹⁰

SCLERITIS AND UVEITIS

- **Medical Treatment as for Epithelial and Stromal AK and:**
 - **Corticosteroids**
 - **Cyclosporin**
 - **Tacrolimus**

MEDICAL TREATMENT

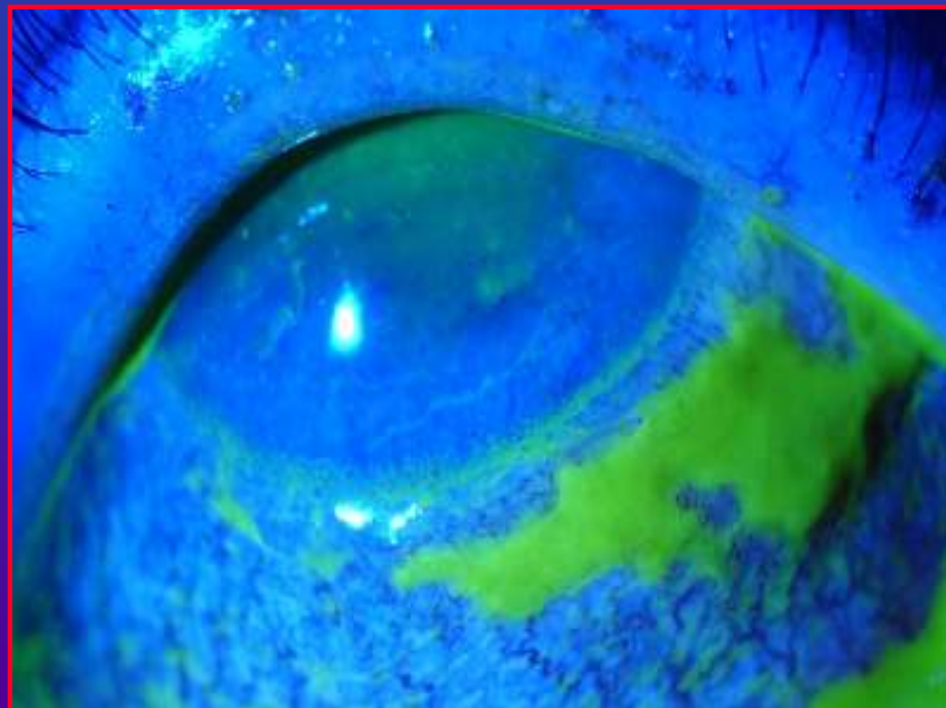
An Approach continued:

- Continue until clinical improvement – reduce frequency as necessary – QID for 1 – 2 months.
- Non-steroidal anti inflammatory drugs for pain.
- Steroids only if definite clinical improvement
- Stop steroids before stopping other drugs
- Total duration of treatment – 2 to 4 months

MEDICAL TREATMENT

An Approach continued:

- Clinically AK non responsive to PHMB can respond to chlorhexidine and vice versa
- Treat raised intraocular pressure with oral acetazolamide in early stages and topical agents in later stages when anti acanthamoeba drugs have been reduced



Drug Toxicity

Differential
congestion and
staining

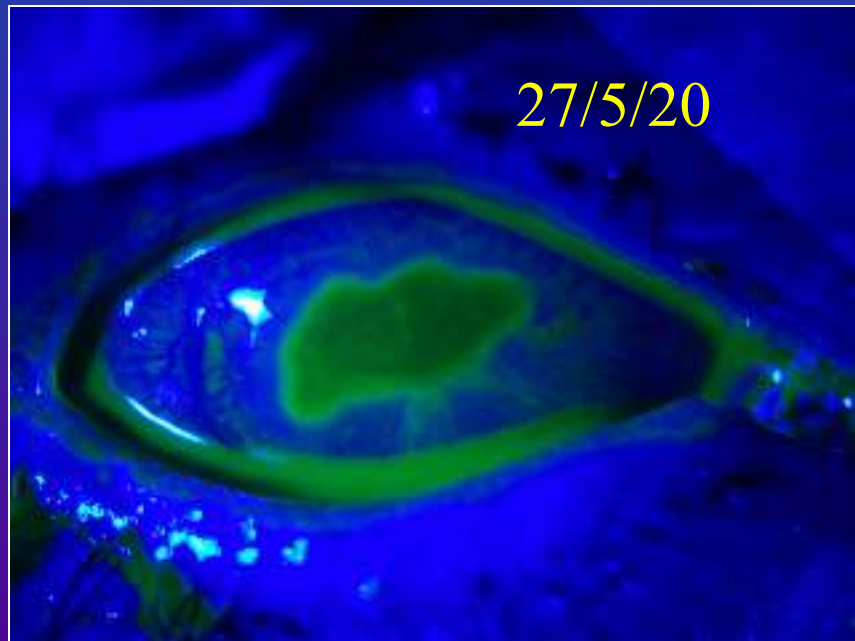
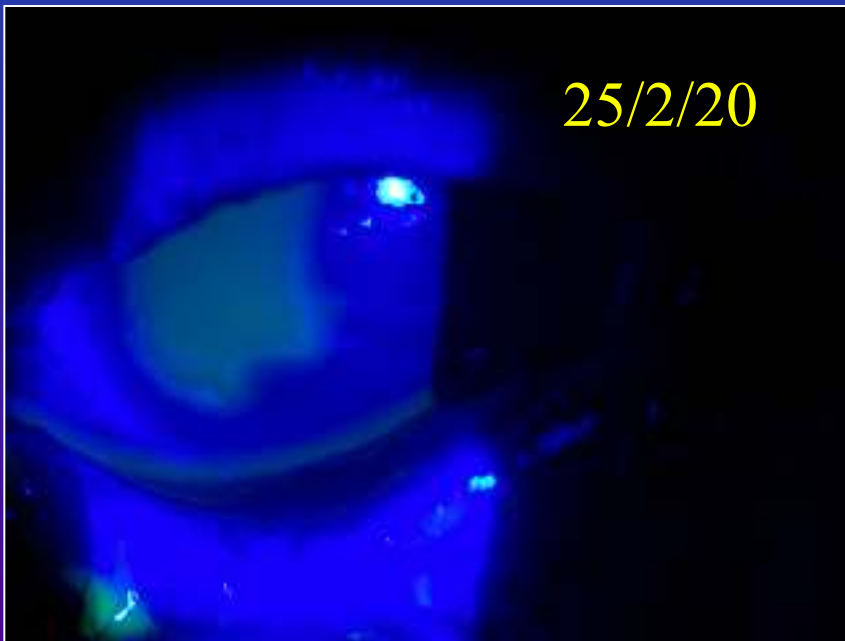
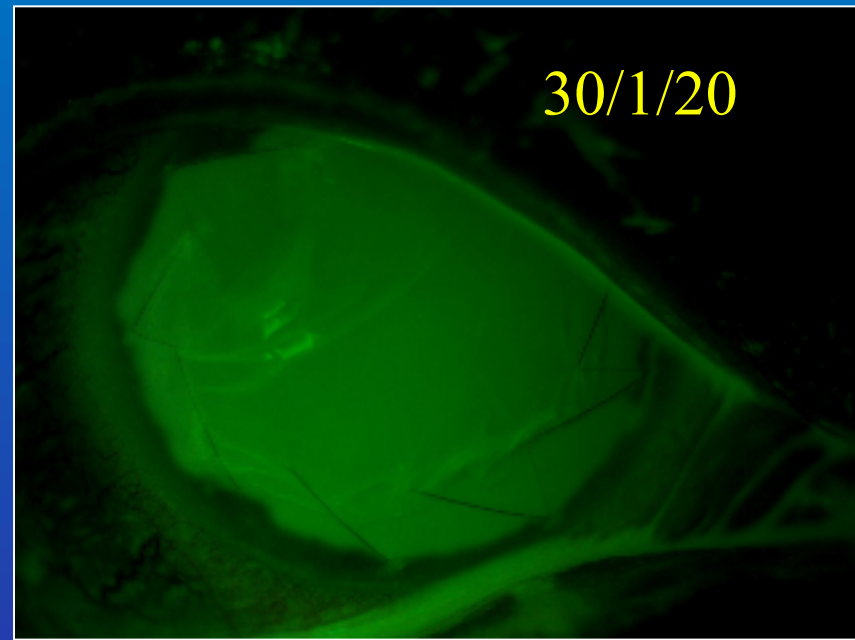
Dua HS. Br J
Ophthalmol. 2012

SURGICAL TREATMENT

- **Epithelial debridement**
- **Penetrating and Lamellar keratoplasty**
 - **To be avoided in acute cases**
 - **Best when done after achieving medical cure**
 - **Occlude vessels with Fine needle diathermy**
- **Collagen cross-linking?**

*A Journey of one of my
most challenging cases*





4/8/20
Tarsorrhaphy



4/8/20: healed
ulcer





Fungal Keratitis

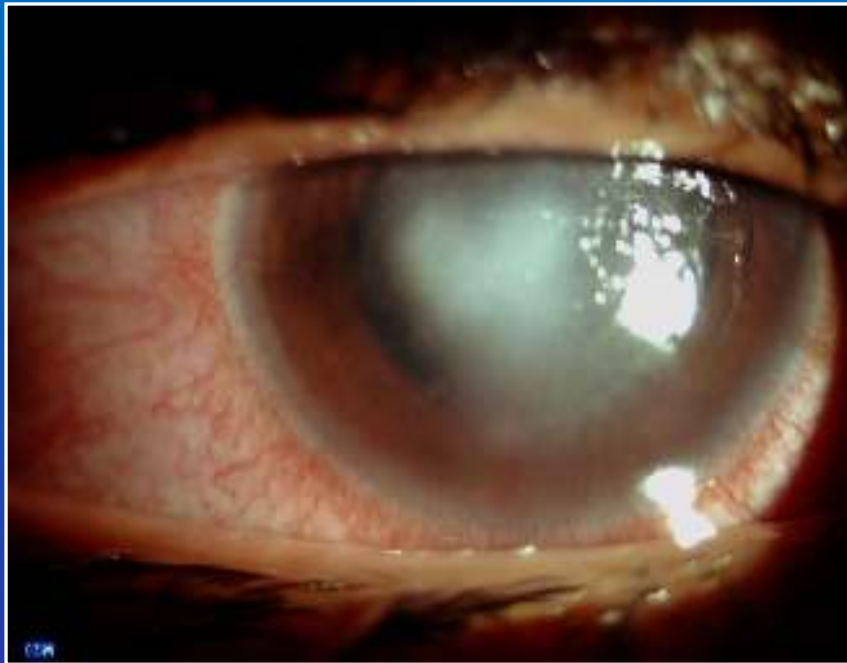
50% of culture positive IK in developing countries

History

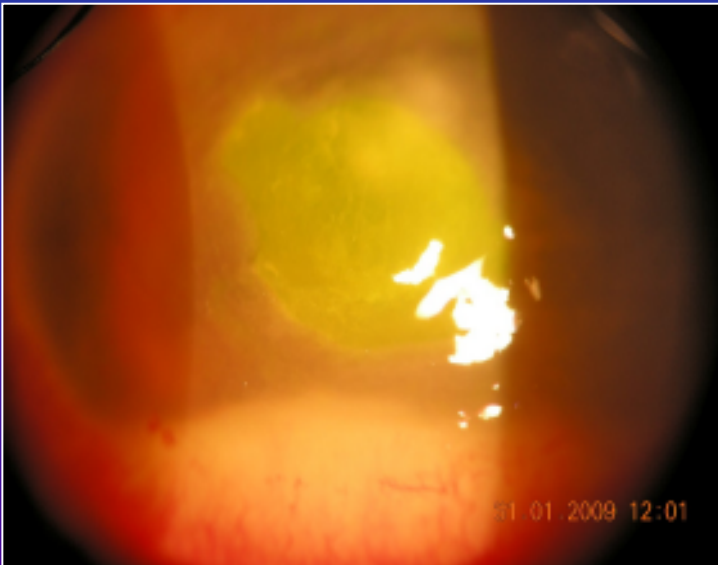
- Vegetable trauma
- CL
- Immunocompromised
- Hot climates
- Slowly lingering infection
- No response antibiotics or no further improvement

Personal risk factors !





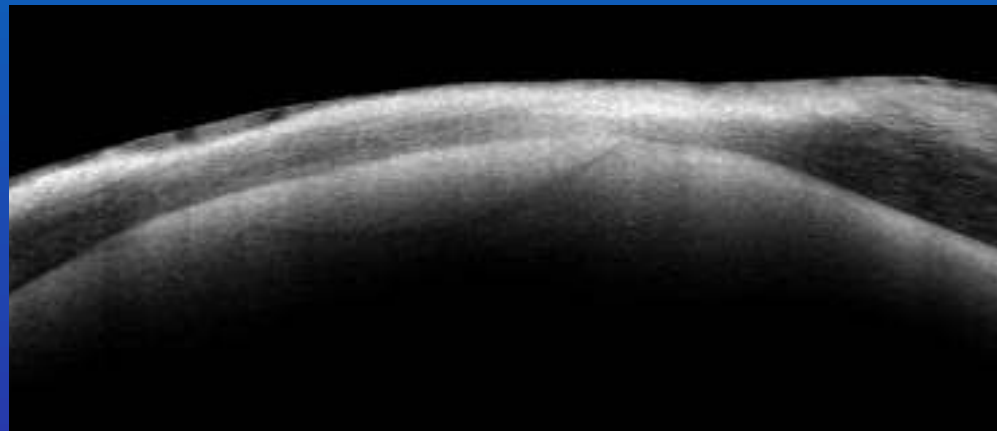
Feathery
edge



□ Inverted
Hypopyon



Endothelial plaque



Satellite lesions



Leathery shield

Scleral or intraocular spread



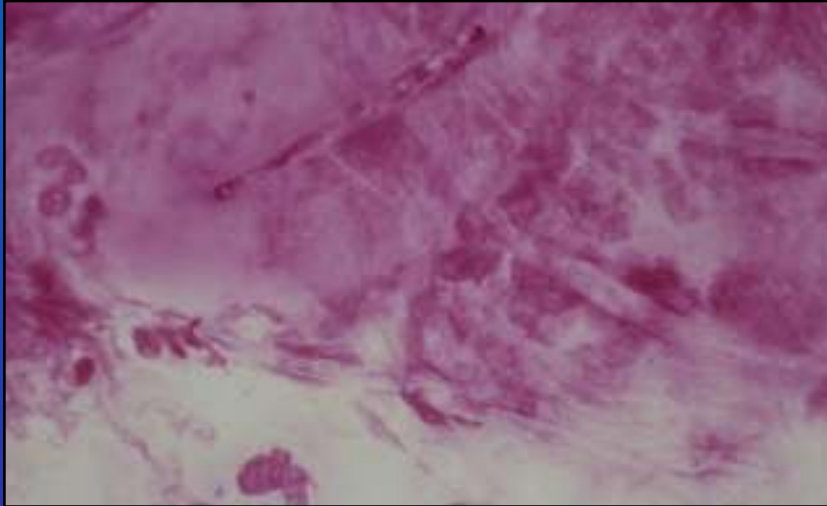
SYSTEMATIC EXAMINATION

□ IOP

□ Corneal sensation

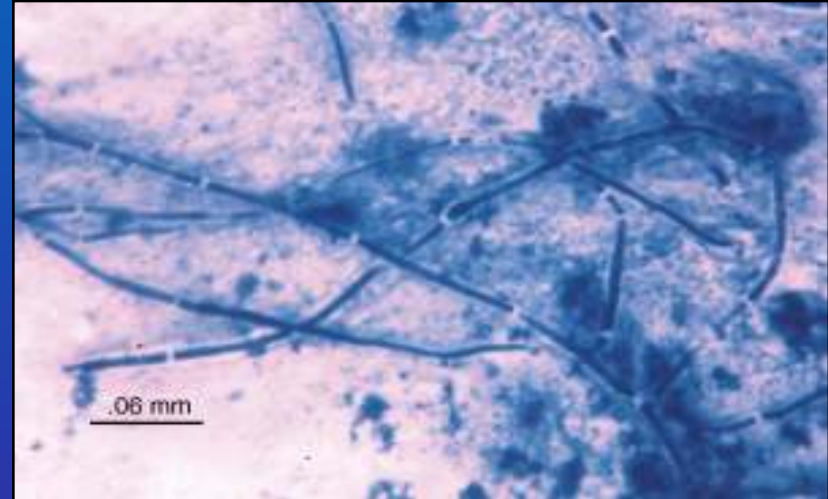
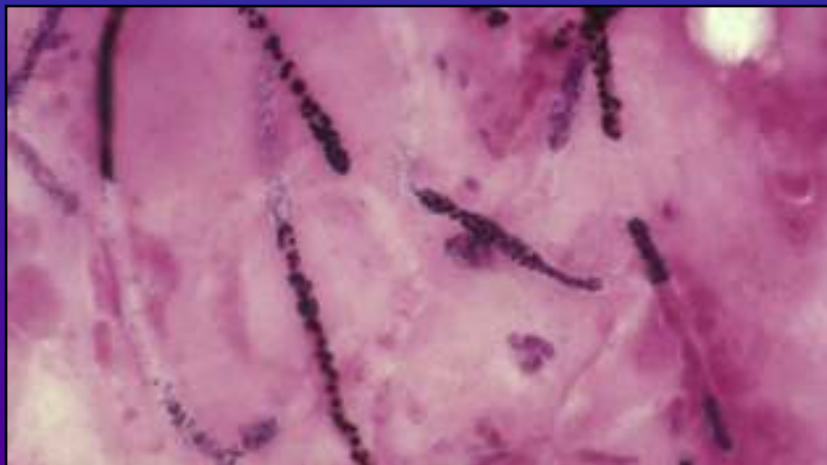


Corneal Smear



Gram (hyphae in negative relief)

Silver



Lactophenol cotton blue

Calcoflor white



Culture

- Blood agar, enrichment media (will grow)
- Sabaraud dextrose agar



Fungi 2.7 days
Bacteria 1.4 days



Biopsy

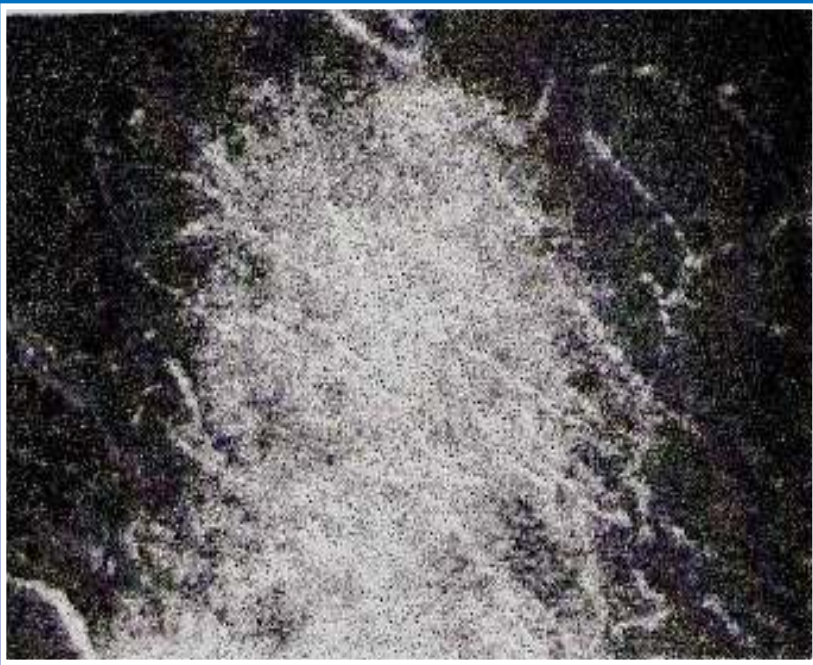
*Can be by biopsy or excisional keratoplasty
- anterior or posterior -*



PAS or Grocott stain

Will tend to miss pre-
Descemet invasion

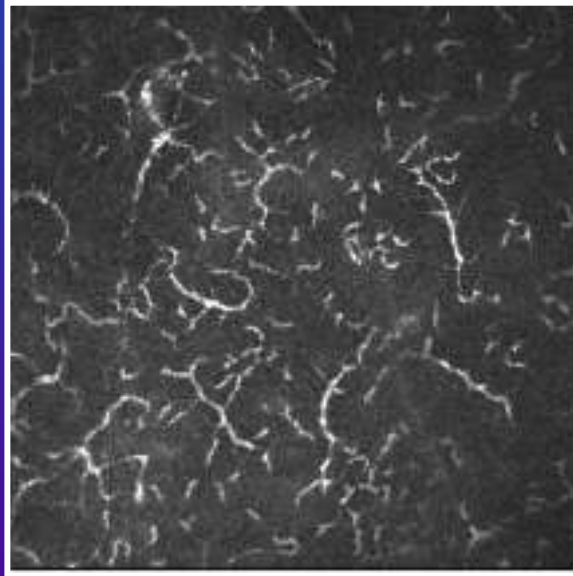
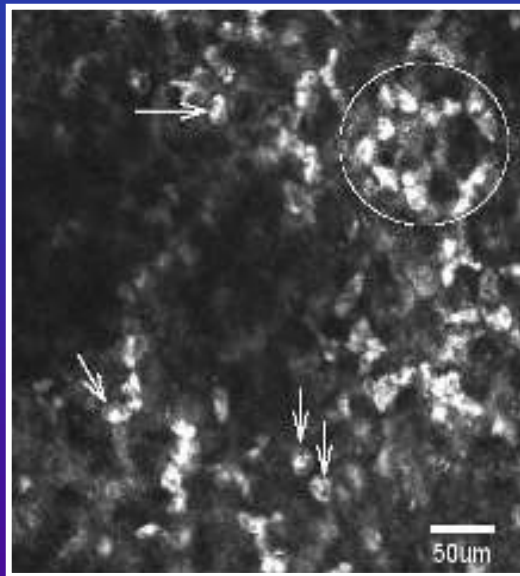




Fungal Keratitis

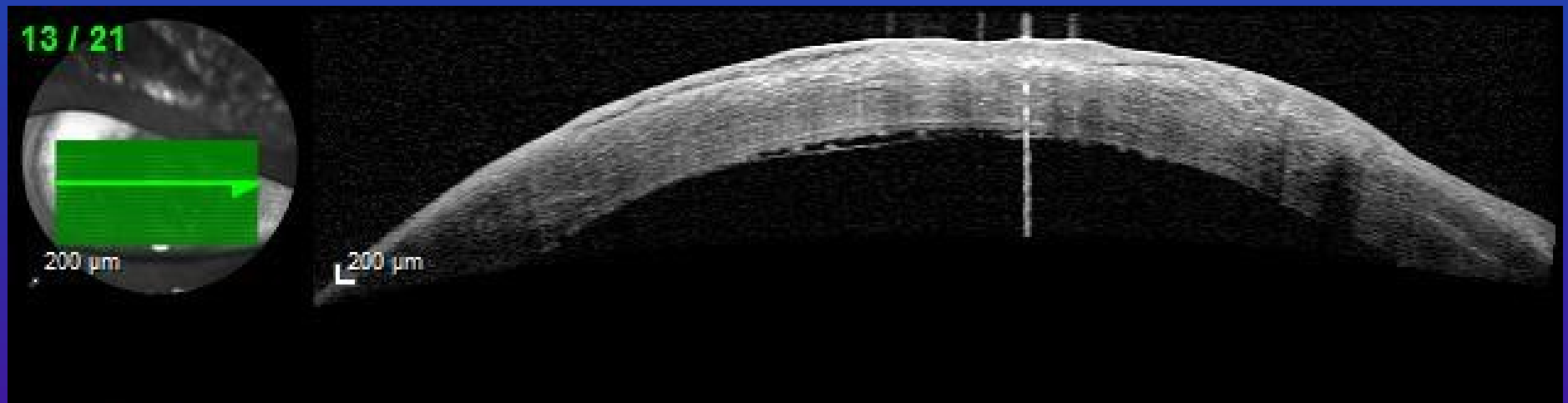
Aspergillus:

- Intra-Stromal bright interlocking filaments
- Dendritic cells





Not Fungal!!



Fungal Keratitis: Topical Treatment

TOPICAL ANTIFUNGAL DROPS

Polyenes

Amphotericin B (candida)
Natamycin 5% (Superficial keratitis,
(allergic reactions))

Azoles

Voriconazole 1% (candida,
aspergillus,
Refractive surgery)

Itraconazole (candida, aspergillus,
Refractive surgery)

Cotrimazole (candida, aspergillus,
Superficial
keratitis)

Miconazole (candida, aspergillus,)

Econazole (fusarium)

Ketoconazole, Fluconazole (candida)

Echinocandins”
Caspofungin 0.5-1%
(minimal experience)
Mainly in
refractory candida

What else can you do?

Systemic Treatment

The Mycotic Ulcer Treatment Trial II (MUTT II) :

Adjuvant oral voriconazole (400 mg BD for 1/7 then 200 mg BD for 20 D)

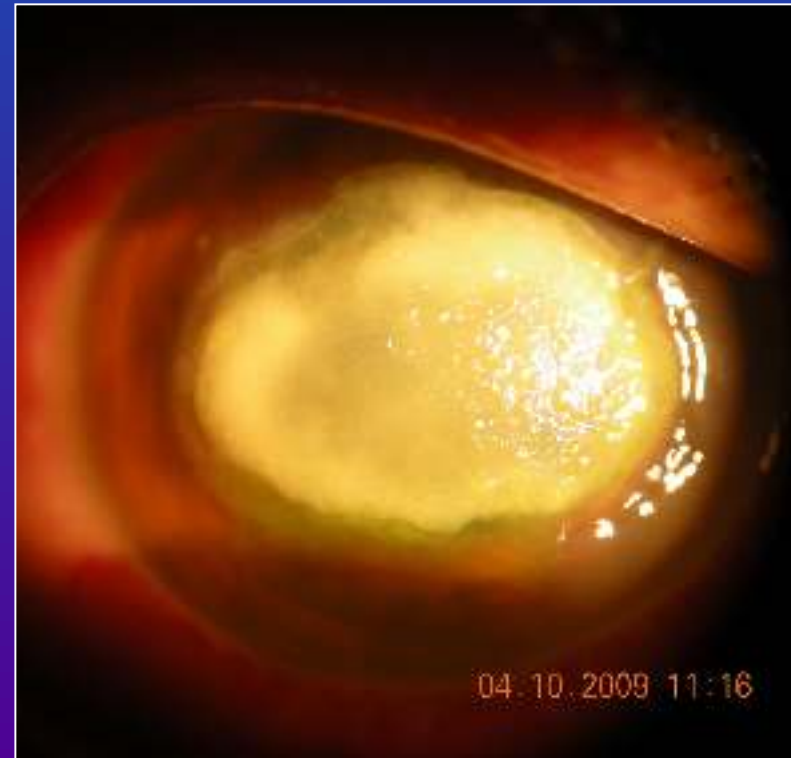
- No difference in rate of healing , BCVA, rate of perforation and/or need for TPK
- Significant adverse events with oral voriconazole

What else can you do?

Systemic Treatment

Debridement

...Better for
superficial keratitis...



What else can you do?

Systemic Treatment

Debridement

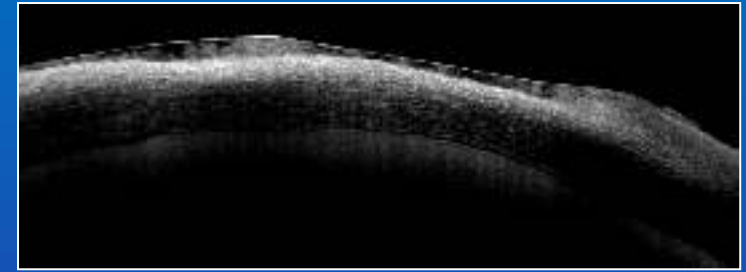
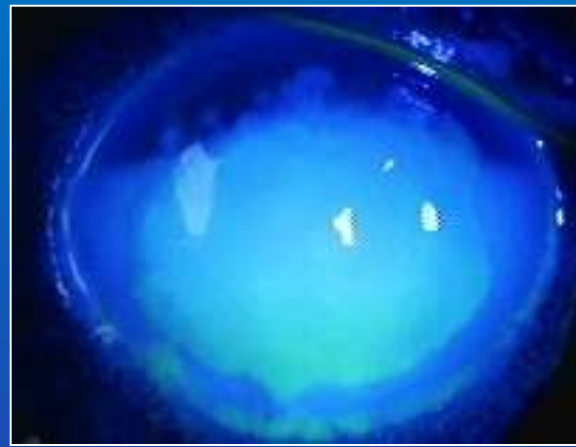
PACK-CXL

- Adjuvant PACK-CXL did NOT confer any additional benefit

Prajna et.al.

- In deep keratomycosis CXL was associated with increased risk of corneal perforation...

Vajpayee et al., Uddaraju et al.



3 days later



2 week post CXL



What else can you do?

Systemic Treatment

Debridement

PACK-CXL

Combination of topical
antifungal therapy

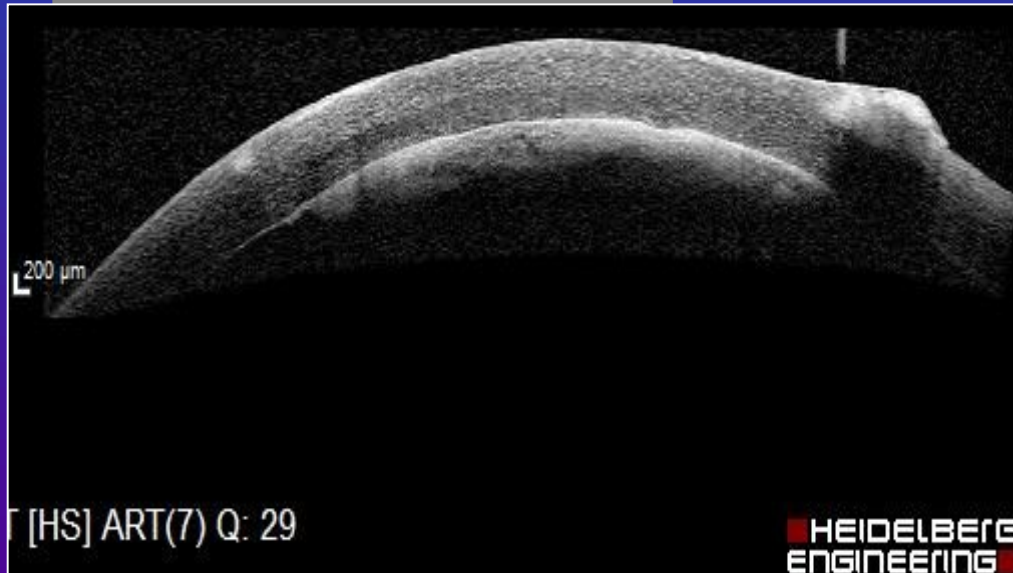
Intracorneal/Intracameral Injections

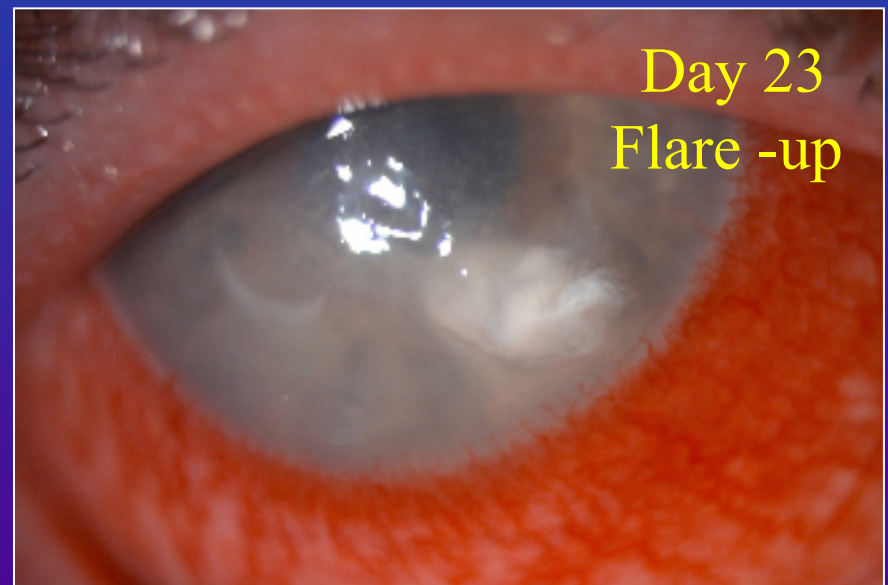
50 ug /0.1ml

Day1:Admision



Day 4

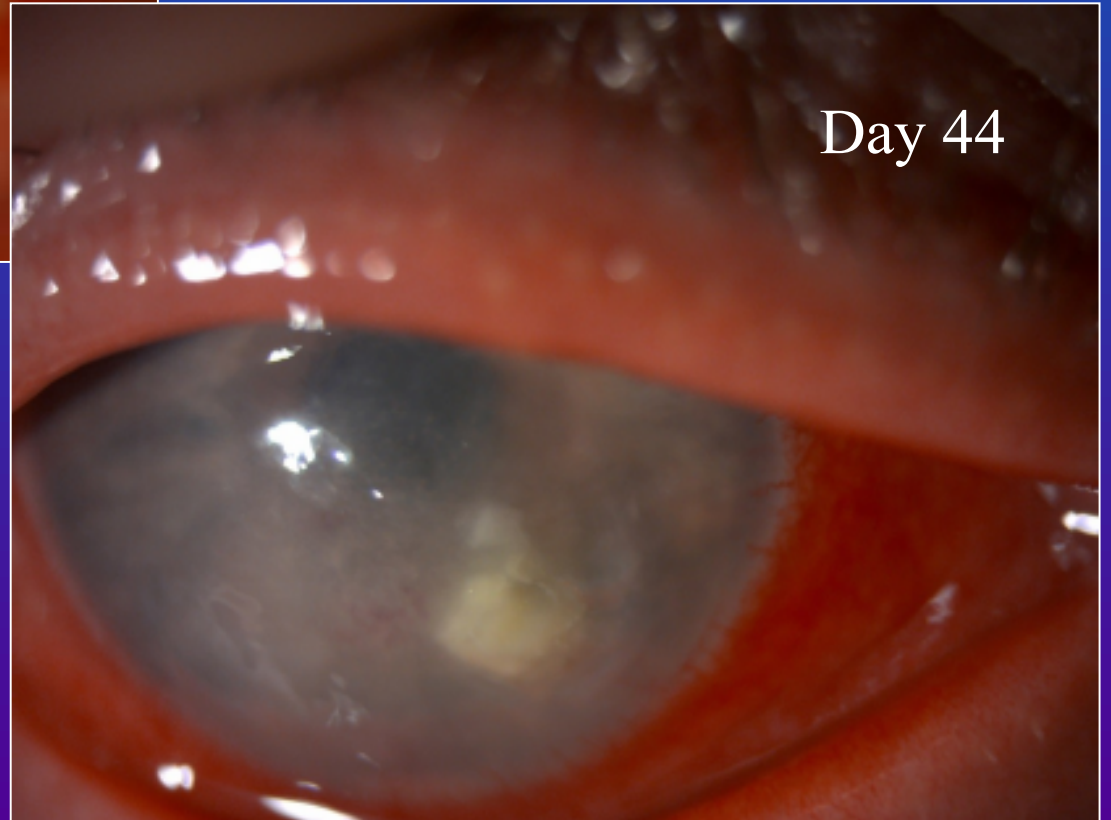




Day 36



Day 44

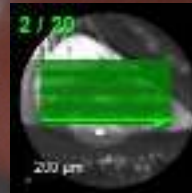


Day 53



STOP Natamycin

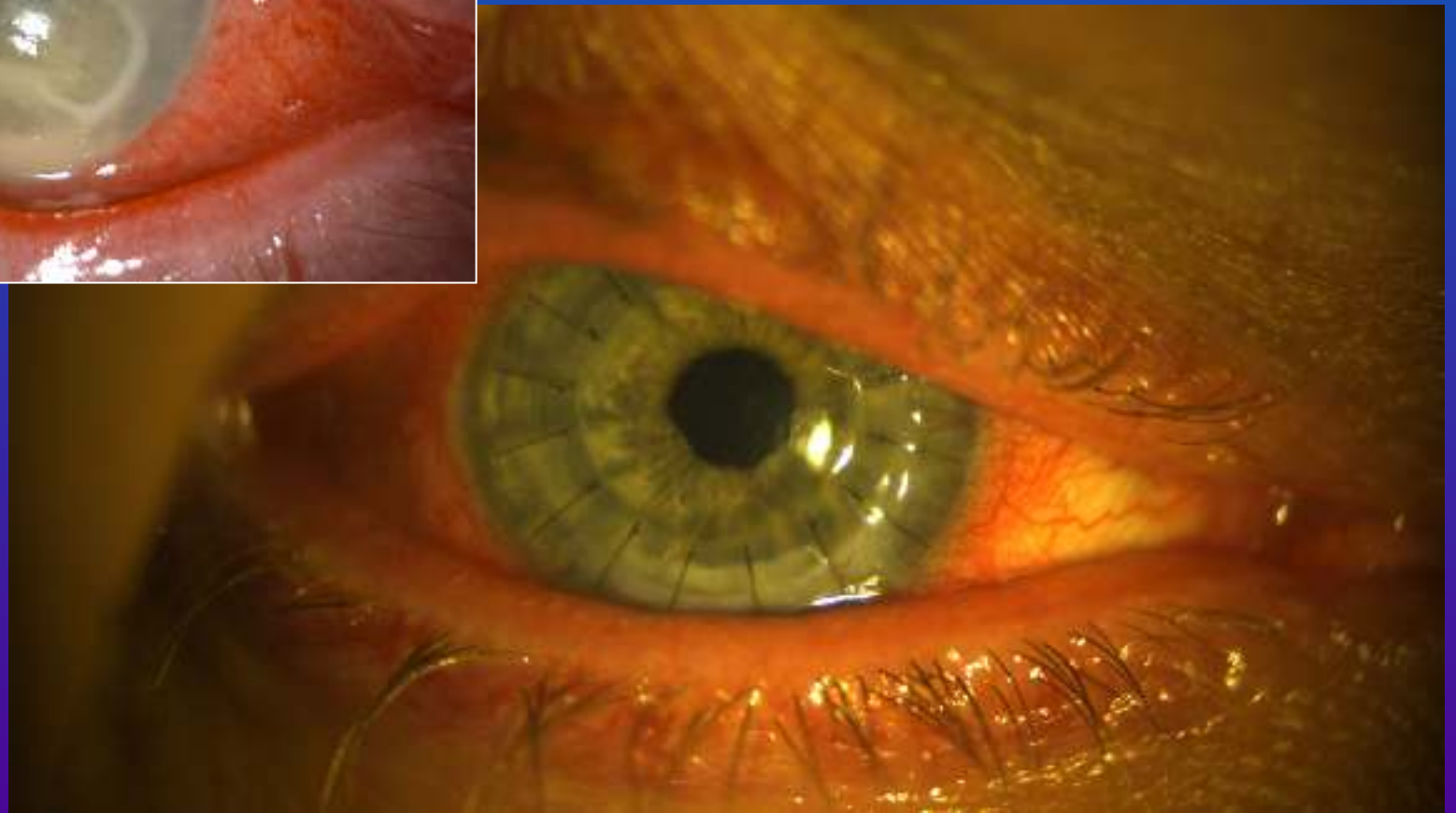
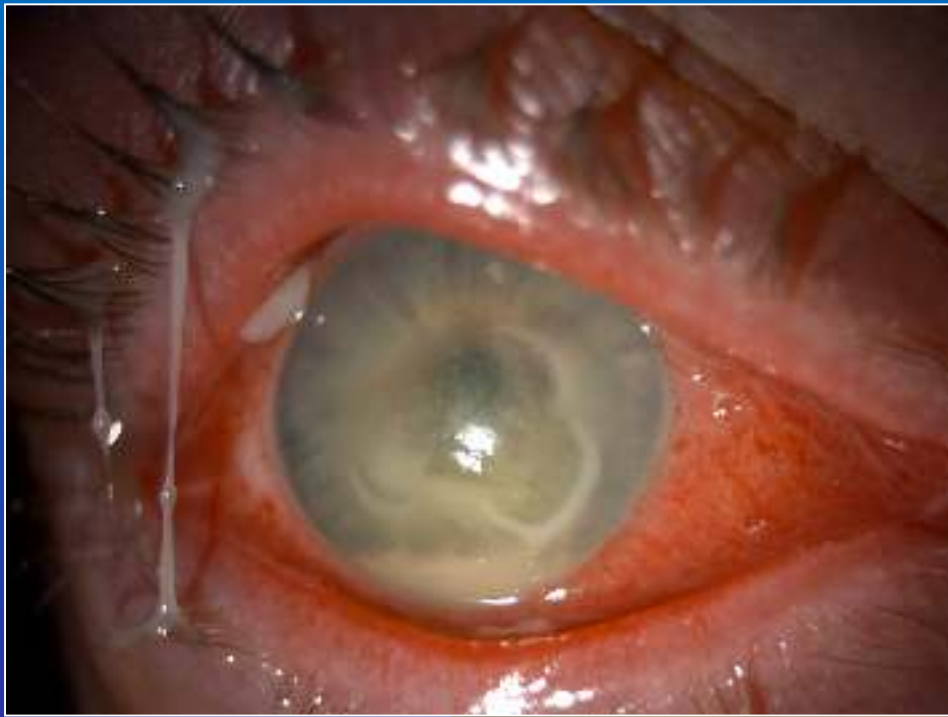
Day 80 Injection 2 times
per week!



05/10/2020, OD

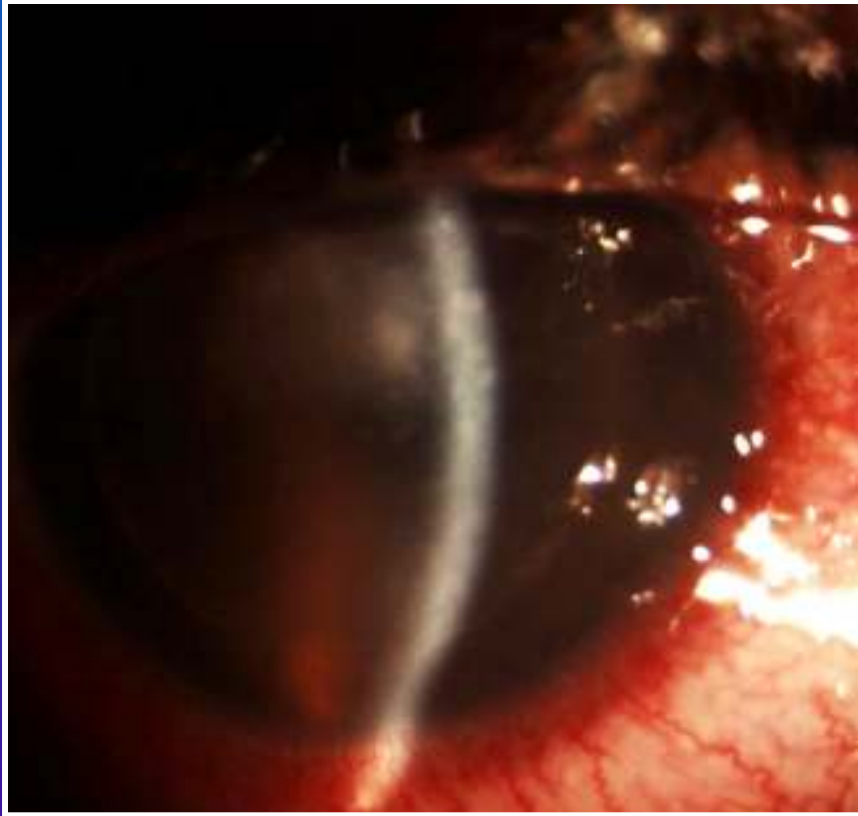
IR&OCT 30° ART [HS] ART(9) Q: 24

HEIDELBERG
ENGINEERING

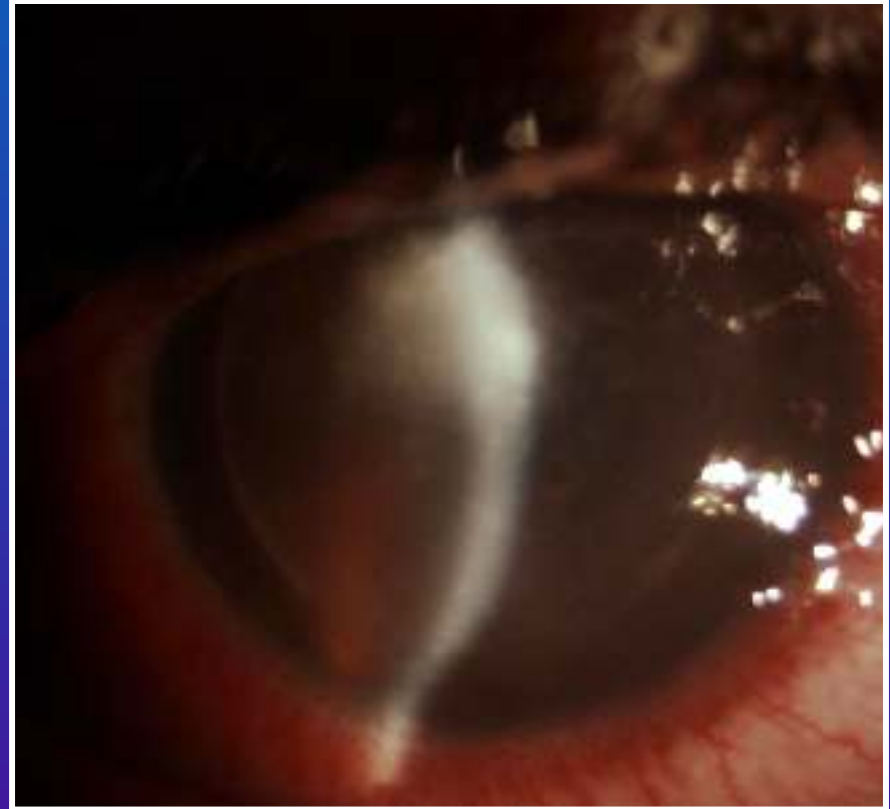


Interface infection

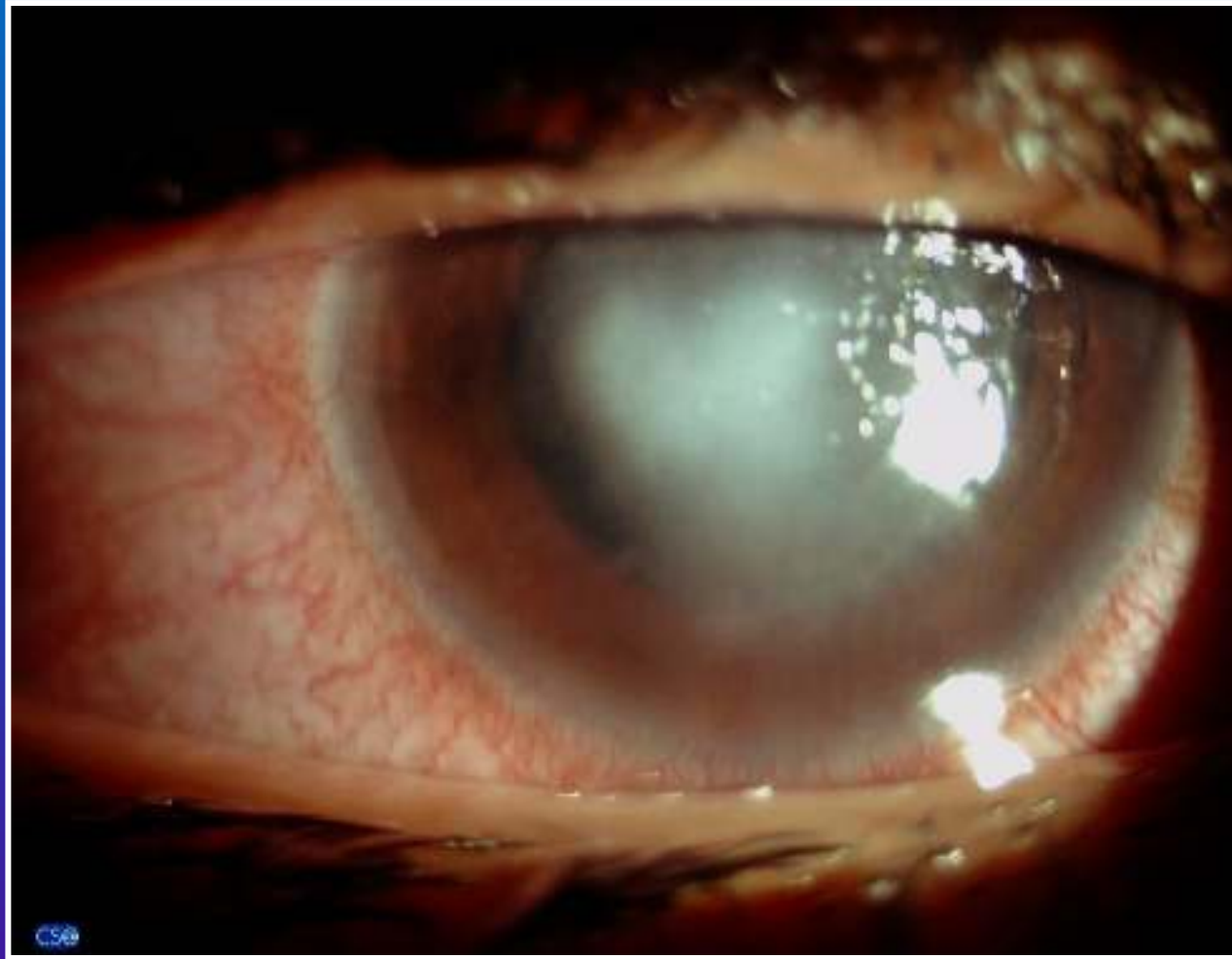
Post LASIK infection



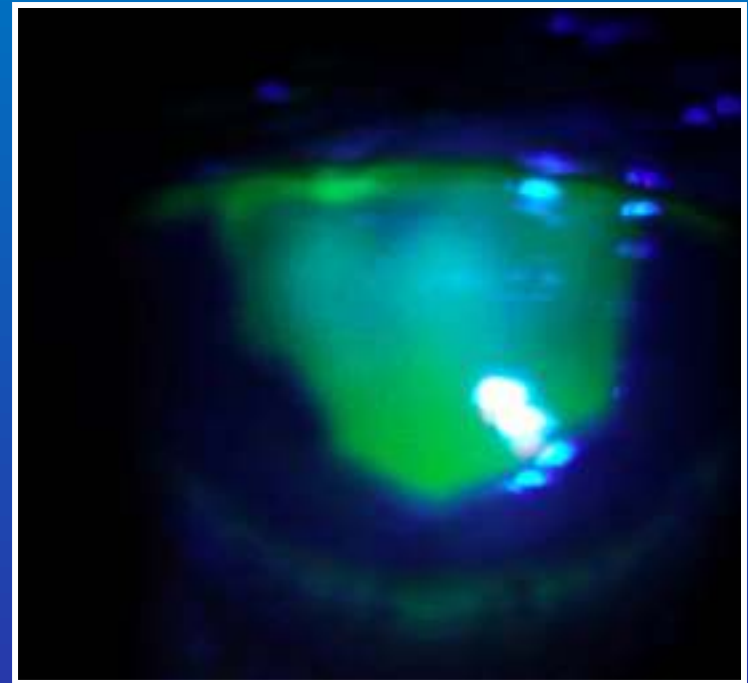
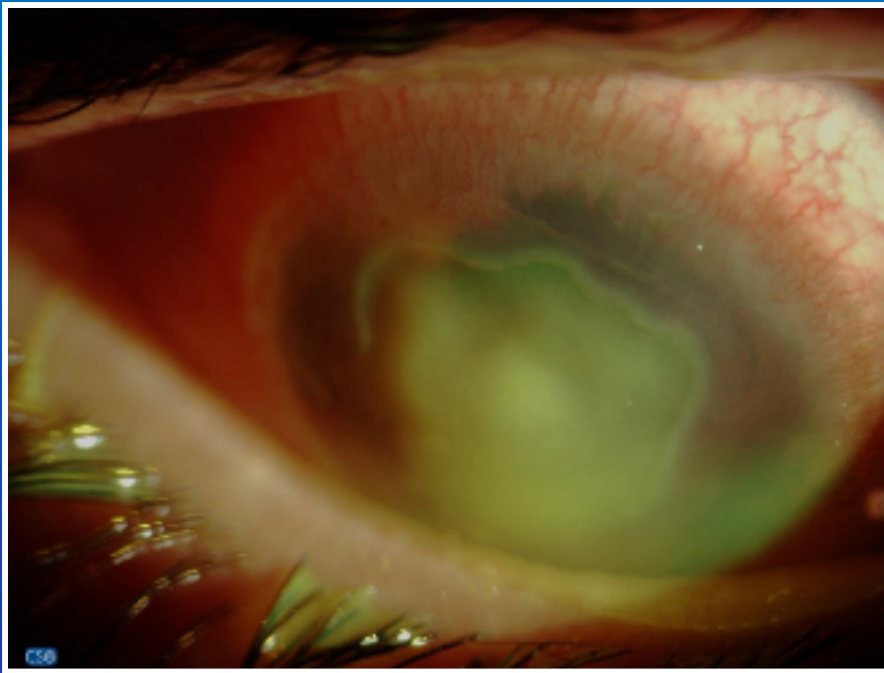
1 Week post LASIK



10 days post LASIK
no improvement
Started fortified drops/systemic antibiotic



2 weeks post op further deterioration



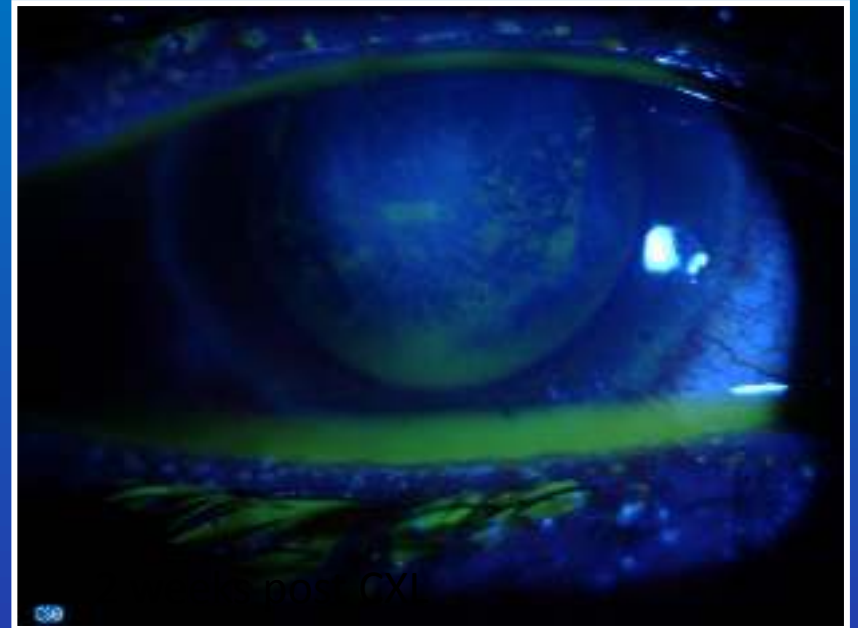
Flap amputated and sent for culture

Pink Yeast cells
(RHODOTURULA)





1 week post CXL



1 month post CXL

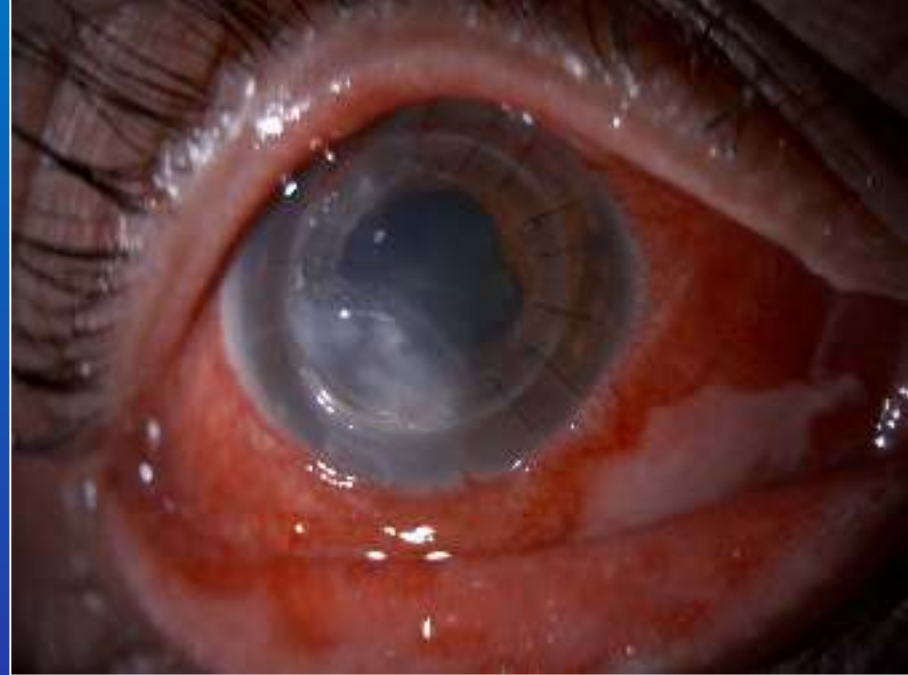
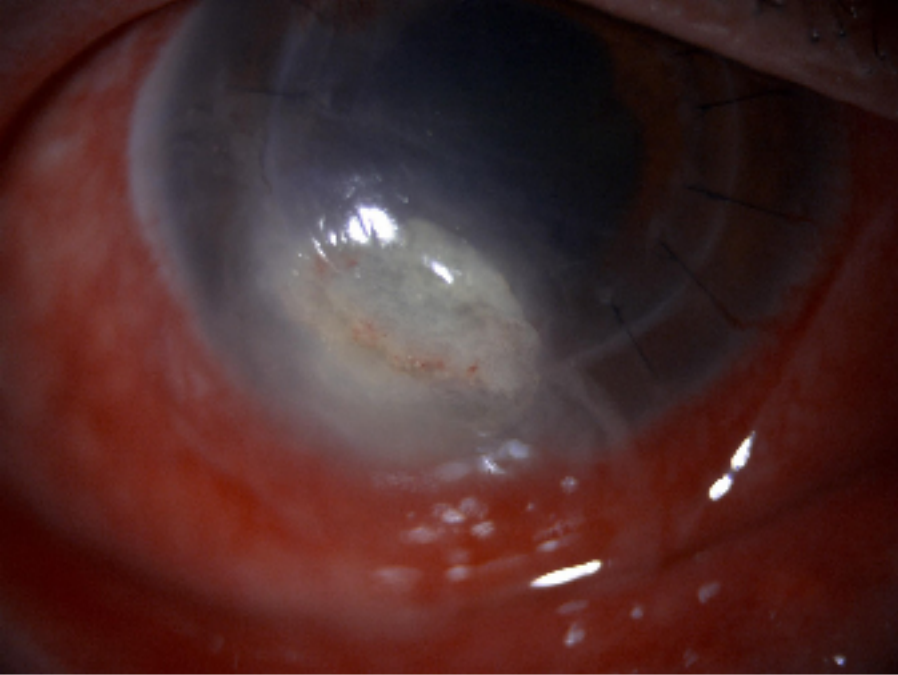
Antifungal drops+ CXL



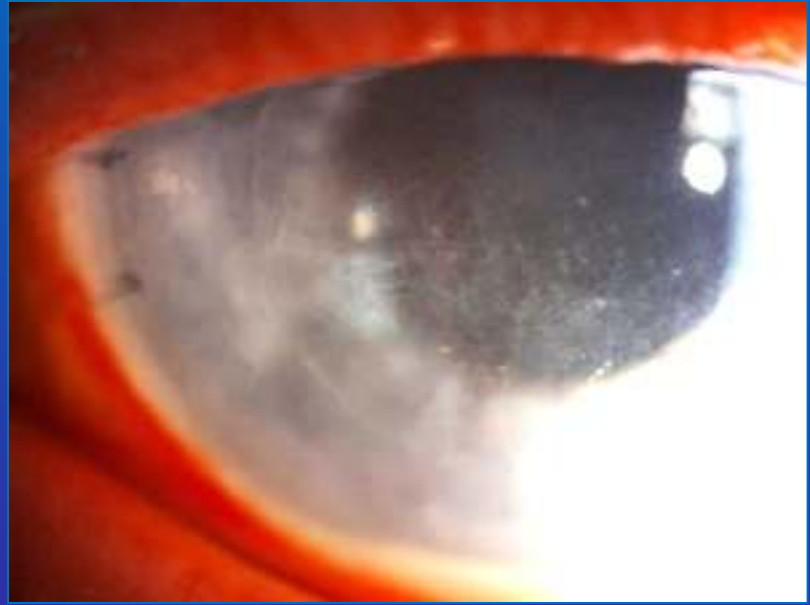
2 months post CXL



5 months post CXL



Interface infection after DSAEK



Excisional Keratoplasty

extension to anterior chamber or sclera

- 2mm clearance
- Remove iris and lens as required
- Peripheral iridectomy
- Cyclodialysis?
- **Voriconazole** 50-100 ug in 0.1ml
- Interrupted sutures

Take Home Message

- Thorough history including personal history
- High index of suspicion for AK particularly in contact lens wearers
- Pain disproportionate signs but not necessary
- Commonly misdiagnosed as HSV and Iridocyclitis
- Radial keratoneuritis pathognomonic
- Ulcer stops improving or gets worse! (another bug or toxicity)

Take Home Message

- **Treat Early/Avoid steroids in CL wearers**
- **Investigate: Culture, PCR, IVCN**
- **Do not stop treatment early**
- **Use an armamentarium of treatment**
- **Avoid therapeutic graft whenever possible**



Thank you for your attention