17th Annual International Meeting of Research Institute of Ophthalmology (RIO)
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Panel: Keratitis Challenges

Herpes Simplex Keratitis

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Chair and Professor of Ophthalmology

RIO

The University of Nottingham

17TH INTERNATIONAL CONFERENCE OF THE RESEARCH INSTITUTE OF OPHTHALMOLOGY
RIO 2025

Declaration of Interests

Consultant: Artic Vision, Santen, Thea

Medical Advisor: NuVision Biotherapies

Shares: Glaxosmithkline, NuVision Biotherapies

Herpes simplex virus keratitis

CLINICAL FEATURES

- **60% of children by age 5 have HSV type 1 infection**
- **6% of them will have primary disease**
- **Less than 1% of primary disease is Ocular**

Clinical classification

- Primary Neonatal (intrauterine infection leading to immune mediated disease is very rare)
- Primary (children and adults)
- Recurrent

Herpes simplex virus keratitis

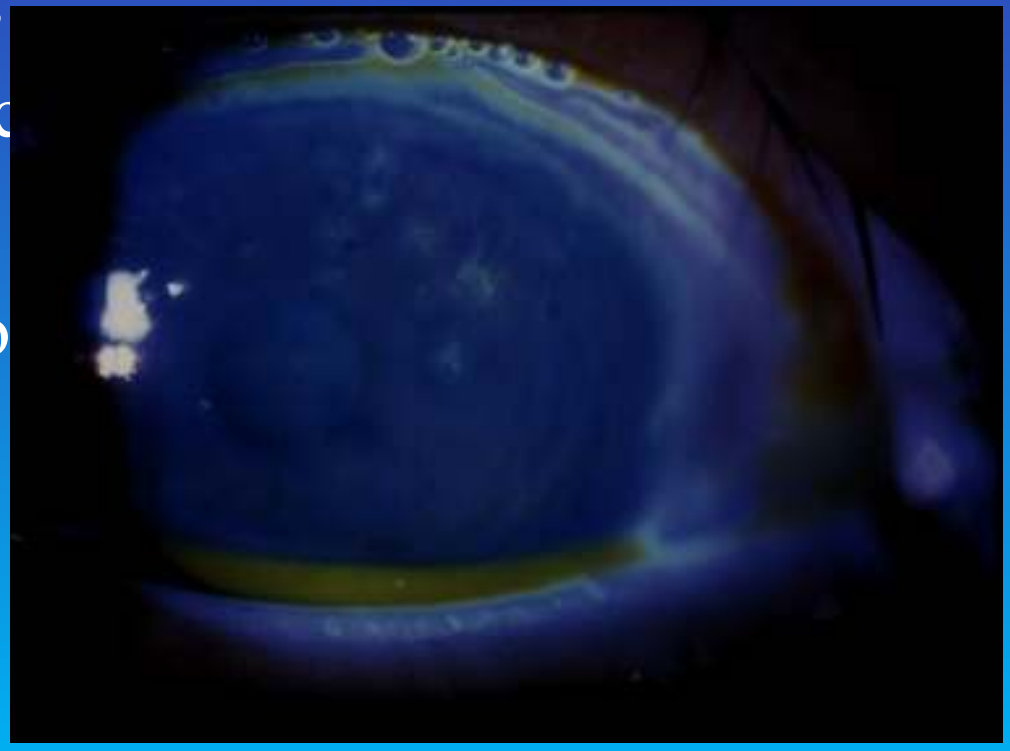
Primary neonatal (non-immune host):

- 80% is type 1 and 20% is type 2
- Significant mortality and morbidity
- **Acute ocular lesions:**
  - Blepharitis
  - Conjunctivitis
  - Keratitis: SPK, microdendrites, serpiginous lesions
  - Stromal keratitis: indicates intrauterine infection and development of host immune capabilities

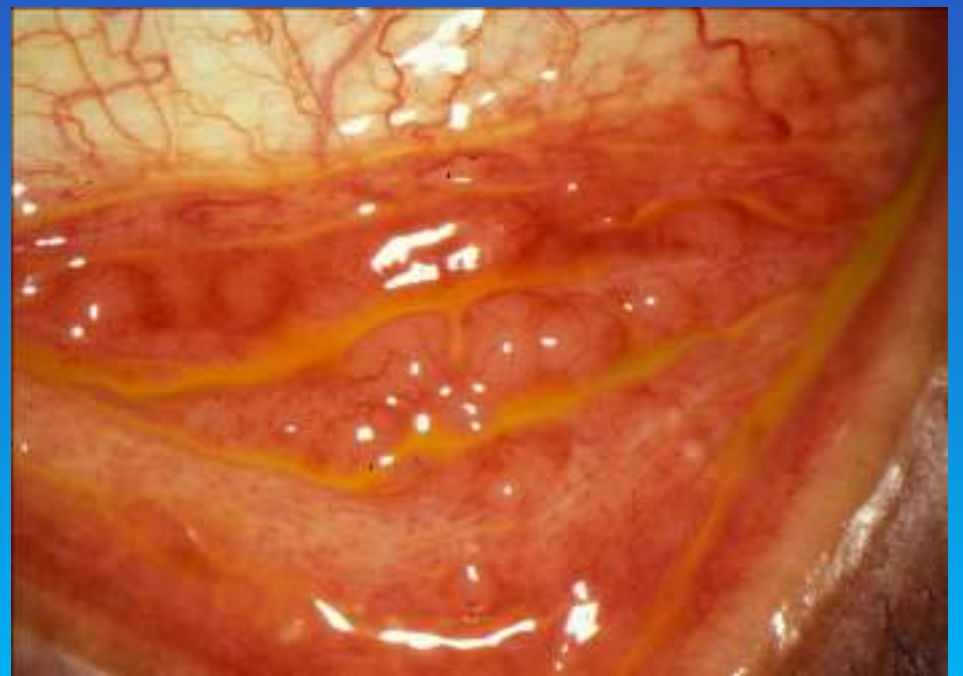
Herpes simplex virus keratitis

Primary ocular (non-immune host)

- Blepharitis
- Conjunctivitis: follicular, pseudomembranous
- Keratitis: SPK, micro-dendrites, diffuse atypic
- Significant skin involvement
  - Peri-ocular haemorrhagic vesicular eruptio
  - Heal with no scars



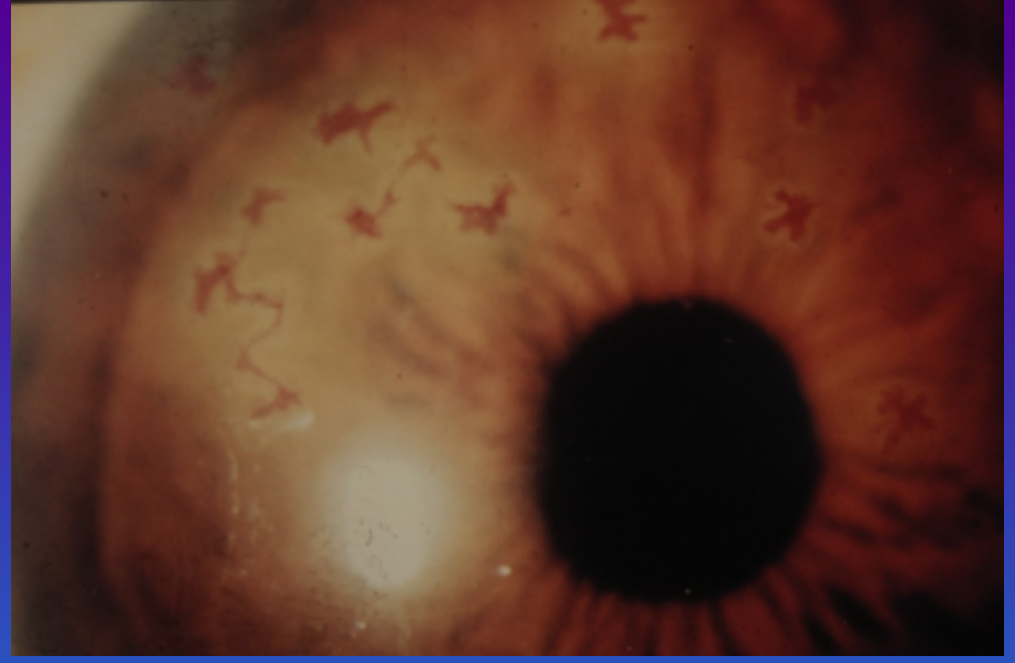
Primary HSV lesions: Periocular and conjunctival



Herpes simplex virus keratitis

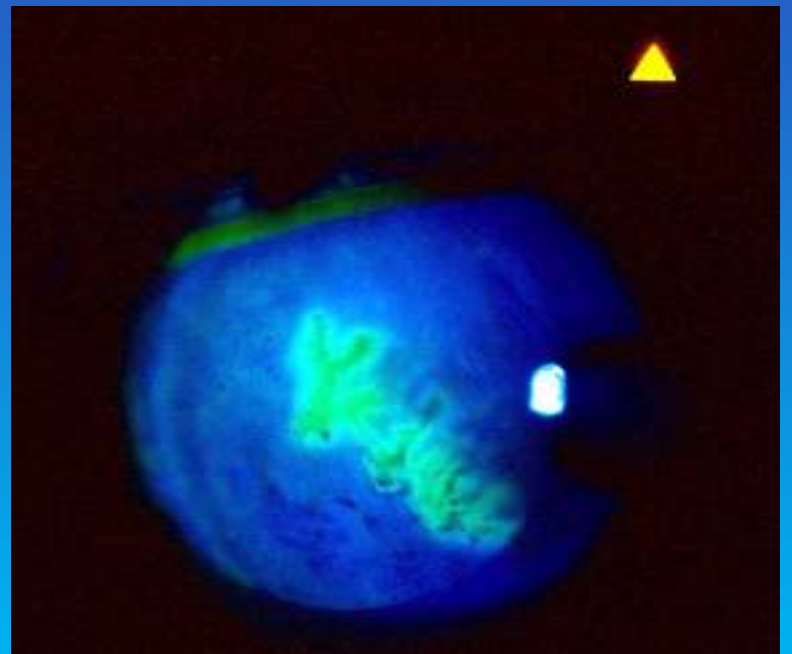
Recurrent ocular (immune host)

- Blepharitis
- Conjunctivitis
- Keratitis:
  - Epithelial:
    - Dendritic, geographic (infective)
    - Neurotrophic keratitis (non-infective)



Micro dendrites

Conjunctival dendrites

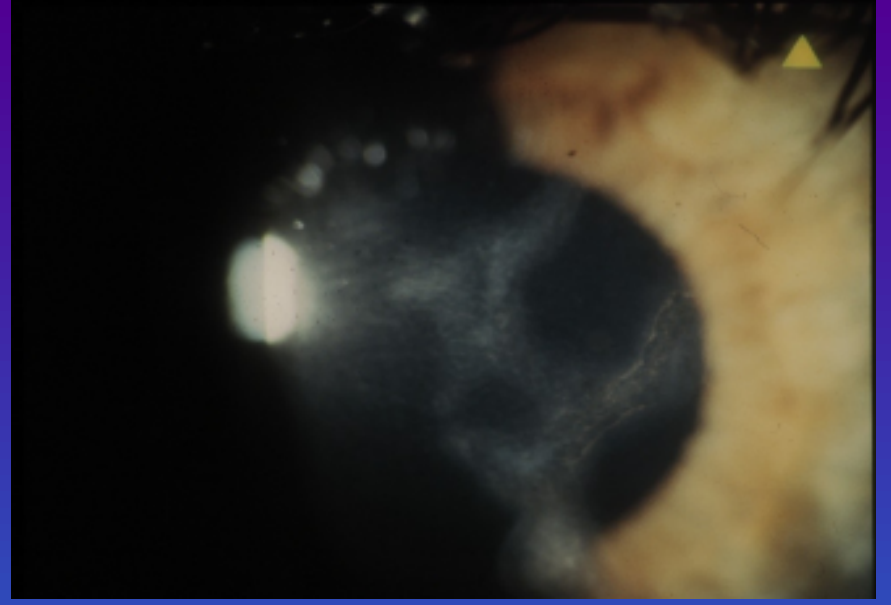


HSVK

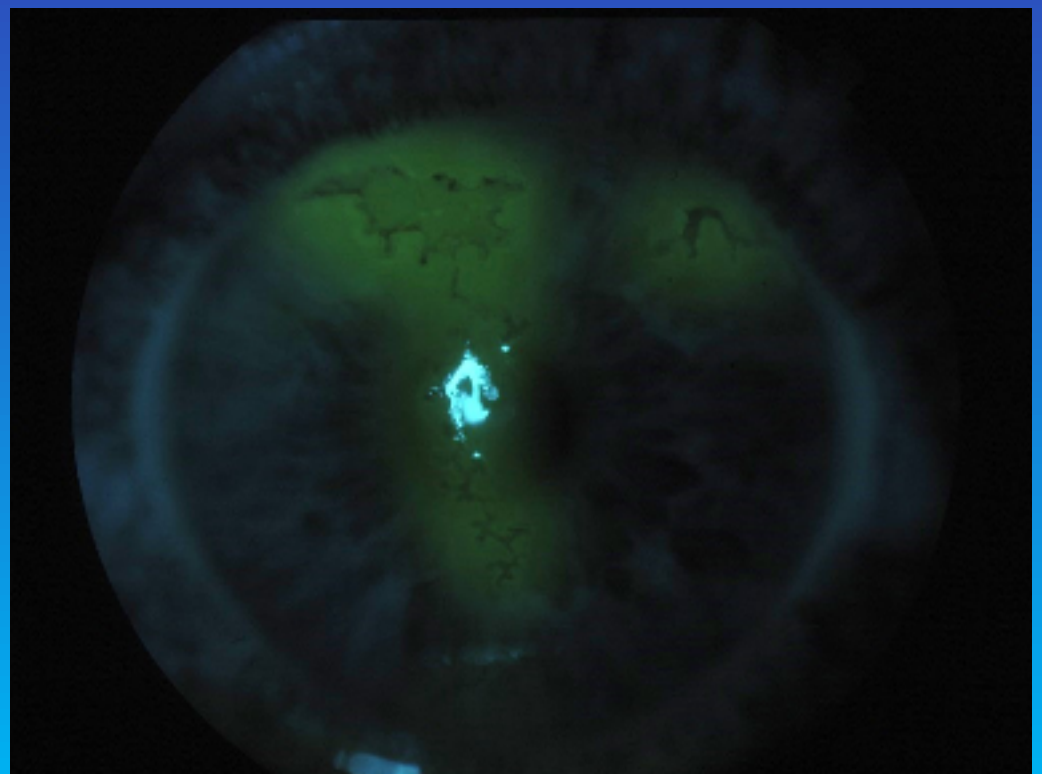
Dendrites

Corneal fluorescein and rose Bengal dye

Ghost
Dendrites

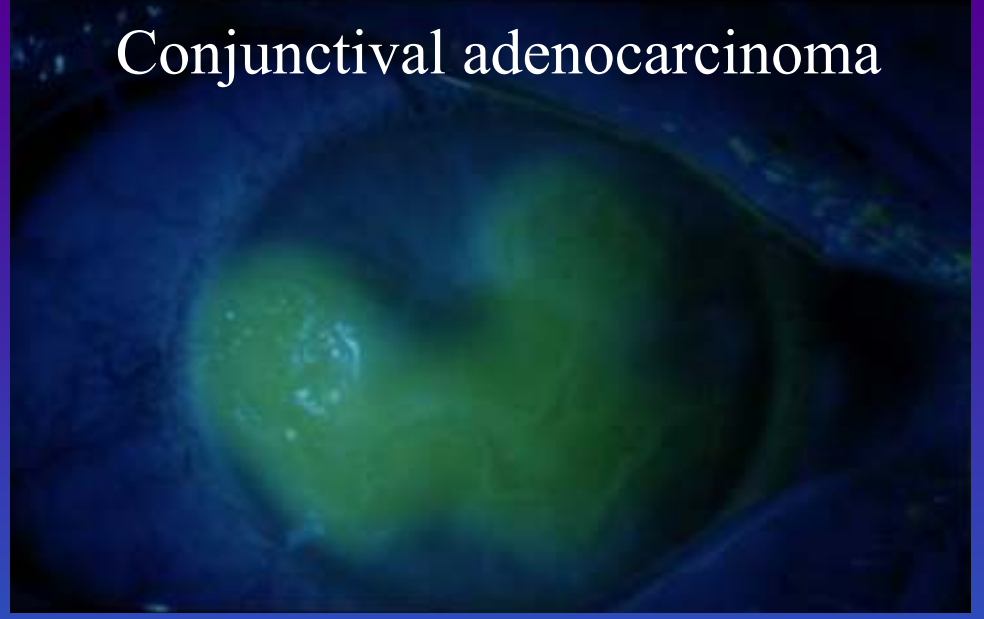


Dendro-
geographic

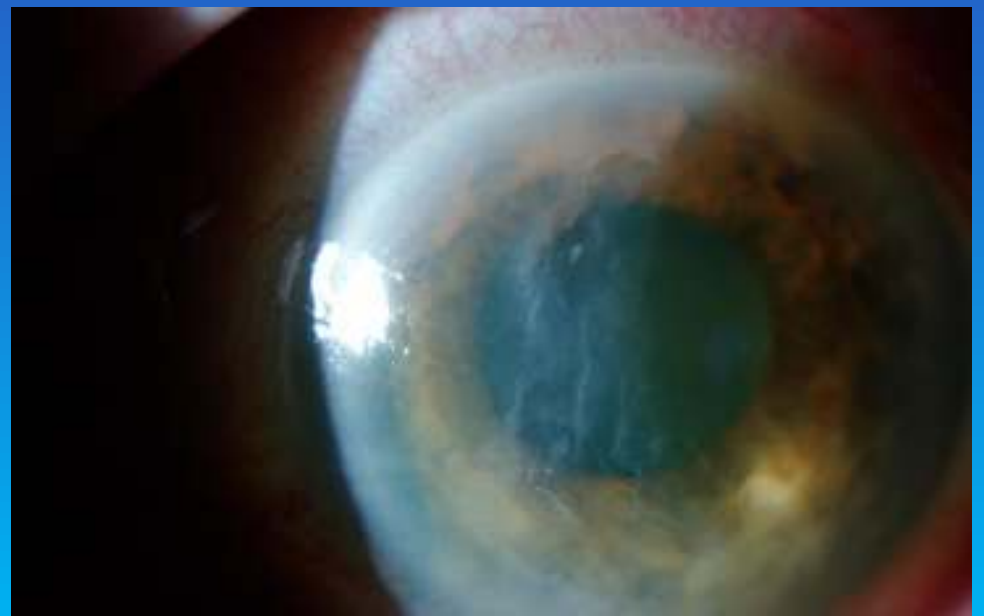


Large ‘map’

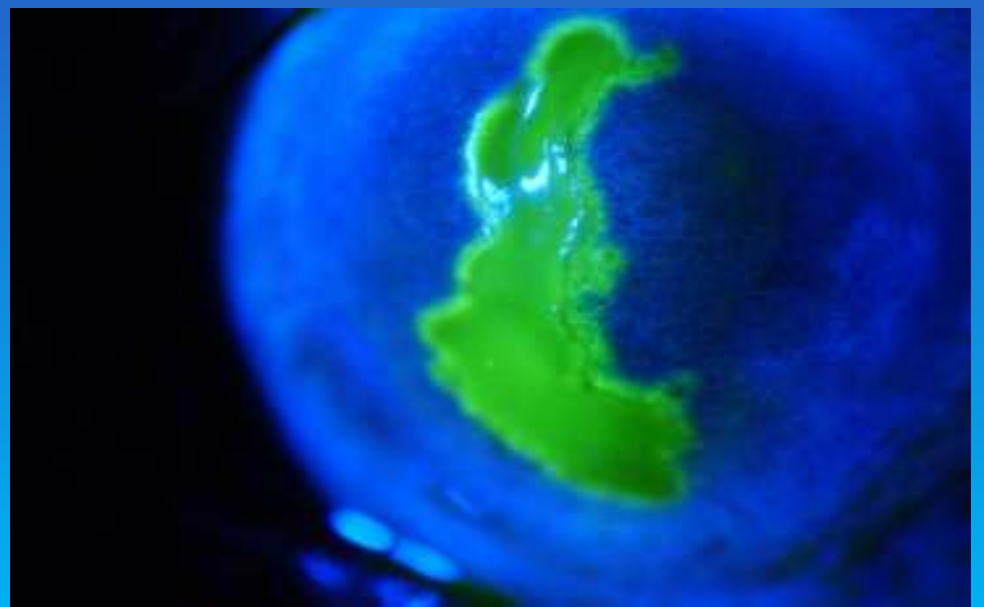
Conjunctival adenocarcinoma



Geographic HSVK



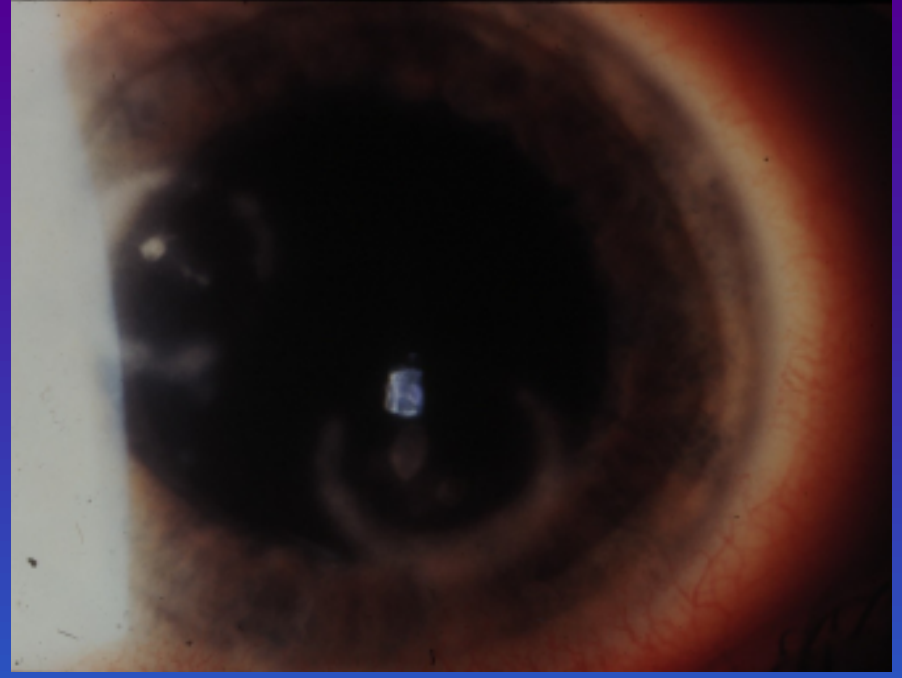
‘PED’



Herpes simplex virus keratitis

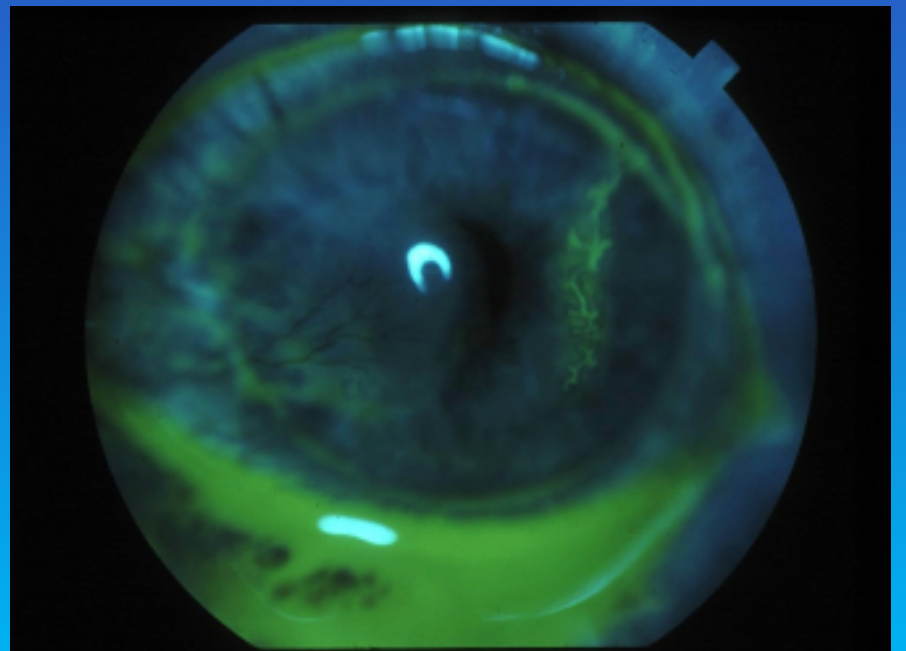
Recurrent ocular (immune host)

- Keratitis:
  - Stromal:
    - Immune complex mediated:
      - Immune rings
      - Interstitial keratitis
      - Limbitis



Immune Rings

Interstitial keratitis

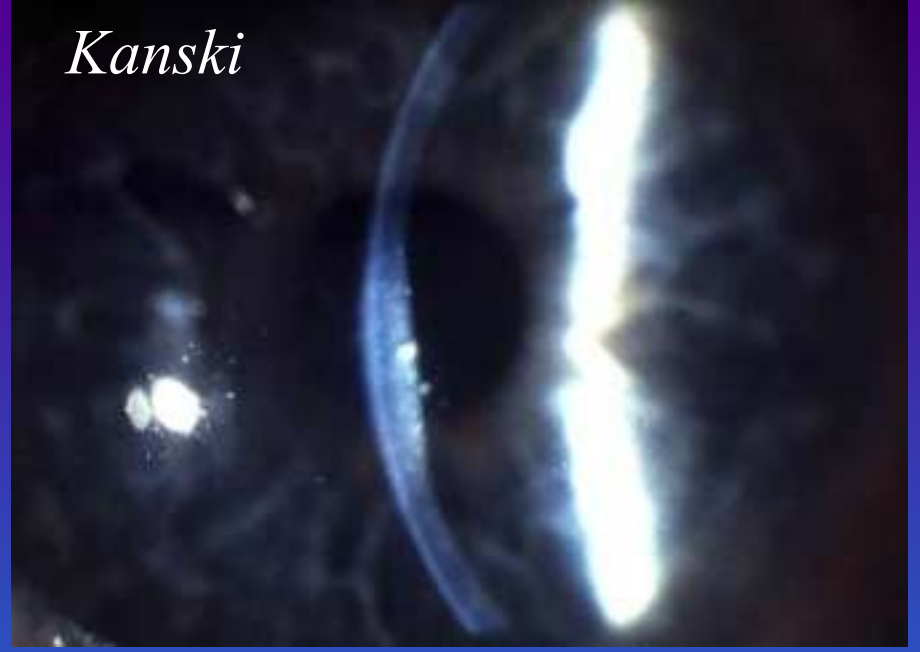


Interstitial keratitis and Limbal vasculitis

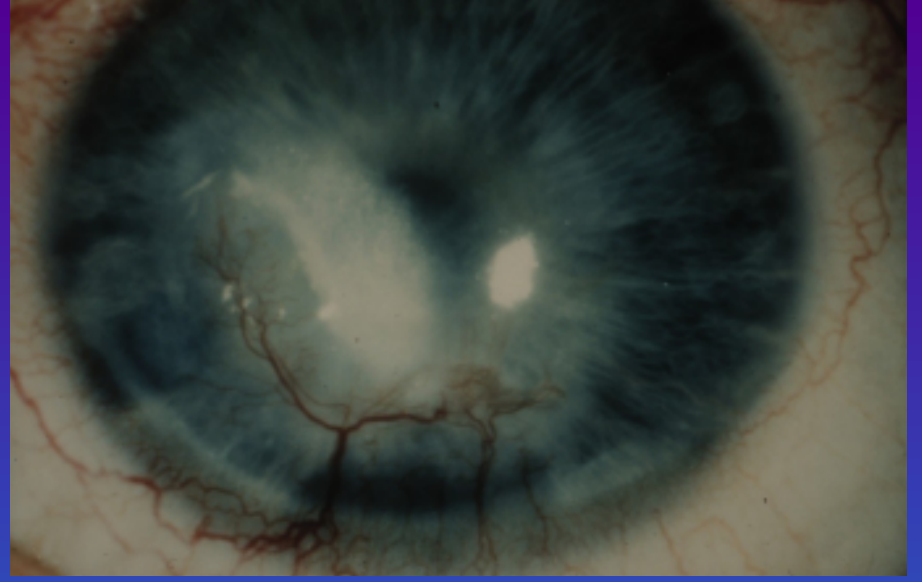
Herpes simplex virus keratitis

Recurrent ocular (immune host)

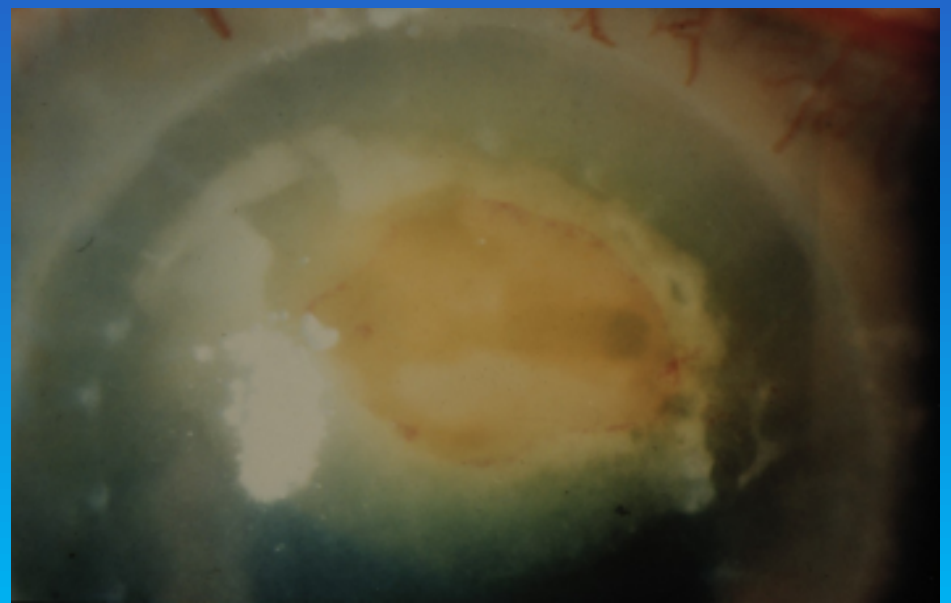
- Keratitis:
  - Stromal:
    - T-cell mediated:
      - Disciform keratitis
      - Endothelialitis

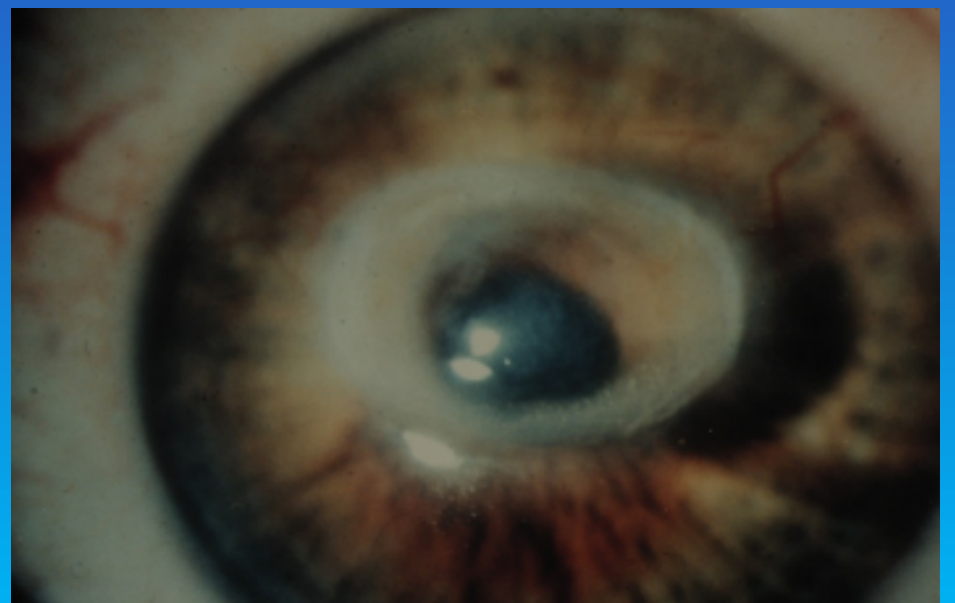


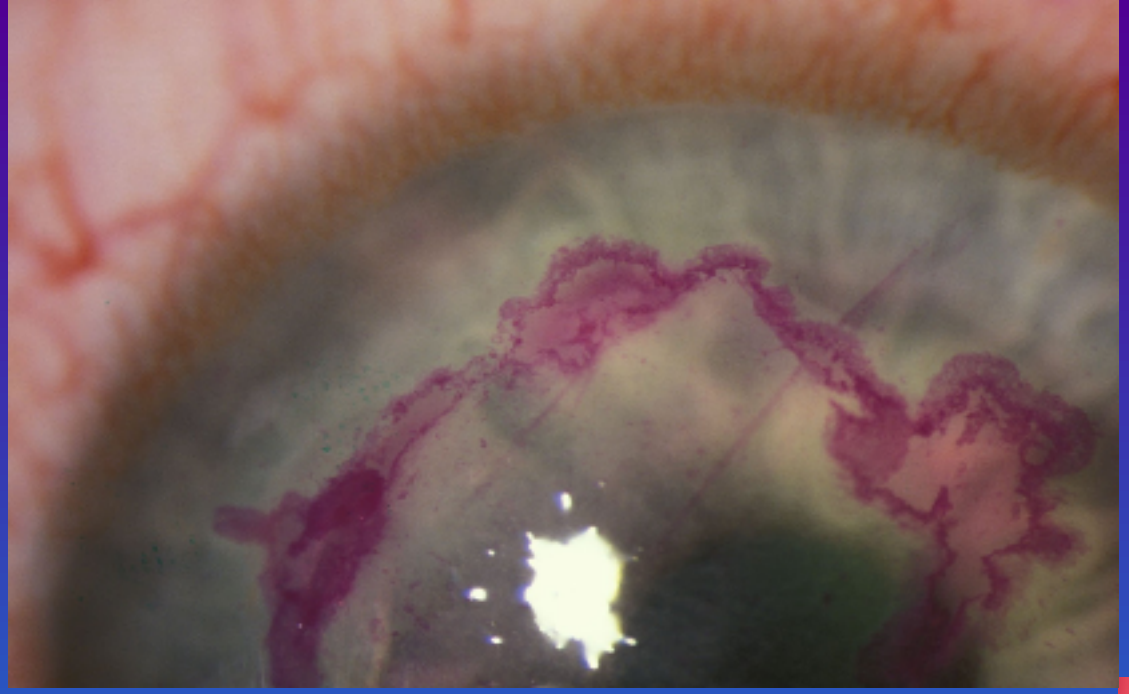
HSV Disciform keratitis



HSVK ‘Mixes and Melts’

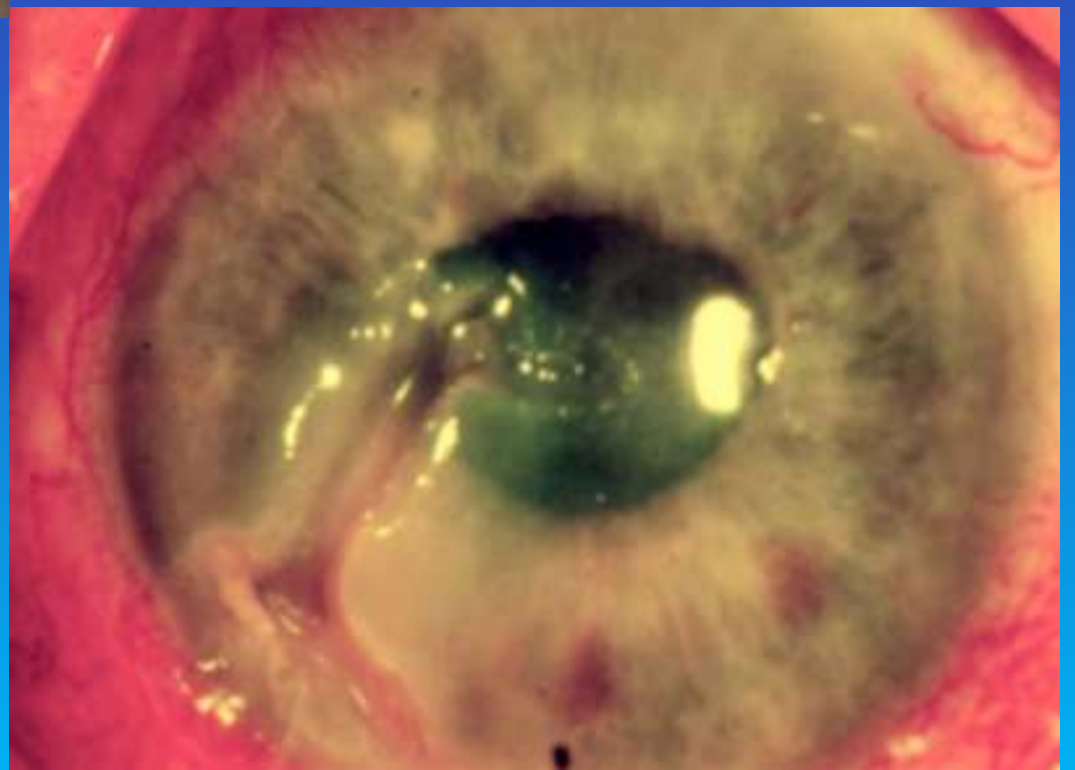


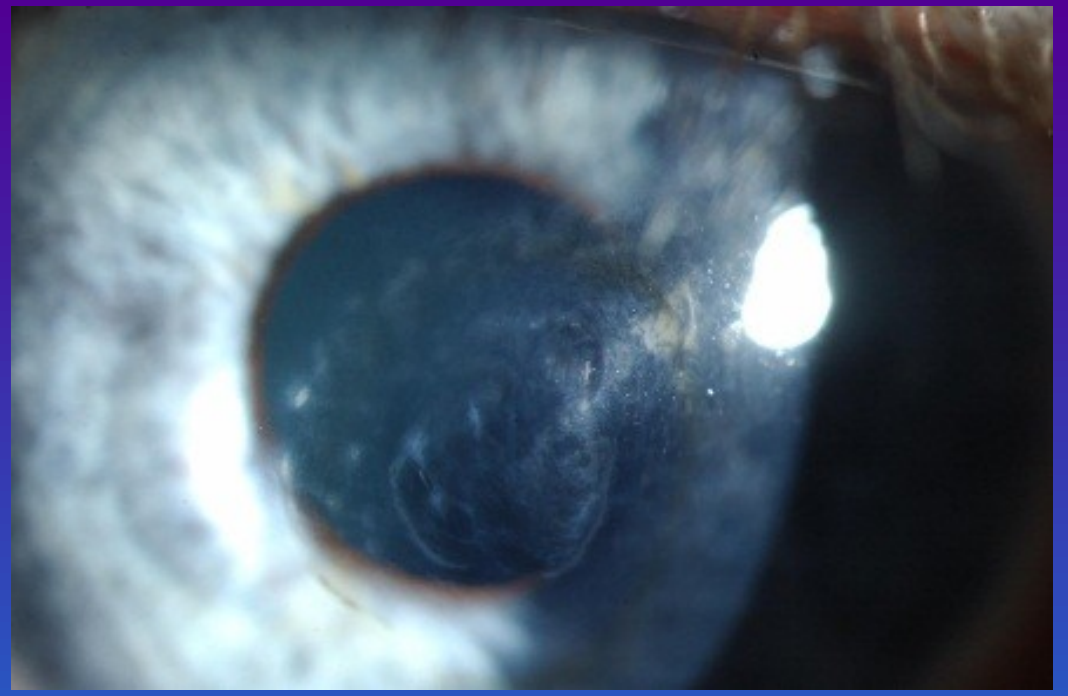


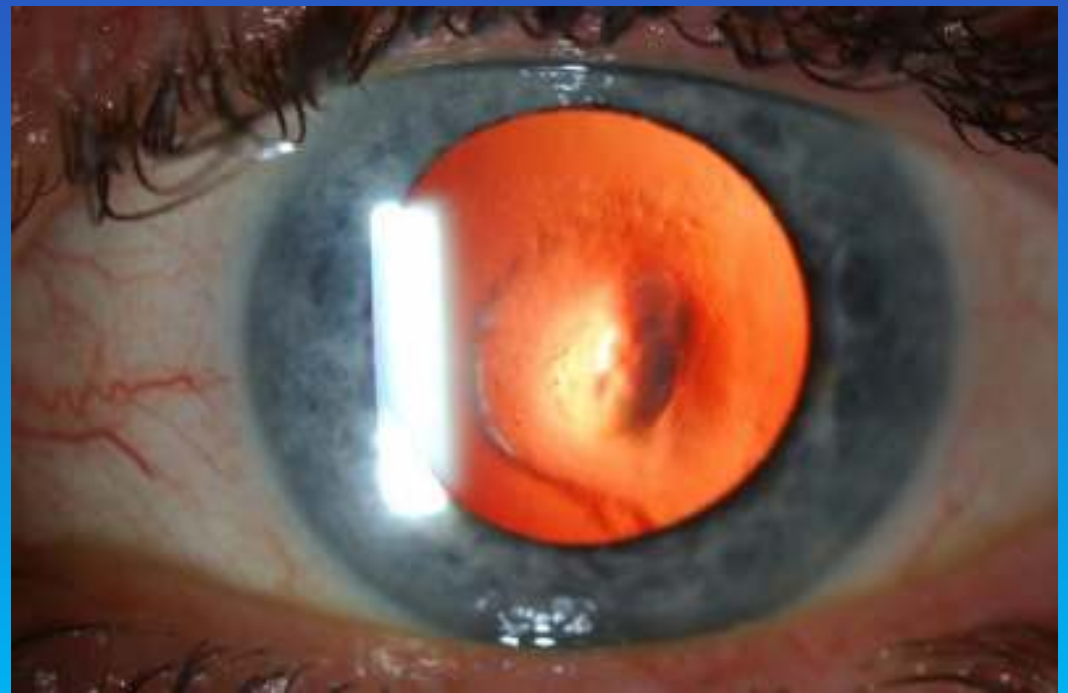


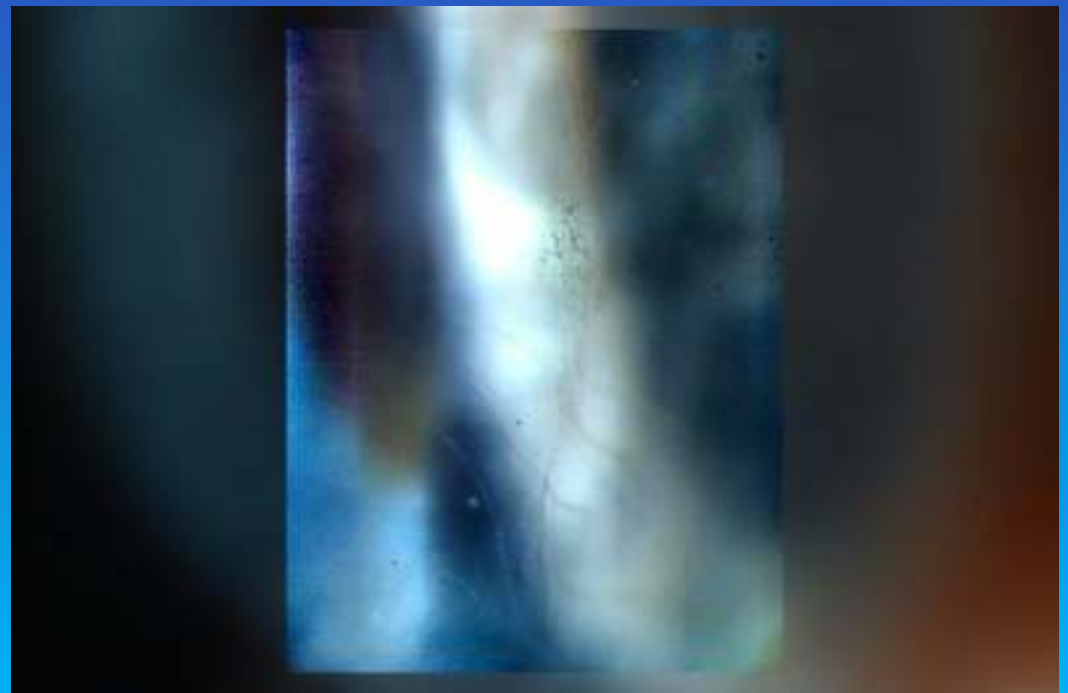
HSV Keratitis

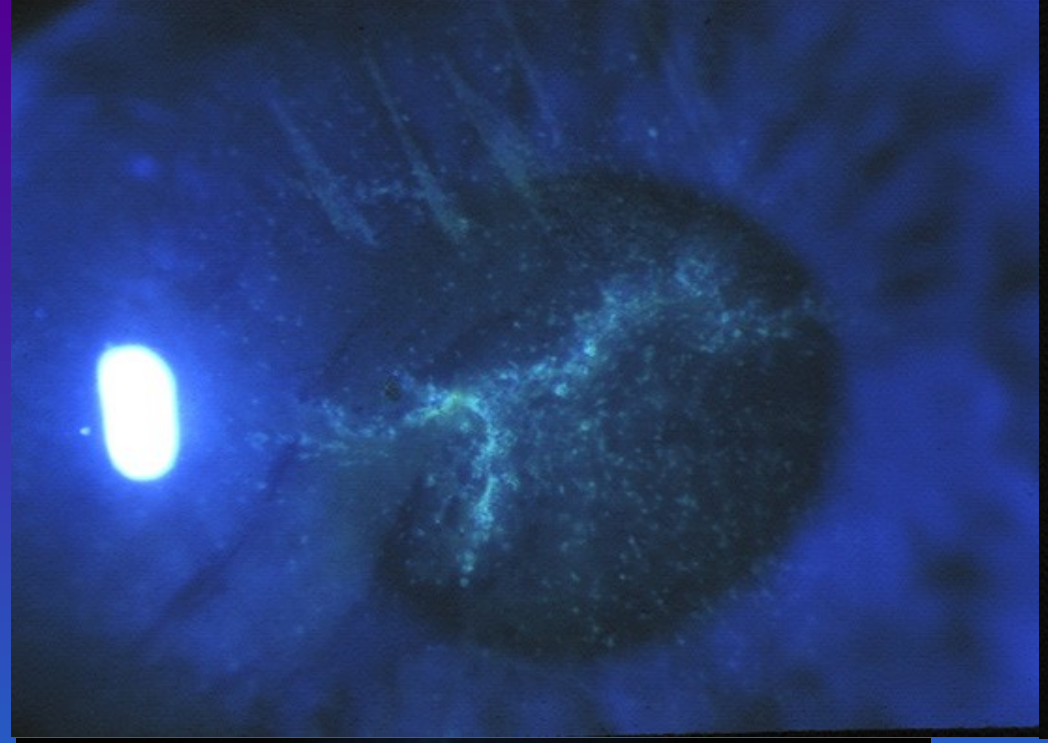
Stromal Melting

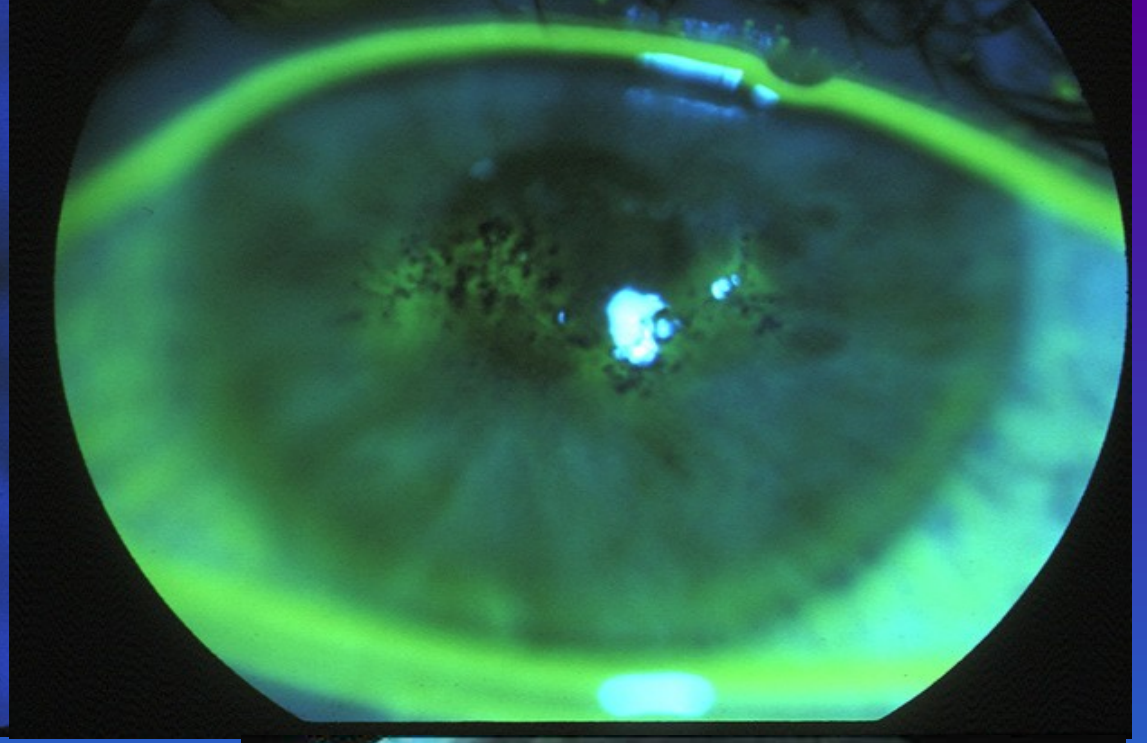


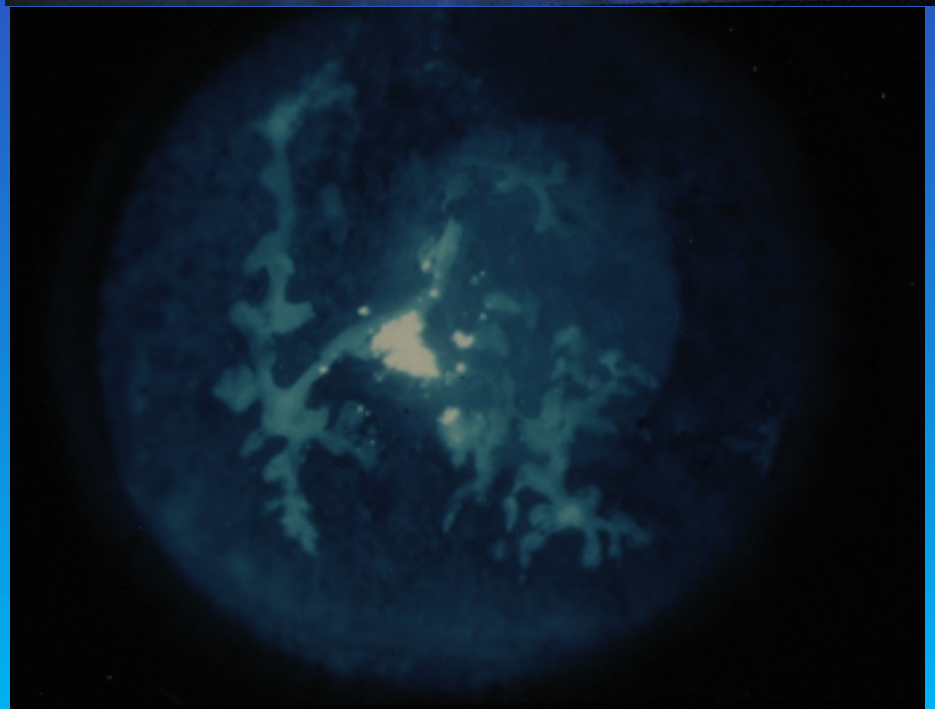


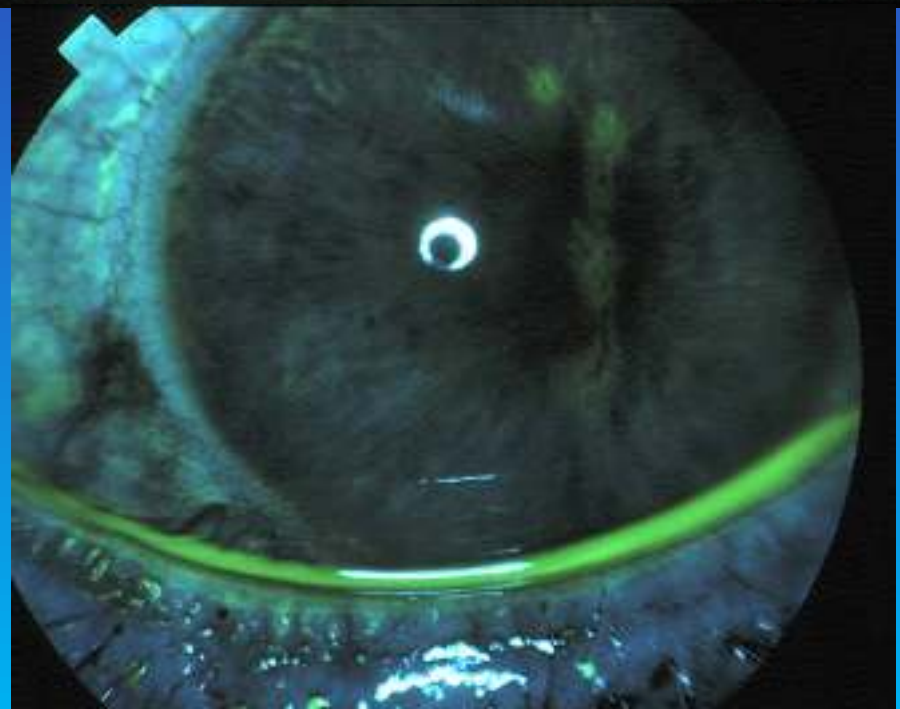












Herpes simplex virus keratitis

DIAGNOSIS

- Clinical: Beware of combined herpetic and bacterial infection. Pain much less than expected for severity of infection.
  - Peripheral ulcerative keratitis

Wagener's

PAN

Systemic Vasculitis

Herpes simplex virus keratitis

DIAGNOSIS

- Laboratory: biopsy or scrapes
  - Culture – Definitive
  - PCR

Herpes simplex virus keratitis

TREATMENT

- Medical:
  - Anti virals (topical and oral)
    - IDU
    - Vira A
    - F3T
    - Aciclovir
    - Famciclovir
    - Ganciclovir
  - Steroids

Herpes simplex virus keratitis

TREATMENT

- Most commonly used - Topical
  - Vira A, F3T (USA)
  - Aciclovir
  - Ganciclovir
  - Steroids

HEDS Herpetic Eye Disease Study

1. After resolution of any form of ocular HSV, 1 year of acyclovir 400 mg twice daily significantly reduced recurrence of herpetic disease during that time and without rebound up to 6 months after acyclovir was stopped.

2. There was no statistically significant benefit of acyclovir 400 mg five times daily for 10 weeks in treating active HSV stromal keratitis already being treated with steroids and trifluridine.

HEDS Herpetic Eye Disease Study

3. Steroids were significantly better than placebo in resolving active stromal keratitis, and postponing steroids slowed resolution but showed no difference in outcome by 6 months.

Avoid steroids BUT in Corneal grafts use it with antiviral prophylaxis

Minimal dose, taper soon, may be required long term

Antiviral cover long term

HEDS Herpetic Eye Disease Study

4. Treatment of iritis with acyclovir 400 mg five times daily for 10 weeks in patients already on steroids and trifluridine may possibly have some beneficial effects.

5. A 3-week course of acyclovir 400 mg five times daily for patients with epithelial keratitis already on trifluridine did not alter the subsequent incidence of stromal keratitis or iritis.

6. Acyclovir 400 mg twice daily for 1 year significantly reduced the recurrence of HSV stromal or epithelial keratitis, with greatest benefit in the stromal group.

HEDS Herpetic Eye Disease Study

7. Previous stromal, but not epithelial, keratitis markedly increased the risk of recurrent similar disease in the future.

8. Psychological stress, sun exposure, contact lens wear, or systemic illness could not be shown to be triggers for HSV reactivation.

HEDS Herpetic Eye Disease Study

9. The number of past episodes of either epithelial or stromal keratitis was strongly associated with the likelihood of a recurrence.

10. Long-term oral acyclovir significantly lowers recurrence of either form of HSK but is more effective in preventing recurrence in stromal than in epithelial disease.

Herpes simplex virus keratitis

TREATMENT

- Oral Acyclovir:
  - 400 mg five times a day for 7 (HSV)
  - 400 mg 8 times a day for 5 -7 days (HZO)

PROPHYLAXIS

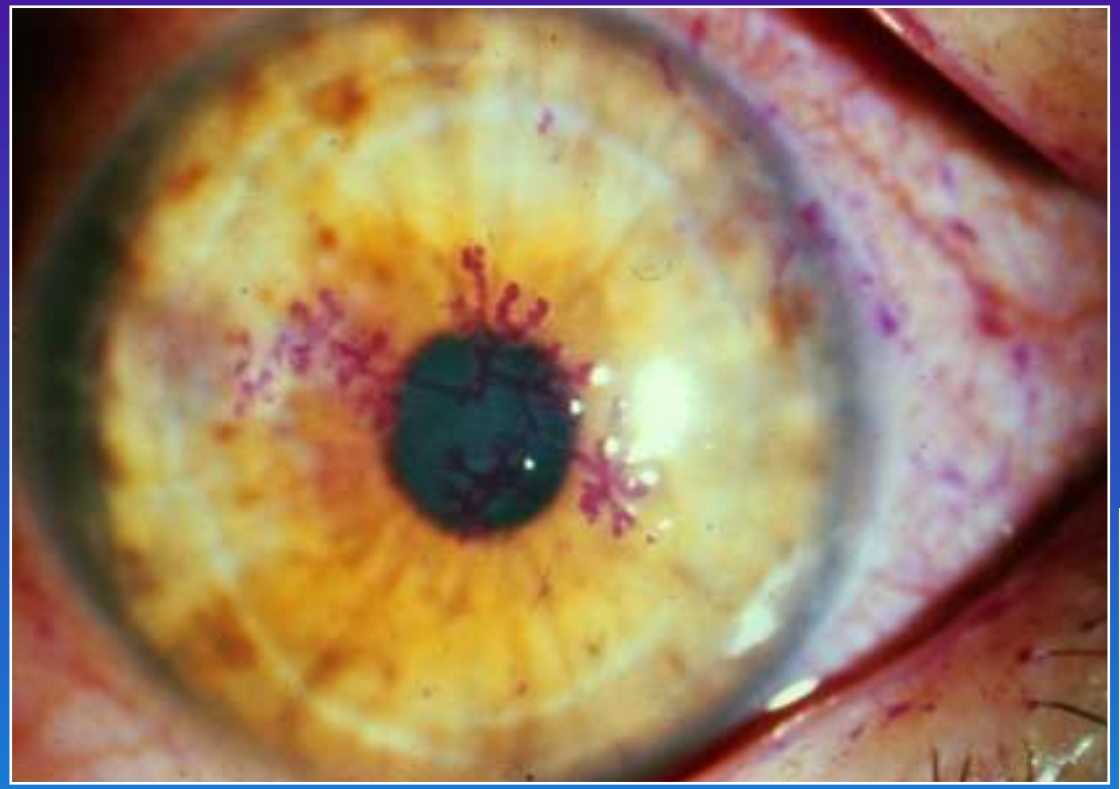
- 400 mg two times a day for one year, 18 months ….indefinitely. In renal failure – titrate dose
- Initiate during episodes of Stress: Anticipating a recurrence
- Topical Acyclovir ointment or ganciclovir gel – one to two times a day.

Herpes simplex virus keratitis

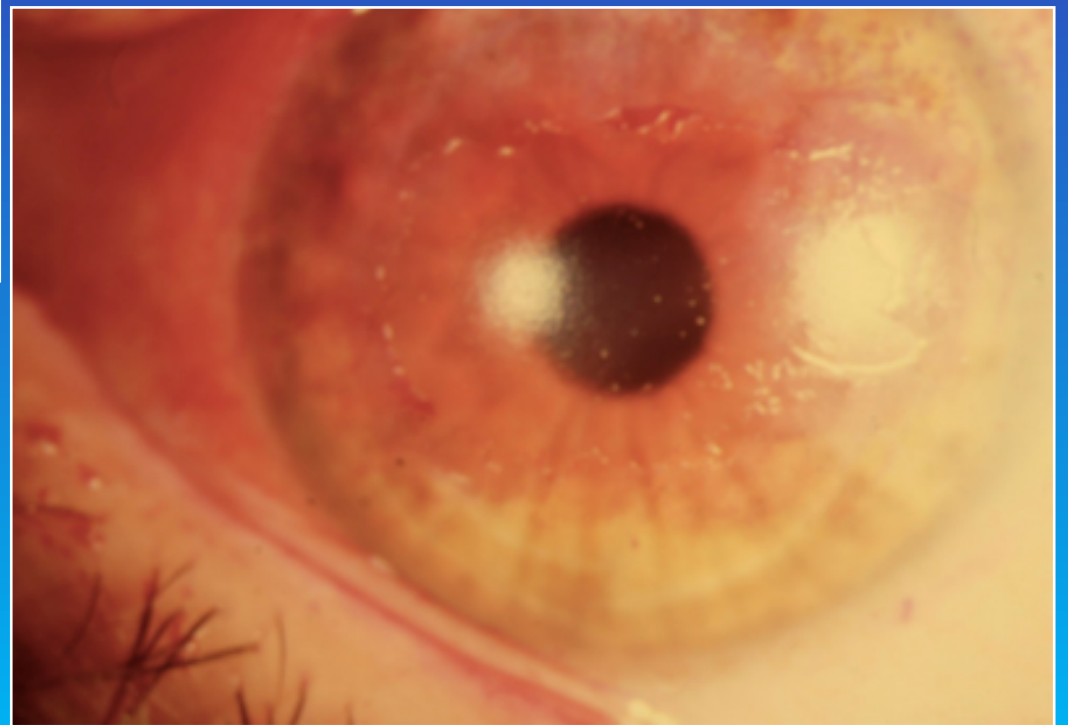
TREATMENT

- Surgical:
  - Debridement
  - Gluing – impending or actual perforation
  - Amniotic membrane stacking – melts
  - Vessel occlusion – prevent recurrence, pregraft
    - Fine needle diathermy
    - Argon laser
  - Corneal graft – therapeutic, tectonic

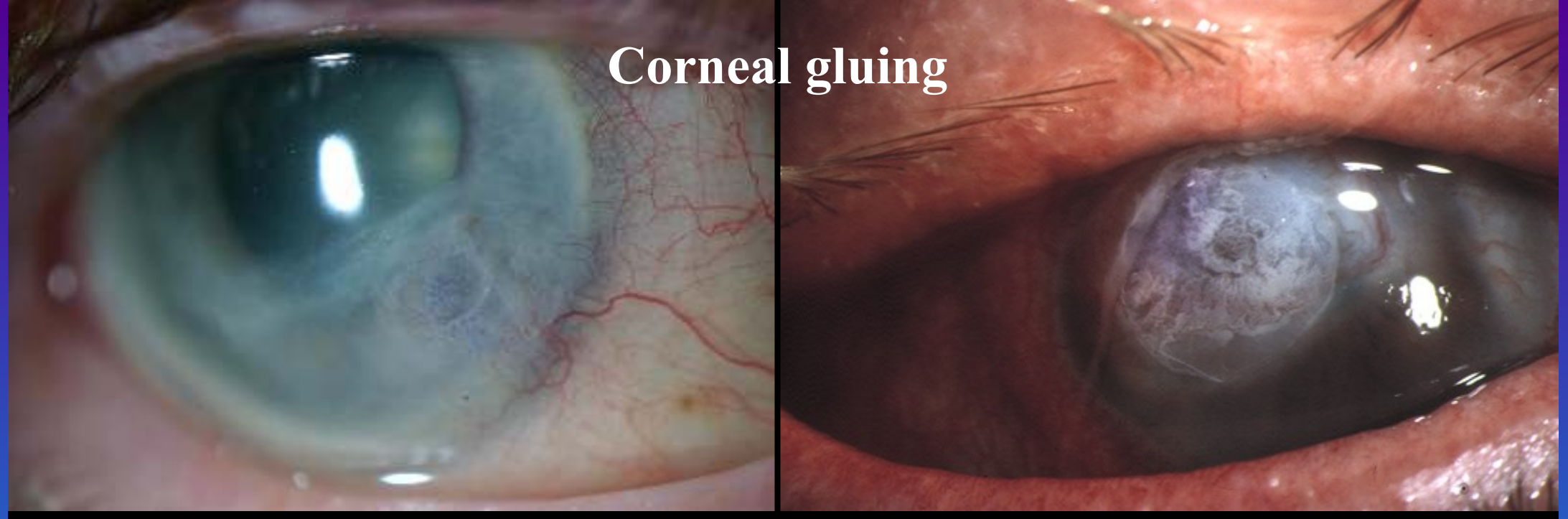
Herpes simplex virus keratitis

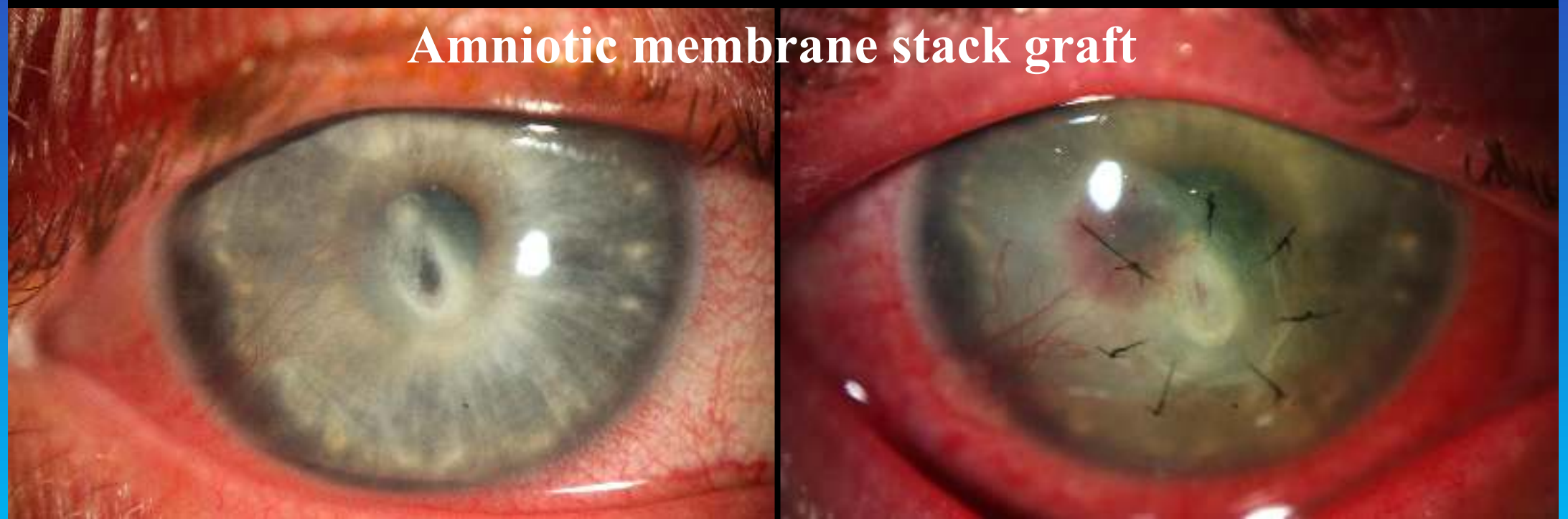


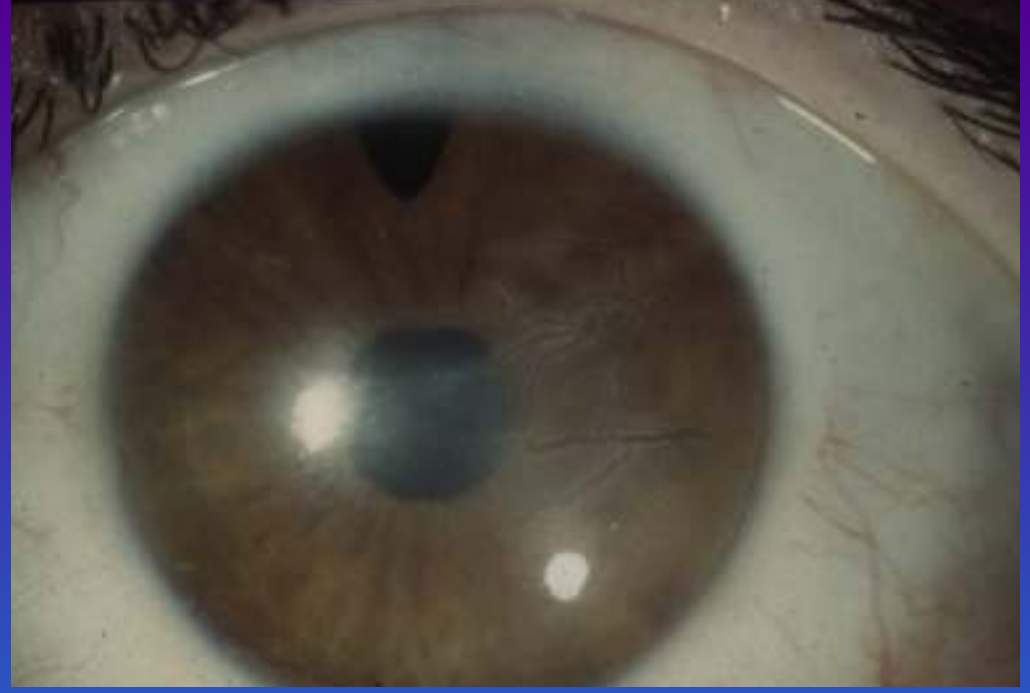
Surgical treatment



Mechanical Debridement

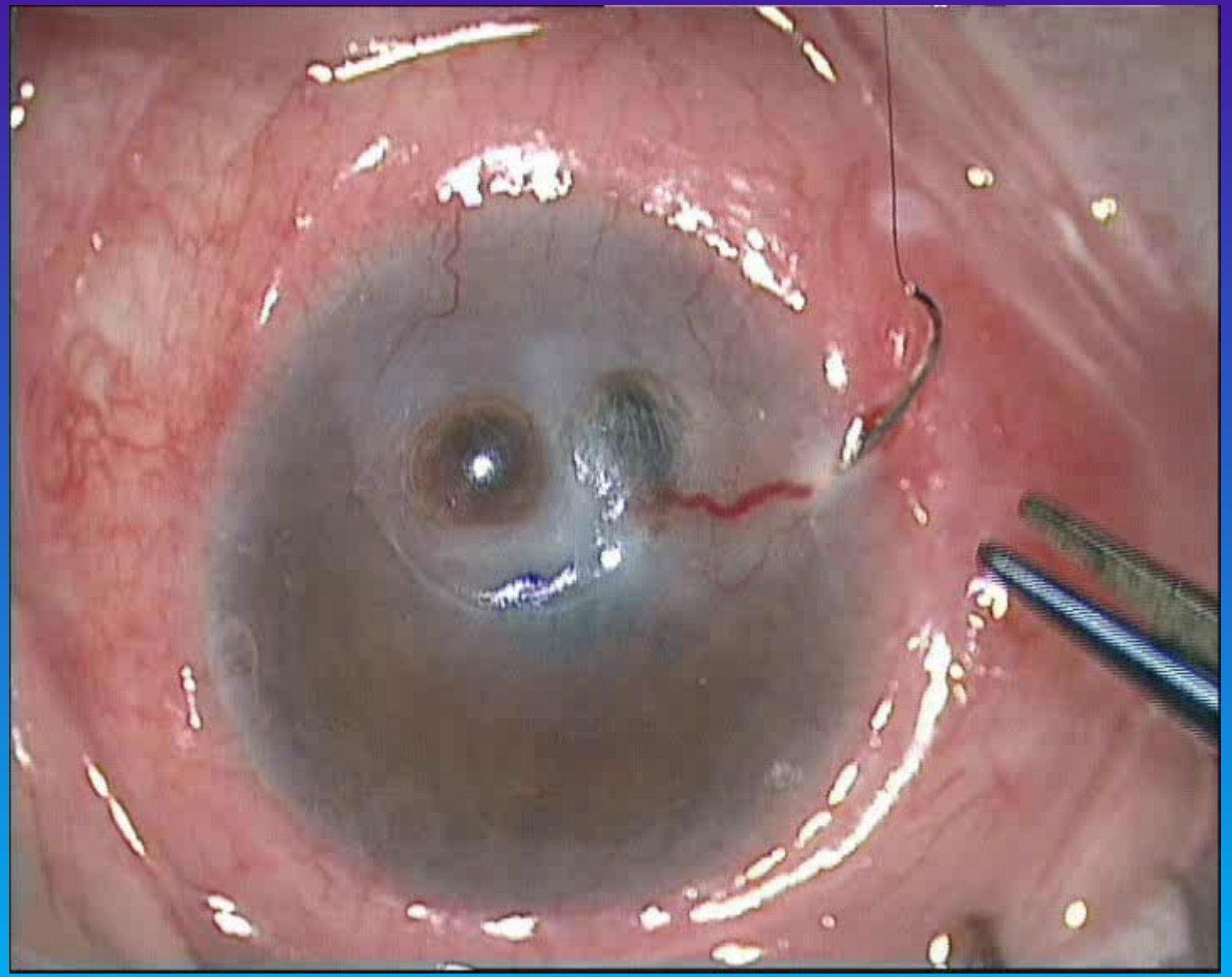

Corneal gluing

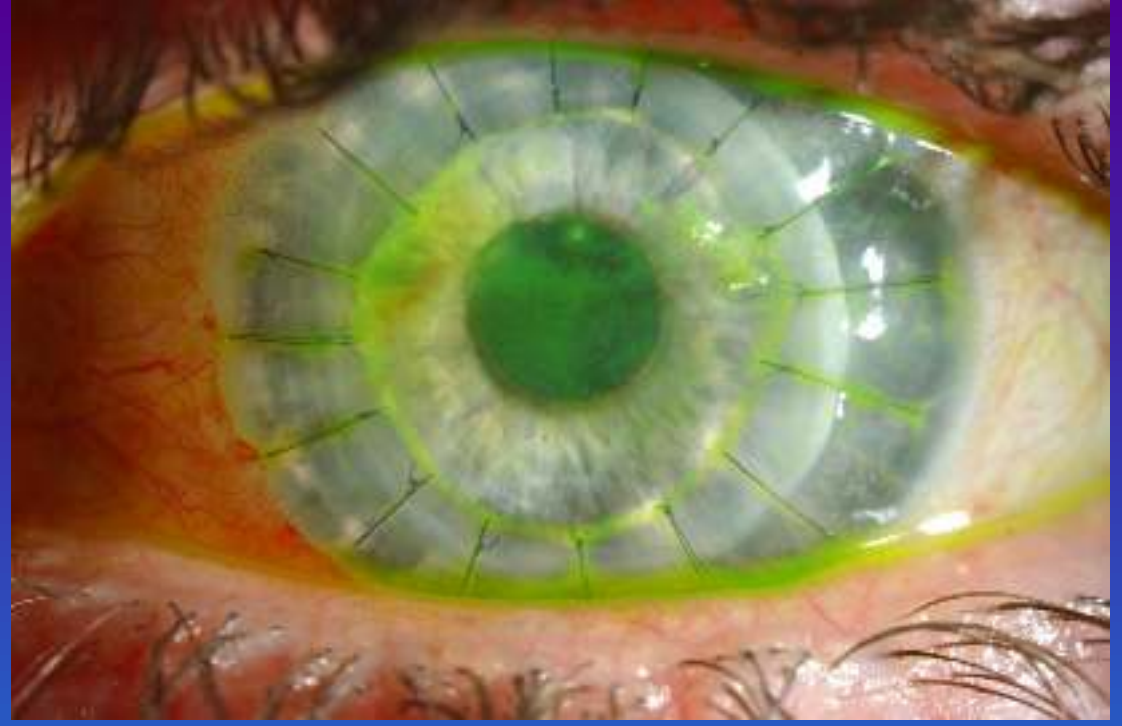

Amniotic membrane stack graft



Vessel occlusion

- Argon laser occlusion attempted
- Fine Needle Diathermy
- Collagen cross linking
- Intravascular mitomycin C injection
- Large PK with all its risks





Penetrating Keratoplasty in HSVK

Recurrence of Dendritic lesion in graft - usually near Graft-Host junction.

Non-healing epithelium

DALK wherever possible

Interrupted sutures over continuous

Donor sizing – graft host bed disparity

Balance of steroids and antivirals

Look out for epithelial defects and manage appropriately

Herpes simplex virus keratitis: Summary

Clinical features can be classical or indeterminate. Reduced corneal sensations are important. Stromal thinning is common.

Commonest cause of corneal vascularisation / lipid keratopathy.

Balance antivirals for epithelial, antivirals and steroids for stromal. Antivirals –topical and/or oral (prophylaxis).

Corneal graft are high risk of rejection / failure.

Recurrences are common

Masquerade: HSVK ↔ Other diseases.

THANK YOU