

# Top Ten Drugs: What's in Your Cabinet

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# Two More Reasons for Practicing Forever



# Disclosure

- I am a consultant for or on the Medical Advisory Board of:
  - Allergan
  - Alcon
  - Novartis
  - Advanced Vision Research
  - TLC Laser Center
  - Carl Zeiss Meditec
  - Synemed
  - IDOC
  - PRN  
Bausch Health
  - Mati

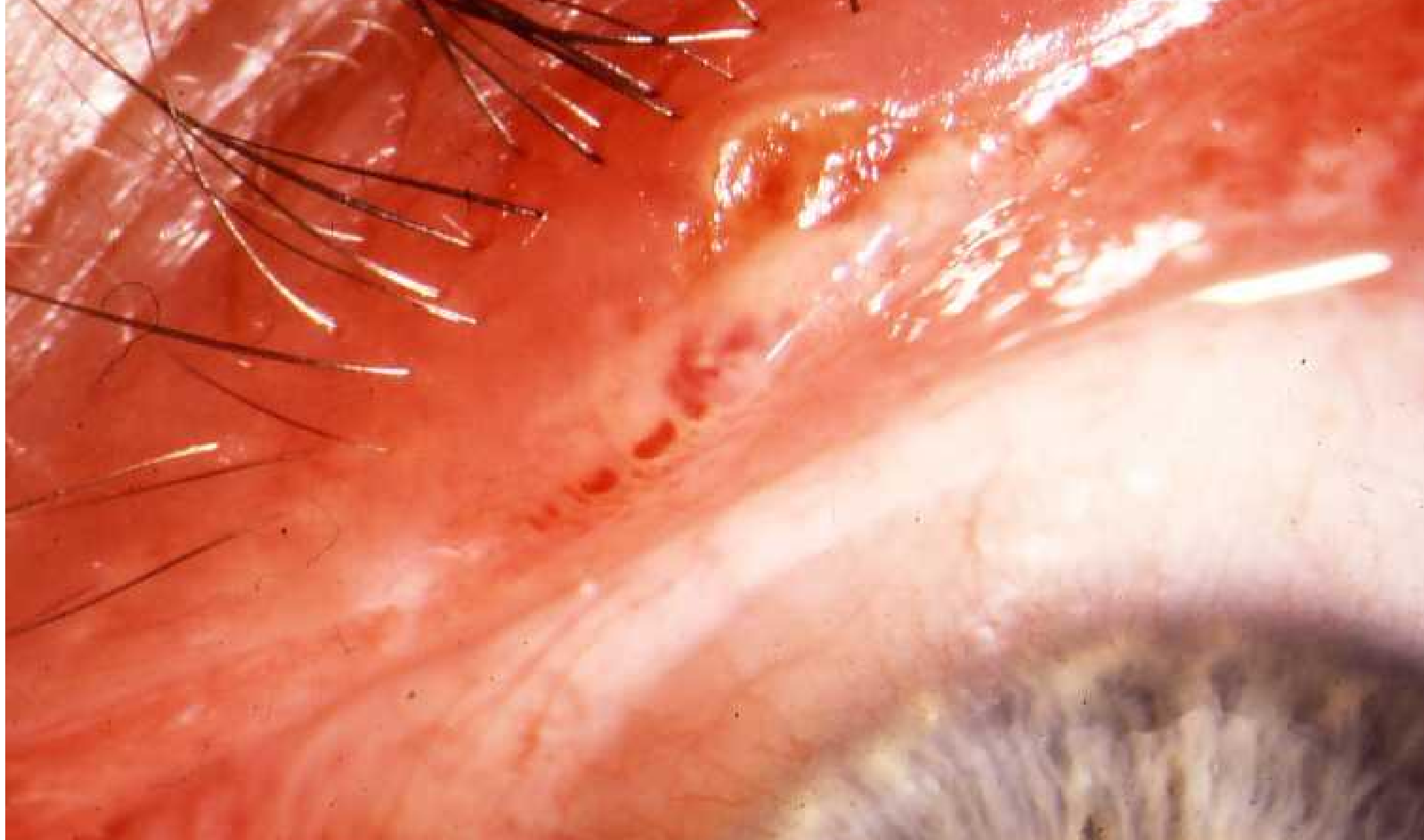
# ANTI-VIRALS

- ACYCLOVIR
- FAMVIR
- VALTREX



# ANTI-VIRALS

- CLINICAL APPLICATIONS
  - ACUTE VS CHRONIC INFECTION
  - PRIMARY LESIONS
  - EPITHELIAL HERPES SIMPLEX
  - STROMAL HERPES SIMPLEX
  - HERPES ZOSTAR
  - HERPETIC IRIDOCYCLITIS







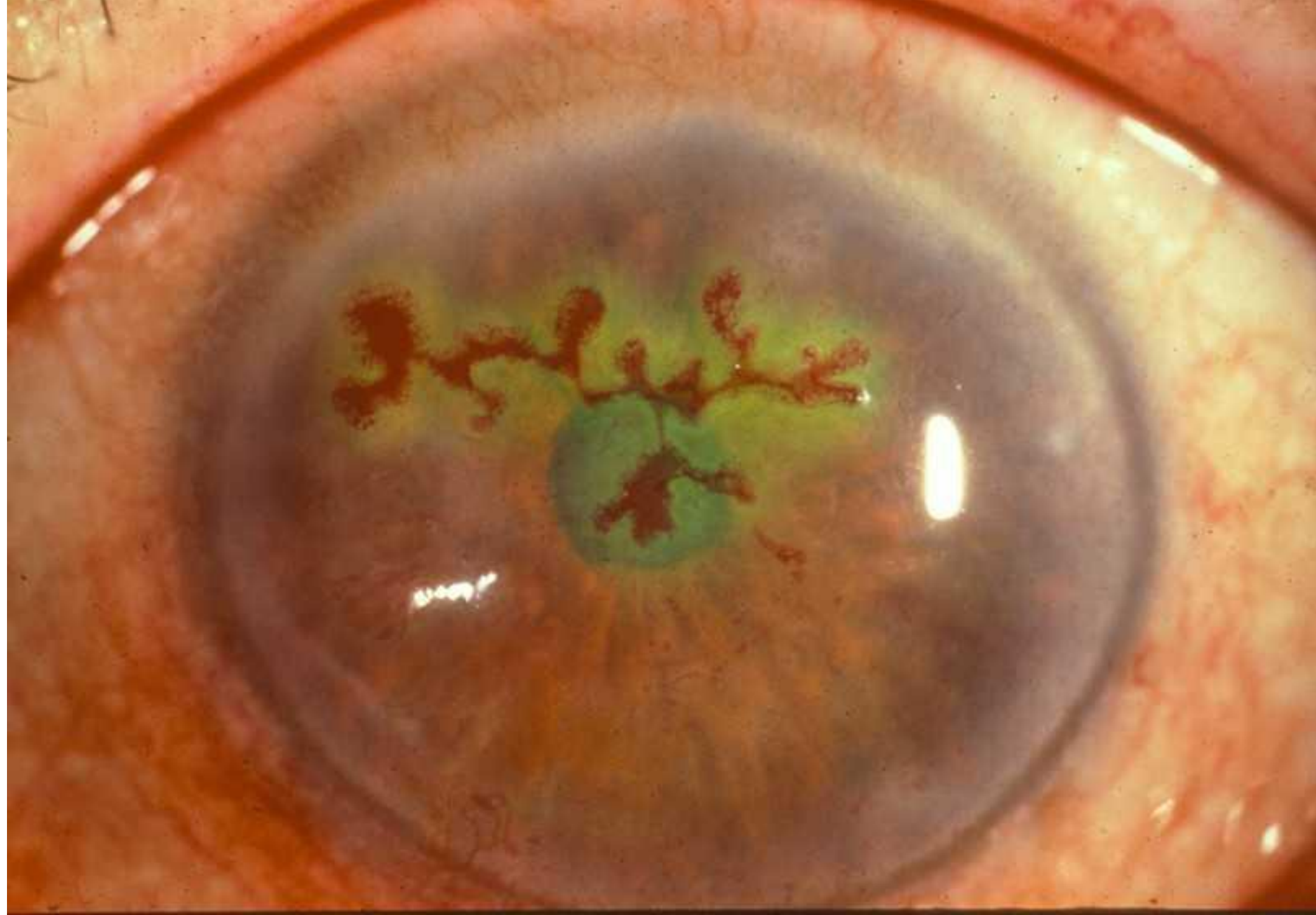




# ANTI-VIRALS

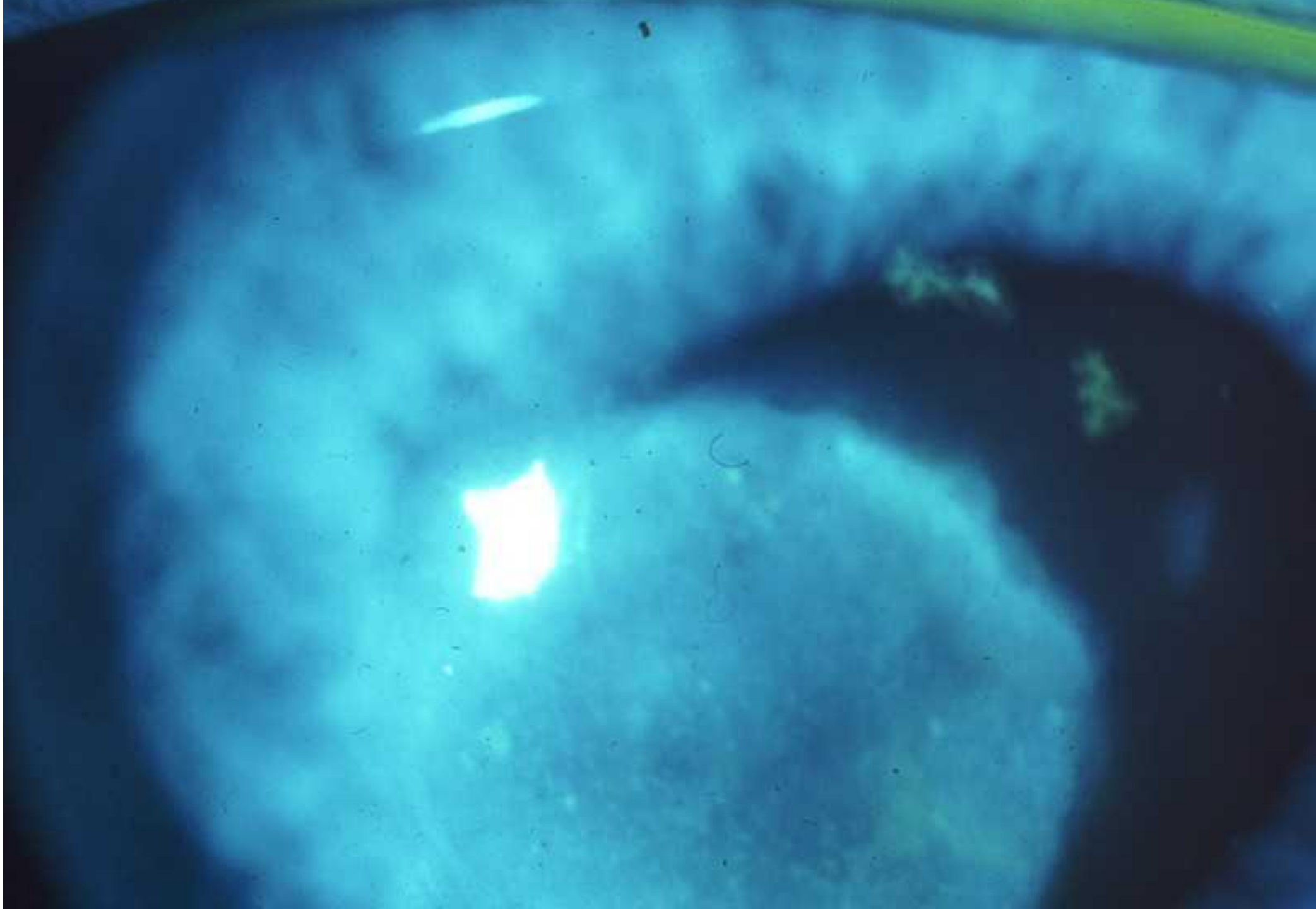
- SIDE EFFECTS
  - RENAL FAILURE/ IMPAIRMENT
  - HYPERSENSITIVITY REACTIONS
  - FACIAL EDEMA
  - VISUAL HALLUCINATIONS



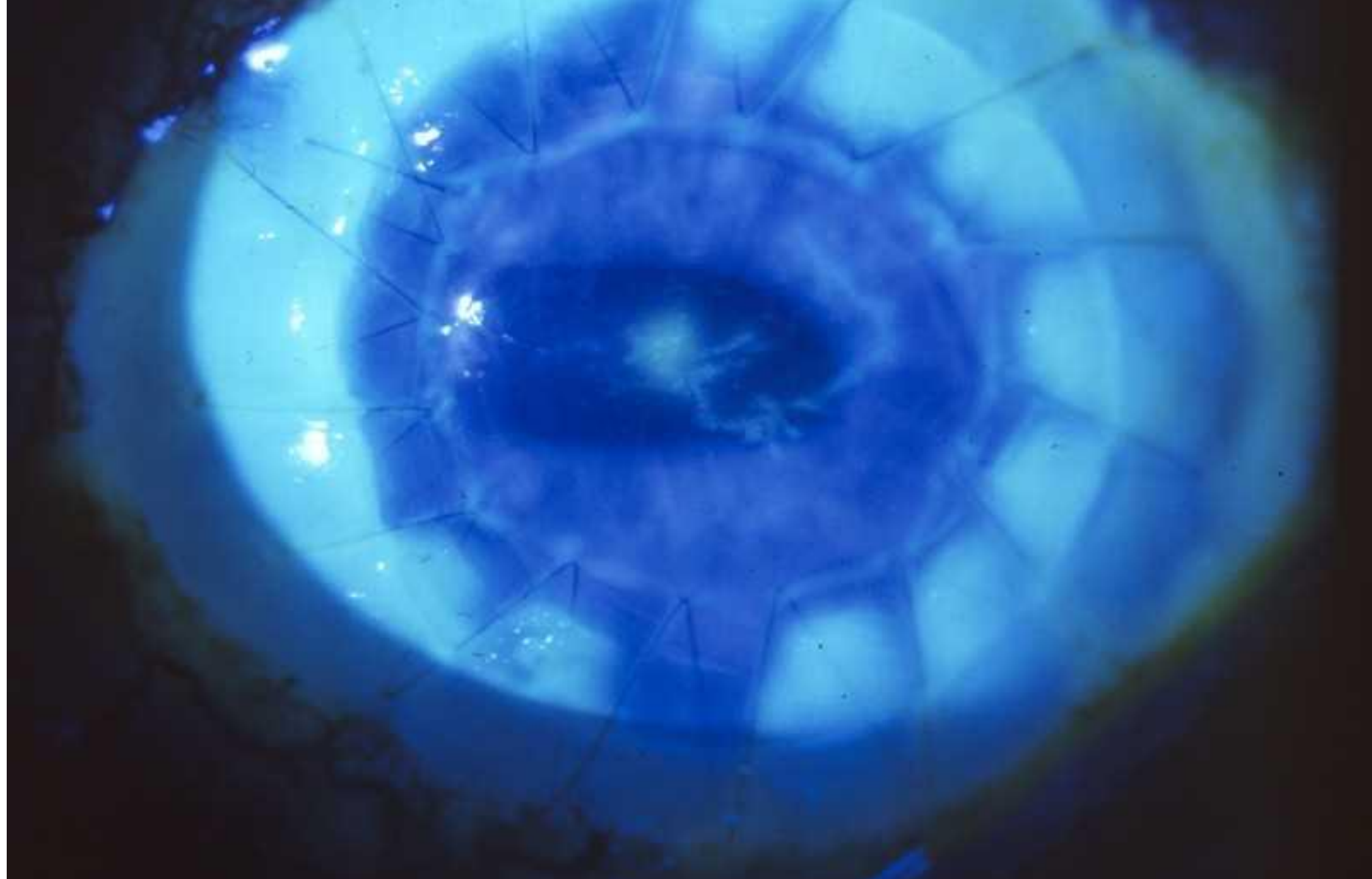






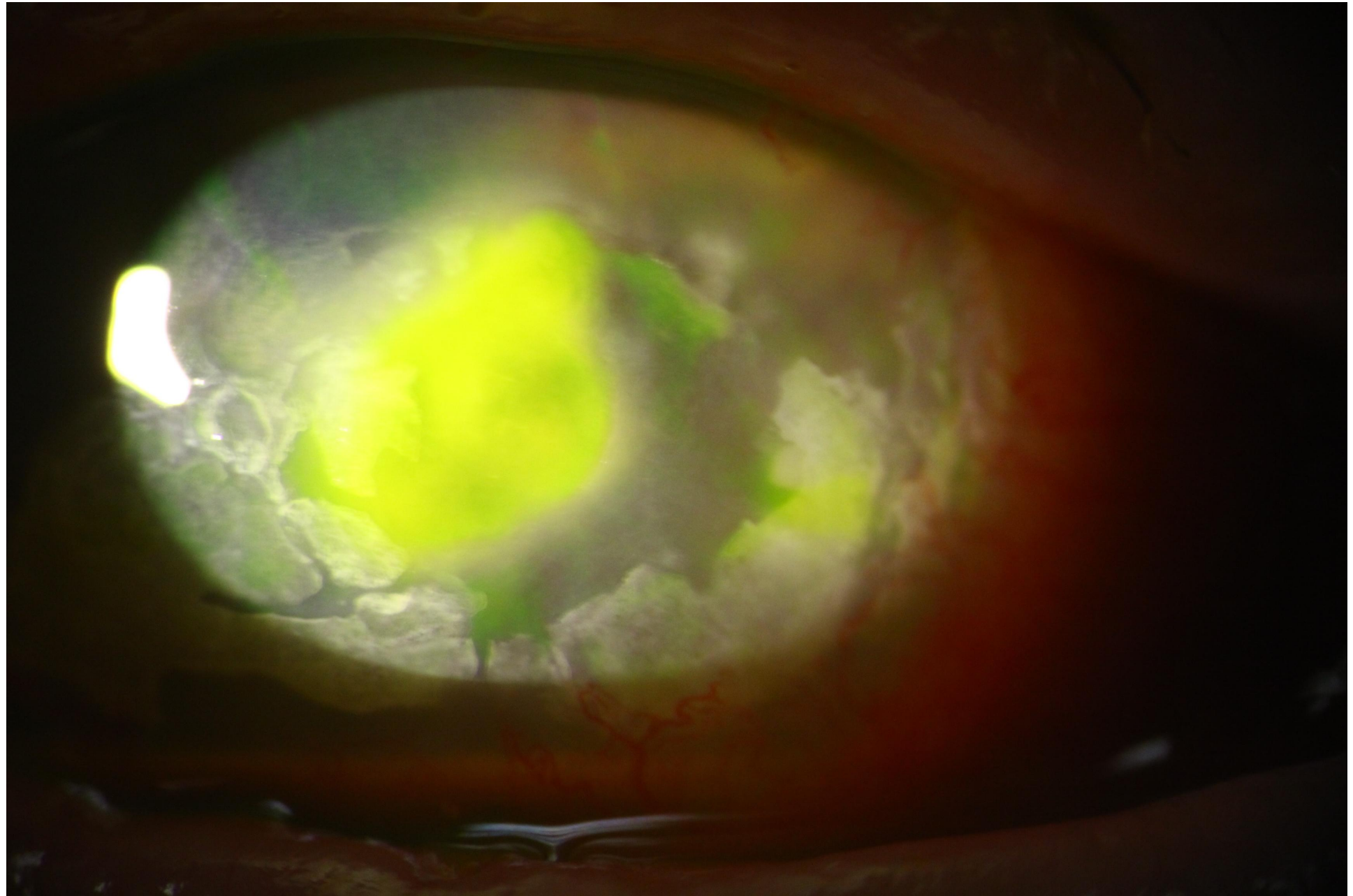


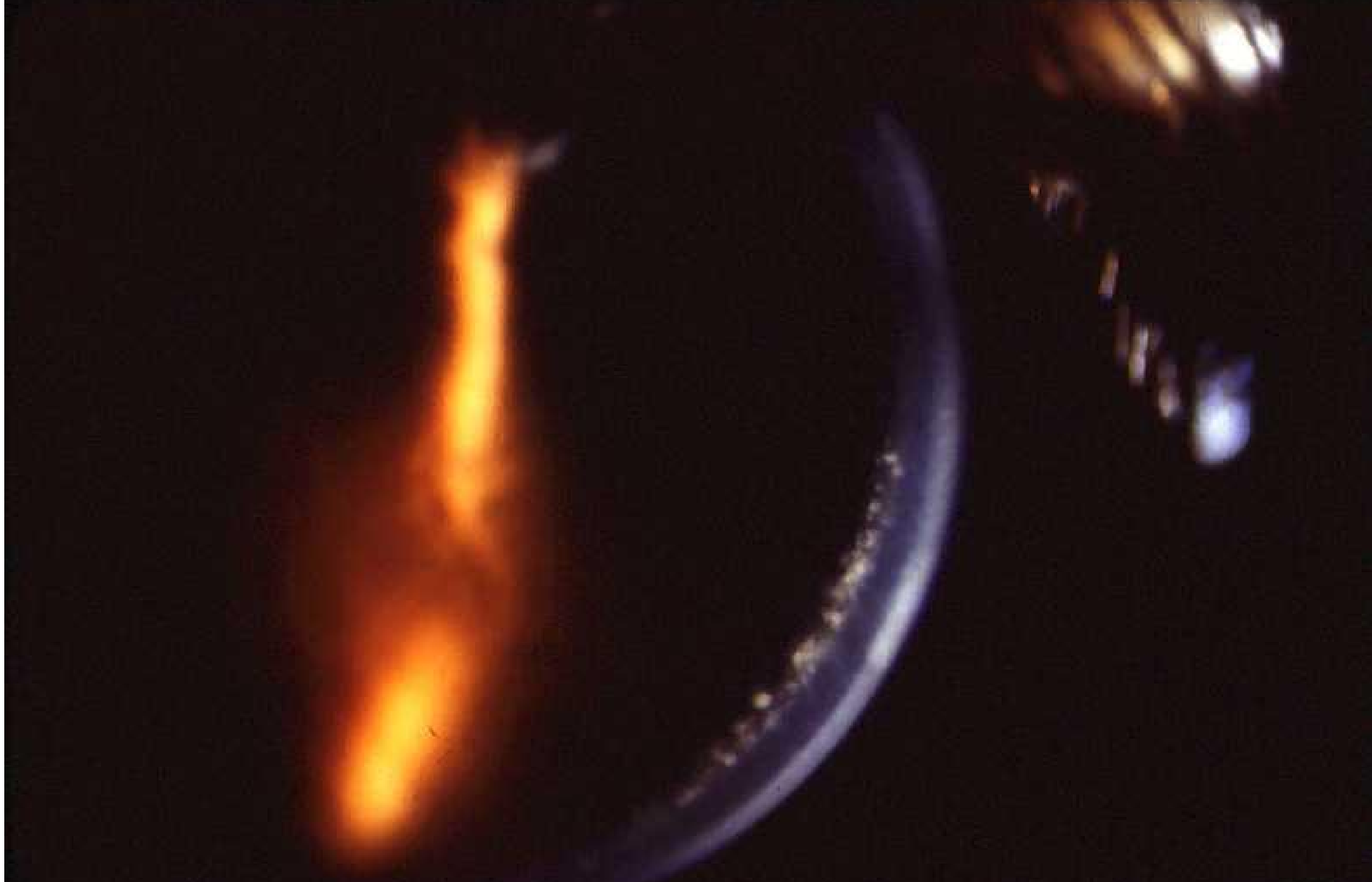












# VARICELLA ZOSTAR- KERATITIS

- PRIMARY INFECTION
  - CHICKEN POX
  - VACCINATION RECOMMENDED BY AMERICAN ACAD of PEDIATRICS
- RECURRENT INFECTION
  - OPHTHALMIC INVOLVEMENT 10-25
  - OPHTHALMIC ZOSTAR > OVER AGE 60









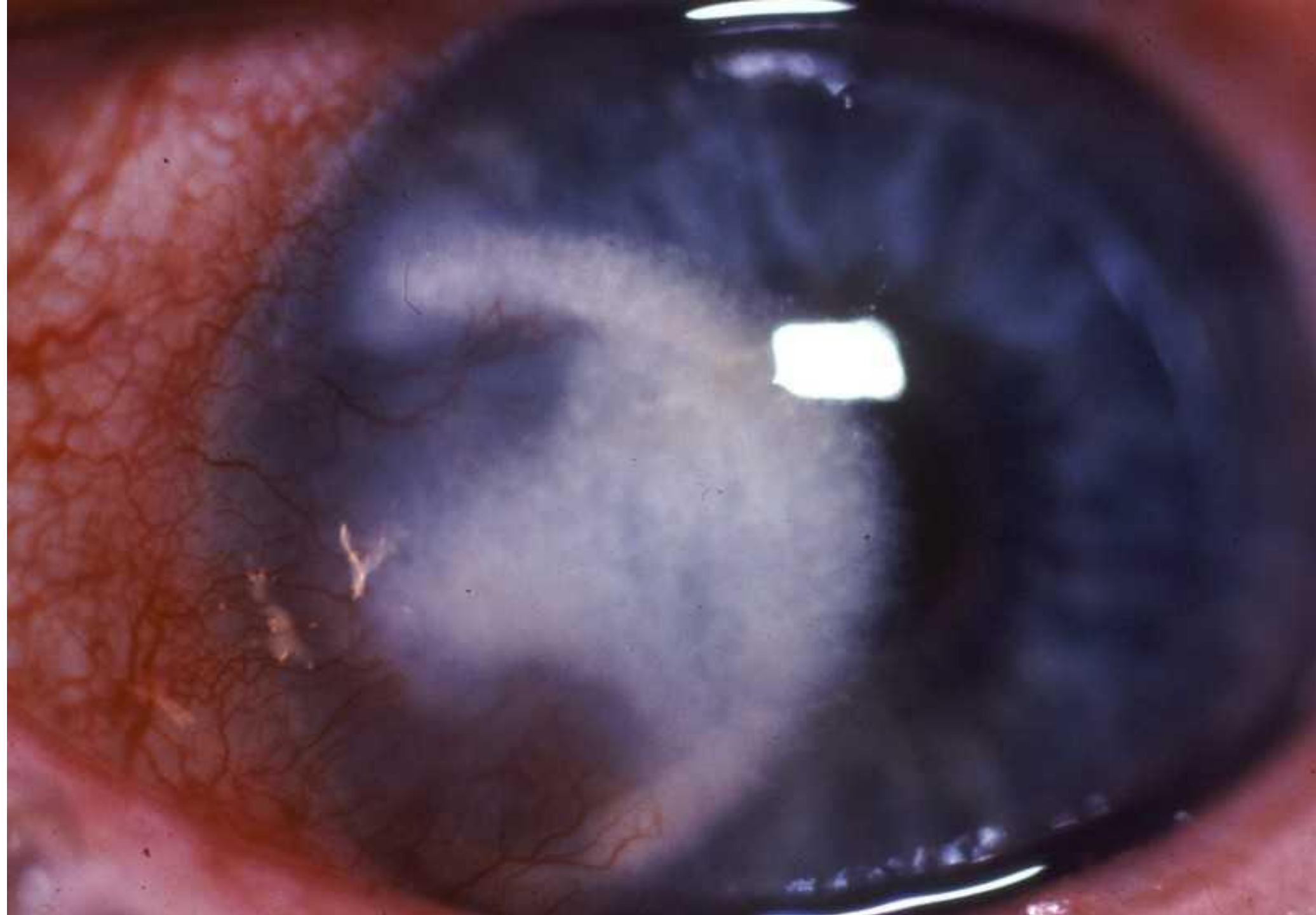




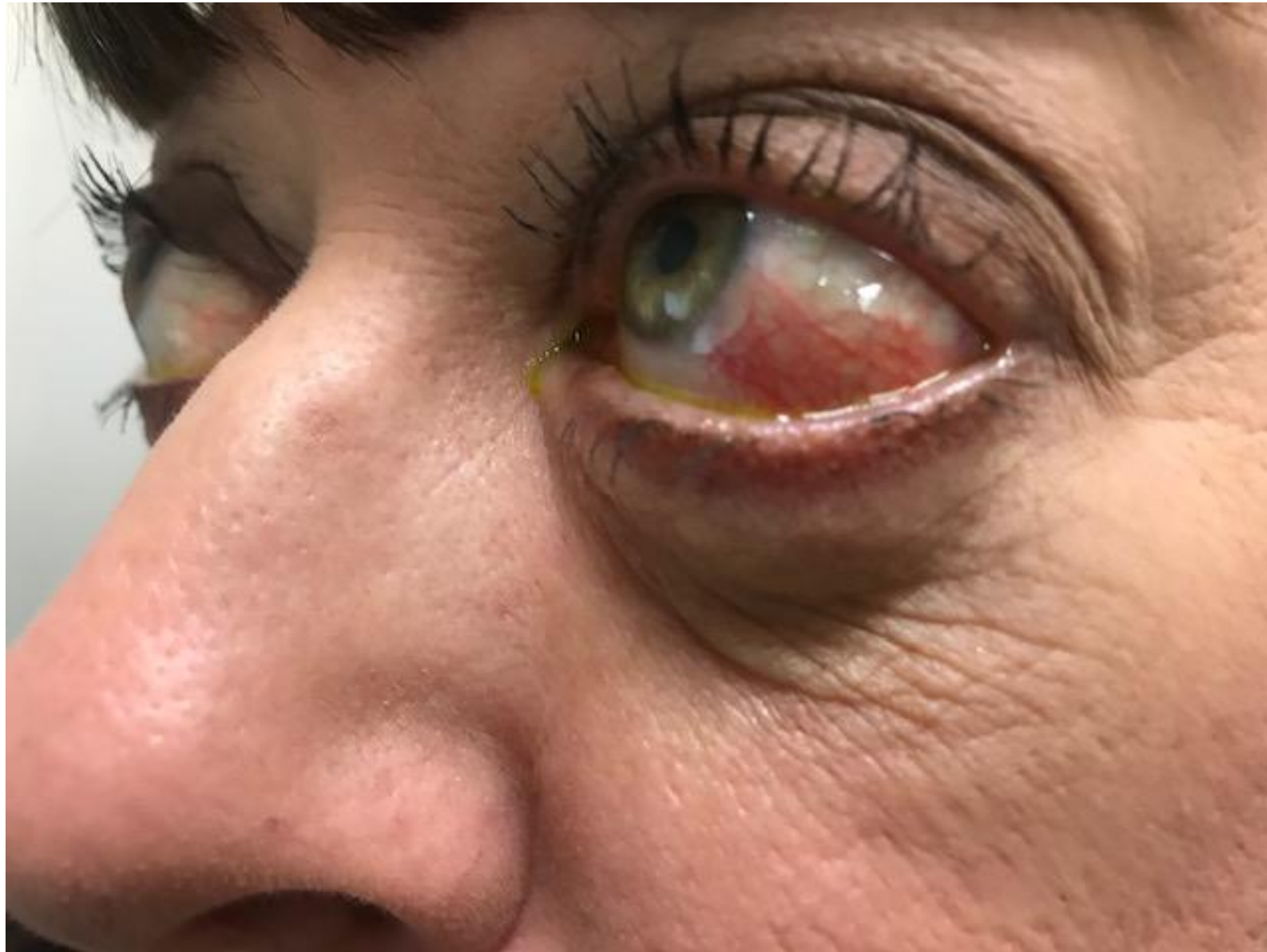








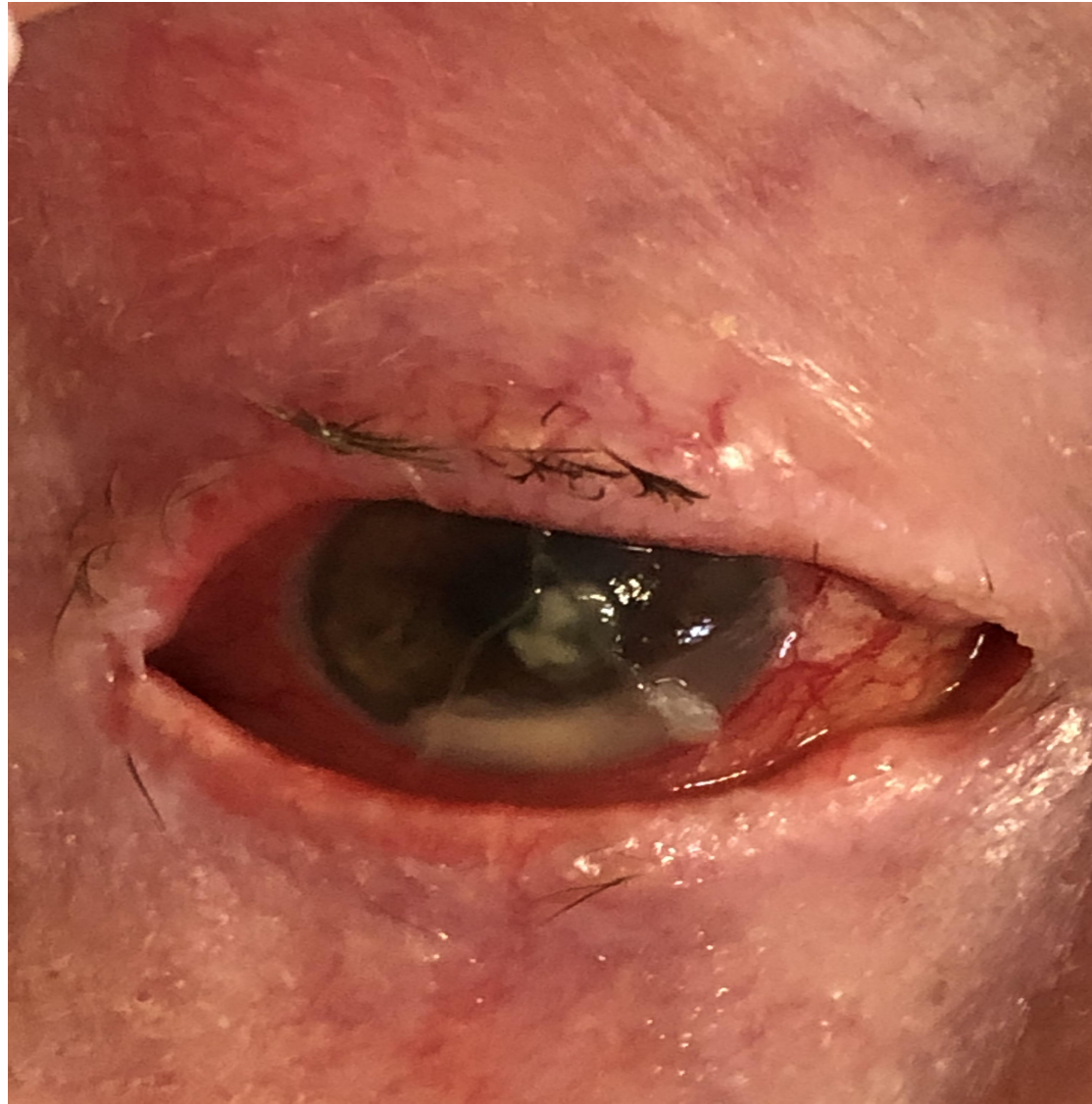




# HZK Keratitis

- Herpes zoster (shingles) is an infection caused by re-activation of the varicella zoster virus, which causes chickenpox. Primary infection usually happens in childhood.
- After the primary infection, the patient is immune to the virus, which then lies inactive in the dorsal root ganglia or cranial ganglia.
- Eventually, as the patient's natural immunity reduces as a result of ageing or disease, the virus can reactivate and spread to the skin, via the afferent nerves, to cause herpes zoster.
- By the time they are 40 years of age, the vast majority (99.6%) of individuals worldwide have antibodies to varicella zoster virus and are therefore at risk of herpes zoster.<sup>[1](#)</sup>

# HZK Keratitis



# HZK Keratitis



# HZK Keratitis/ Uveitis

- Patients can develop complete corneal anesthesia after HZO, known as neurotrophic keratitis. This can lead to sight loss, as the anesthetic cornea is at risk of developing an epithelial defect, secondary infection, vascularization and scarring.
- Frequent lubricating drops are helpful to prevent epithelial breakdown. A chronic epithelial defect may heal with a temporary tarsorrhaphy, bandage contact lens or amniotic membrane graft.
- Unfortunately, a proportion of patients eventually require a permanent tarsorrhaphy or conjunctival flap to protect the eye.
- Severe post-herpetic neuralgia may be helped by giving oral analgesics, anticonvulsants (e.g., gabapentin) or tricyclic anti-depressants.



# The Cyclines

- Tetracycline, Doxycycline and Minocycline
  - Isolated from Streptomyces
  - Effective against Gram +/ Gram -/Aerobic/ Anerobic/  
Spirochetes/Rickettsia/Chlamydia
  - Similar action / different duration

# Tetracyclines

- Tetracycline (Sumycin)
- Doxycycline (Vibramycin)
- Coated doxycycline (Doryx)

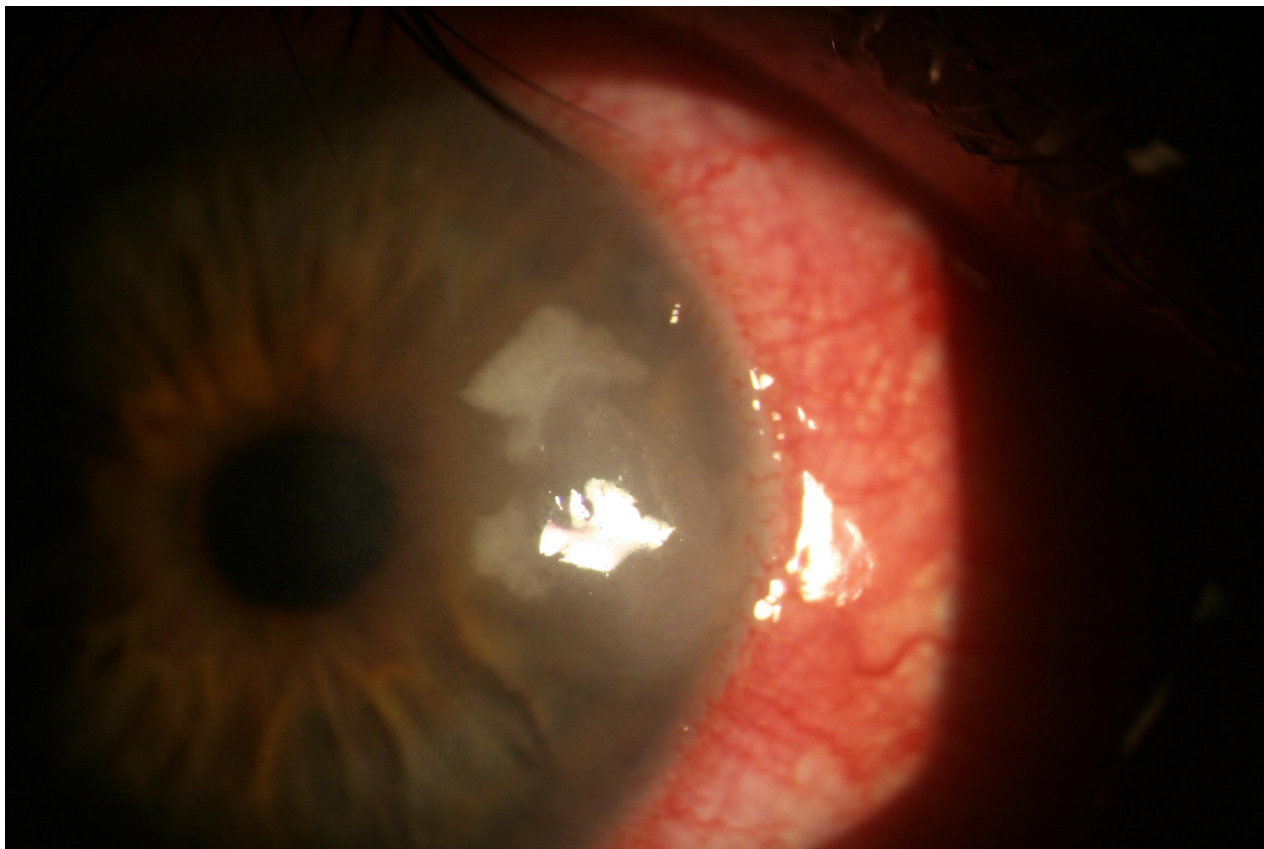
# Doxycycline (Vibramycin)

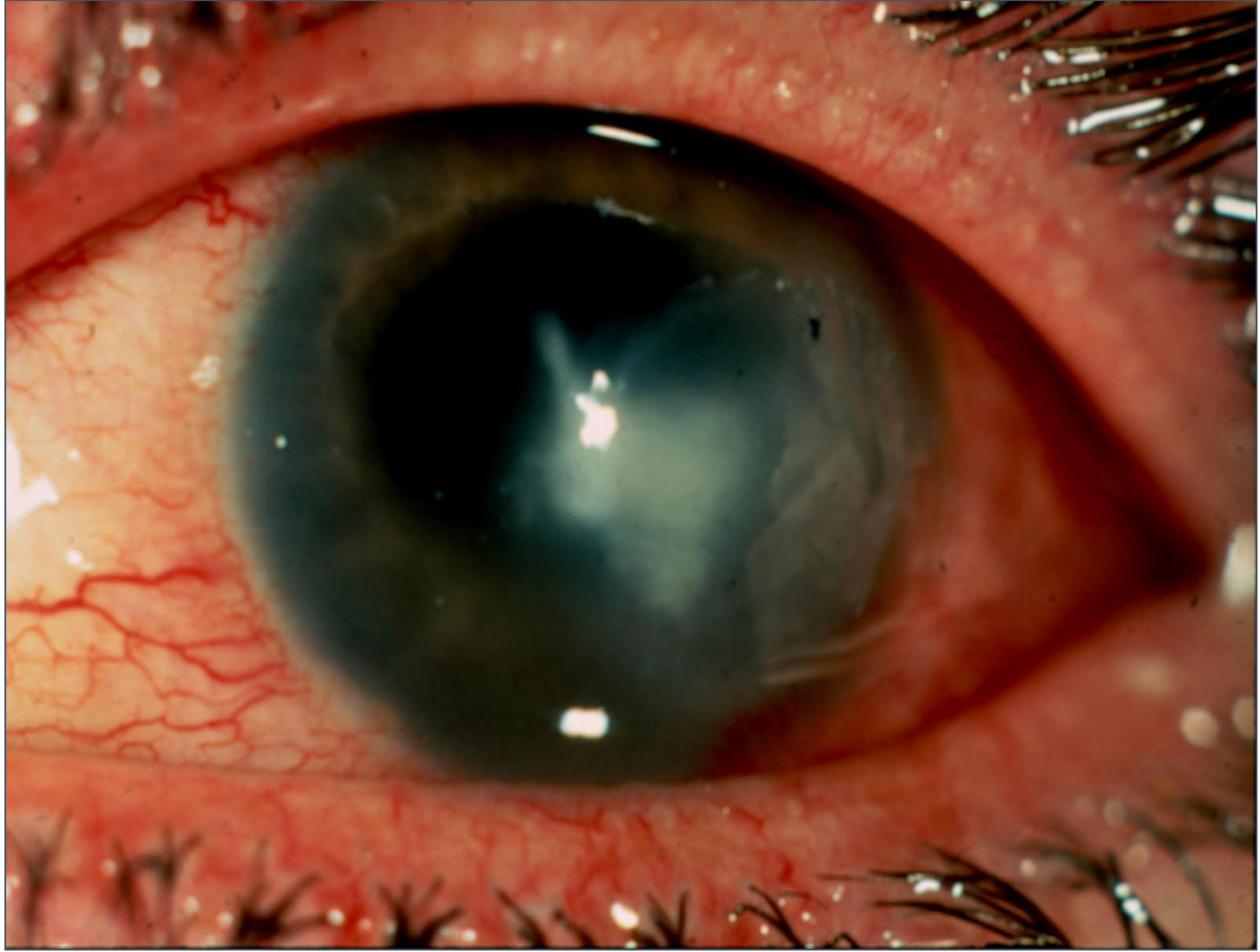
- Formulations
  - 50mg, 100mg capsules: 100mg tablet: suspension 25/tbs: syrup 50mg/tsp
- Dosages
  - 50mg, 100mg q.i.d
- Oracia
  - 40 mg sustained release/ regular
- Periostat
  - 20 mg
  - Most common use in dentistry

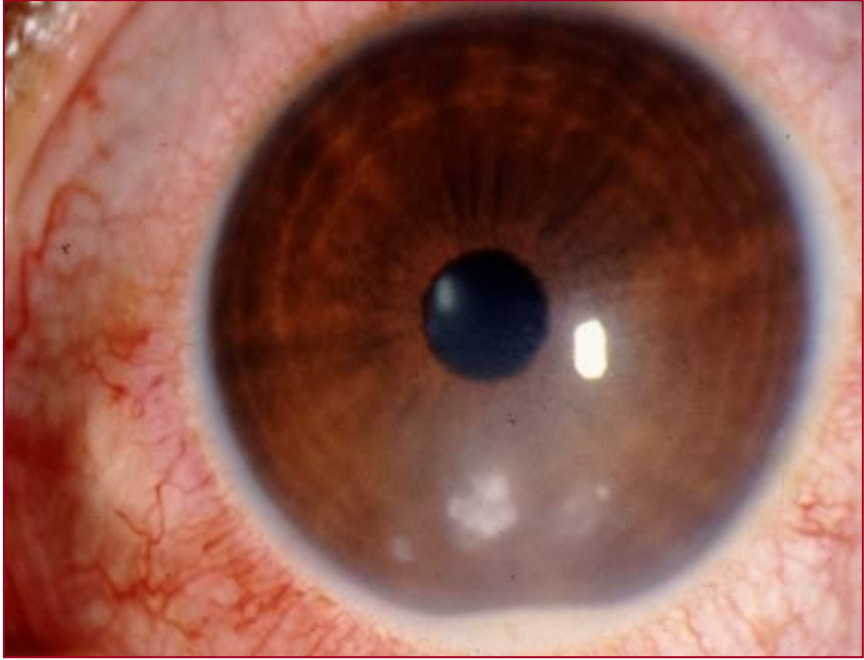


# The Cyclines

- ▶ Clinical Applications
  - ▶ Brucellosis
  - ▶ Rickettsia ( Rocky Mountain Spotted fever)
  - ▶ Lyme Disease
  - ▶ Chlamydia/ Trachoma
  - ▶ Primary Meibomianitis
  - ▶ Gonococcal Prophylaxis
  - ▶ “Corneal melting” Syndrome
  - ▶ Non Healing Corneal lesions
  - ▶ Rosacea















# MK Treatment Protocol

- Gram negative coverage
  - Fluoroquinolone
  - Fortified Tobramycin
- Gram positive coverage
  - Polytrim
  - Fortified Vancomycin
- Night time
  - Neosporin unguent
- Oral
  - Doxycycline
  - Vitamin C

# Oral Antibiotics

- PCN's
- Cephalosporin's
- Macrolides

# Oral Agent Therapy

## Posterior Blepharitis

- ▶ Hordeola
- ▶ Canaliculitis
- ▶ Conjunctivitis
- ▶ Keratitis
- ▶ Dacryocystitis
- ▶ Dacroadenitis
- ▶ Preseptal/orbital cellulitis
- ▶ Endophthalmitis



# Bacterial Flora of the Normal Eye/Adults

|                                     |             |
|-------------------------------------|-------------|
| Staphylococcus <i>epidermidis</i>   | 75-90%*     |
| Diphtheroids ( <i>C. xerosis</i> )  | 20-33%      |
| Staphylococcus <i>Aureus</i>        | 20-25%*     |
| Streptococcus ( <i>S. viridan</i> ) | 2-6%        |
| Hemophilus influenza                | 3% or more  |
| Streptococcus <i>pneumoniae</i>     | 1-3%*       |
| Gram negative rods                  | 1% or more* |
| Pseudomonas <i>aeruginosa</i>       | 0-5%*       |

\* *Dominant organisms in microbial keratitis*

# Body Depots of Bacterial Organisms

- ▶ Skin: Lids/hands: Staph/Gr. (+)
- ▶ Nose/nasopharynx: Staph and GR (+)
- ▶ Kids: Hemophilus
- ▶ Oropharynx: Staph and StrepGr (+)
- ▶ Mouth: Strep/Bacteroides
- ▶ Stomach: Helicobacter pylori and rosaceae
- ▶ Small Intestine: Gr (+) cocci and bacilli
- ▶ Large intestine: Greatest conc of bacteria in body (10<sup>11</sup> organisms/gm) anerobes-enterobacteria, enterococcus feacalis, E. coli
- ▶ Genito-urinary tract: Chlamydia, E. coli, Neisseria gonorrhoea (Ophthalmia neonatorum)

# Bacterial Conjunctivitis

- In adults, 75% of cases caused by Gram positive pathogens
  - *Staphylococcus epidermidis*, *S. aureus*, *Streptococcus pneumoniae*
- Very common in children under 6 years
- Causal agents of pediatric cases:
  - 42% *Haemophilus influenzae*
  - 35% *S. pneumoniae*

# Gram (-) species

- Pseudomonas
- Hemophilus
- Klebsiella
- Serratia
- Moraxella
- Neisseria

# Important Penicillin's

- ▶ Ampicillin: Broad spectrum oral-QID dosing
- ▶ Amoxicillin: Pro-drug of Ampicillin, improved absorption with lower GI side-effects
- ▶ Cloxacillin/Dicloxacillin: Intrinsic beta-lactamase resistance
- ▶ Augmentin: Amox + Clavulanate
- ▶ Methicillin: IV prep for penicillinase producers
- ▶ Amp + Sulbactam: Unasyn: IV
- Ticarcillin + Clavulonic acid: IV better penicillinase protection than methacillin



# Augmentin

## Amoxicillin/Clavulanate

- ▶ Broad spectrum penicillin (Staph, Strep, Hemophilus)
- ▶ Effective against penicillinase producers-clavulanate blocks penicillinase@@@
- ▶ High therapeutic index
- ▶ Bacteriocidal
- ▶ Low GI side-effects
- ▶ Safe in pregnancy
- ▶ Watch out for allergy
- ▶ Cheap\*\*\*

# Wow! What Happened While I was Asleep?

- JR a 23 year old Caucasian female awoke with a pain, swelling and a pulsing ache over her left eye.
- Pt. denies h/o trauma, prior occurrence or vision loss.
- PEX: VA 20/20 OD , 20/20 OS
- EOM: Full without pain
- VF: CFTFC/ OU

# Wow: What Happened While I Was Asleep?

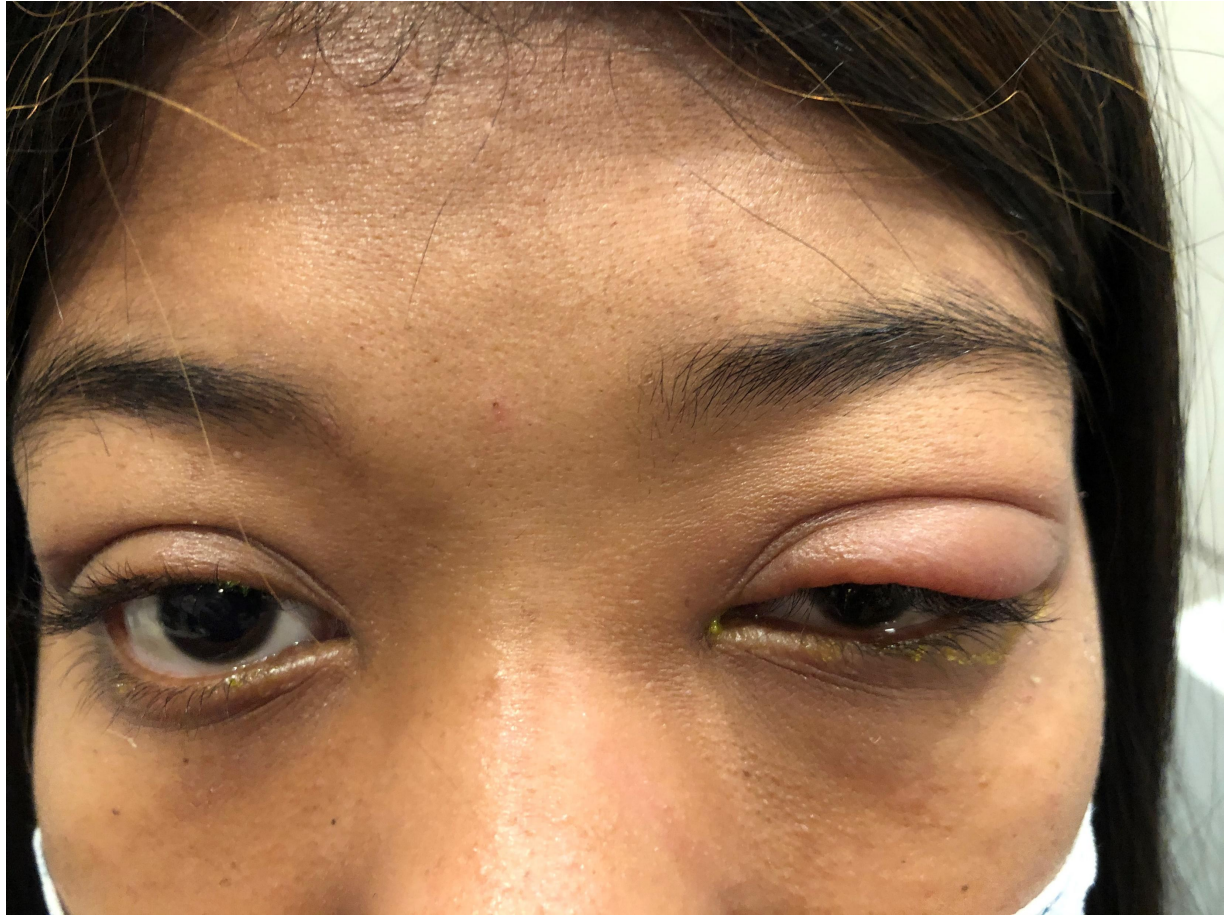
- Ta: 18/19
- SLE: 2+3 Tender lid edema. Cornea clear, AC=D&Q. Negative discharge.
- DFE: 0.2 OU
- Dx: ?
- Tx:























# Keep Your Eyes Open!





# Another Look at MRSA!

- Asbell, P; Topics in Ocular Antiinfectives
- Ocular TRUST II 2008 ( Tracking Resistance in United States Today)
- 155 ocular isolates in US sent to reference labs for centralized in vitro testing
- 84/155 ( 54%) were Methicillin resistant compared to Ocular TRUST I 2005 data which showed predominant response to be Methicillin sensitive.
- MSSA Sensitivities:
  - Trimethoprim 97%
  - Tobramycin 95%
  - FQ's 93%
  - Azithromycin 62%
- MRSA Sensitivities:
  - Trimethoprim 95%
  - FQ's 18%
  - Tobraymycin 50%
  - Azithromycin 8%
- Strep P. Sensitivities
  - FQ's 100%
  - Trimethoprim 80%
  - Tobramycin 2%
- H Flu Sensitivities
- All drugs 100% except Trimethoprim @ 85%

I Just Wanted to Look a Little Better



# One Week Later





2 Weeks Later





MRSA



**MRSA**



# Plan B: The Cephalosporins

- Mechanism: Same as penicillin
- Bacteriostatic
- Low toxicity
- 3% allergic to pen are allergic to Ceph.
- Better penicillinase resistance than penicillins

# Know Your Generations

First Generation: Good GR (+) activity against penicillinase producers/poor Gr (-) activity especially Hemophilus (children)

- Cefadroxil: Duricef-PO
- Cephazolin: IV- Ancef- Keratitis
- Cephalexin: PO-Keflex
- Cephadrine: PO- Velosef

Second Generation:  
Greater Gram (-) activity,  
especially Hemophilus

- ▶ Cefaclor: PO-Ceclor
- ▶ Cefuroxime: PO-Ceftin

Third Generation: Reduced GR (+) activity (Staph sp) with  
marked Gr (-) activity

- ▶ Cefixime: PO- (Suprax)
- ▶ Cefpodoxime: PO - Vantin
- ▶ Cefprozil: PO - Cefzil

# Pre-Septal Considerations

- ▶ JAMA 2013 Dec.
- ▶ Dual cohorts of 95,000 each, older adults (mean 76) who were users of Calcium Channel Blocker's
- ▶ Clarithromycin (inhibits CYP3A4 which can cause increased CCB levels) vs: Azithromycin ( non inhibitor)
- ▶ Measured for 30 days post treatment
  - ▶ Risk for hospitalization 0.44% vs 0.22% due to acute kidney injury
  - ▶ All cause mortality 1.02% vs.0.59%



# Azithromycin (Zithromax)

- Formulations
  - 250mg, 500mg 600mg tablets: suspension 100mg/5ml, 200mg/ml Z-PAK six 250 mg tablets, TRI-PAK three 500mg tablets
- Dosages
  - 1 gm one dose administration for *Chlamydia*: 500mg q.d. followed by 250mg q.d for four days

# Fluoroquinolones

- **Levofloxacin (Levaquin)**
- **Ciprofloxacin (Cipro)**
- **Gatifloxacin (Tequin)**
- **Moxifloxacin (Avelox)**

# Fourth Generation FQ's & Diplopia

- Ophthalmology; Sept. 2009; Oregon Health Sciences
- 171 cases of diplopia associated with FQ use
- 76 men/ 91 women/ 4 non-gender
- Median dose was wwnl for package insert recommendations
- Median time to onset 9.6 days
- Meds d/c in 53 patients all resolved
- WHO rating: Possible
- Mechanism? Tendinitis of the EOM

# STEROIDS

- INHIBIT PROSTAGLANDIN AND LEUKOTRIENE ACTIVITY BY BLOCKING ACTION OF ENZYME PHOSPHOLIPASE A2.

# Steroids

- 99 % topical use in eye care
- Medrol Dose Pack most common
- Pred Forte Generic since January 2009
- Lotemax/ Alrex & Durezol

# Clinical Applications

- Scleritis
- Dermatitis
- Severe anterior uveitis
- Posterior uveitis
- Inflammatory preseptal cellulitis
- Progressive thyroid eye disease
- DLK



# Methylprednisolone (Medrol)

- Formulation
  - 2mg, 4mg, 8mg, 16mg, 24mg and 32mg tablets
  - Medrol Dose Pak 21 4mg tablets
- Dosage
  - Varies based on condition

# Prednisone (Deltason)

- Formulation
  - 2.5mg, 5mg, 10mg, 20mg and 50mg tablets; 5mg/5ml solution/syrup
- Dosage
  - Varies based on condition









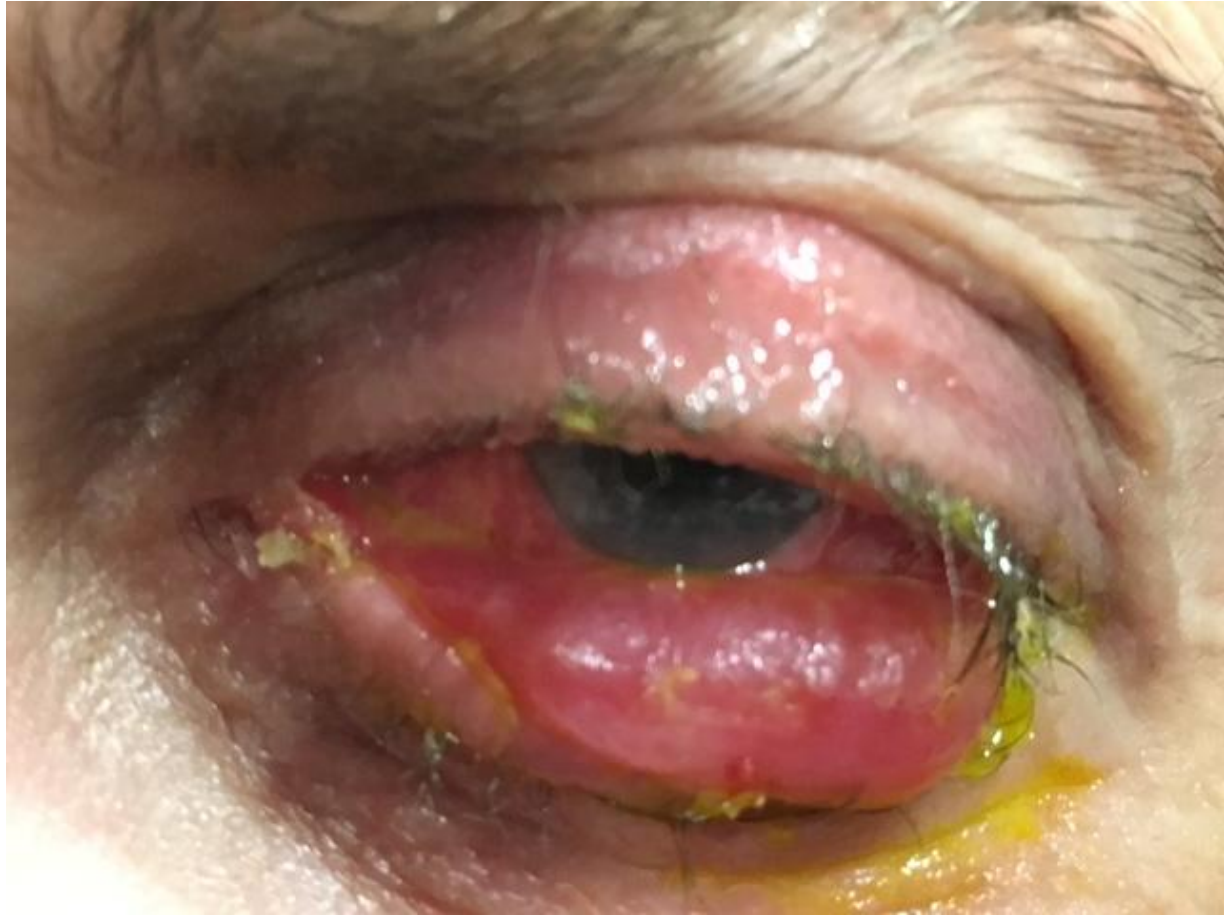














# Interesting Steroid Facts

- In steroid responders, onset of IOP elevation occurs after about two weeks of use
- Time of onset often longer for systemic steroids
- Complex pathophysiologic factors result in increased resistance to aqueous outflow



# New Therapies for “ Old” Diseases

- Oxervate
- Regenerize

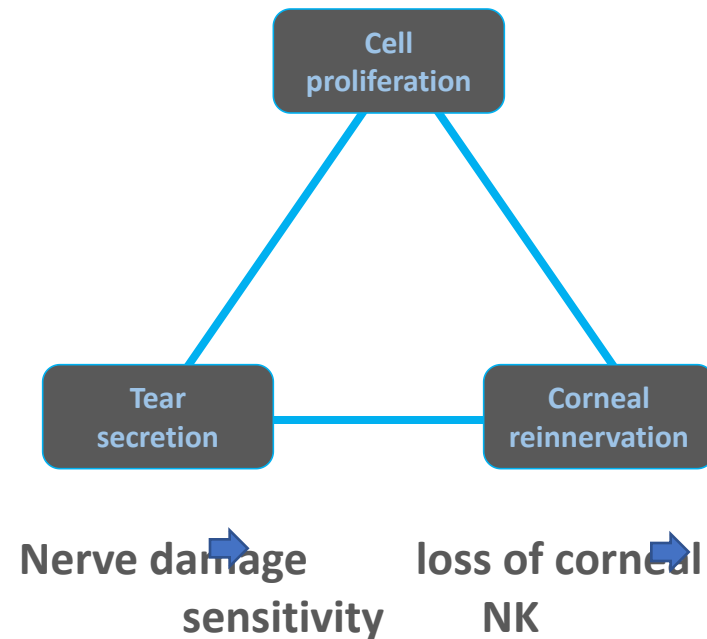
# OXERVATE

## Endogenous nerve growth factor (NGF) and its role in NK:

Neurotrophic keratitis (NK) is a result from **impaired trigeminal corneal innervation**

- ↓ Lacrimation and blink reflex
- ↓ Epithelial cell vitality, metabolism, mitosis
- ↓ Epithelial trophism and repair
- ↑ Stromal and intracellular edema
- ↓ Microvilli
- ↓ Development of the basal lamina

Endogenous NGF maintains corneal integrity by three mechanisms



# Cenegermin-bkbj: Recombinant human NGF (rhNGF)

## Proprietary treatment developed by Dompé

~10x more potent than murine NGF  
based on in vitro studies

### Phase I study (74 healthy subjects)

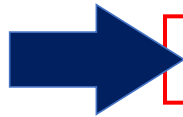
- Favorable safety and tolerability
- No immunogenicity and no significant changes in serum NGF

BioDrugs (2014) 28:275–283  
DOI 10.1007/s40259-013-0079-5

ORIGINAL RESEARCH ARTICLE

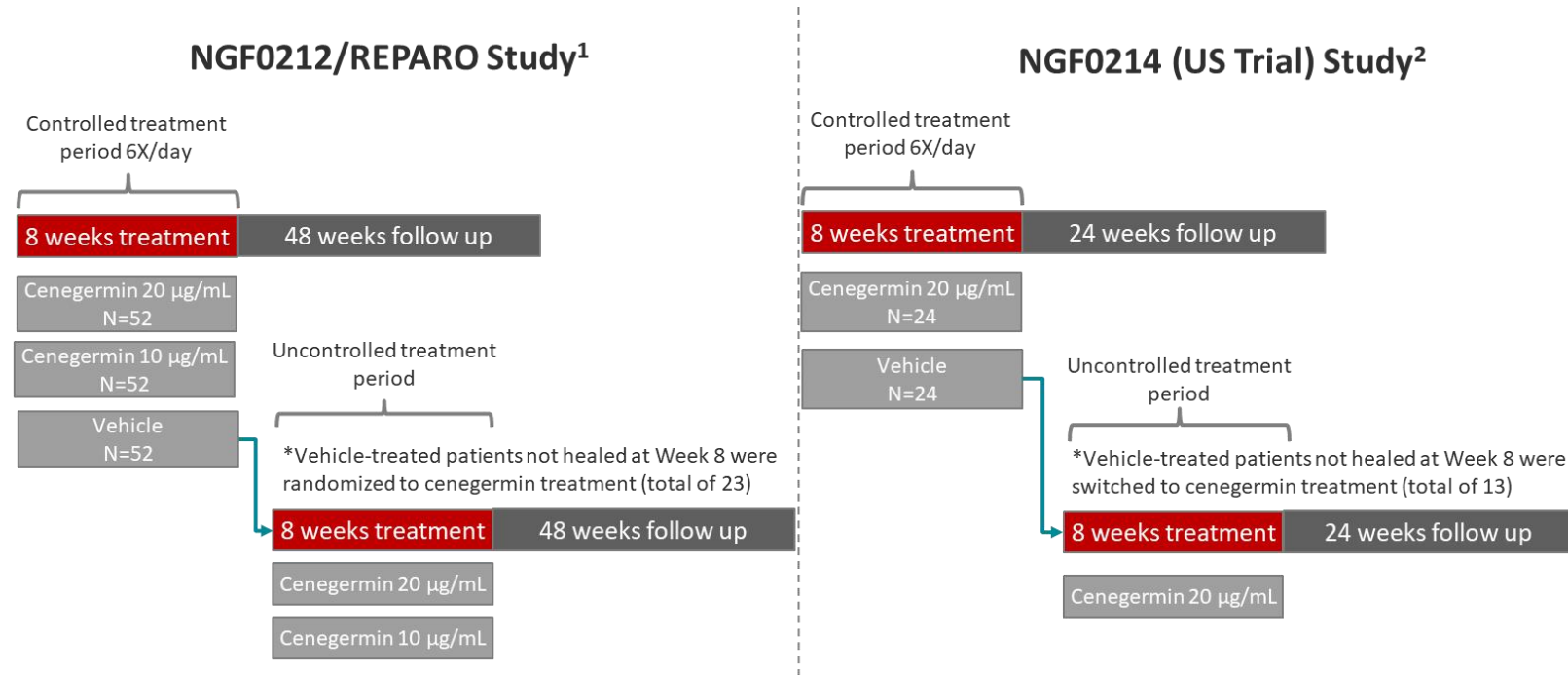
### Safety and Pharmacokinetics of Escalating Doses of Human Recombinant Nerve Growth Factor Eye Drops in a Double-Masked, Randomized Clinical Trial

Mauro P. Ferrari · Flavio Mantelli · Marta Sacchetti · Maria Irene Antonangeli ·  
Franca Cattani · Gaetano D'Anniballe · Francesco Sinigaglia · Pier Adelchi Ruffini ·  
Alessandro Lambiase



Resulting product: A more potent, patient-compatible NGF

# OXERVATE™ (cenegermin-bkbj) ophthalmic solution 0.002% Pivotal Trials Study Design



The primary efficacy endpoint, which was determined by a central reading center, was “complete corneal healing” defined as 0 mm staining in the lesion area and no persistent staining in the rest of the cornea

1. Bonini S, Lambiase A, Rama P *et al.* Phase II Randomized, Double-Masked, Vehicle-Controlled Trial of Recombinant Human Nerve Growth Factor for Neurotrophic Keratitis. *Ophthalmology* 2018;125:1332-1343.
2. Chao W, J. BDC, R. D *et al.* Data on file. Healing of persistent epithelial defects or corneal ulcers by recombinant human nerve growth factor eye drops in patients with stage 2 or 3 neurotrophic keratitis. Presented at: Congress of the European Society of Ophthalmology (SOE) 10–13 June, 2017, Barcelona, Spain. 2017.

# Study Criteria

## Main inclusion criteria

- Adult NK patients with stage 2 or 3 NK
- Unilateral NK only in NGF0212/REPARO
- Unilateral or bilateral NK permitted in NGF0214
- Evidence of decreased corneal sensitivity (<40mm by Cochet-Bonnet aesthesiometer) within the area of the PED or corneal ulcer and outside of the area of the defect, in at least 1 corneal quadrant
- Refractory to  $\geq 1$  nonsurgical tx
- No improvement in in 2 weeks prior to enrollment

1- ClinicalTrials.gov Identifier: NCT01756456

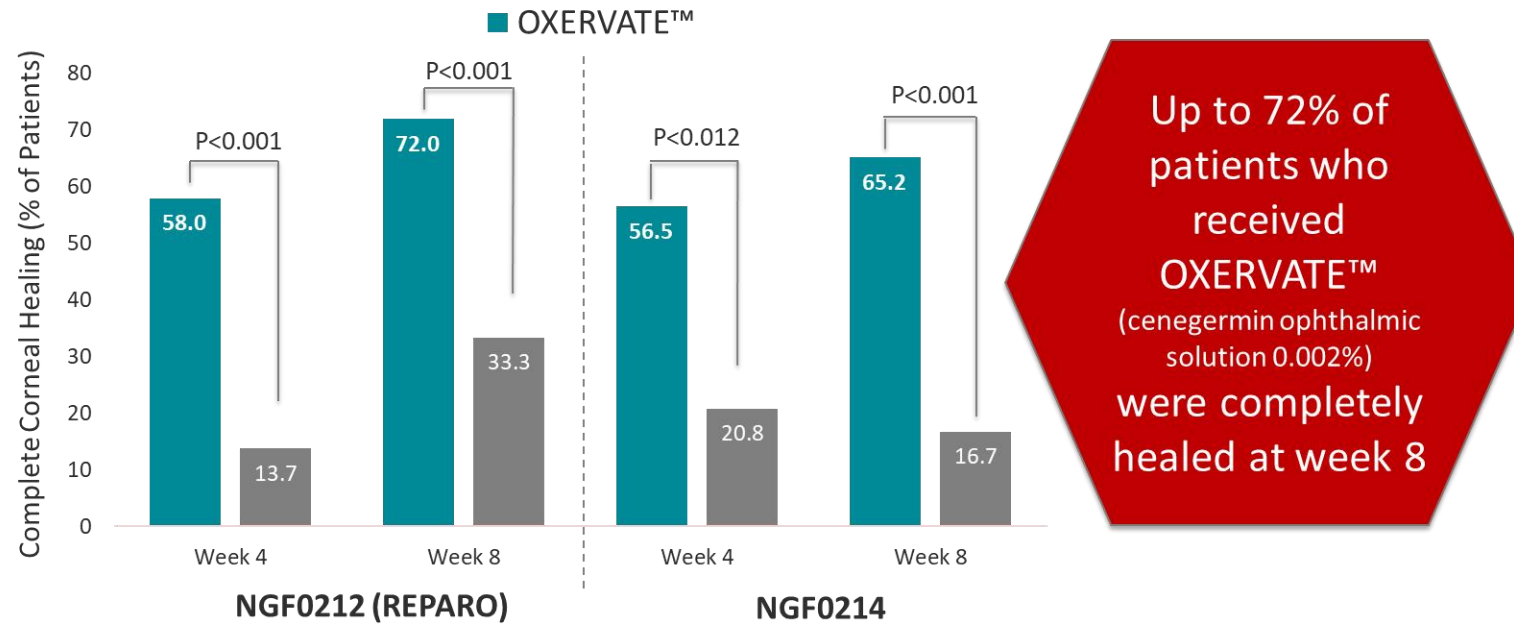
2- ClinicalTrials.gov Identifier: NCT02227147

## Main exclusion criteria

- Infection, inflammation, other ocular disease requiring topical tx
  - Glaucoma patients were switched to systemic meds during the study
- Severe blepharitis or MGD
- Prior surgical tx for NK
  - Exception for AMT performed > 6 weeks prior or membrane disappeared > 2 prior
- Stromal involvement in posterior third, corneal melting, or perforation in study eye

## Efficacy established as early as week 4

Endpoint of complete corneal healing: **0 mm staining in the lesion area and no persistent staining in the rest of the cornea** (last post-baseline observation carried forward; chi-squared test).



1. Bonini S, Lambiase A, Rama P *et al.* *Ophthalmology* 2018;125:1332-1343.
2. Chao W, J. BDC, R. D *et al.* Data on file. Healing of persistent epithelial defects or corneal ulcers by recombinant human nerve growth factor eye drops in patients with stage 2 or 3 neurotrophic keratitis. Presented at: Congress of the European Society of Ophthalmology (SOE) 10–13 June, 2017, Barcelona, Spain. 2017.



# Study Conclusions

Up to 72% of patients achieved complete corneal healing;  
80% of healed patients were recurrence free after 1 year\*

After 8 weeks of treatment,  
6 times daily

In the majority of patients across two clinical studies OXERVATE™ (cenegermin ophthalmic solution 0.002%) was well tolerated and more effective than vehicle in promoting complete corneal healing of moderate or severe NK.



**Study NGF0212  
(REPARO)**  
(N=52 per  
group)  
European patients  
with NK in one eye  
  
NCT01756456



**Study NGF0214  
(N=24 per  
group)**  
U.S patients with  
NK in one or both  
eyes  
  
NCT02227147



Of patients who healed  
after one 8-week course of  
treatment...

80%

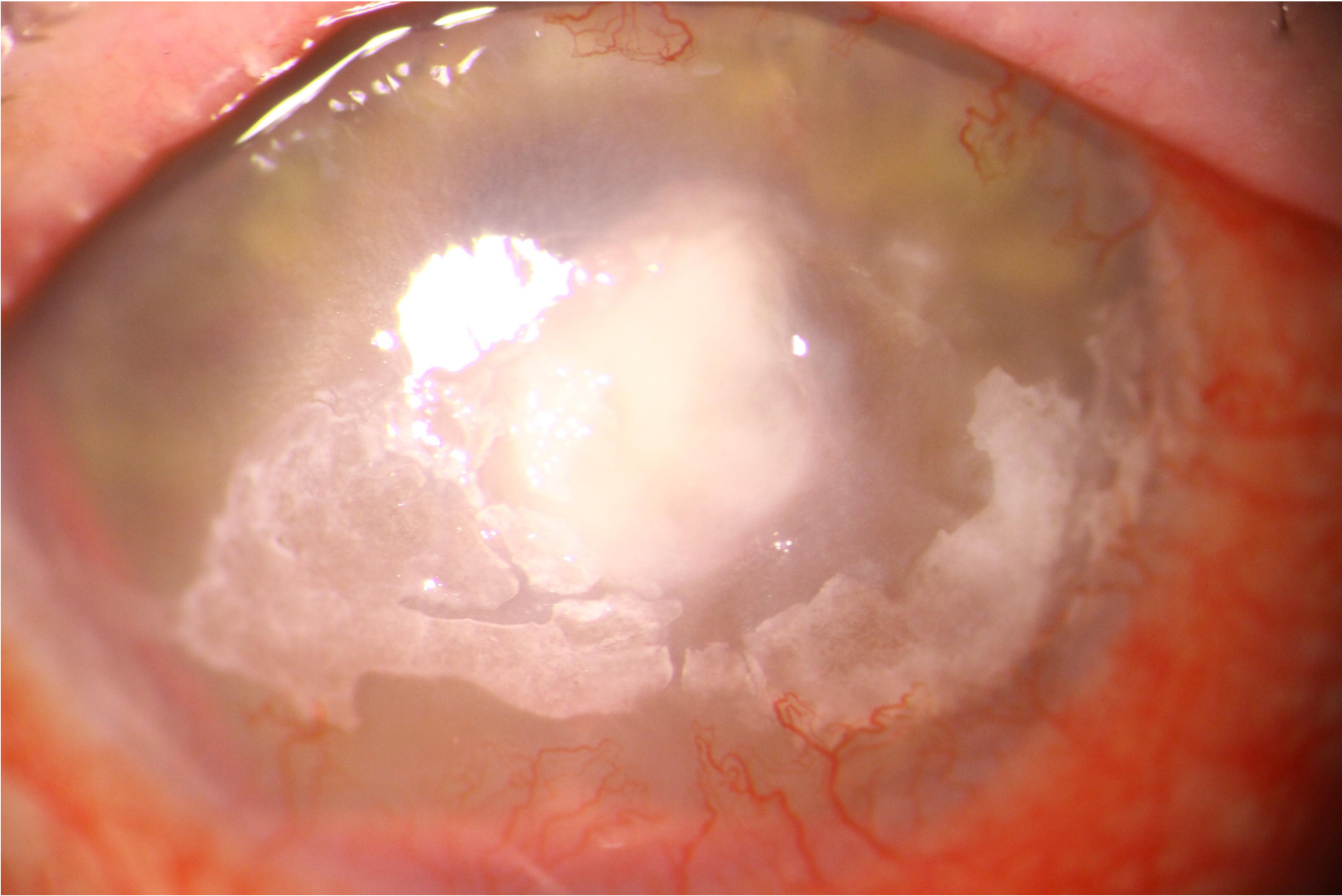
Remained healed for  
one year\*

\*Based on REPARO, the study with longer follow-up

1. Bonini S, Lambiase A, Rama P *et al.* *Ophthalmology* 2018;125:1332-1343.
2. Chao W, J. BDC, R. D *et al.* Data on file. Healing of persistent epithelial defects or corneal ulcers by recombinant human nerve growth factor eye drops in patients with stage 2 or 3 neurotrophic keratitis. Presented at: Congress of the European Society of Ophthalmology (SOE) 10–13 June, 2017, Barcelona, Spain. 2017.

# Neurotrophic Ulcer



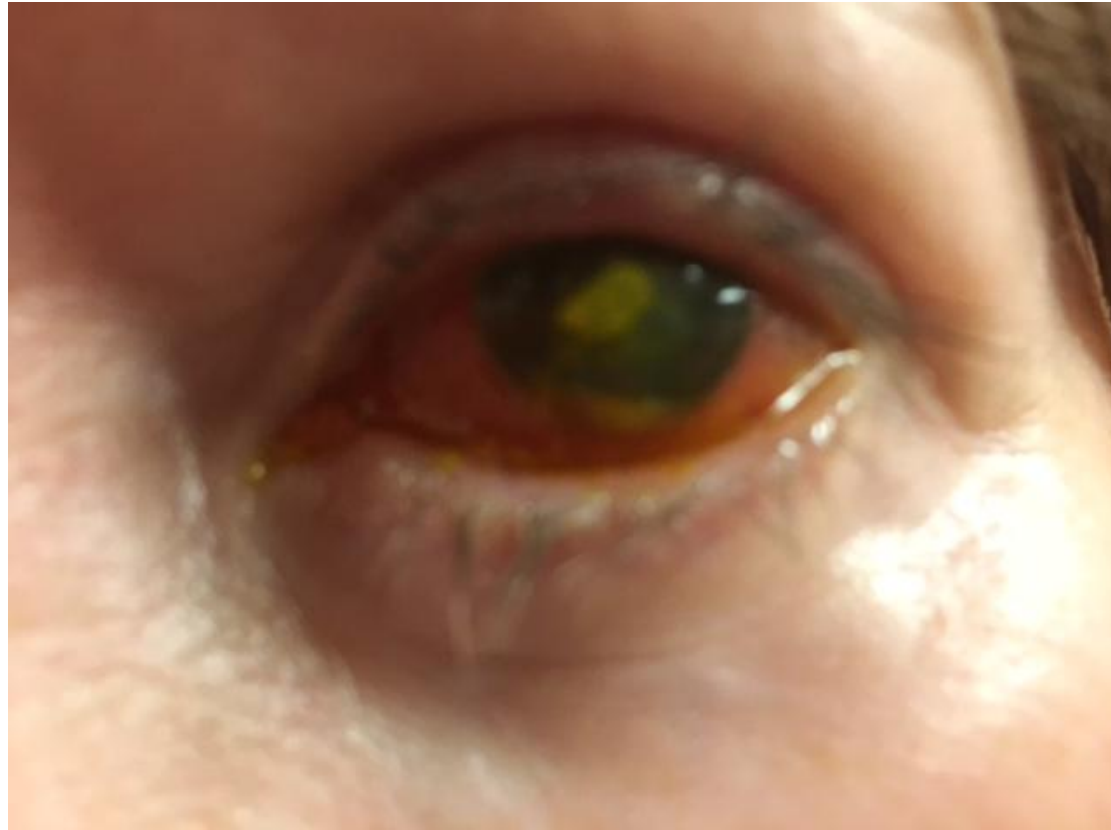




# Neurotrophic Ulcer

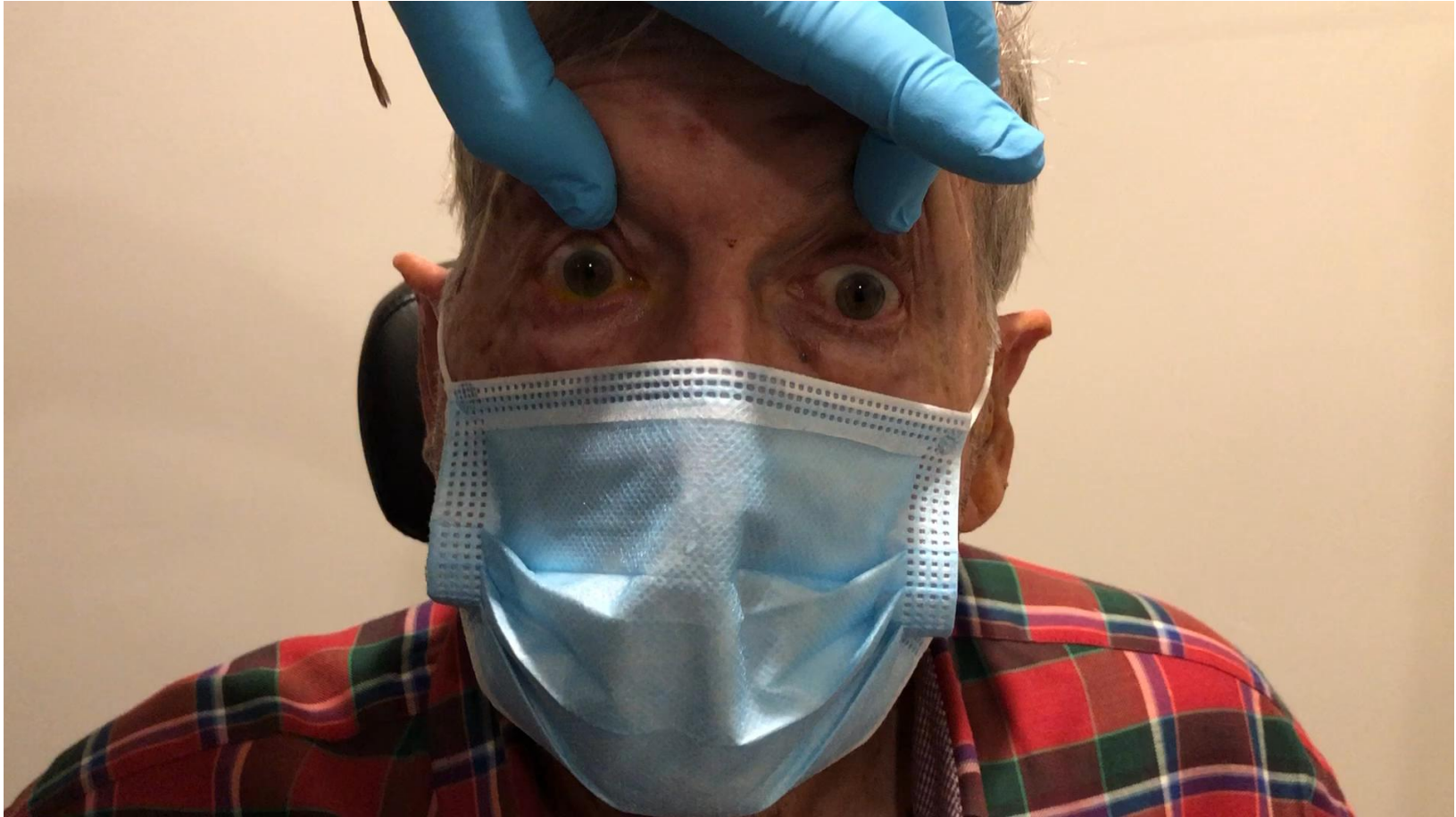


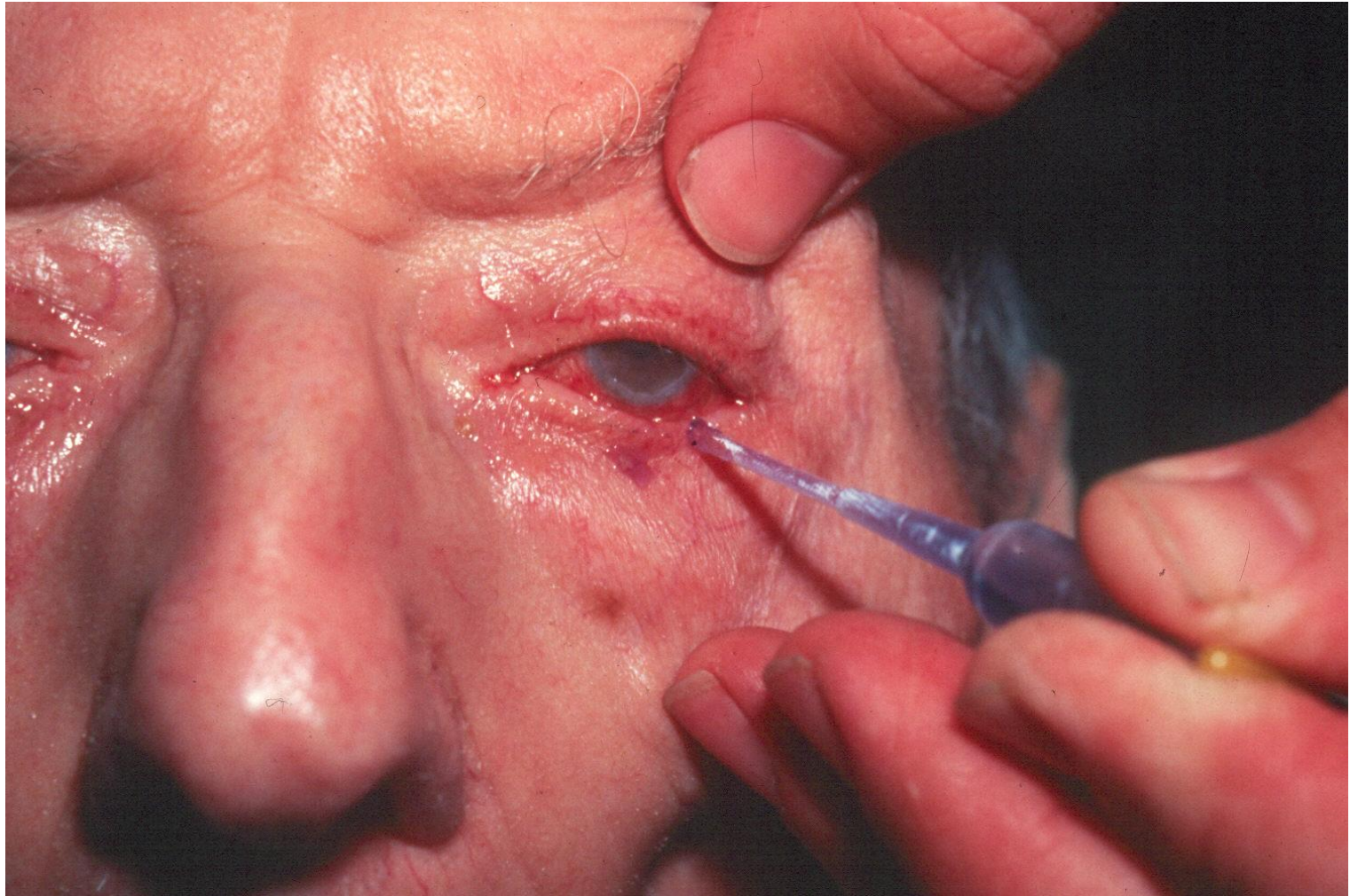
# Neurotrophic Ulcer



















# Duxipent

- **Dupixent** works by blocking a type of protein called an interleukin, or IL, from binding to their cell receptors. Interleukins contribute to a functioning **immune system** by helping to fight off viruses or bacteria in **our** bodies. ... **Dupixent** works on two interleukins thought to contribute to atopic diseases: IL-4& II-13

## **The most common side effects of Duxipent**

- Injection site reactions.
- Eye and eyelid inflammation, including redness, swelling and itching have been seen in patients with atopic dermatitis.
- Pain in the throat (oropharyngeal pain)
- Cold sores in your mouth or on your lips
- Subcutaneous injection q 2 weeks



# Case Three

- 19 y/o white male with c/o severe itching and FBS OU
- Increased x last 2 weeks
- H/o asthma, Tx with inhalers, topical therapy and rescue steroids
- Perennial allergies
- VA: Clear at 10 ft

















# Pain Management

Topiramate

- Narcotics
- NSAIDS
- Acetaminophen
- Lyrica
- Neurontin

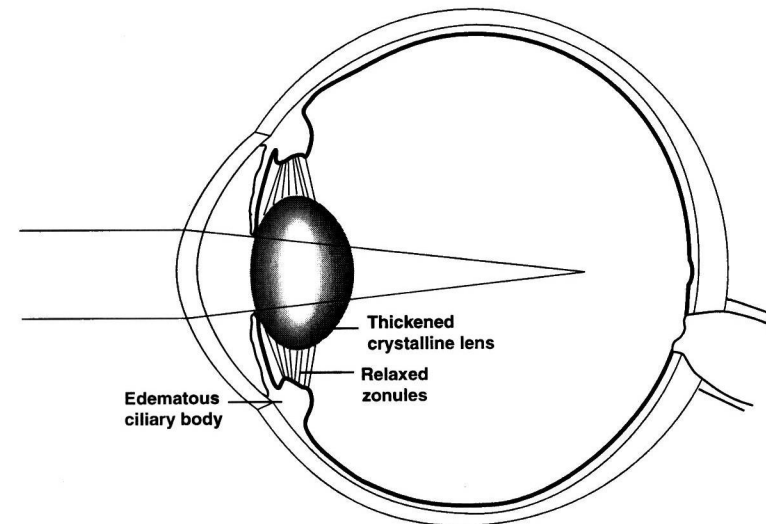
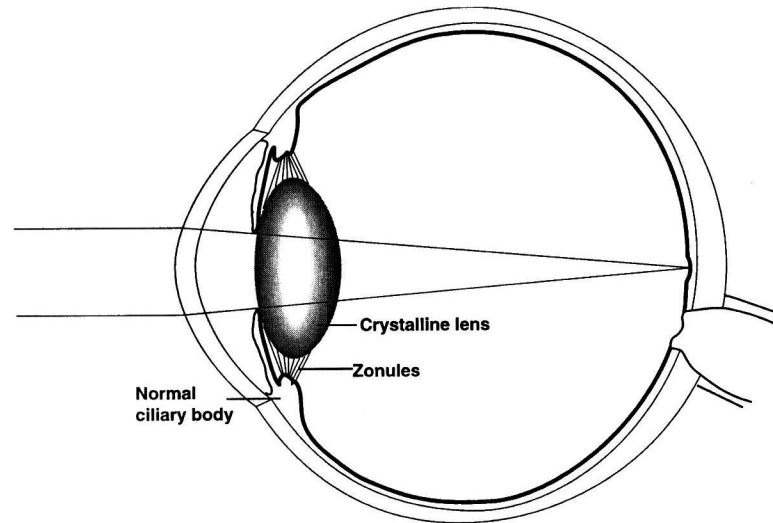
# Topiramate

- **Used to treat seizures, migraine headache, bipolar disorders**
- **Side Effects:**
  - **1. Acute myopia**
  - **2. secondary angle-closure glaucoma**
  - **3. suprachoroidal effusions**
- **85% of cases of mostly bilateral, acute angle-closure glaucoma occur within the first two weeks of treatment**

# Drugs That Can Cause Secondary Angle Closure

- Sulfonamides
- Diuretics
- Carbonic anhydrase inhibitors
- Isotretinoin
- Topiramate (Topamax)
  - Also a component of Qsymia (weight loss drug FDA-approved on July 18, 2012)

# Mechanism



## New Weight-Loss Drug Containing Topiramate

### *Obesity*

*Indicated as an adjunct to a reduced-calorie diet and exercise for chronic weight management in adults with an initial BMI  $\geq 30$  kg/m<sup>2</sup> (obese), or BMI  $\geq 27$  kg/m<sup>2</sup> (overweight) in the presence of at least 1 weight related comorbidity (eg, hypertension, type 2 diabetes mellitus, dyslipidemia)*

*Initial: 3.75 mg/23 mg PO qDay for 14 days, THEN  
Day 15: Increase to 7.5 mg/46 mg PO qDay for 12 weeks, then evaluate weight loss*



# CONVERSION

mg-to-mg<sup>3</sup>

Total  
daily dose

Twice-daily<sup>2</sup>  
**Topamax**

Once-daily<sup>3</sup>  
**Trokendi XR**

25 mg



25 mg/day



25 mg/day

50 mg



50 mg/day



50 mg/day

# RECOMMENDED TOTAL DAILY DOSE

100 mg



100 mg/day



100 mg/day

200 mg



200 mg/day



200 mg/day

Trokendi XR may be taken without regard to meals. Swallow capsule whole and intact.  
Do not sprinkle on food, chew, or crush.<sup>3</sup>

Tablets and capsules shown are not actual size.

# New Weight-Loss Drug Containing Topiramate



# Narcotic agents

- **Directly affect opioid receptor**
- **Agonist, partial agonist, or mixed**
- **Bind to opioid receptors in brainstem, cortical areas and spinal cord**
- **Mimic endorphins, producing a morphine like effect whether natural or synthetic**

# Narcotic Side Effects

- Drowsiness
- Dizziness
- Blurred vision
- Nausea/vomiting/constipation
- Take with food to avoid GI distress
- Avoid Etoh or other CNS agents
- Breathing distress

# Narcotic Contraindications

- ▶ Bronchial asthma
- ▶ COPD
- ▶ Emphysema
- ▶ Pregnancy
- ▶ Hypersensitivity
- ▶ Prior addiction
- ▶ Renal/Liver dysfunction
- ▶ H/O Etoh use, Concurrent use of CNS agents(Tricyclic antidepressants, Phenothiazines)

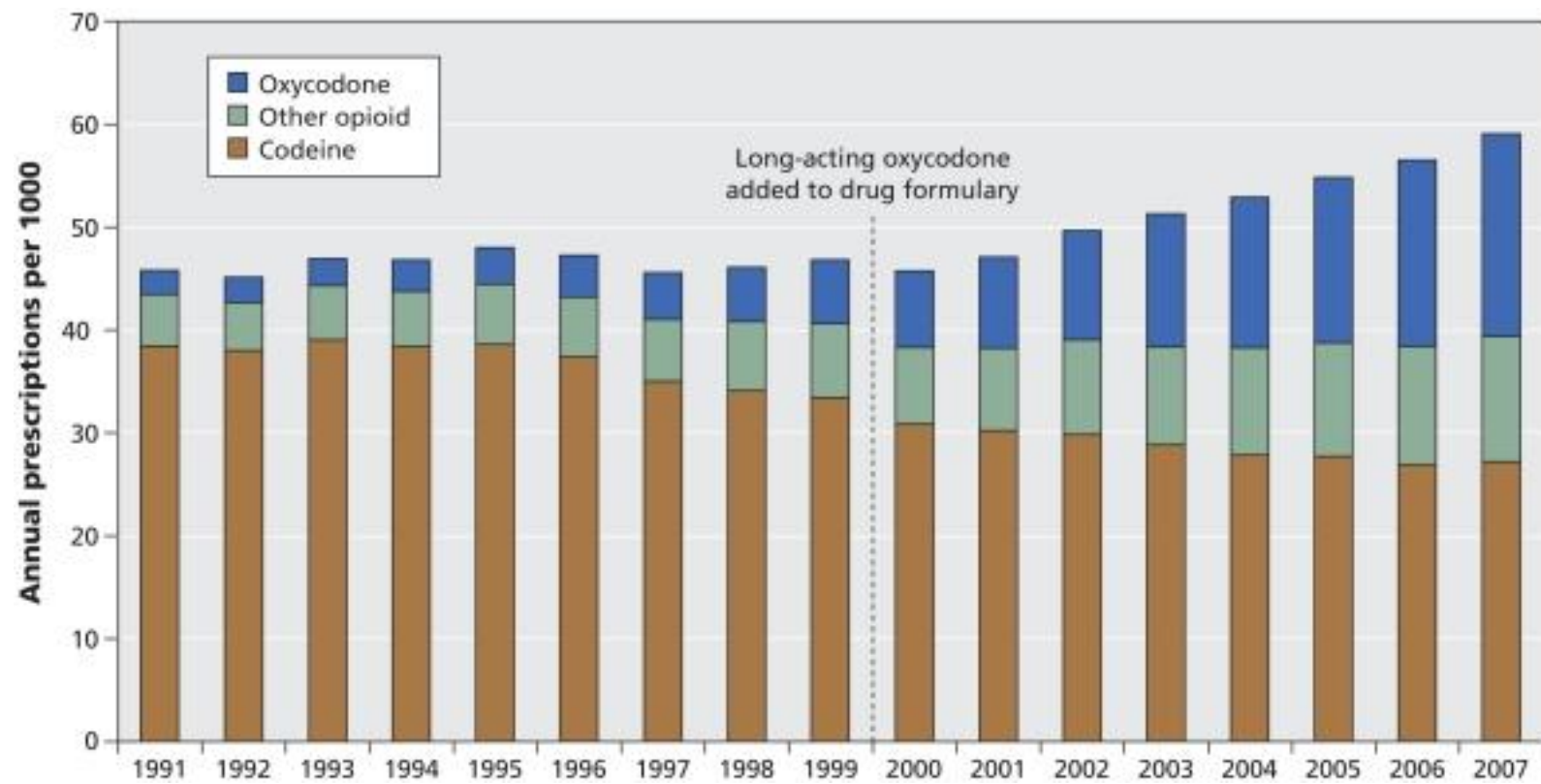
# Narcotic Agents

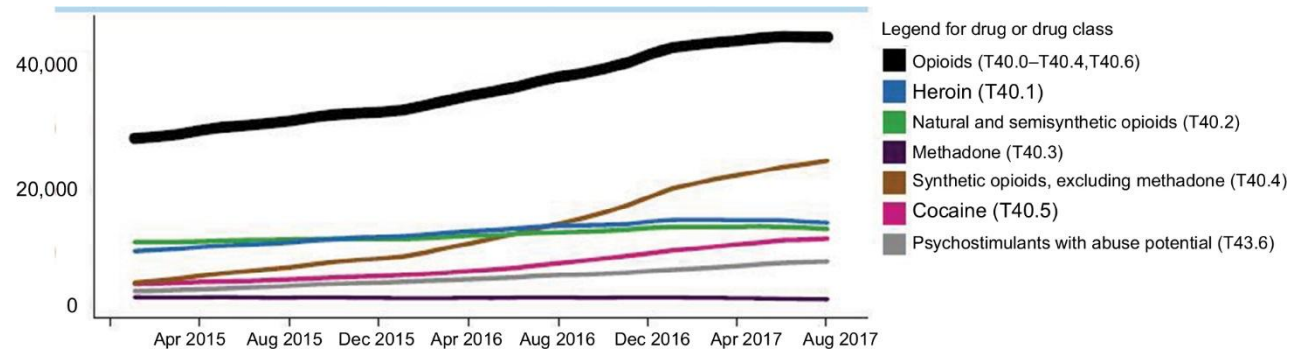
- **Hydrocodone**
- **1. 5/10 mg -325 mg Acetaminophen**
- **. Vicodin/ Lortab**
  
- **2.Oxycodone**
- **A. 5/10 mg -325 mg Acetaminophen**
- **B. Percoset**
- **3. Tramadol**
  - **50 mg qid**

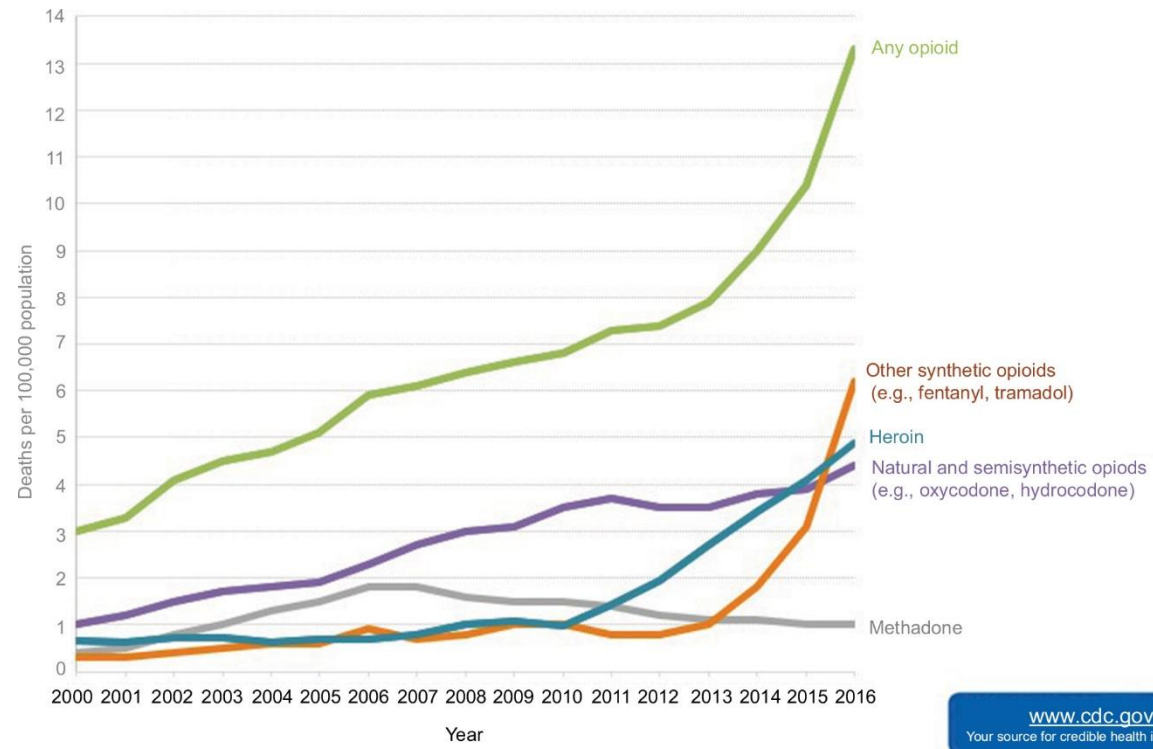


# Addictive Properties of Short Term Narcotics Use

- Shah, A et al
- Journal of Morbidity & Mortality 3/ 2017
- 1,294,000 patients analyzed
- Among persons prescribed at least 1 day of opioids, the probability of continued opioid use at 1 year was 6.0% and at 3 years was 2.9%
- The probabilities of continued opioid use at 1 and 3 years for persons starting on hydrocodone short acting (5.1% at 1 year; 2.4% at 3 years), oxycodone short-acting (4.7% at 1 year; 2.3% at 3 years)







- Since a previous contribution to this journal in 2012, the epidemic of opioid abuse has become increasingly frightening and tragic. Of an estimated 62,632 drug overdose deaths in the US in 2016 about 2/3 were from opioids, more than deaths from traffic fatalities. Preliminary data for 2017 indicates an even higher opioid overdose death count.

# A Light at the End of the Tunnel

- Morphine has four basic receptors
- Three of which are structurally similar
- mu / delta / kappa
- Mu is the main driver for pain relief and addiction
- Korsuva only targets Kappa receptors that can avoid the addictive potential
- Also inhibits the sensation of itch ( 45 million patients / year)



# A Light at The End of the Tunnel

Korsuva: Cara Therapeutics

1. 5 micgograms po
2. Phase II clinical trials
  1. 39% pain reduction vs placebo in hip patients
  2. 35% in knee pain patients
  3. Much lower potential for abuse
  4. Significantly lower “ would take it again” compared Talwin

# Lyrica ( Pregabalin)

- **Indications:**

- 1. Treat neuropathic pain caused by [nerve damage](#) due to [diabetes](#), [shingles](#) ([herpes zoster](#)) infection, or spinal cord injury. This medication is also used to treat pain in people with [fibromyalgia](#).
- 2. It is also used with other [medications](#) to treat certain [types of seizures](#) (focal [seizures](#)).
- **Dose: 100mg tid**
- **Side Effects:** Blurred [vision](#), unusual bleeding/bruising, unsteadiness, confusion, [muscle pain](#)/tenderness/[weakness](#)(especially if you are tired or have a fever), swelling of hands/legs/feet, signs of [kidney](#) problems (such as change in the amount of urine)

# Neurontin

- **Dosage For Postherpetic Neuralgia**
- In adults with postherpetic [neuralgia](#):
  - 1. Day 1 as a single 300 mg dose
  - 2. Day 2 as 600 mg/day (300 mg two times a day)
  - 3. Day 3 as 900 mg/day (300 mg three times a day).
- The dose can subsequently be titrated up as needed for pain relief to a dose of 1800 mg/day (600 mg three times a day).
- In clinical studies, efficacy was demonstrated over a range of doses from 1800 mg/day to 3600 mg/day with comparable effects across the dose range; however, in these clinical studies, the additional benefit of using doses greater than 1800 mg/day was not demonstrated.

# Neurontin

## • SIDE EFFECTS

- Drug Reaction with [Eosinophilia](#) and Systemic Symptoms (DRESS)/Multiorgan Hypersensitivity
- [Anaphylaxis](#) and [Angioedema](#)
- [Somnolence](#)/Sedation and Dizziness
- Withdrawal Precipitated [Seizure](#), [Status Epilepticus](#)
- Suicidal Behavior and Ideation
- Neuropsychiatric Adverse Reactions (Pediatric Patients 3–12 Years of Age)
- Sudden and Unexplained Death in Patients with [Epilepsy](#)

# Analgesics & Nonsteroidal Anti-Inflammatory Agents

- ▶ Nonsteroidal Anti-Inflammatory Agents - peripheral acting agents, prevent stimulation or discharge of nociceptors, more effective for inflammatory related conditions, may have ceiling effect
  - ▶ Acetylsalicylic acid (ASA) 325-500 mg q4-6h
  - ▶ Ibuprofen (Motrin, Advil, Nuprin) 400 mg q4-6h
  - ▶ Naproxen sodium (Aleve) 450 mg loading dose, then 225 mg q6-8h

# NSAID'S

- CLINICAL APPLICATIONS
  - ANALGESIA
  - ANTI-INFLAMMATORY
  - MUSCULOSKELATAL/ MYOSITIS
  - ACUTE GOUT
  - DYSMENNORRHEA
  - CME



# NSAID'S

- CORNEAL OPACITIES( WHORL)
- TINNITUS
- FLUID RETENTION
- EPISTAXIS
- BREAST CHANGES
- ANEMIA/BLEEDING
- CONSTIPATION

# NSAIDS , H Pylori and Gastric Ulcers

- Lancet 2002 Jan 5; 359: 14-22
  - 1625 NSAID users
  - Peptic ulcer disease
    - 42 % H Pylori patients
    - 26% of non-infected patients
  - Peptic ulcer disease
    - 36 % of NSAID users
    - 8% of non users
  - Risk of bleeding ulcer (6.1x> in H Pylori on NSAIDS0

# Erectile Dysfunction

# Erectile Dysfunction

- 1. Viagra ( Sildenafil)
- 2. Cialis ( Tadalafil)
- 3. Levitra ( Vardenafil)

# Sildenafil

- **Mechanism of action:**
- To obtain an erection, nitric oxide is released in the corpus cavernosum of the penis.
- This activates the enzyme guanylate cyclase, which leads to a subsequent increase in the levels of cyclic guanosine monophosphate (cGMP).
- The nitric oxide-cGMP pathway relaxes smooth muscle in the penis, which in turn increases blood inflow and closes venous drainage channels.
- As the cavernous bodies become engorged with blood, the erection ensues. The enzyme cGMP-specific phosphodiesterase type 5 (PDE 5) then breaks down cGMP. This causes the erection to end.

# Sildenafil (Viagra)



- Mild, transient, dose-related impairment of color vision
- Peak effect is 30 min to 2 hr after ingestion
- Visual side effects occur in 3-10% of users
- Bluish-tinged, pink-tinged, or yellowish-tinged vision
- Symptoms last several min to several hours
- Effects are due to inhibition of PDE-6, involved in retinal phototransduction



# Viagra

- [Am J Ophthalmol](#). 2001 Dec;132(6):872-4.
- **Acute effects of sildenafil citrate (Viagra) on intraocular pressure in open-angle glaucoma.**
- [Grunwald JE<sup>1</sup>](#), [Jacob SS](#), [Siu K](#), [Piltz J](#), [Dupont J](#).
- **PURPOSE:**
  - To assess the acute effects of sildenafil citrate (VIAGRA) on the intraocular pressure (IOP) of patients with chronic open-angle glaucoma.
- **DESIGN:**
  - This was a double-blind, randomized, placebo-controlled, crossover study, in which 15 patients received a single oral dose of sildenafil 100 mg or matching placebo on two separate occasions.
- **METHODS:**
  - Fifteen subjects aged 63 +/- 14 years (mean +/- SD) with bilateral chronic open-angle glaucoma were administered a single oral dose of sildenafil 100 mg or matching placebo on two separate occasions at least 3 days apart. IOP was measured in both eyes by Goldmann ap-planation tonometry at baseline and then at 1-5 hours after dosing. Brachial artery systolic and diastolic blood pressures were determined by sphygmomanometry, and heart rate was also monitored at baseline and 1-5 hours after dosing.
- **CONCLUSION:**
  - At the maximum therapeutic dose of 100 mg, sildenafil did not produce any significant acute change in IOP in men with chronic open-angle glaucoma. This information is of importance for patients with glaucoma receiving sildenafil for treatment of erectile dysfunction.

# Sildenafil (Viagra)

- Several dozen published cases of optic neuropathy
- Etiology for NAION with ED drugs is controversial and unproven
- NAION associated with sildenafil is considered “possible” by WHO causality classification
- (Pfizer, the manufacturer of sildenafil, states that in more than 100 clinical studies (more than 13,000 patients) of their drug, no cases of NAION were reported. They also state that more than 170 million sildenafil prescriptions have been administered to 23 million men (equivalent to 1 billion doses), so the overall occurrence of NAION is an extremely infrequent event.)

# OTC ED Food “Supplements”

## Public Notification: “Instant Hard Rod” Contains Undeclared Drug Ingredient

**[4/20/2012]** The Food and Drug Administration (FDA) is advising consumers not to purchase or use “Instant Hard Rod,” a product for sexual enhancement manufactured by Enhance Nutraceutical and sold on various websites, including [www.instanthardrod.com](http://www.instanthardrod.com).

FDA laboratory analysis confirmed that “Instant Hard Rod” contains aminotadalafil. Aminotadalafil is an analog of tadalafil, an FDA approved prescription drug used to treat Erectile Dysfunction (ED). This drug may interact with nitrates found in some prescription drugs such as nitroglycerin and may lower blood pressure to dangerous levels. Men with diabetes, high blood pressure, high cholesterol or heart disease often take nitrates.

Consumers should stop using this product immediately and throw it away. Consumers who have experienced any negative side effects should consult a health care professional as soon as possible.

Healthcare professionals and patients are encouraged to report adverse events or side effects related to the use of these products to the FDA’s MedWatch Safety Information and Adverse Event Reporting Program:

- Complete and submit the report Online: [www.fda.gov/MedWatch/report.htm](http://www.fda.gov/MedWatch/report.htm)
- Download form or call 1-800-332-1088 to request a reporting form, then complete and return to the address on the pre-addressed form, or submit by fax to 1-800-FDA-0178

Note: This notification is to inform the public of a growing trend of products marketed as dietary supplements or conventional foods with hidden drugs and chemicals. These products are typically promoted for sexual enhancement, weight loss, and body building, and are often represented as being “all natural.” FDA is unable to test and identify all products marketed as dietary supplements on the market that have potentially harmful hidden ingredients. Consumers should exercise caution before purchasing any product in the above categories.

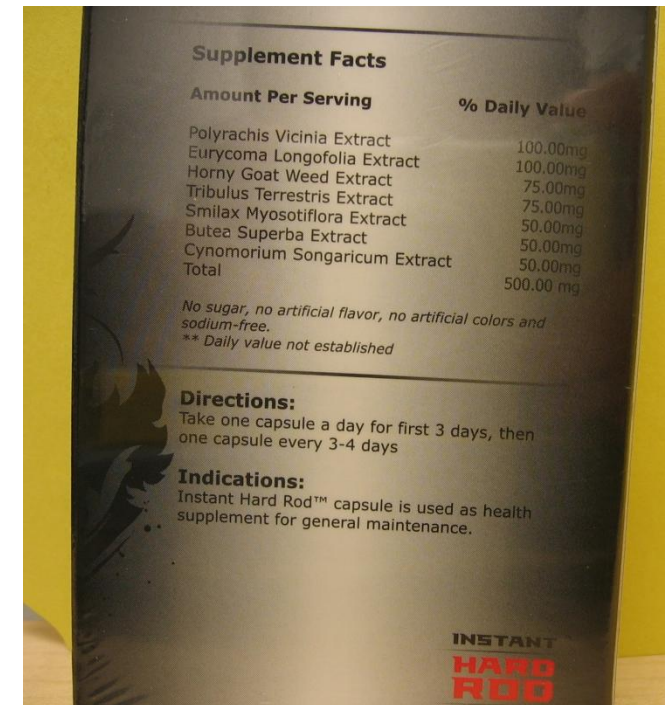
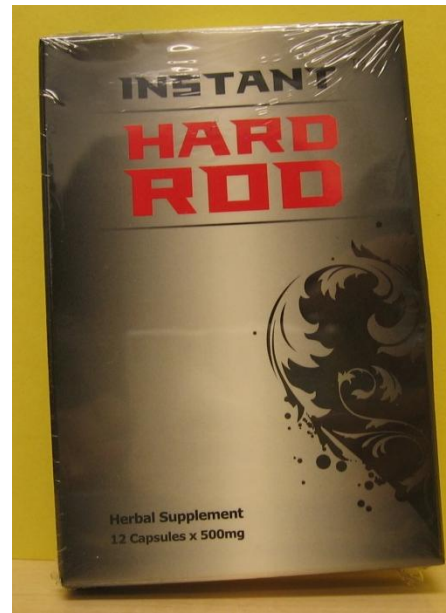


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## **Urgent News About** **Your Sexual Health**

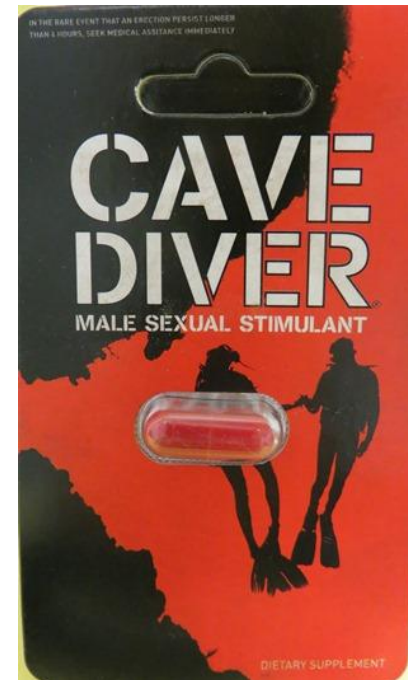
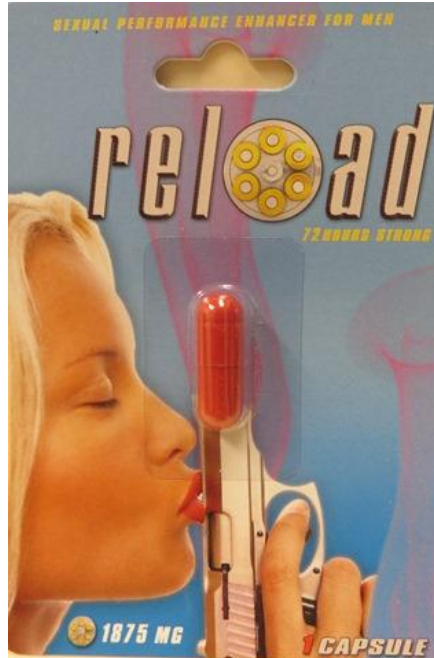
If you have not read this Amazing information concerning male enhancement discovery yet, then by all means get your hands on this right away

# The **NEW** **Male Enhancement** **Discovery**





# Other Products with Undeclared ED Components

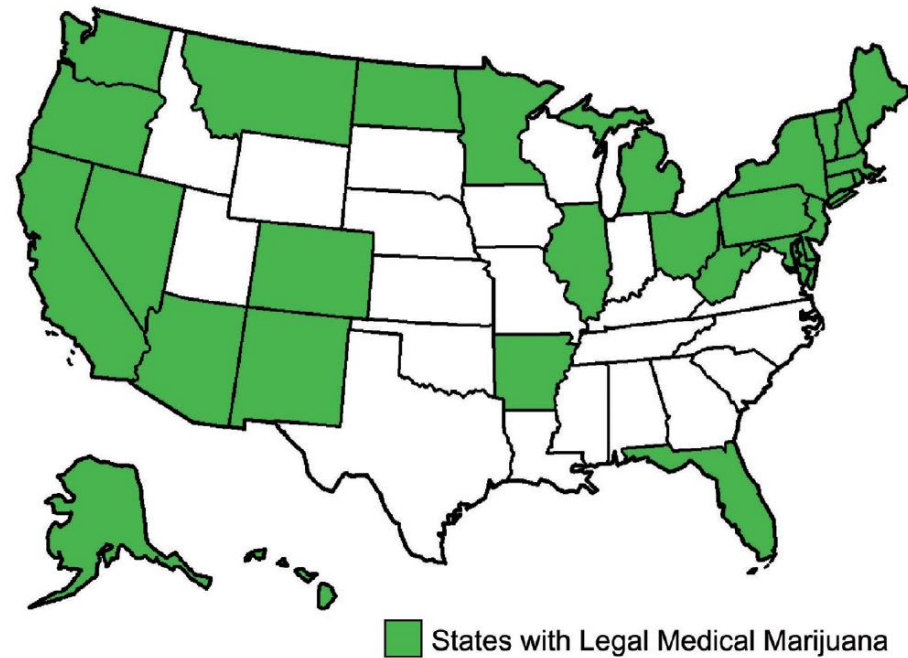


# Cannabinoids

Welcome to  
COLORADO



# Current Trends in Marijuana Laws





# Marijuana & Glaucoma

**TABLE 1. MARIJUANA SIDE EFFECTS\*<sup>5,14</sup>**

**OCULAR**

- Conjunctival hyperemia
- Decreased lacrimation
- Photophobia
- Ptosis
- Blepharospasm
- Nystagmus
- Impairment of accommodation

**SYSTEMIC**

- Tachycardia
- Decreased blood pressure
- Orthostatic hypotension
- Euphoria or dysphoria
- Impaired coordination
- Difficulty with concentration, problem solving, memory
- Decreased testosterone
- Impaired immunity

*\*Any route of administration*

# Journal of Cannabis and Cannabinoid Research 2016

- Collectively, this research indicates that although the results of experimental studies with healthy adults are mixed, there is converging evidence to support the notion that cannabis can produce acute pain-inhibitory effects among individuals with chronic pain.
- This observation is consistent with determinations made by authors of the recent National Academies report on cannabis that there is “conclusive or substantial evidence” of benefit from cannabis or cannabinoids for chronic pain.
- However, it is important to also highlight their statement that more research is needed to better understand the efficacy, dose–response effects, routes of administration, and side effect profiles for cannabis products that are commonly used in the United States.<sup>8</sup>

# Cannabinoids

- Smoking and ingesting marijuana significantly reduces IOP
- Have been administered orally, topically, and by inhalation as a means of reducing IOP
- After smoking a single marijuana cigarette, maximal ocular hypotensive response occurs 60 to 90 min. after inhalation and lasts approximately 4 hours

# Mechanisms of Cannabis in Glaucoma ( GT 4/18)

- Marijuana and THC have been shown to lower IOP in 60% to 65% of both normal individuals and patients with glaucoma. Mean IOP reduction in one study was about 25%.<sup>5</sup>
- An ocular hypotensive effect has been reported when the drug is smoked or ingested and when THC is inhaled or administered orally, sublingually, or intravenously.<sup>6</sup>
- The duration of action is short, about 3 to 4 hours.
- There appears to be a dose-response relationship between the amount of marijuana consumed and the degree of IOP reduction, although the length of efficacy does not improve at higher doses.<sup>5</sup>
- Topical administration of THC to the eye does not lower IOP.<sup>7,8</sup>
- THC is a highly lipophilic compound and cannot be administered in a water-based vehicle.
- In one placebo-controlled double-masked study using an oil-based vehicle, no IOP-lowering effect was demonstrated. Both the placebo (vehicle) and the study drug caused significant ocular irritation.<sup>7</sup>

# Marijuana & Glaucoma

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• 5. Green K. Marijuana smoking vs cannabinoids for glaucoma therapy. *Arch Ophthalmol*. 1998;116(11):1433-1437.

• 6. Tomida I, Azuara-Blanco A, House H, et al. Effect of sublingual application of cannabinoids on intraocular pressure: a pilot study. *J Glaucoma*. 2006;15(5):349-353

# WHAT'S IN A WORD

- Surgery 2002 Jul; 132: 5-9
  - 57 surgeons / 114 office encounters
  - Relationship between tone of voice and malpractice experience was evaluated
  - audio clips were collected and reviewed for ten traits ( warmth, interest, hostility, concern, sincerity etc.)
  - Surgeons with a Hx of malpractice were 5x more likely to demonstrate dominant voice tones



# Alcohol and Dementia

- Rottenberg A et al
- Lancet 2002 Jan 26:359:281-6
- 7983 males/females/ 5395 non-dementia @ baseline
- 6 year f/u standardized questionnaire
- Suspected dementia- neuro consult/MRI
- 197 - dementia/ 0.58 risk ratio for 1-3 drinks /day

# I don't drink should I?

- Wannamethee,SG etal
- Heart 2002 Jan;87:32-6
  - 7735 males ( 40 -59 y/o)
  - 6503 without CAD/ 874 CAD events
- Outcomes
  - stable ,moderate, etoh- lowest CHD/Mortality
  - new regular drinkers- no change in CAD
  - no protection for CAD/ Increased risk of other cause of death

# Friendship and longevity

- Fratigioni, L etal
- Lancet 2000 Apr 15: 355; 1315-9
- “Influence of Social Network on occurrence of Dementia”
- 1203 patients non-demented
- 75 yrs or older
- 3 yr f/u 176 developed dementia
- single alone 1.9 vs married together 1.0

# What are friends for?

- Laurence Roy Stains
- Men's Health Oct 2001
- "Bowling Alone" Dr Robert Putnam
  - Loners are 2-5 x more likely to die prematurely