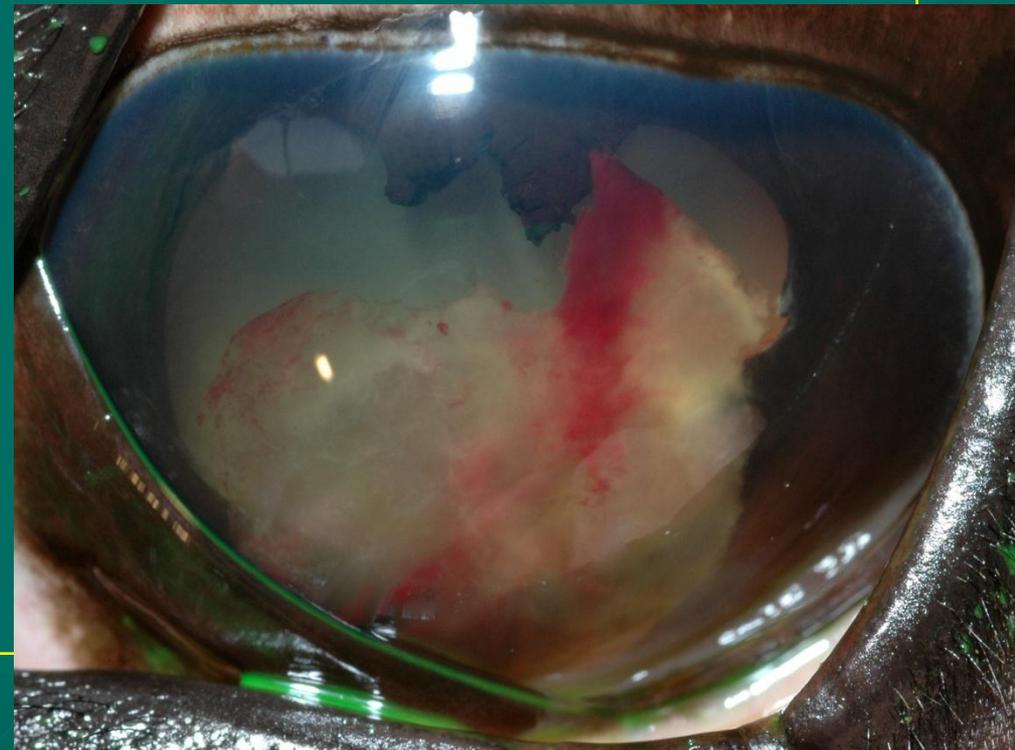
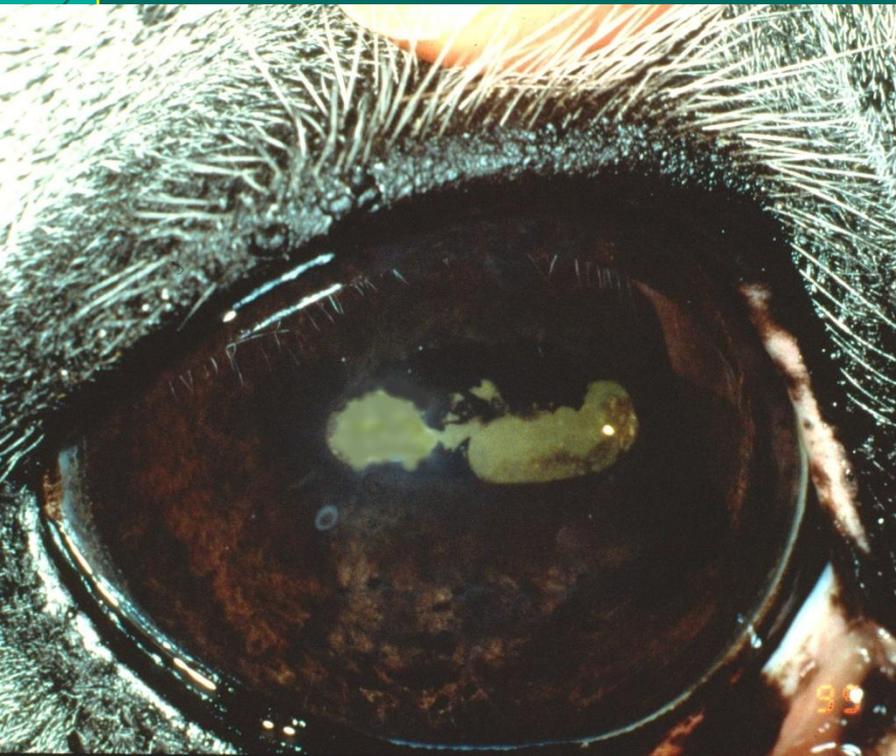


# Equine “Recurrent” Uveitis is a “Persistent” Problem in Horses

Equine Ophthalmology Service  
University of Florida



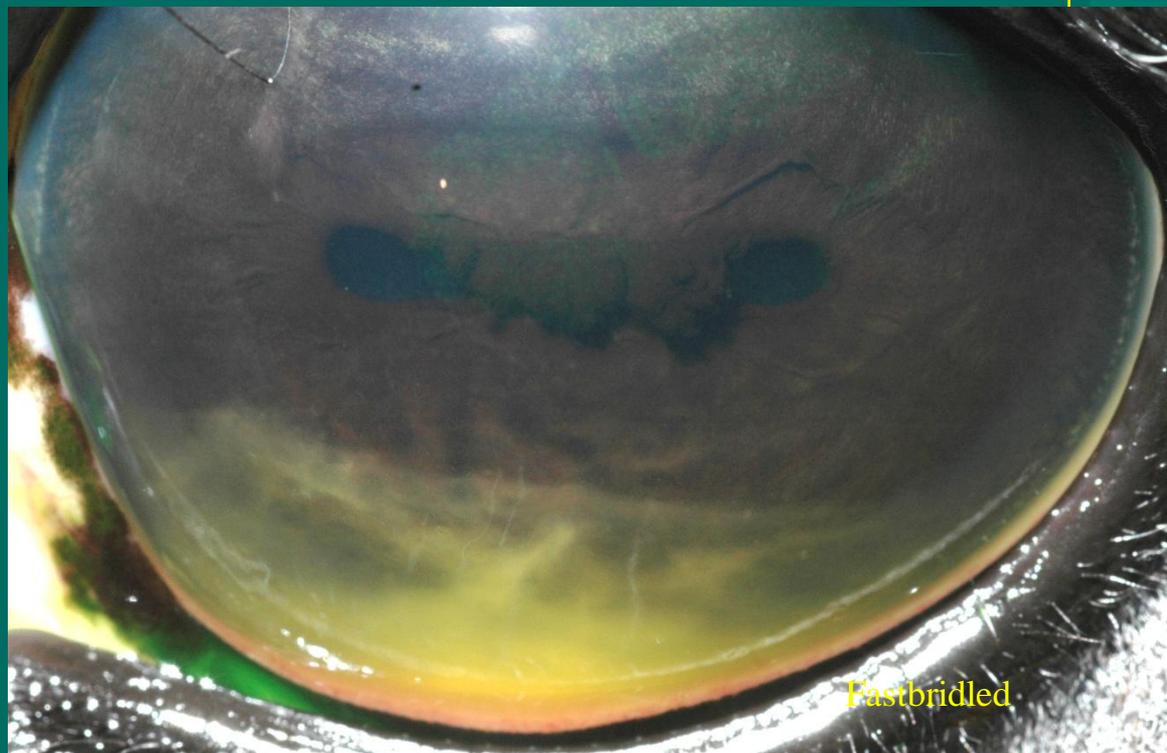
# UVEITIS IN THE HORSE



- UVEITIS is the LEADING CAUSE OF BLINDNESS IN HORSES
- Not a single disease: SYNDROME, MANY subsets!

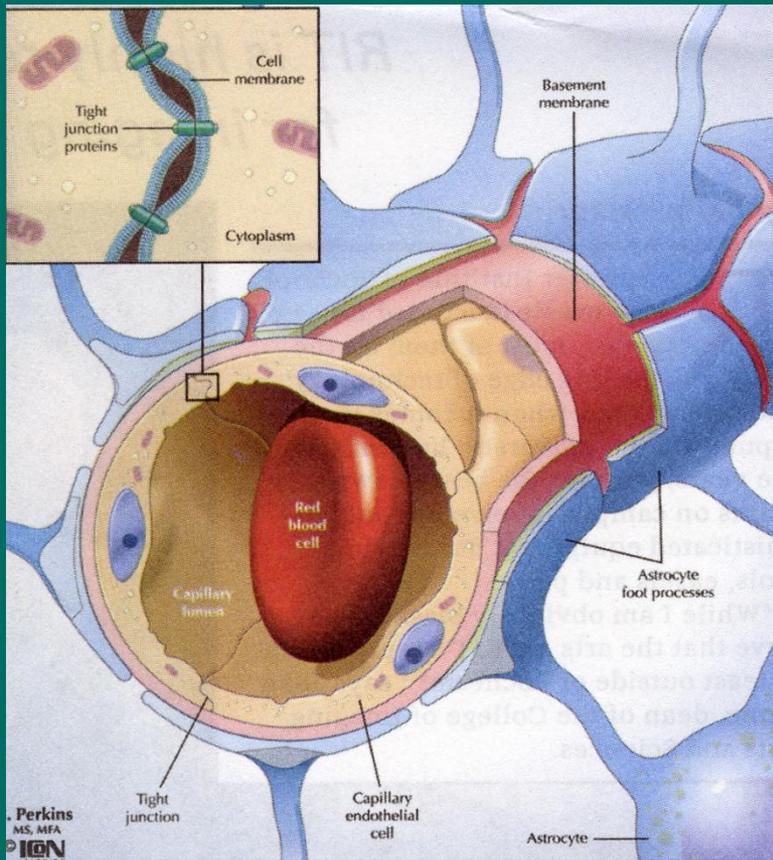
# UVEITIS is like LAMINITIS...

- Variety of triggers
- Poorly understood, but BAD for the horse
- Variable response to therapy
- Multiple tissues in key functional area involved



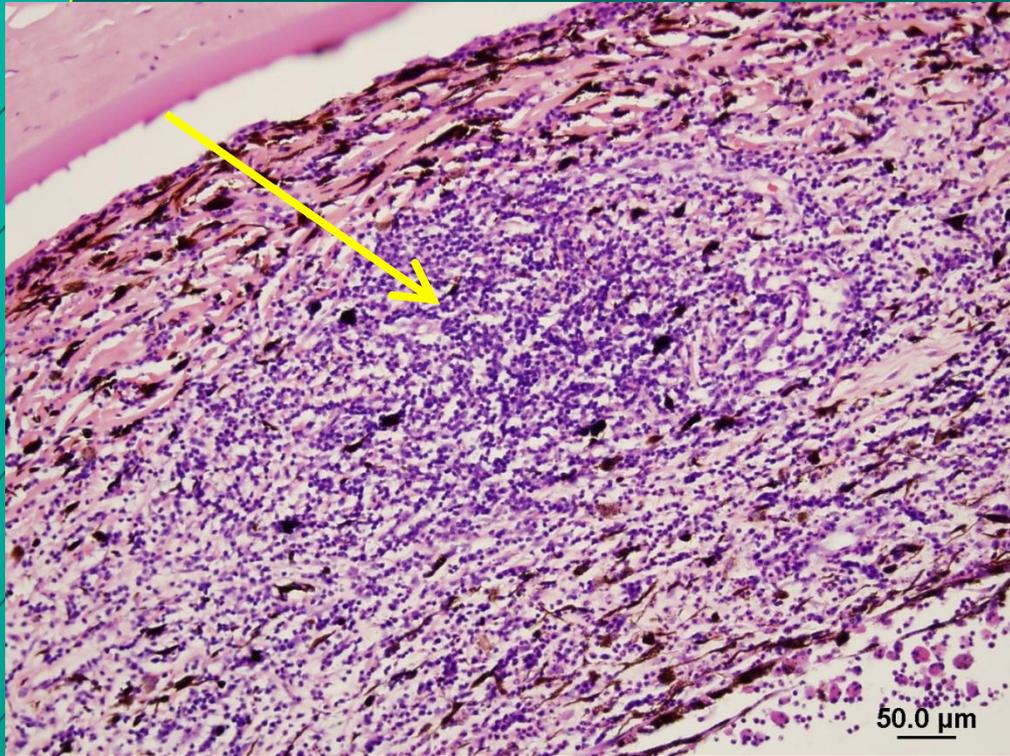
Fastbridled

# Uveitis starts as blood-ocular barrier compromise!



- Blood vessels of iris, CB and choroid become thickened, congested and “leaky”
- Cells and mediators enter the eye
  - PMNs then LCs
  - Inflammatory cytokines

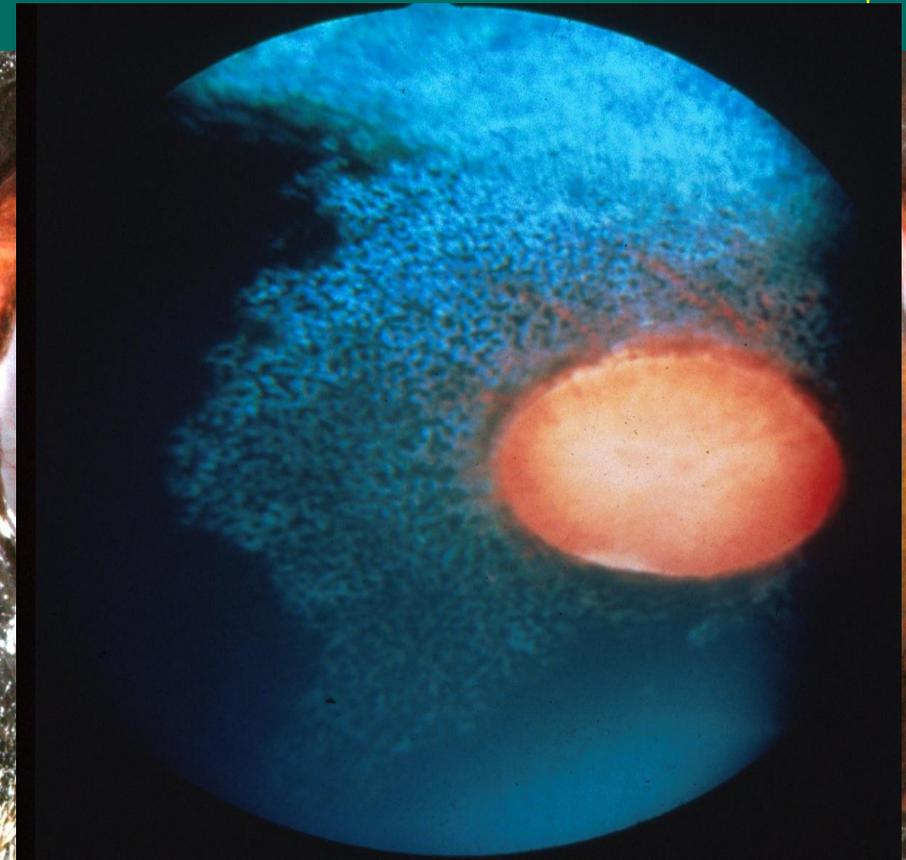
# Lymphocyte infiltration



- Heavy influx of LC into uveal and other eye tissues
- Clusters of LC resembling follicles in ciliary body
- T-LCs predominate, MHC Class II reactive

## “periodic ophthalmia, moon blindness”

- Cavalry horses in ancient Egypt
- “oculus lunaticus”- Vegetius 300AD
- Etiology - autoimmune disease.
  - “Catch-All” term. Group of diseases with same signs
  - Suspected inciting stimulus: Leptospira, Onchocerca, Brucella, Toxoplasma, EHV-1 and -4, Lyme’s, others?
- Diagnosis: It tends to recur!!  
Worse in Appaloosas
- 20% OU in non Apps
- 80% OU in Apps
  - a. Painful ~~X~~ - tearing, conjunctivitis
  - b. Miotic pupil; hypotony ~~X~~
  - c. Negative fluorescein retention
  - d. Hypopyon, flare, hyphema
  - e. Retinal degeneration, “butterfly lesions“
  - f. “hypertensive” uveitis



# Comments

- ERU prevalence in the USA is 1-8%
  - 9.2 million horses in the USA (2005)
  - 736,000 cases!!
- ERU with leptospirosis is a bad form
- ELA-A9 in German Warmbloods may be a heritable form of ERU
- Appaloosas genetically predisposed.
  - UM011 microsatellite had greater 182 allele in Apps with ERU.
  - EqMHC1 microsatellite had greater 206 allele in Apps with ERU.
- Acute and Chronic quiescent clinical phases

- Homing and Molecular Mimicry in ERU
  - Mucous membranes communicate!!!
  - Antigens in the eye reach the lymphatic system, and vice versa!!
  - Infectious agents may only activate ERU. Lepto antigen and horses.
  - Self-antigens perpetuate the disease.
- Bystander activation
- Epitope (a single antigenic site on a protein against which an antibody reacts) spreading
  - **Shifts** in immunoreactivity may cause the waxing/waning character of ERU
  - Shifts in immune response to S-antigen and IRBP occur in horses with ERU
  - **These shifts occur in quiet clinical phases**
- The retina and vitreous have many T-cells.
  - Th lymphocytes in the uveal tract.
- Chorioretinitis occurs at all stages of ERU.
- Pinealitis is present.

# Theories on the “Lepto Link”

- Is equine uveitis due to **DIRECT TOXICITY** of intraocular infection?
  - This may be the case in Europe.
  - ERU is actually “ocular leptospirosis” not ERU
- Is it as **AUTOIMMUNE DISORDER** triggered by molecular mimicry?
- Are leptospira somehow **MODULATING THE IMMUNE RESPONSE** in the eye?



# Testing for Leptospirosis

- Most significant are *L. pomona* and *L. grippityphosa*
  - *L. pomona* most important in USA
  - Titers  $\geq$  1:400 are significant
  - Rarely will rising titer be found in paired samples--sampling too late in course of disease.
- Uveitis from lepto occurs later than the systemic infection.
- Some horses with lepto in eyes are seronegative!

- Persistent Leptospirosis may sustain the auto-immune attacks and be a subset of ERU.
  - **ERU Eyes:** *L. gryppotyphosa* cultured from vitreous of 52% uveitis eyes in Germany and *poimona* from aqueous humor of 20% (70% DNA+) uveitis eyes in USA
- Locally produced antibodies against Lepto cross react with the cornea, lens and retina (S-antigen and IRBP).
- Not all horses positive for *L. poimona* have uveitis.
  - The serologic evidence of *poimona* infection is more frequent than the incidence of ERU.

# Breed and Uveitis



*Color pattern more at risk*



*Color pattern less at risk*

- In Western NY, Appaloosas are 8.3 times more likely to suffer from uveitis than other breeds
- At risk individuals tend to have coat patterns with overall roan or light coats, little pigment around eyelids, sparse manes and tails
- Germany: Warmbloods at risk, ELA genetics theorized.

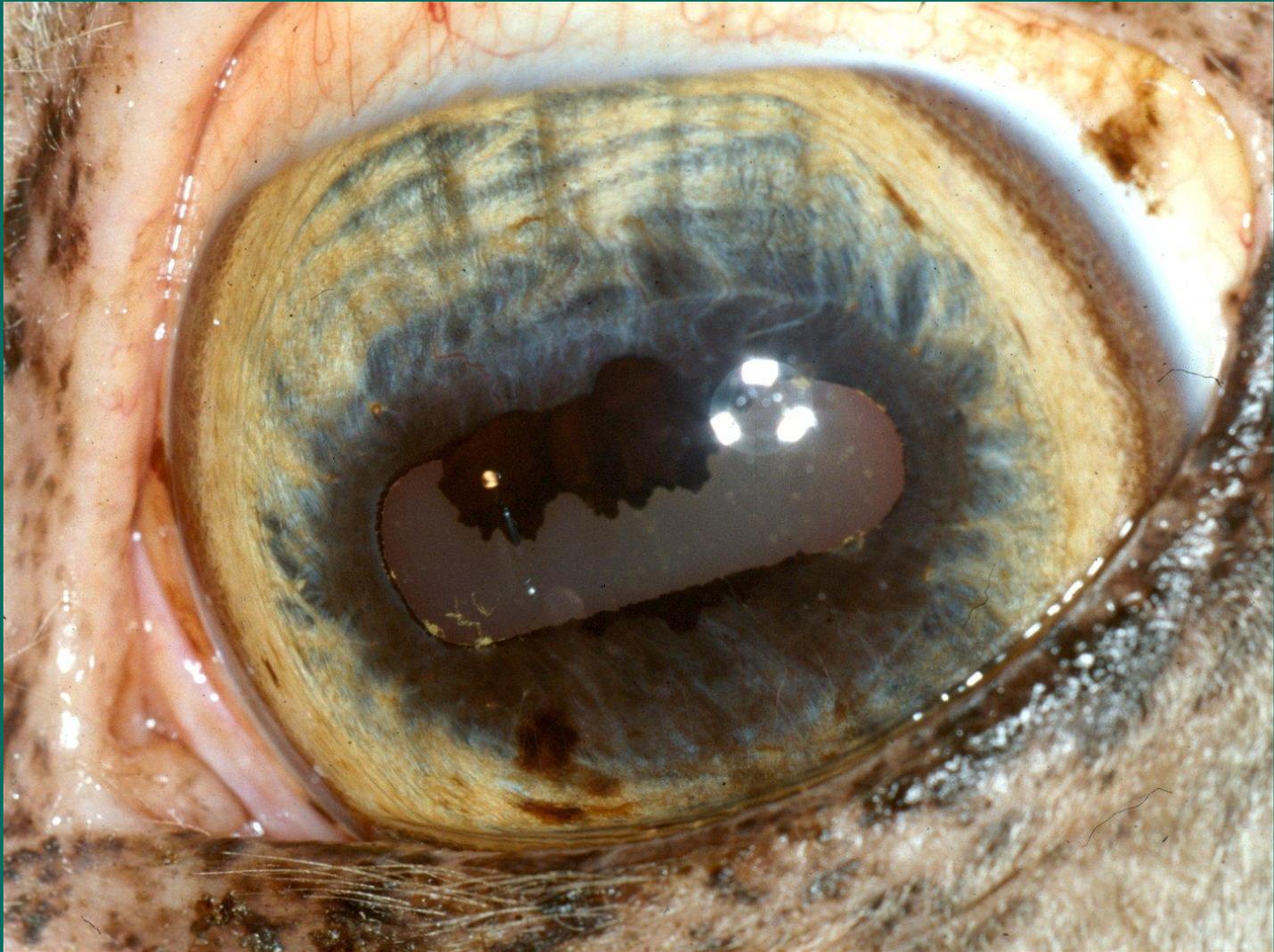
■ Percentage of horses with uveitis losing sight in at least one eye if Lepto + (11 yrs):



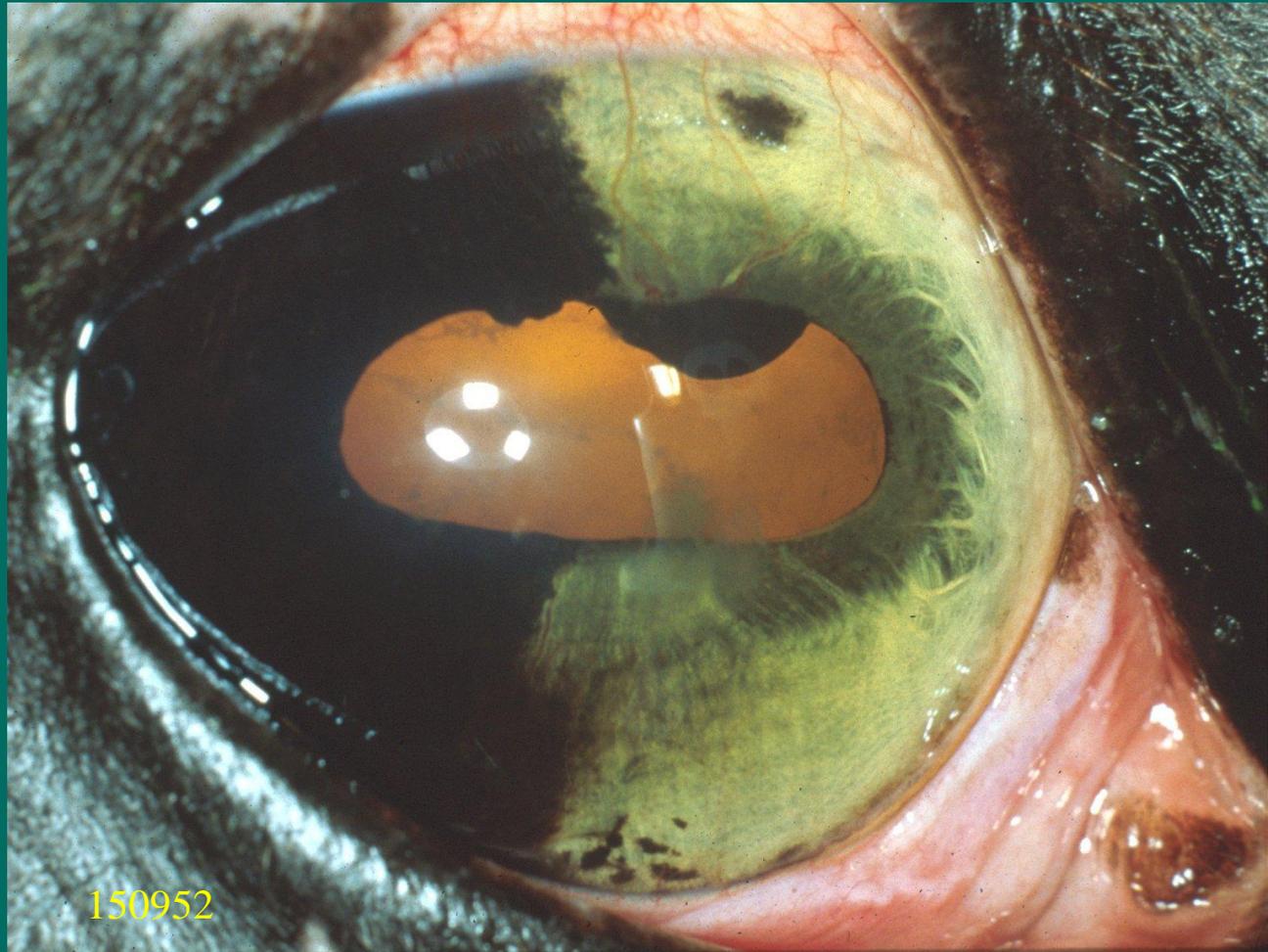
- + Appaloosa 100%
- Appaloosa 71%
- + nonAppaloosa 52%
- nonAppaloosa 34%



The more pigment, the less ERU, and the less CSNB!

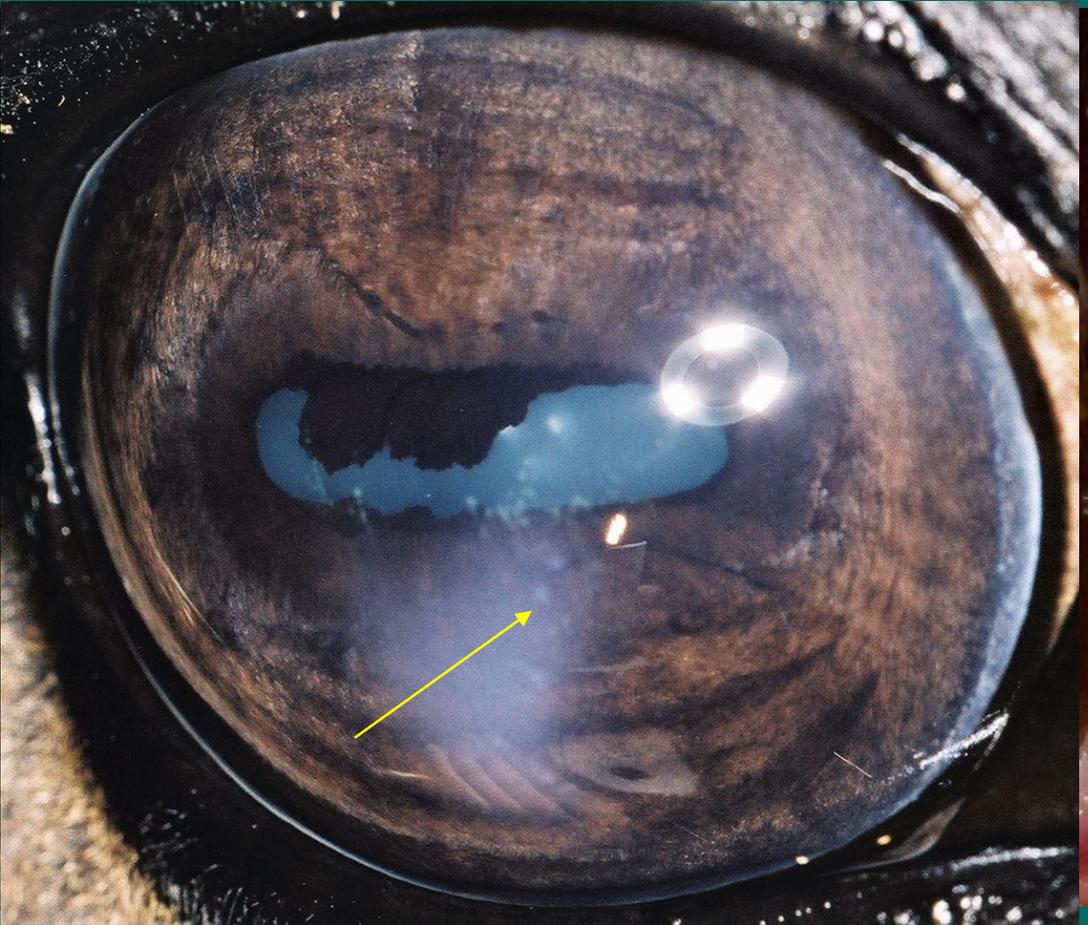
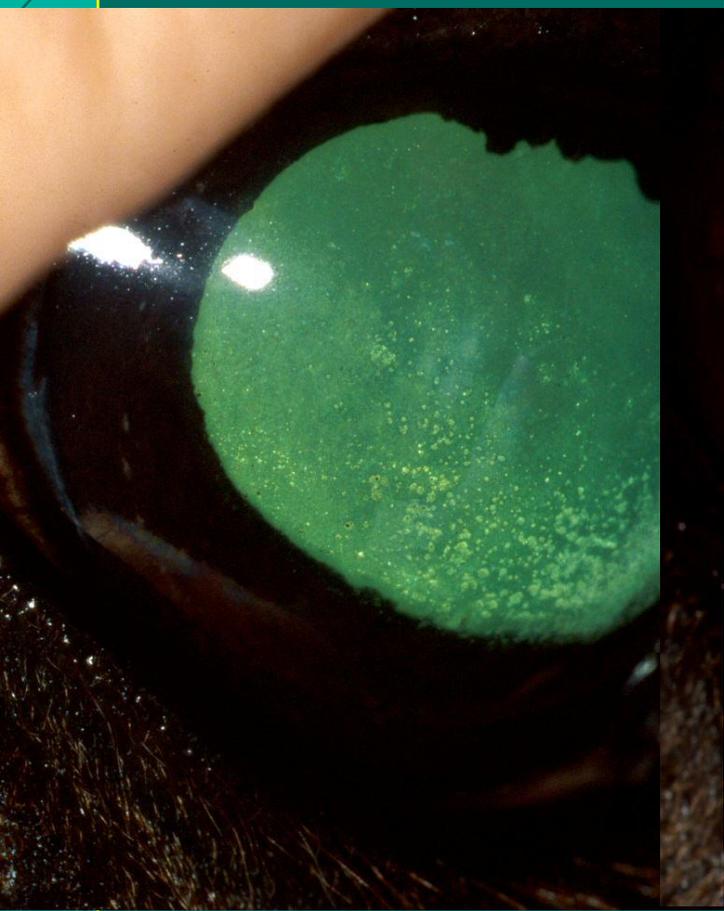


Iris color changed to brown



150952

# Keratic Precipitates (KPs)

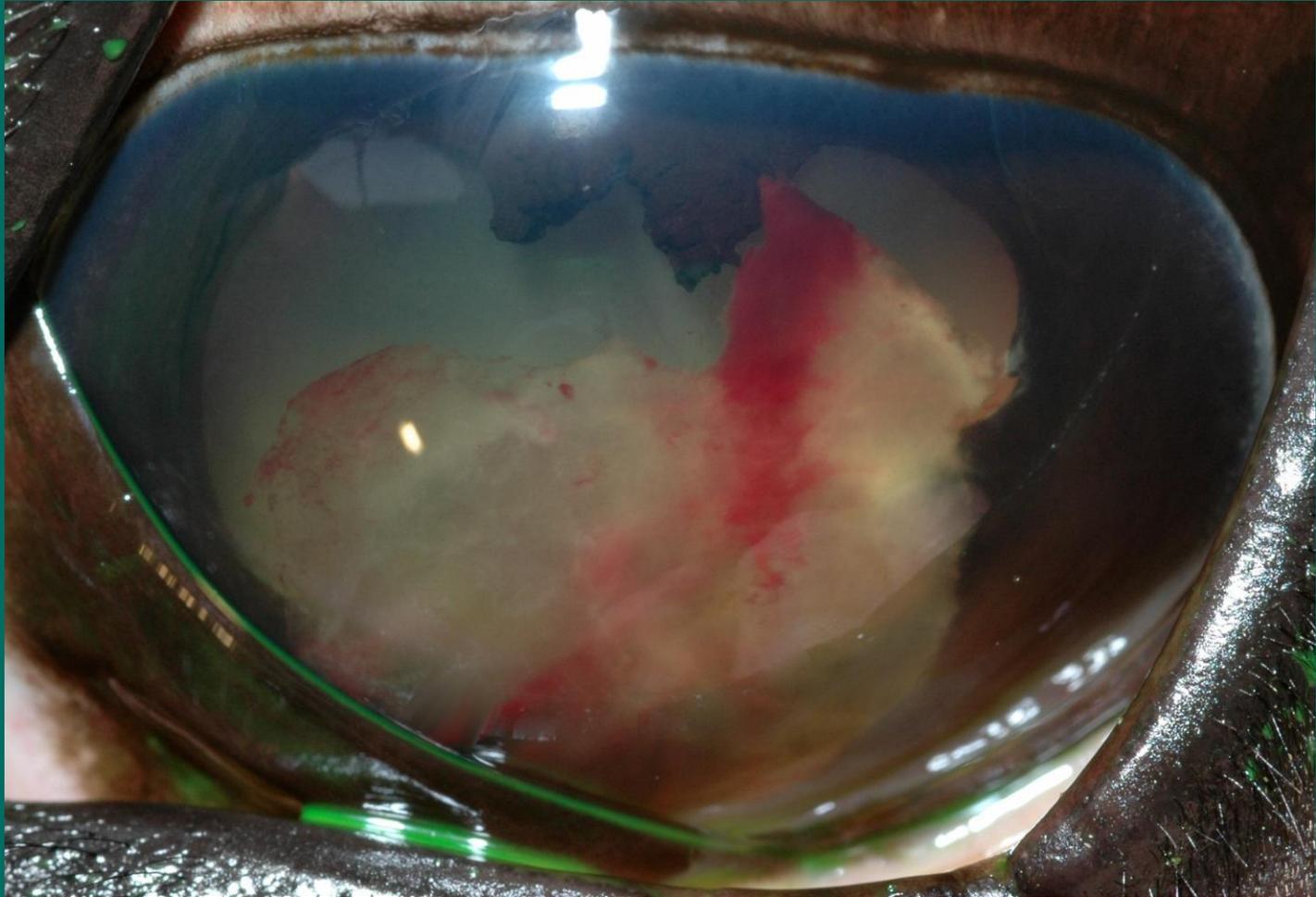




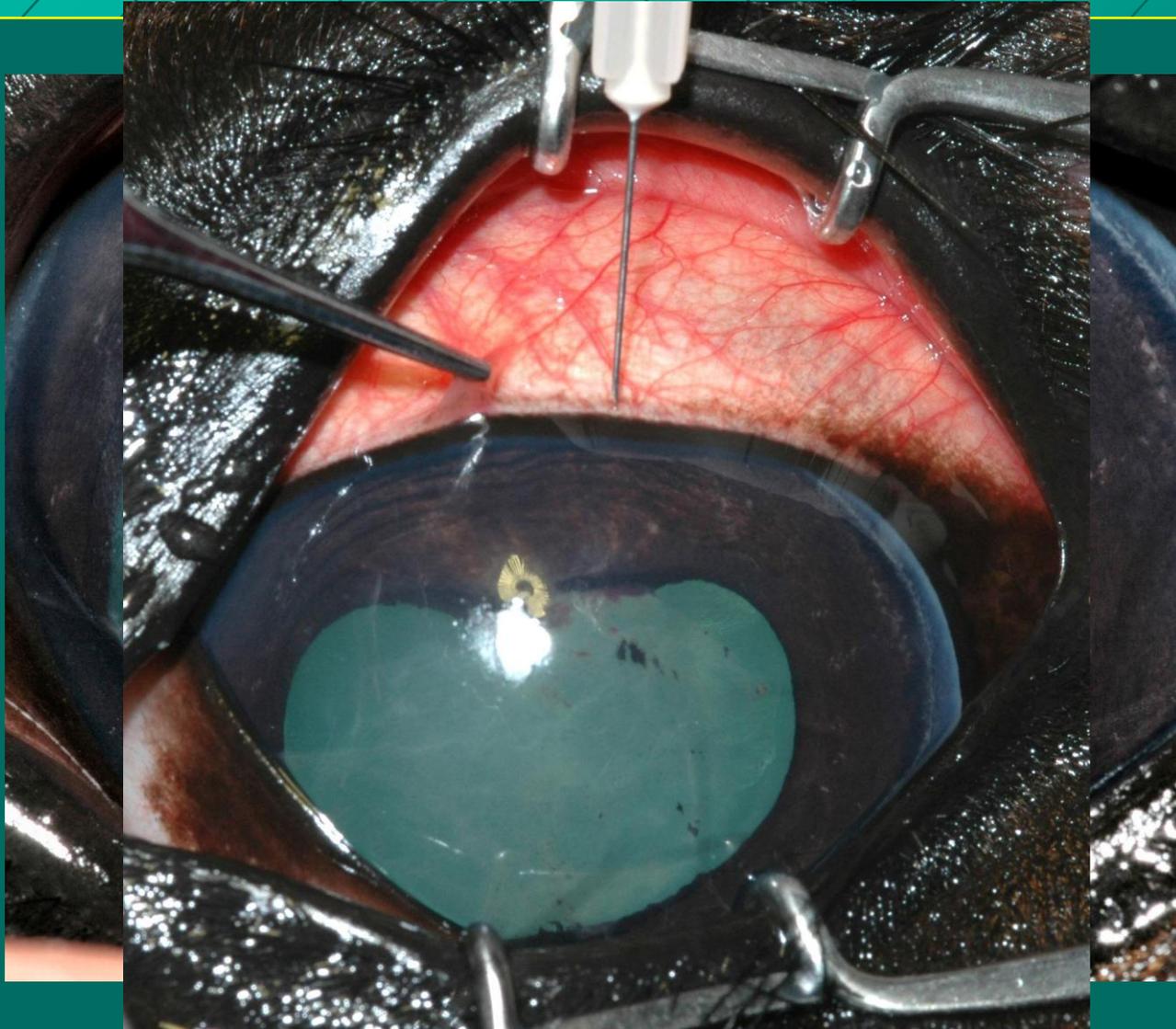
PMNs give a green appearance in ERU.



210202



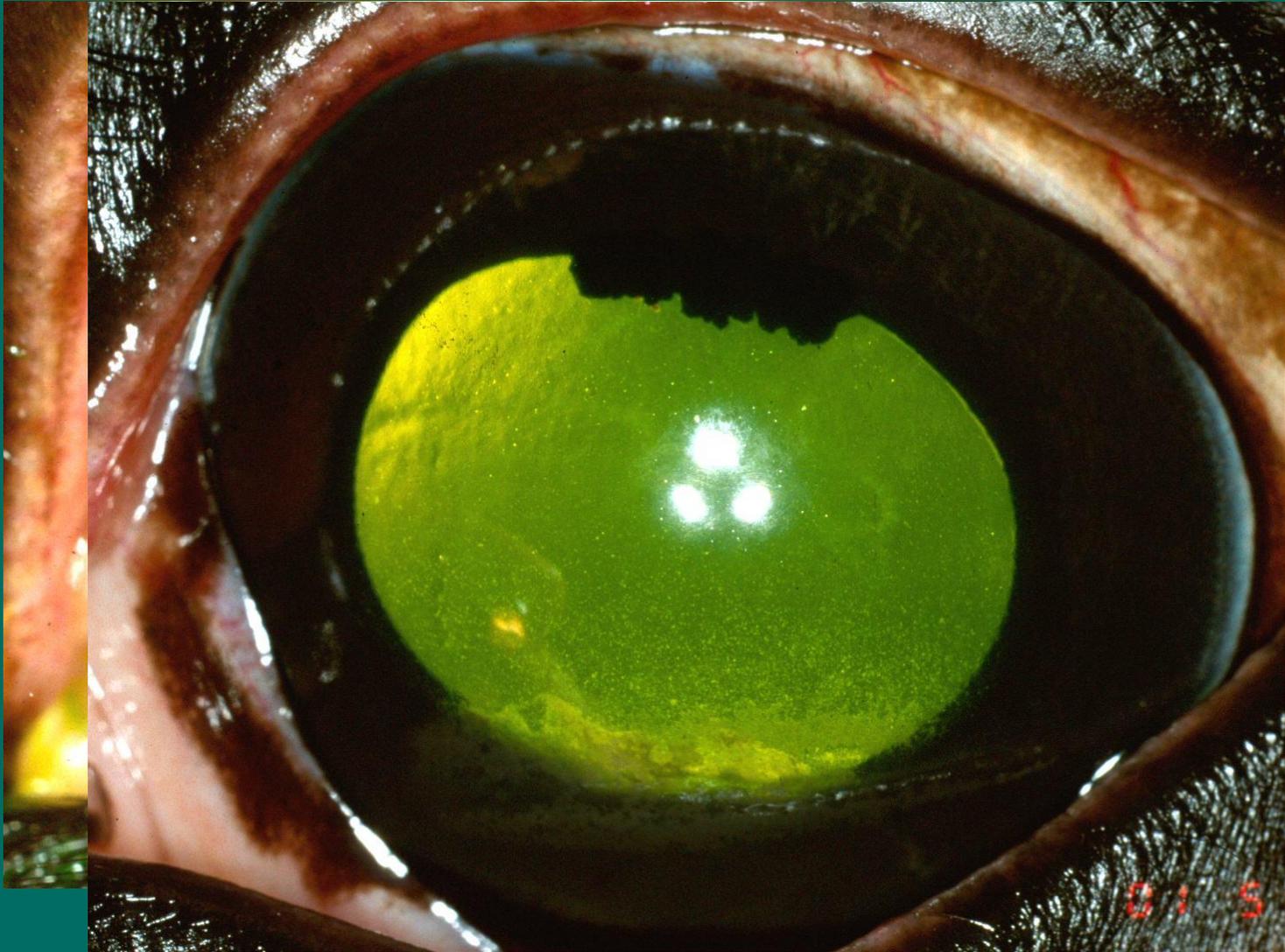
ERU and fibrin (Cookie)



Gypsy and Tissue Plasminogen Activator



Fibrin is removed by TPA



156113

# Tissue Plasminogen Activator

- Cathflo Activase® (Alteplase®) Genentech:
  - 100 µgm/0.1ml
  - \$121/14 doses

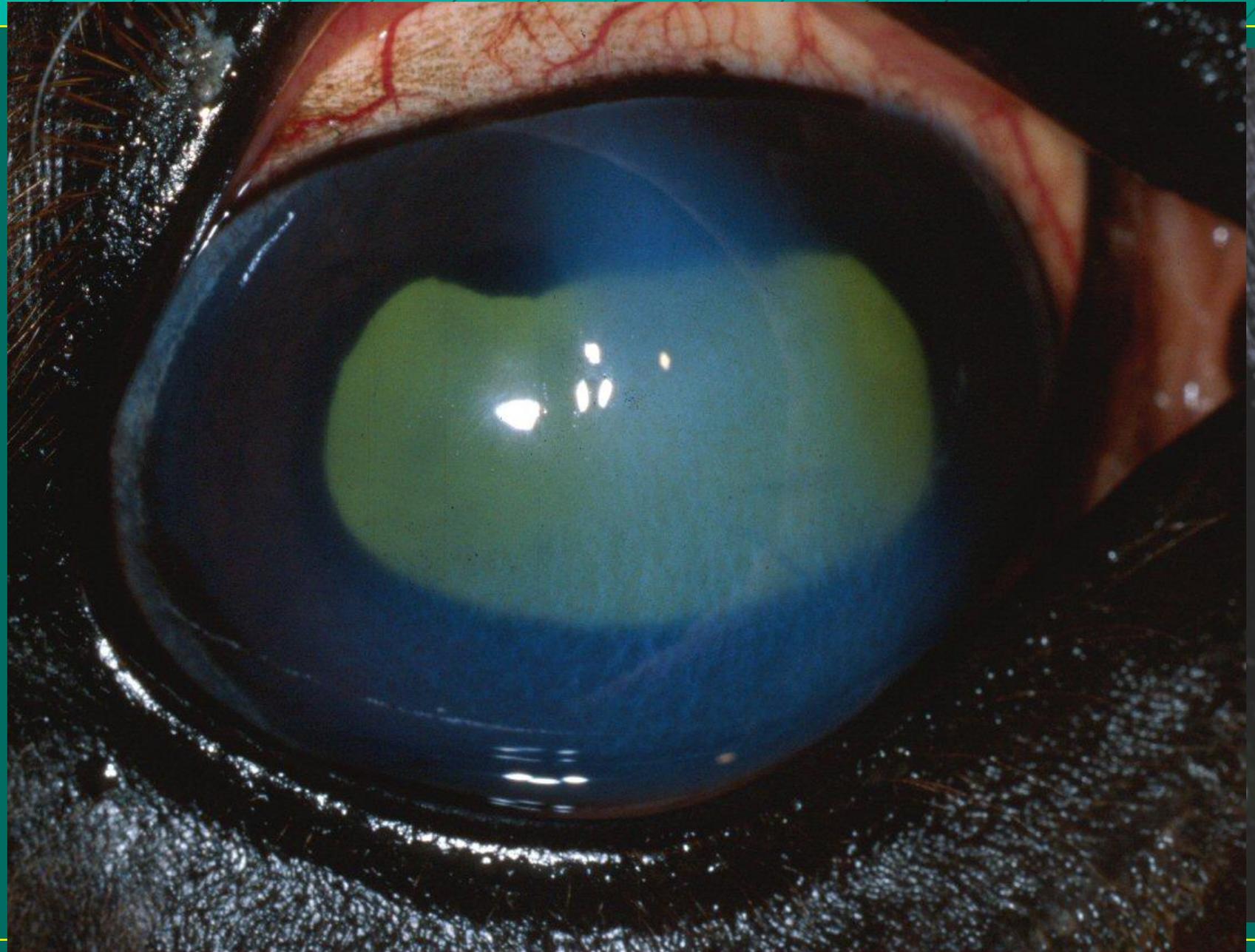


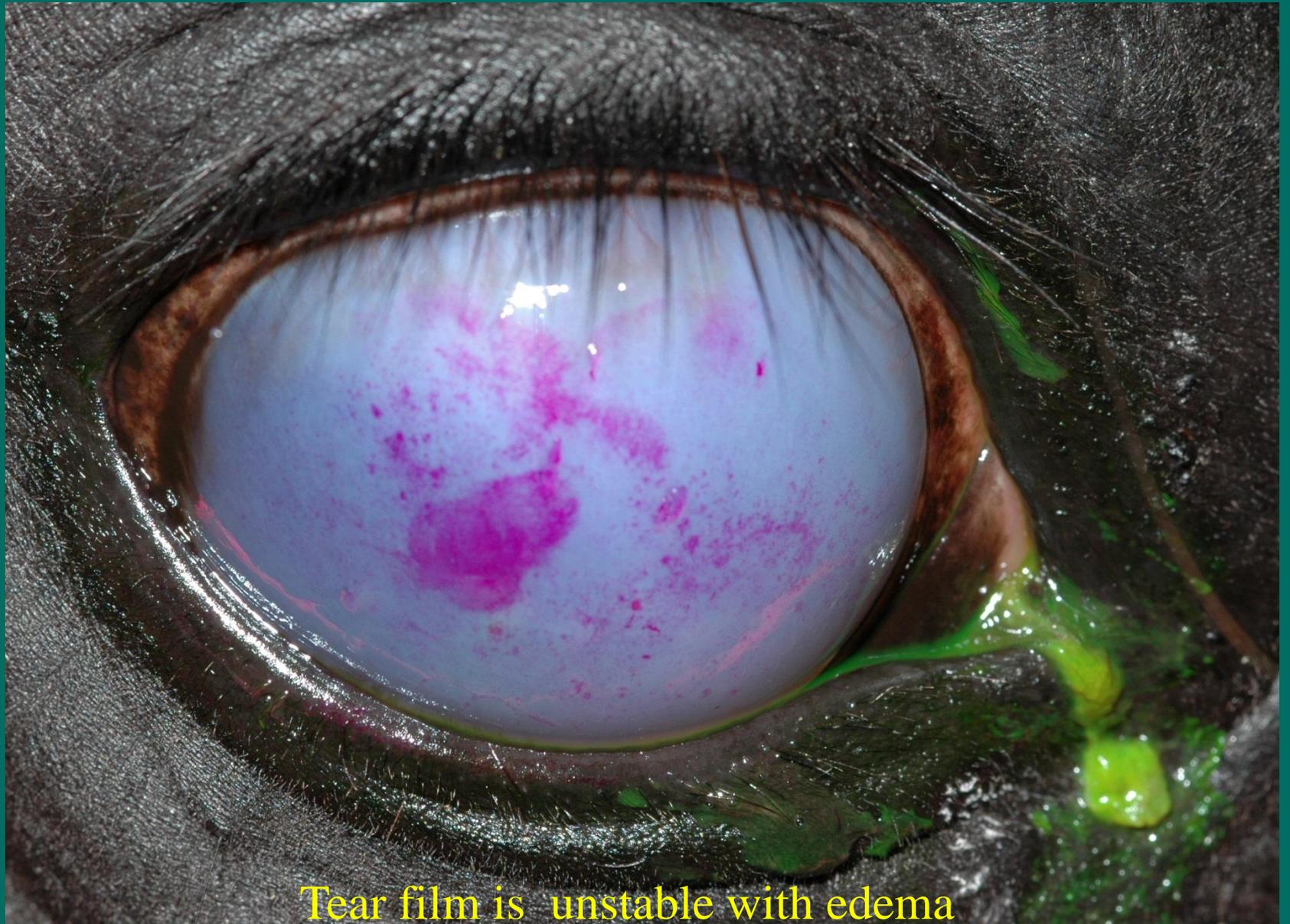


Corpora nigra atrophy in ERU

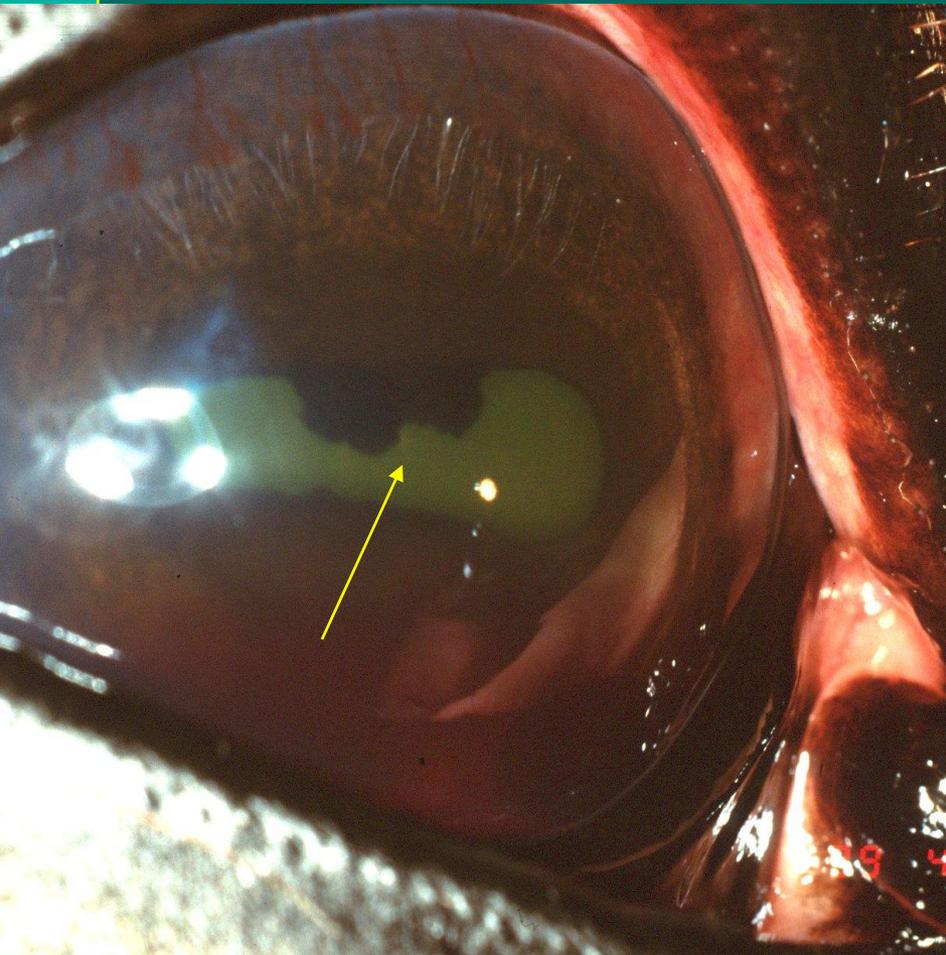


Endotheliitis: precursor of glaucoma??

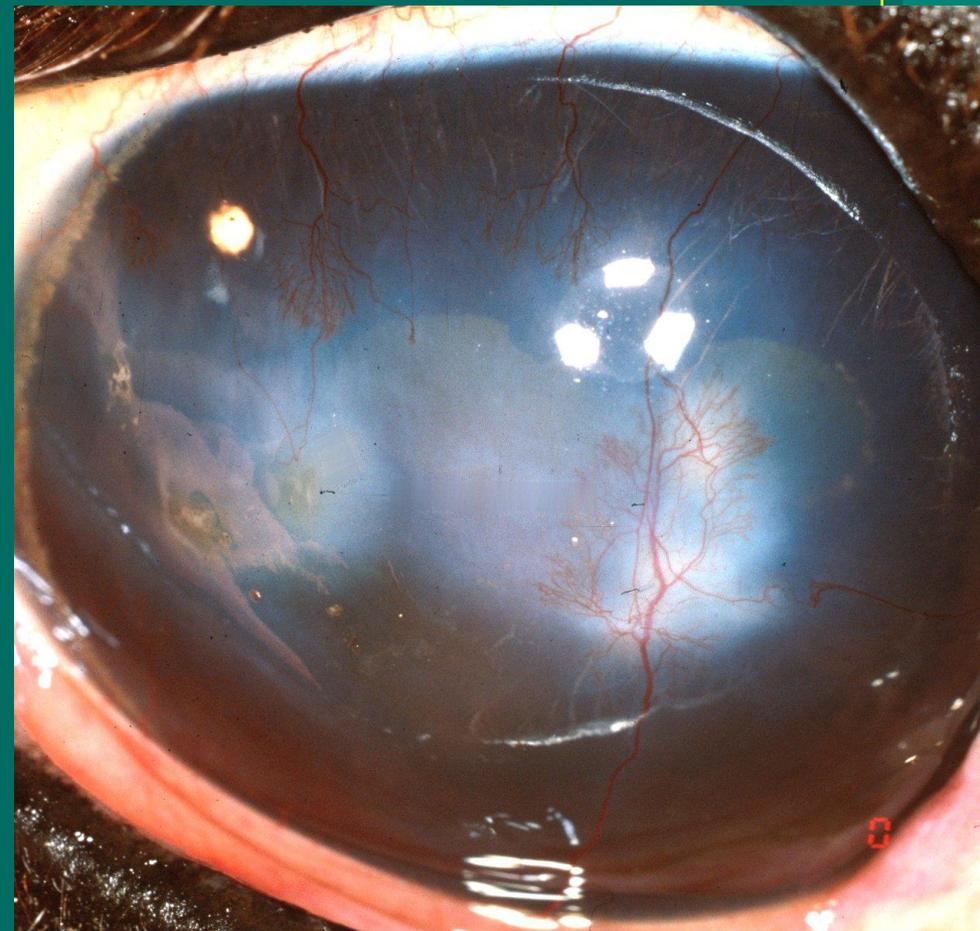




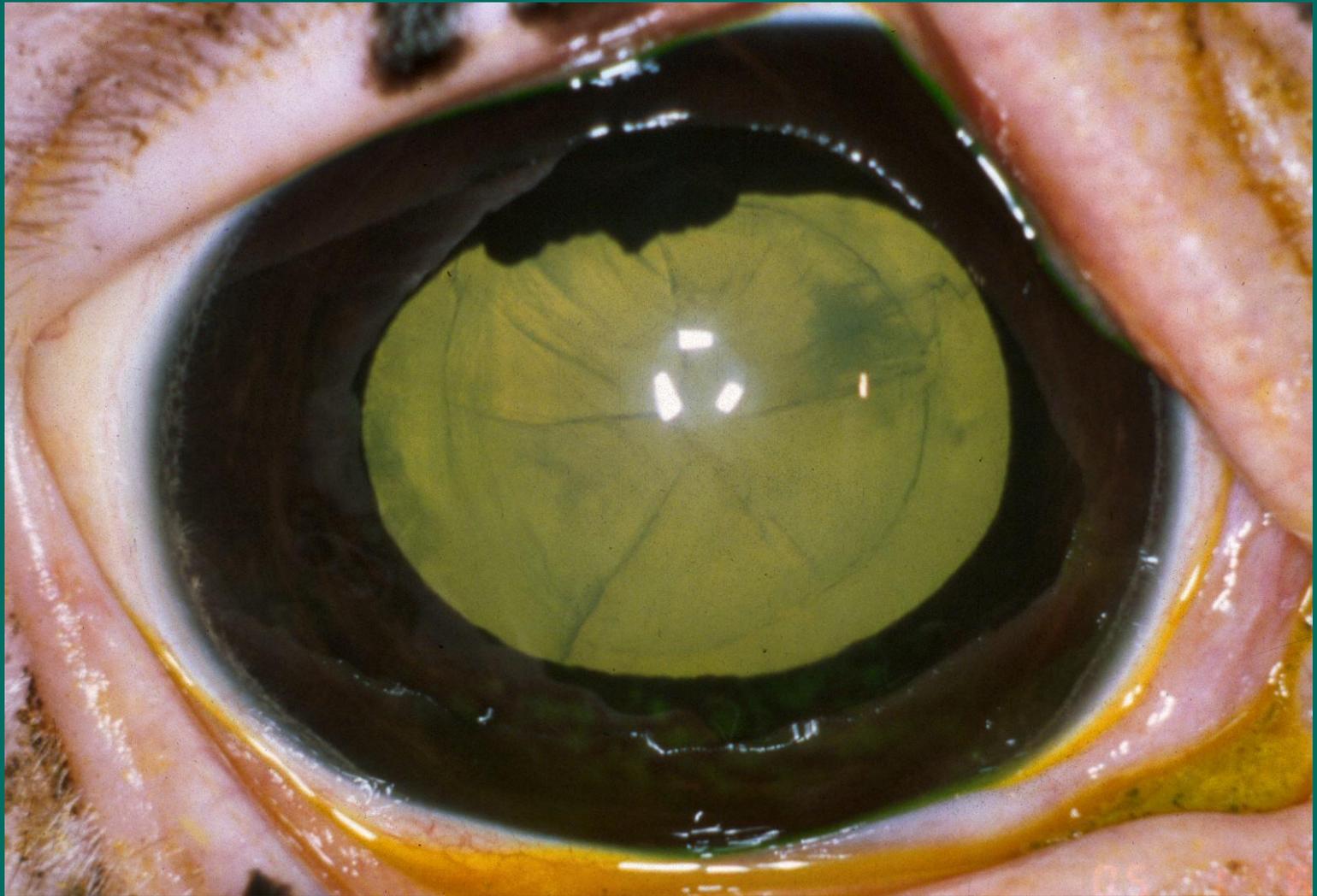
Tear film is unstable with edema

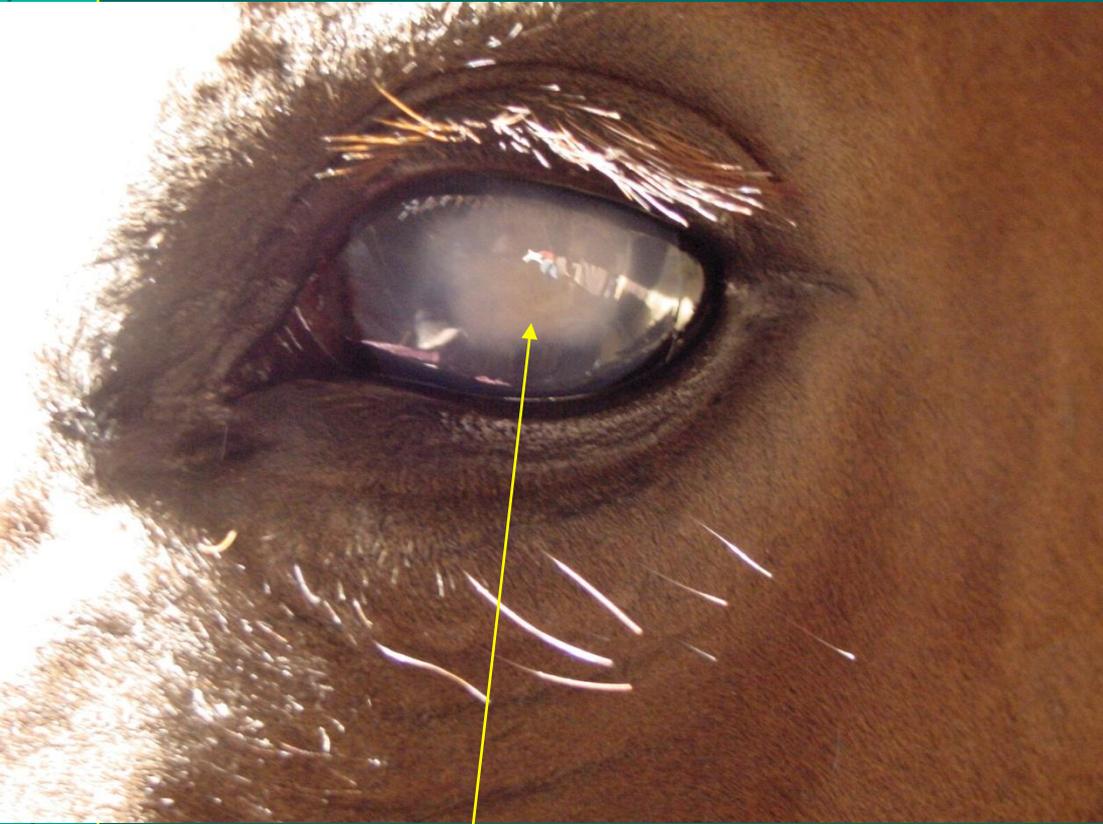


Miosis

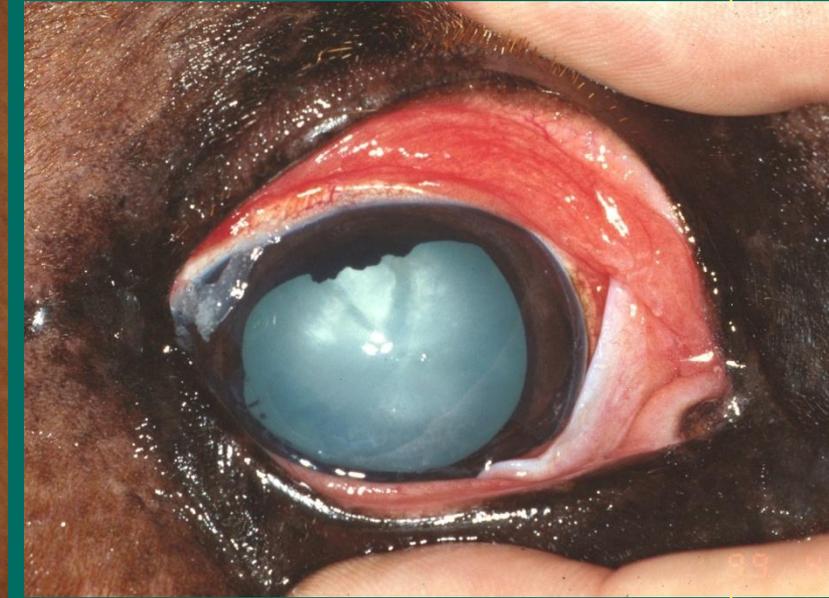


Corneal scarring



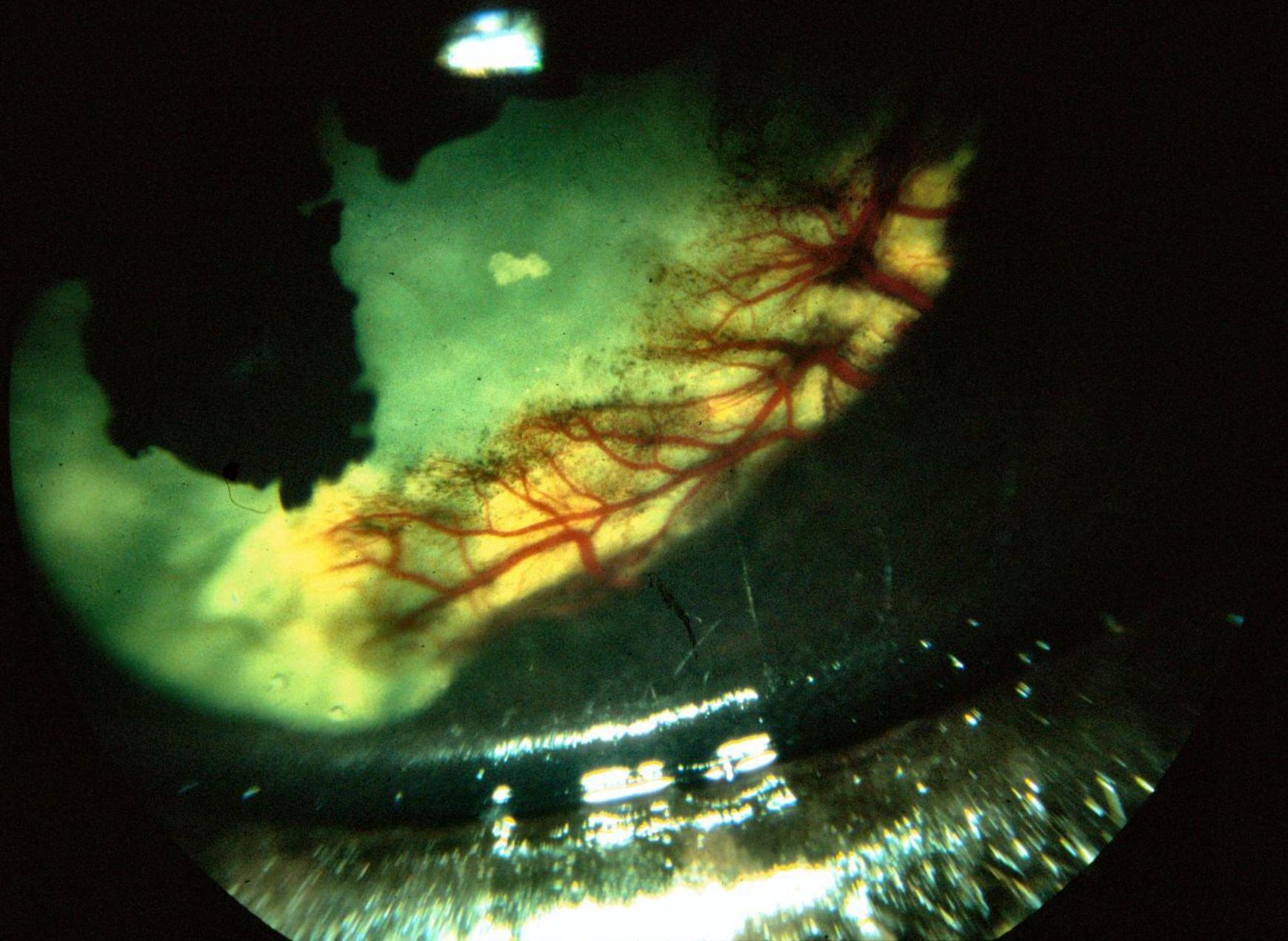


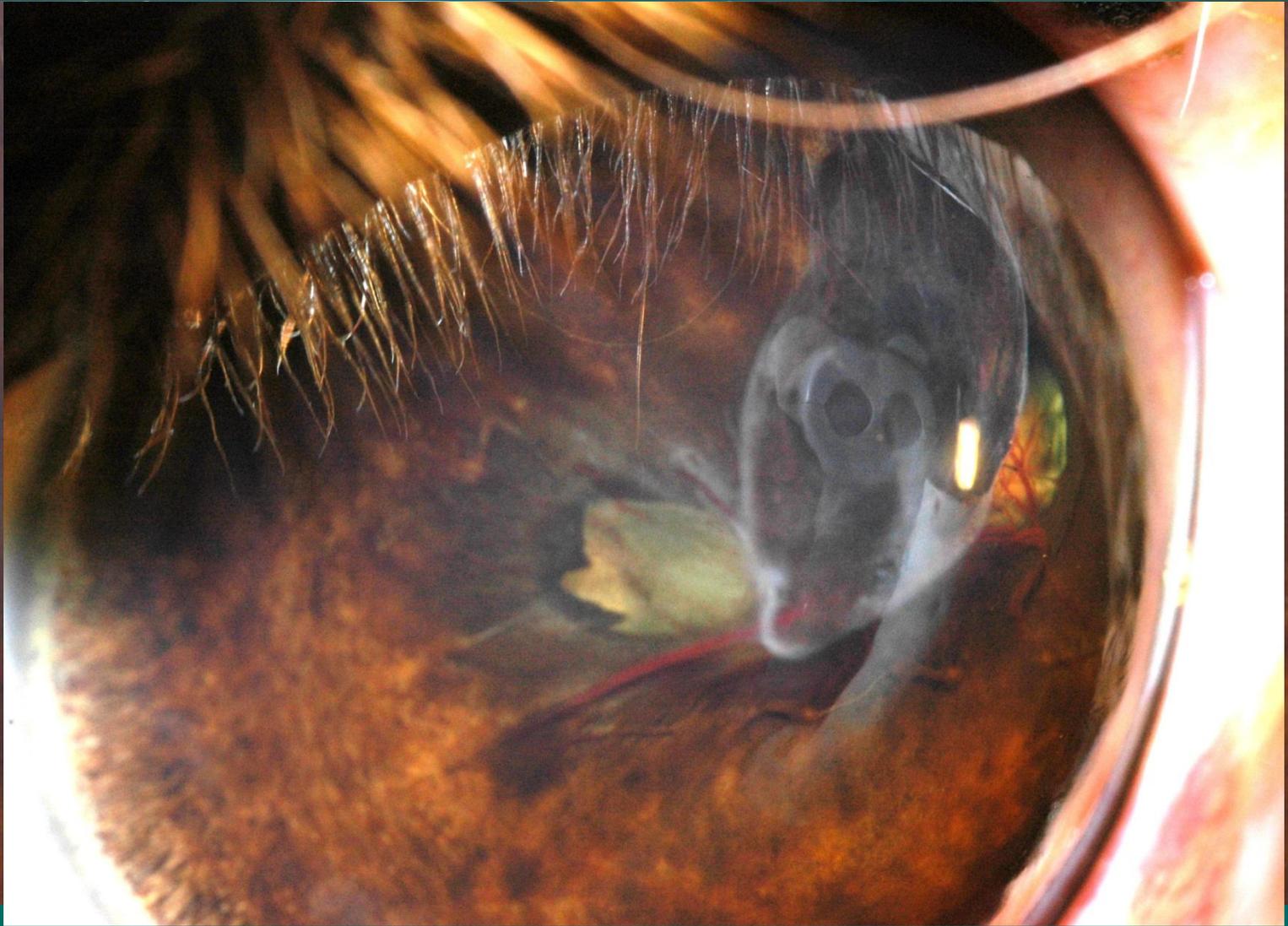
Fibrin plaque in pupil.



ERU causes cataracts. Some feel oral aspirin reduces this.

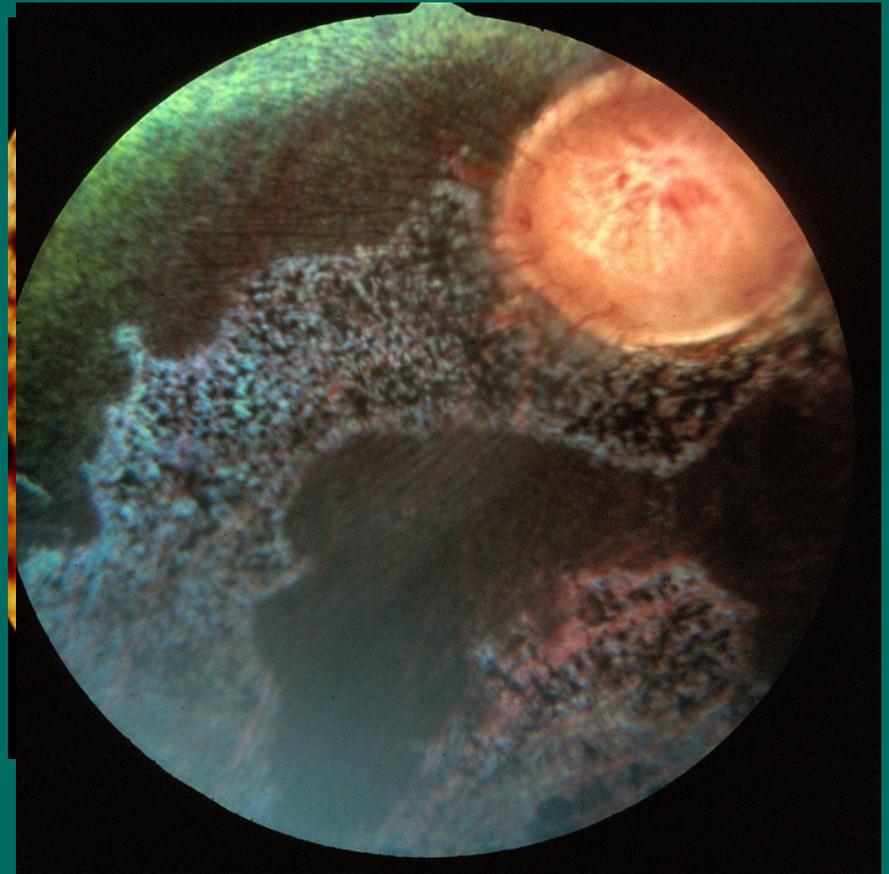
Why is the pupil dilated?



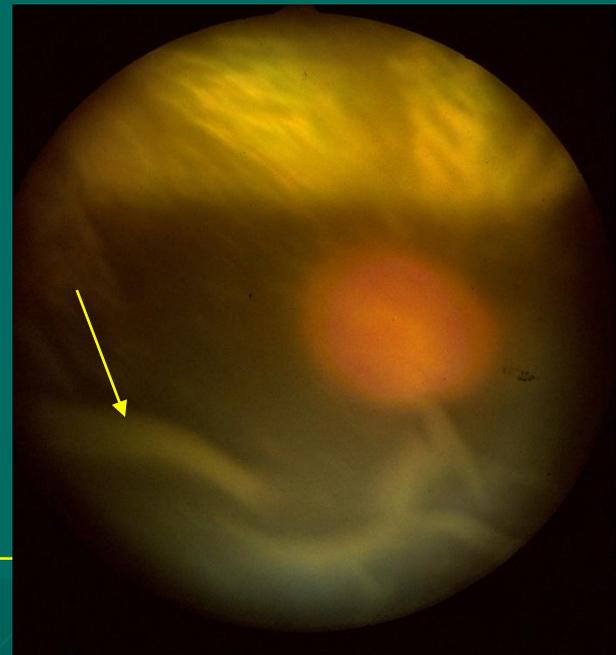
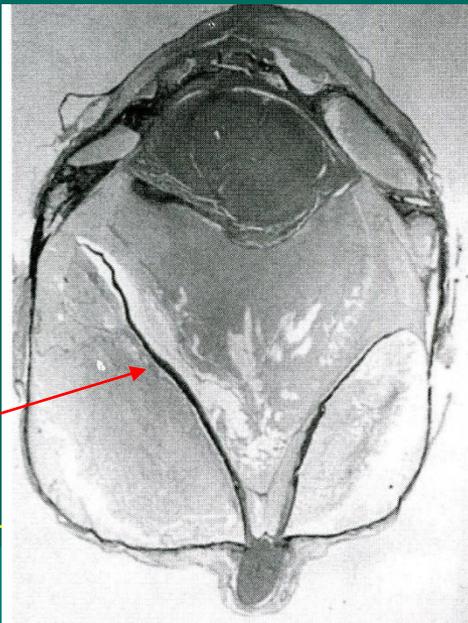
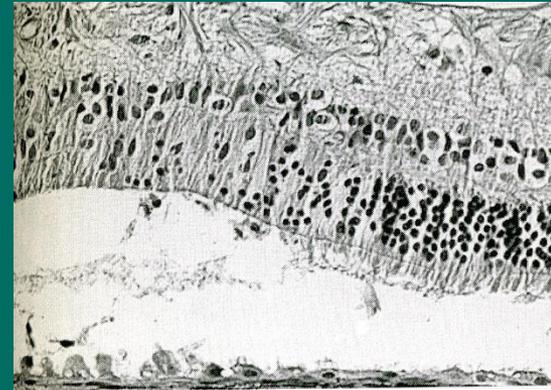
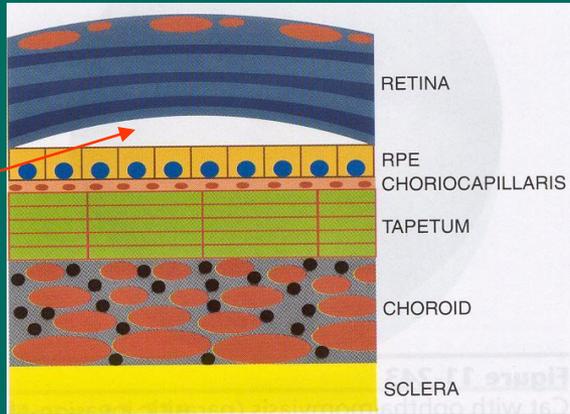


# Chorioretinitis

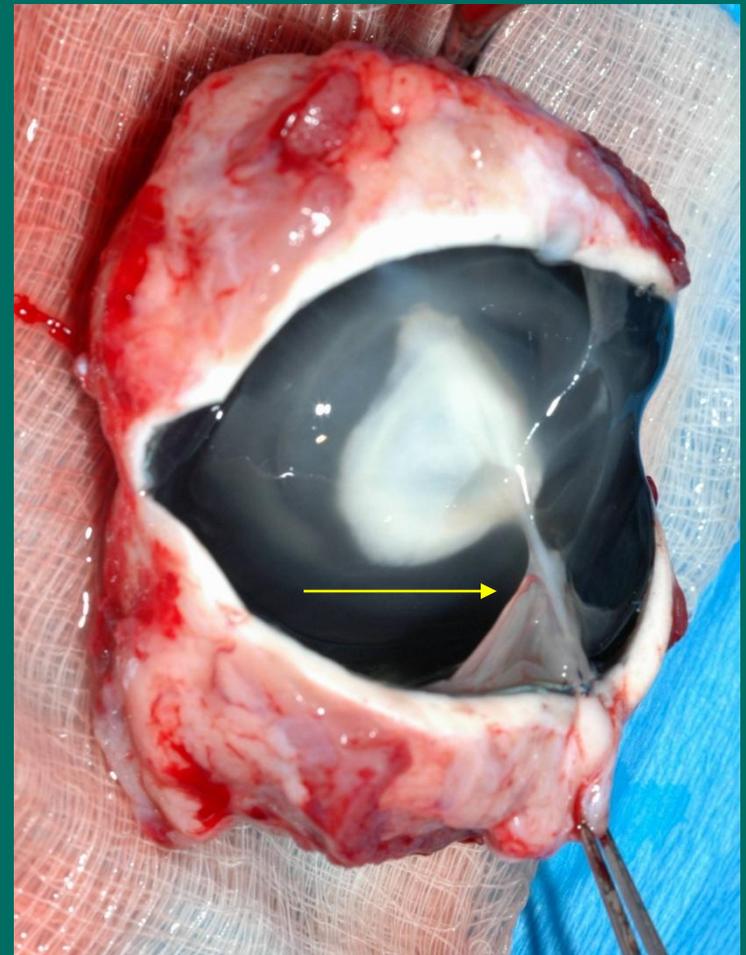
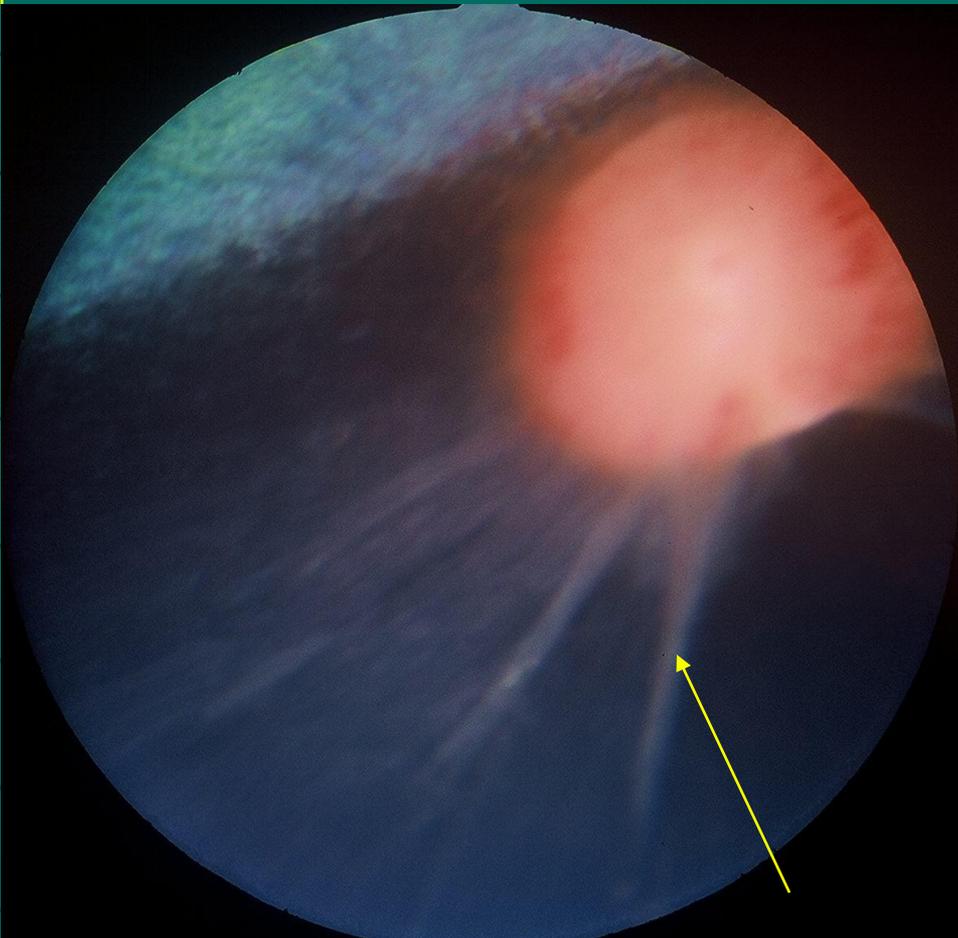
- Found at all stages of ERU!



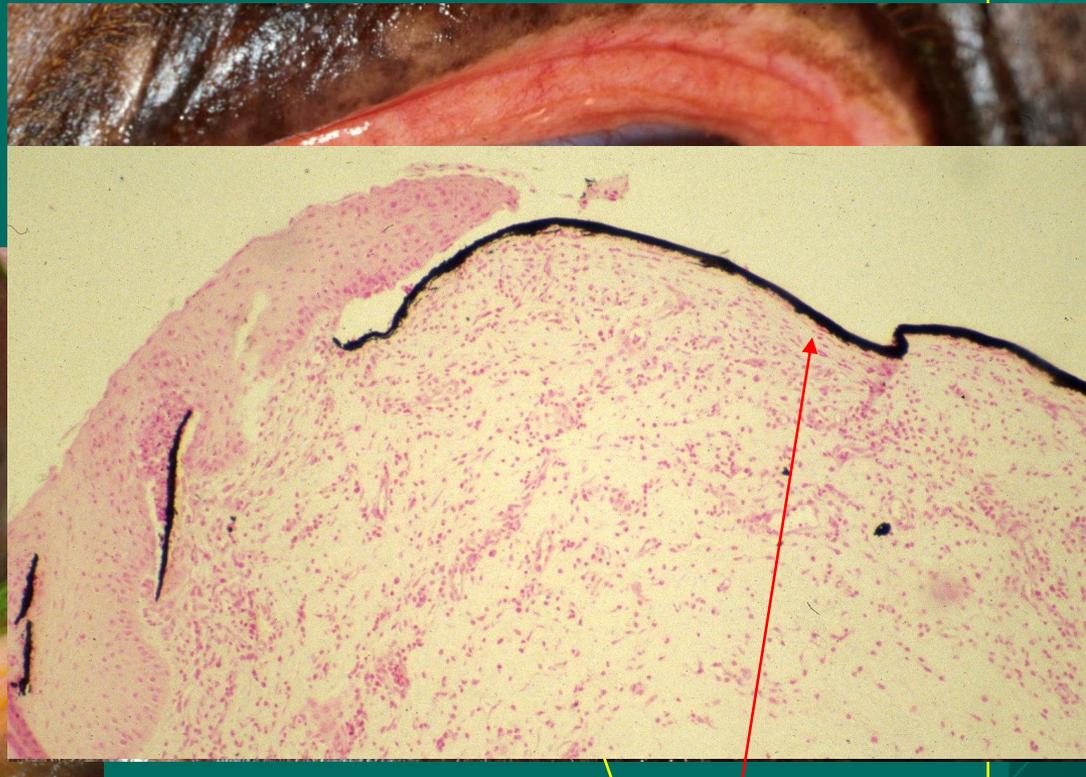
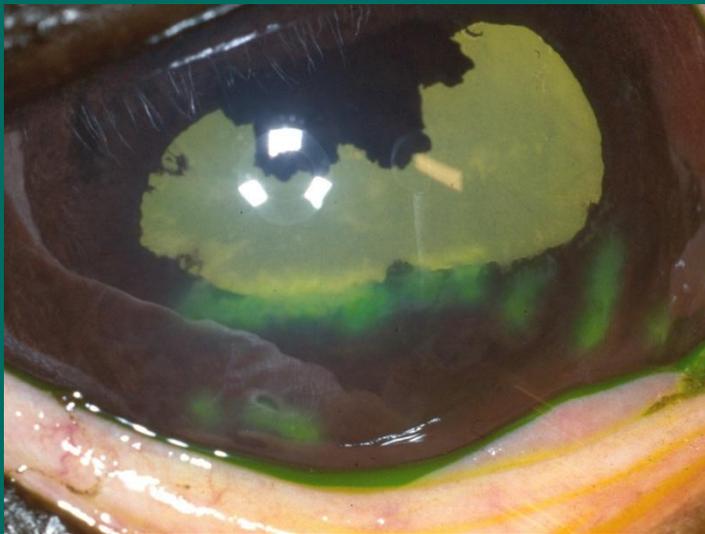
# Detachment of Retina



# Retinal Detachment

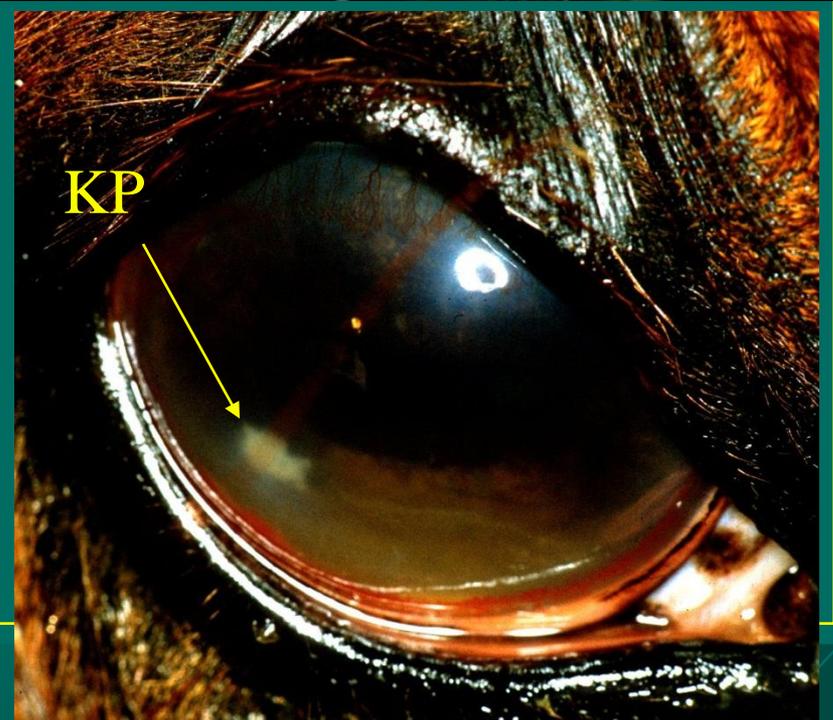
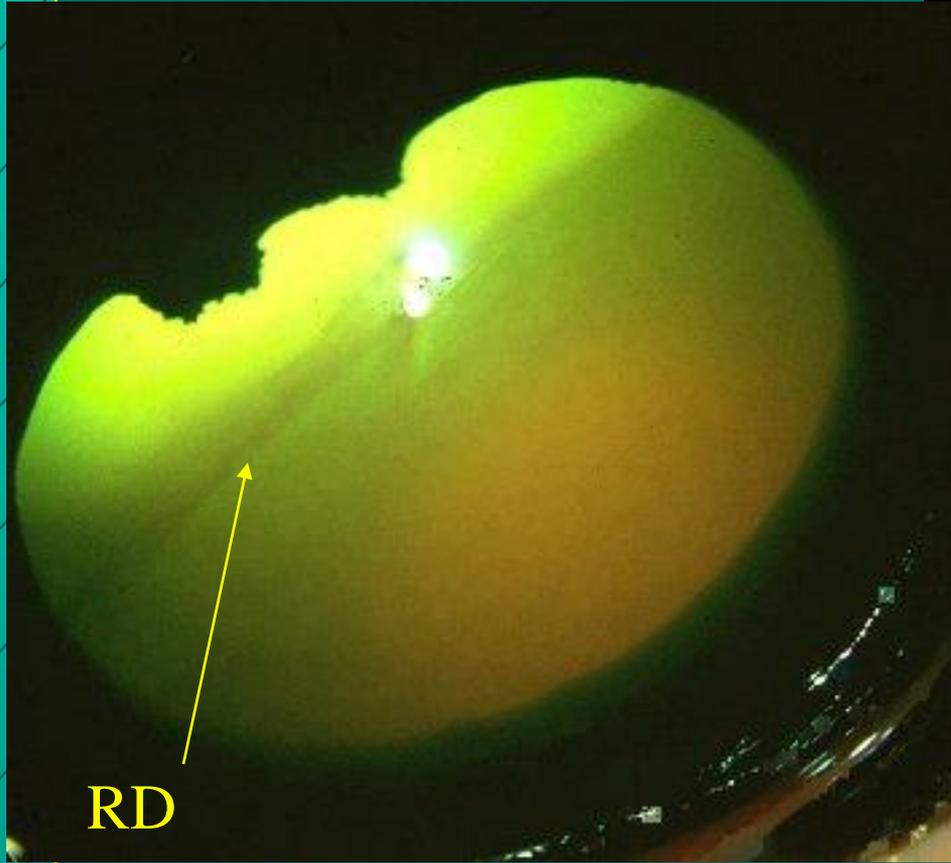


# Band Keratopathy: chronic ERU- 6% of cases

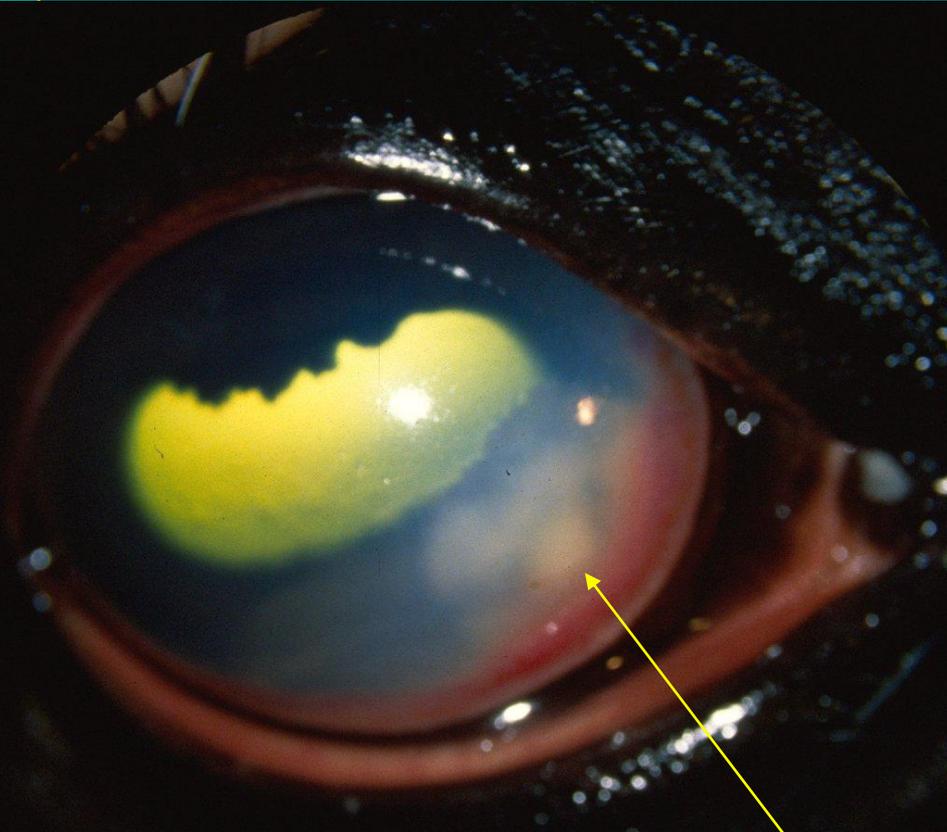


Treatment is EDTA topically.  
BK occurs in treated horses??

calcium



# Differentials for ERU



ERU resembles SA.

3 wks later

# KEY POINTS: Treatment



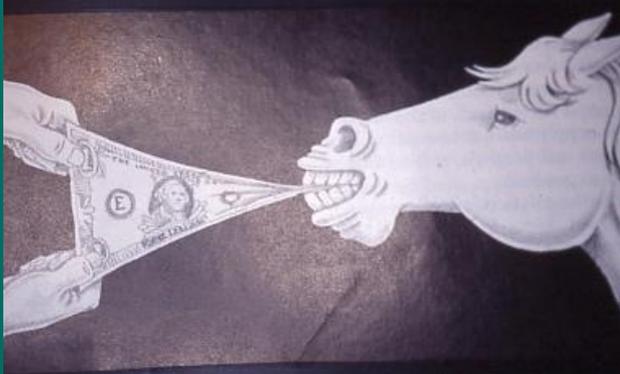
- Initially, owners may be very diligent about therapy
- Adherence to therapy is good

# KEY POINTS: Treatment



- But eventually, it wears them out!
- They do not persist in the therapy.

# KEY POINTS: Treatment



- Fatigue, burnout, and \$\$ concerns may tempt owners to self treat painful eyes
- But >25% of horses with uveitis suffer corneal ulcers over time, steroid treatment is dangerous!

# KEY POINTS: Outcome



- Tell owners that no matter WHAT they do, many uveitic horses go blind.
- SOME horses have to be euthanized.
- OTHERS may lead productive lives as family pets.

# ERU Medical Therapy

- Topical mydriatics: 1% atropine to effect. Critical!!!!!!!
- Topical corticosteroids: Prednisolone acetate. Treat 30 days past last attack!!
- Topical NSAIDs: flurbiprofen, Voltaren
- Topical cyclosporine A: 2% is best
- Systemic gentamicin (2.2 mg/kg IV BID)
- Intravitreal gentamicin (4 mg total in 0.1 ml injected 8 mm posterior to limbus at the 12 o'clock position); 17/18 had no recurrence with vision in 6.

## ■ ERU Medical Therapy

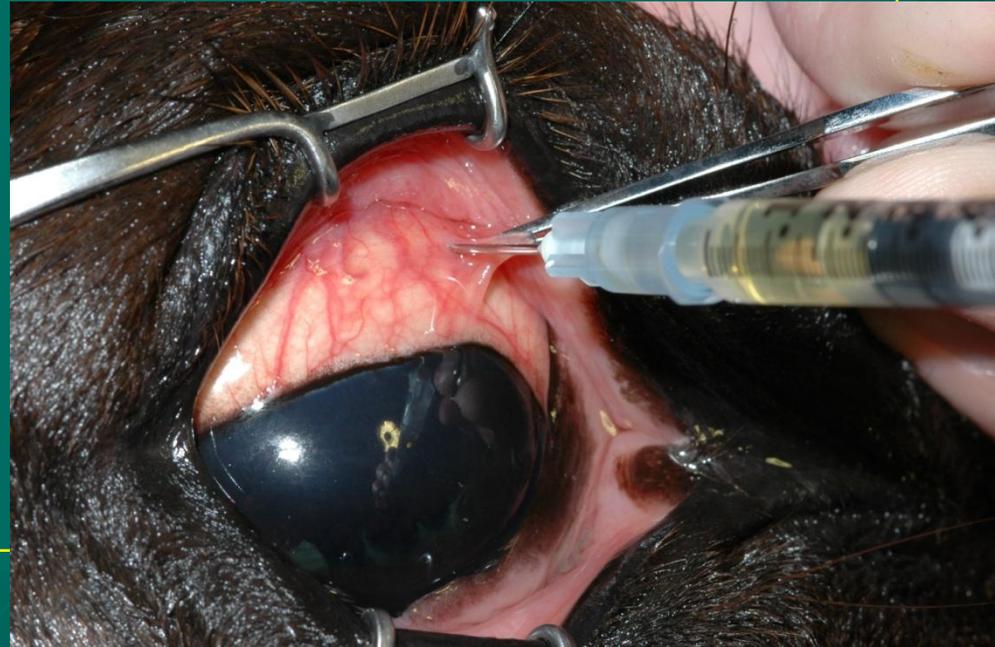
### – Systemic NSAIDs:

- Flunixin meglumine: 0.5 mg/lb SID - BID initially
- Phenylbutazone: 1-2 gm BID PO - 2nd choice
- Aspirin: 10-40 mg/kg PO SID long term!!!!
  - Methyl-Sulfonylmethane (MSM): 15 mg BID PO

### – Systemic Corticosteroids:

- Prednisolone/Prednisone: 0.75 mg/lb SID and decrease dose
- Dexamethasone: 0.05-0.2 mg/kg PO SID

- IRAP: Interleukin-1 Receptor Antagonist Protein
  - Homeopathic remedies: check the internet for the latest
  - “Cold Laser”
  - Magnet polarity
    - Green wavelength light!!
    - Damage the good eye for a “sympathetic effect”!?!?
- (William Percivall MRCVS 1876)



# Intracameral Medications for ERU

- TPA: 200 micrograms in anterior chamber
- Gentamicin: 4 mg in vitreous
- Triamcinolone: 2 mg in vitreous. \*\*\*

# Intravitreal Injection

- 4 mg gentamicin



# Intracameral Administration

- Tremendous drug concentration
- For intraocular infection or to remove fibrin in uveitis
- Many risks
  - Hemorrhage, cataract
  - Retinal detachment, retinal degeneration
  - Infection



Fibrin and TPA

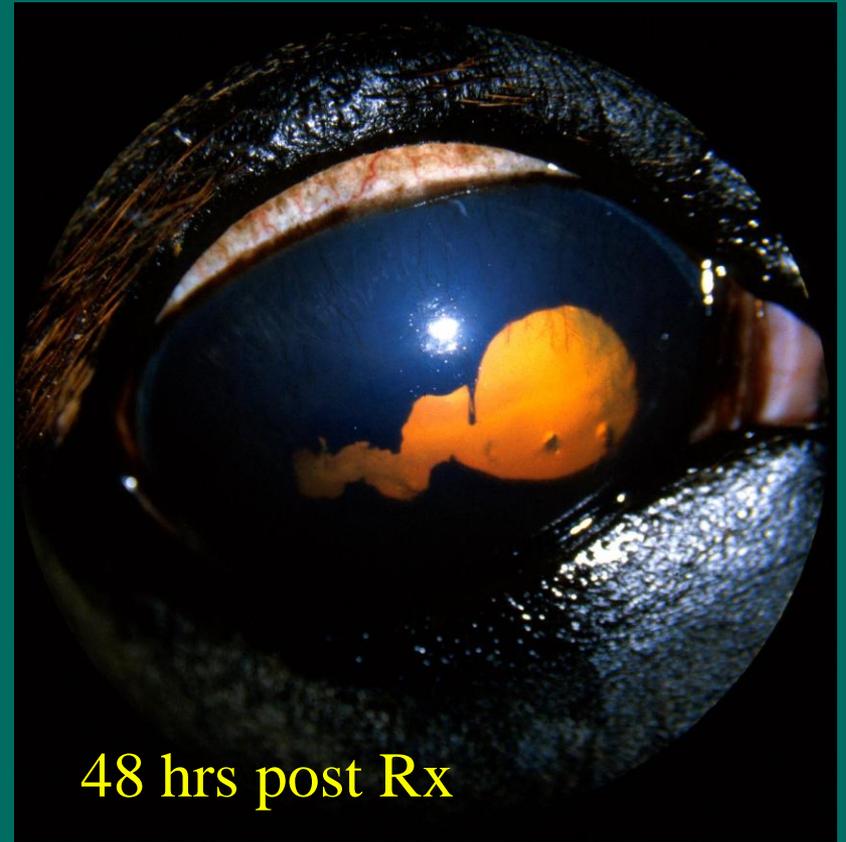
# Medical Treatment “Works”



Miosis and fibrin

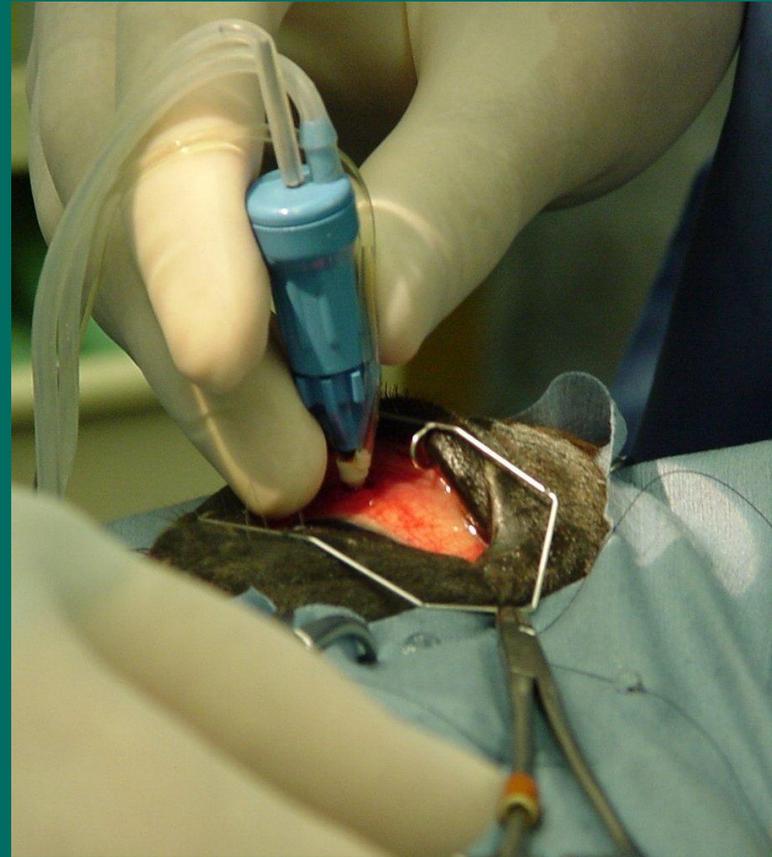


Pupil dilated and fibrin consolidating



48 hrs post Rx

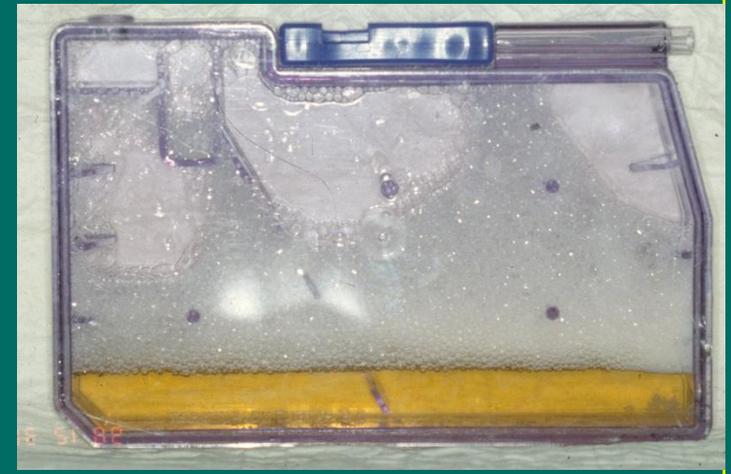
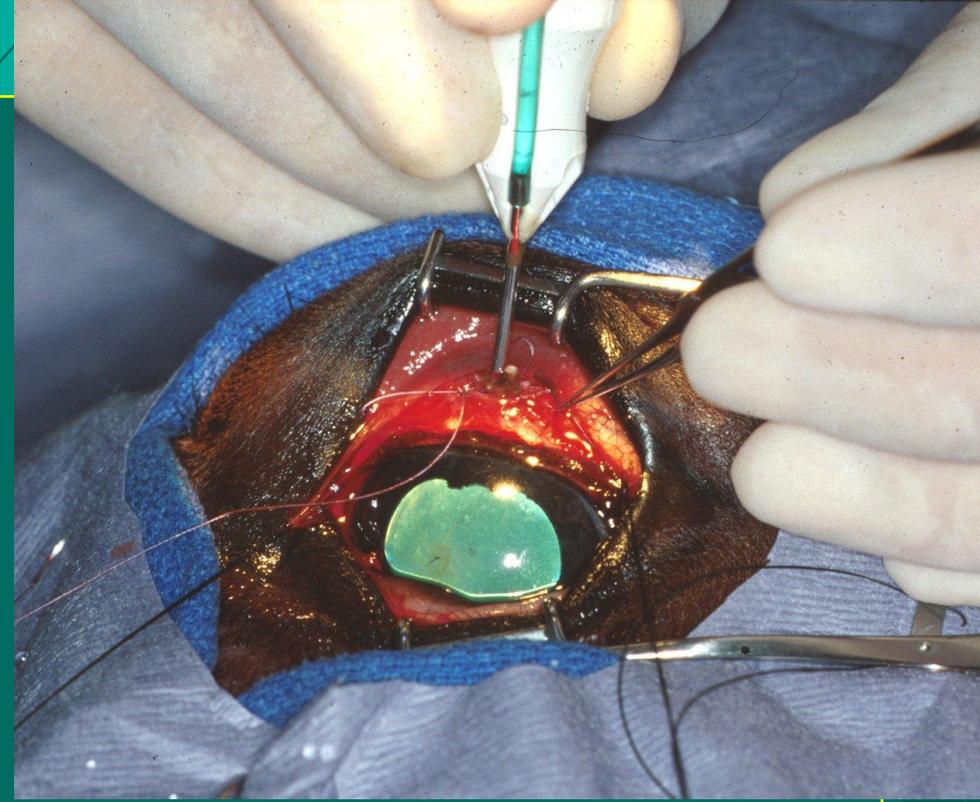
# Surgical Vitrectomy for ERU



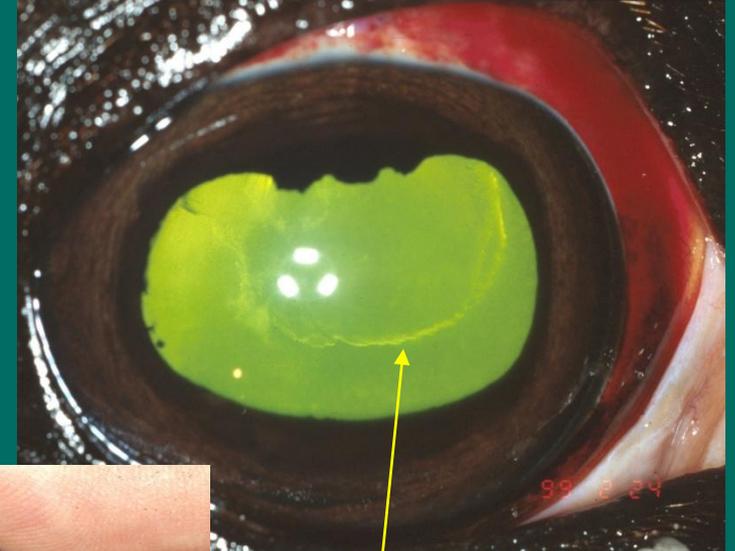
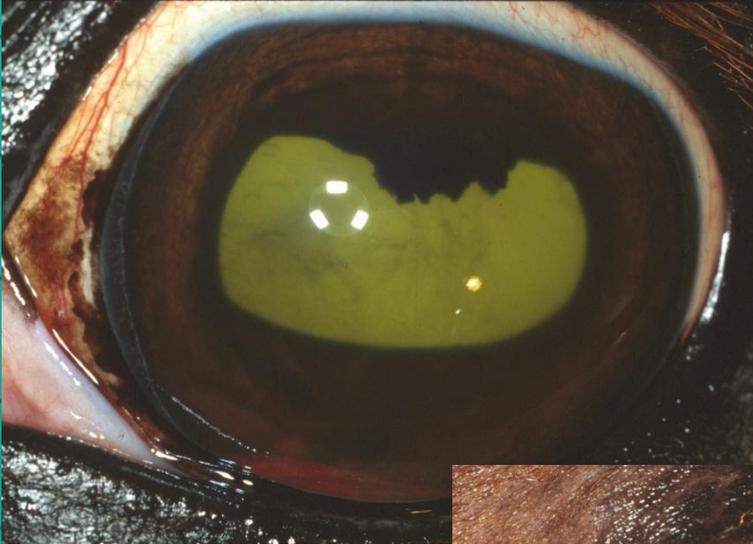
## ■ Vitrectomy

- Europe: 98% have less inflammation; 3-25% cataracts
- USA: 69% have less inflammation; 49% cataracts

- The European cases may be a subcategory of ERU, ocular leptospirosis.



- Subtotal vitrectomy to remove fibrin framework and antigens.



# Cyclosporine A implants

- (Slow release at 4 $\mu$ g/day for 5 years)
  - Intravitreal
  - Suprachoroidal
- 81% have less inflammation and attacks
- 87% visual at 14 months postop

CSA

