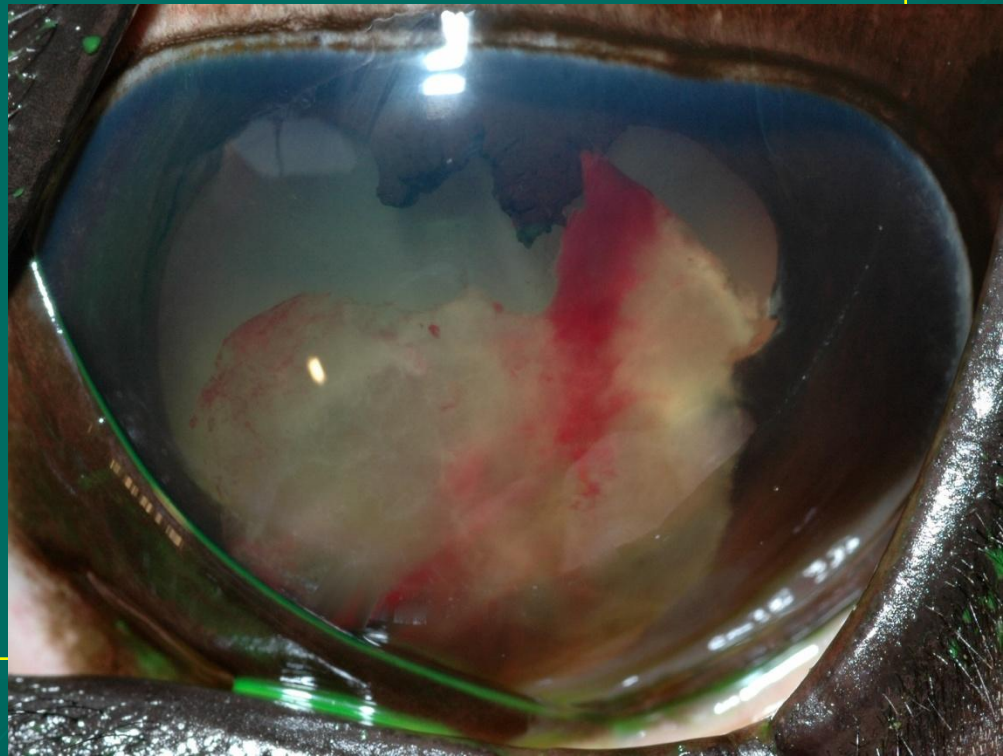
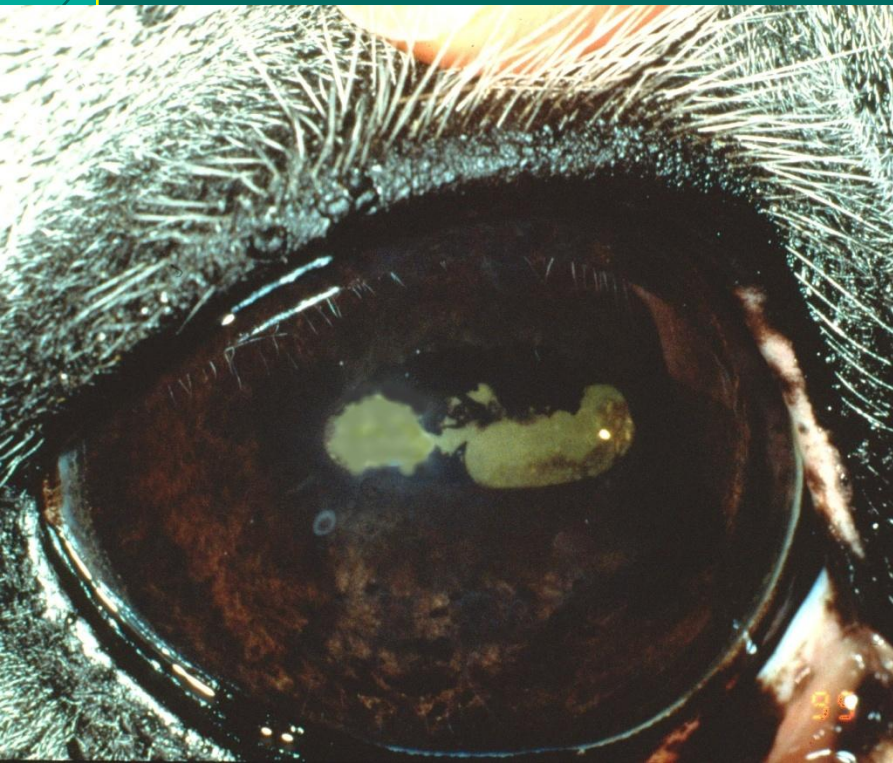
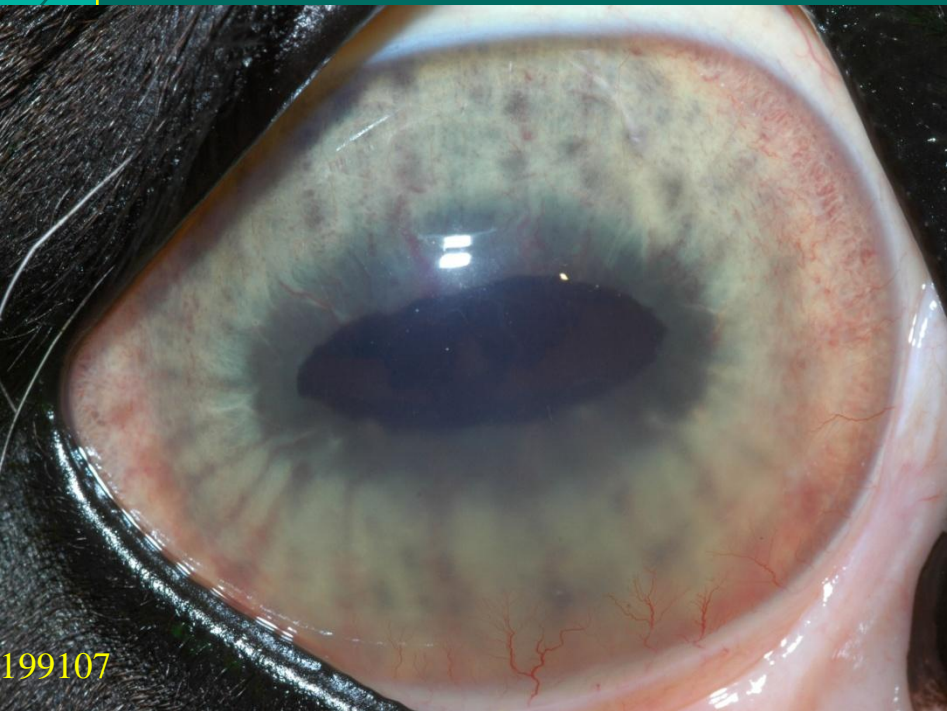


Equine “Recurrent” Uveitis is a “Persistent” Problem in Horses

Equine Ophthalmology Service
University of Florida



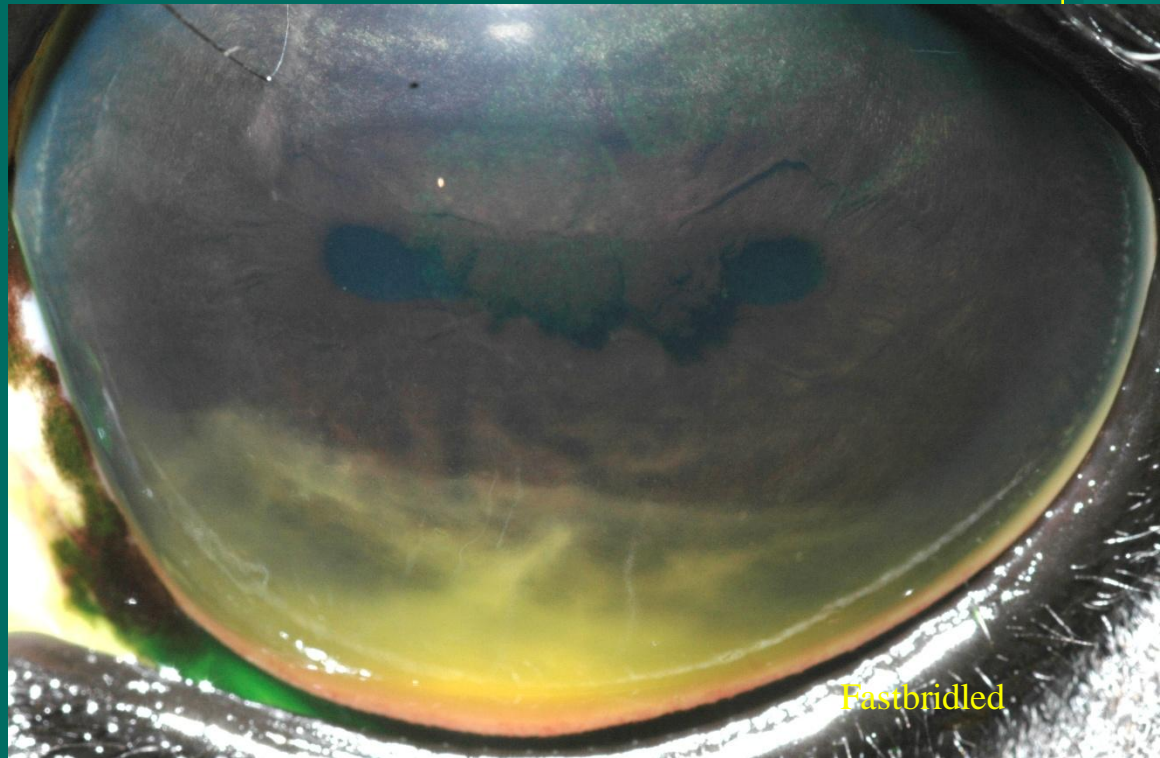
UVEITIS IN THE HORSE



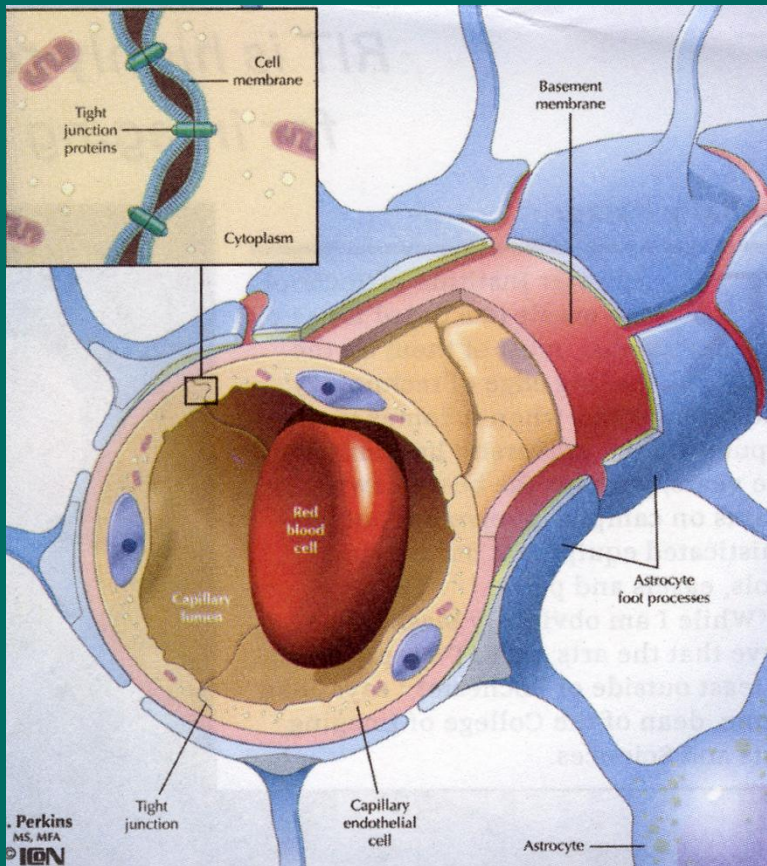
- UVEITIS is the LEADING CAUSE OF BLINDNESS IN HORSES
- Not a single disease: SYNDROME, MANY subsets!

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

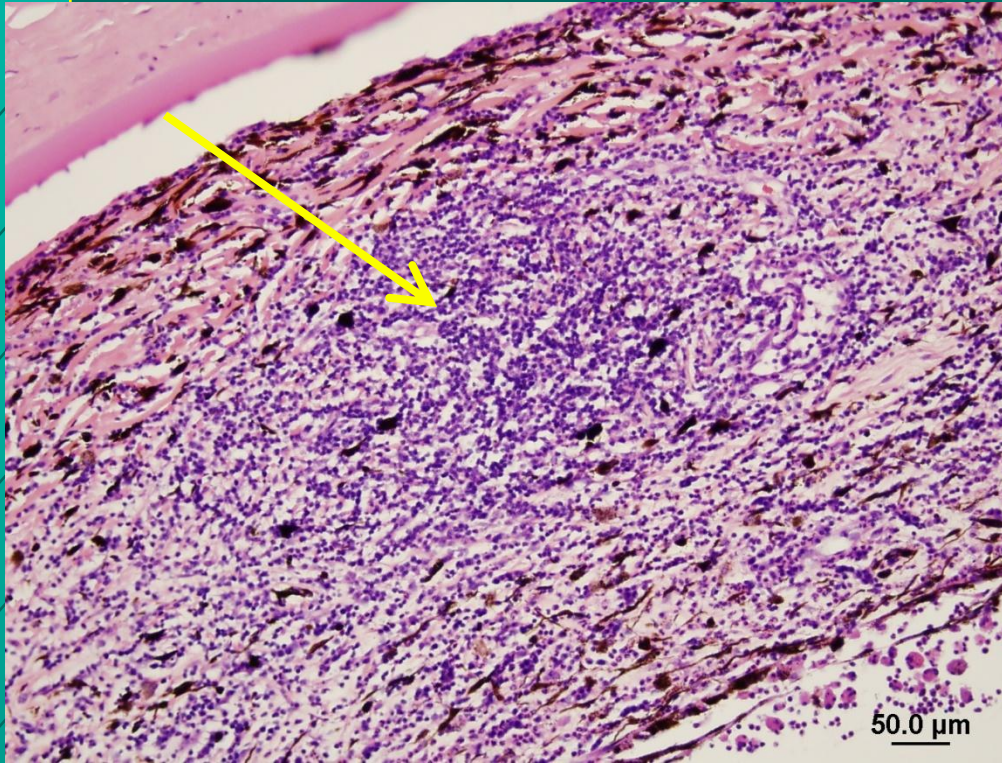


Uveitis starts as blood-ocular barrier compromise!



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

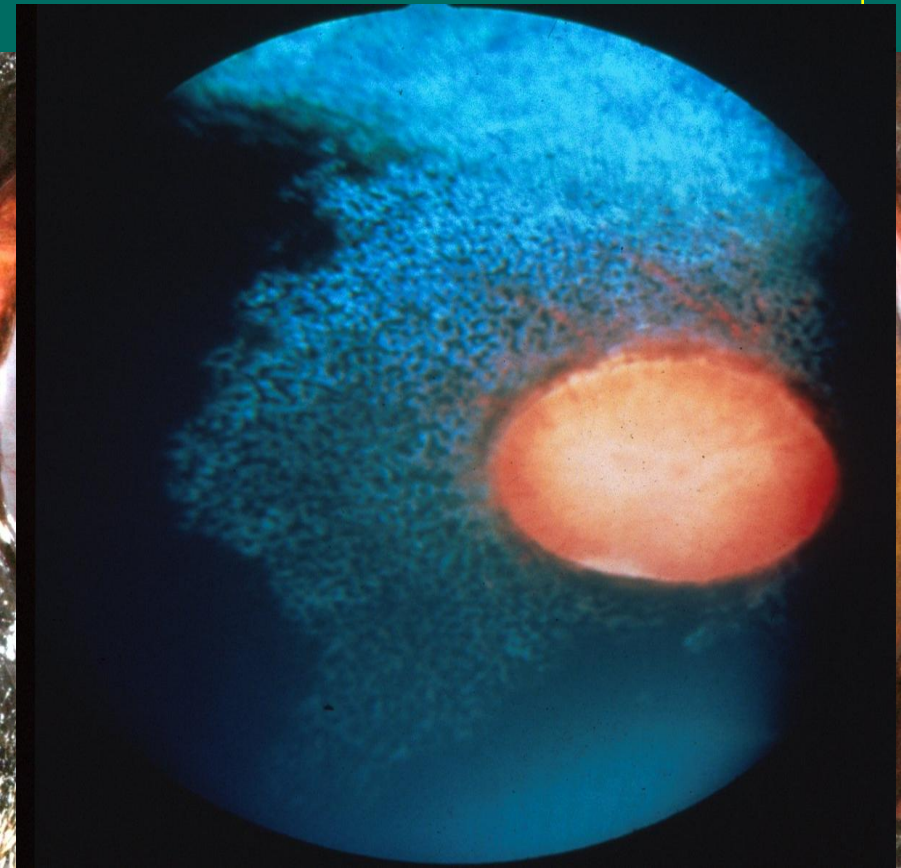
Lymphocyte infiltration



- 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 - tearing, conjunctivitis
 - b. Miotic pupil; hypotony
 - c. Negative fluorescein retention
 - d. Hypopyon, flare, hyphema
 - e. Retinal degeneration, “butterfly lesions”
 - f. “hypertensive” uveitis



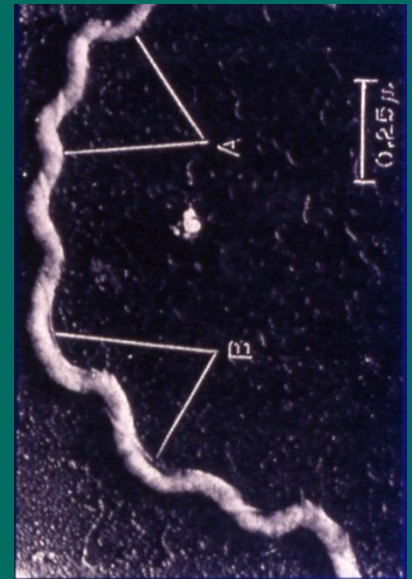
Comments

- 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. grippotyphosa*
 - *L. pomona* most important in USA
 - Titters $\geq 1:400$ 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 *pomona* 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. pomona* have uveitis.
 - The serologic evidence of *pomona* 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.

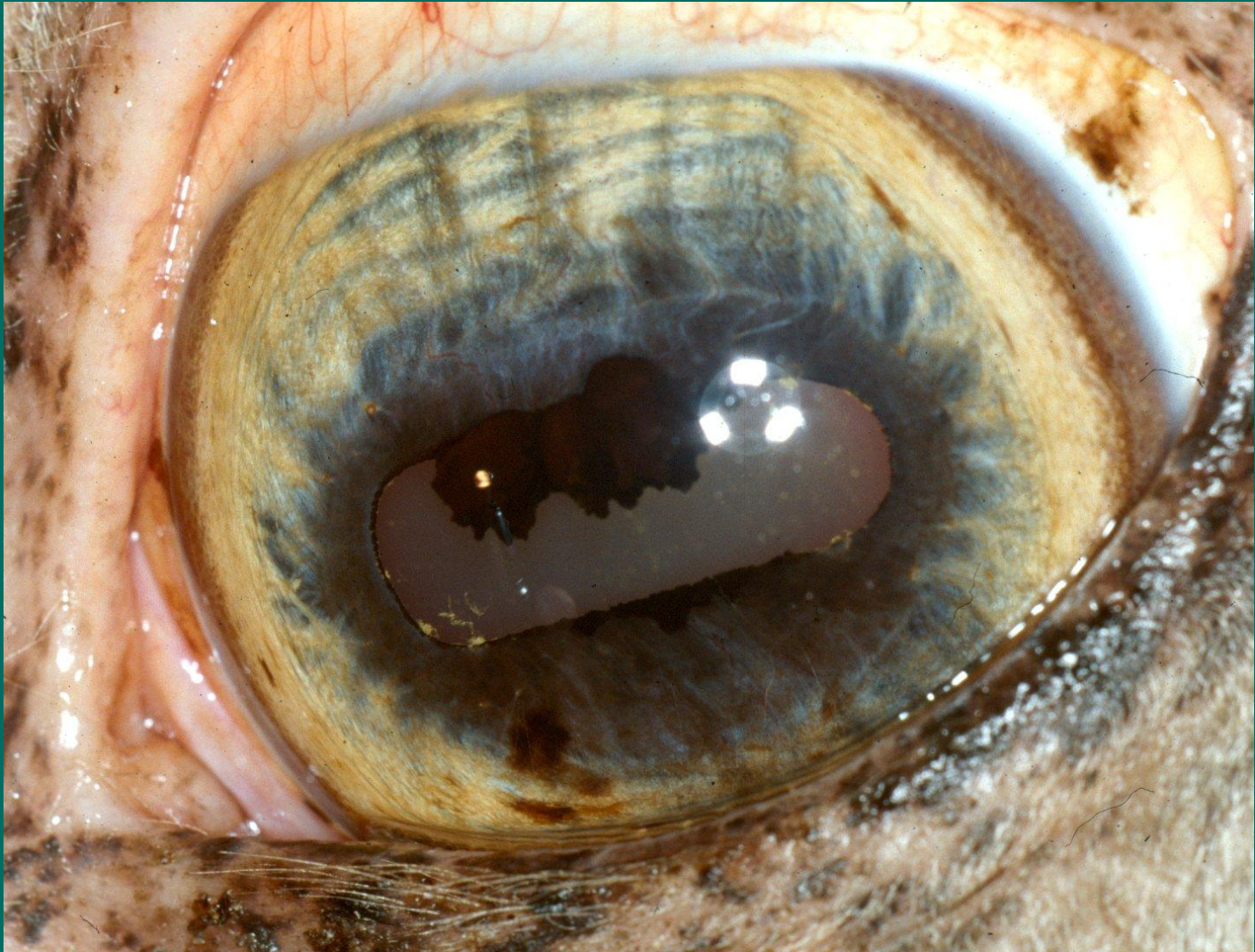
■ Percentage of horses with uveitis losing sight in at least one eye if Lepto + (11 yrs):



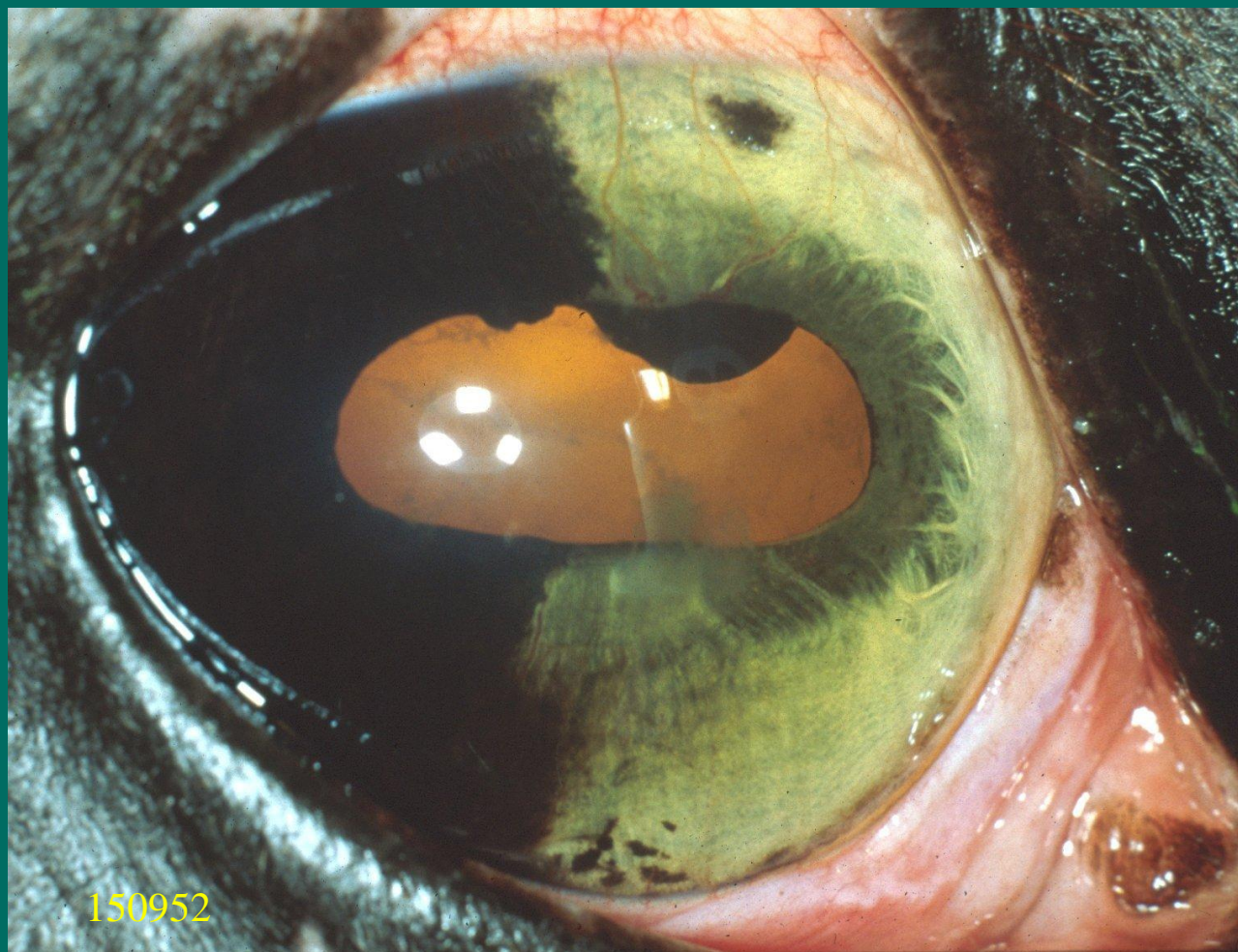
- + Appaloosa 100%
- Appaloosa 71%
- + nonAppaloosa 52%
- nonAppaloosa 34%



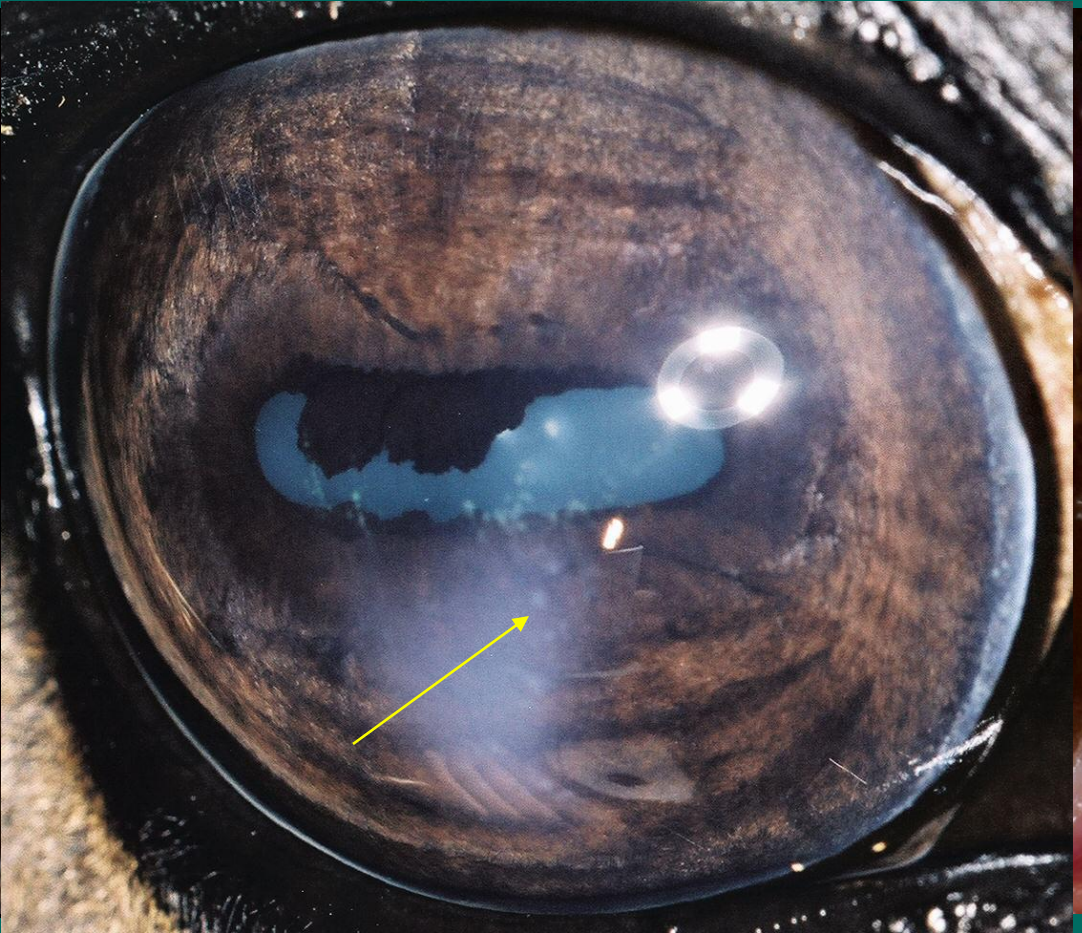
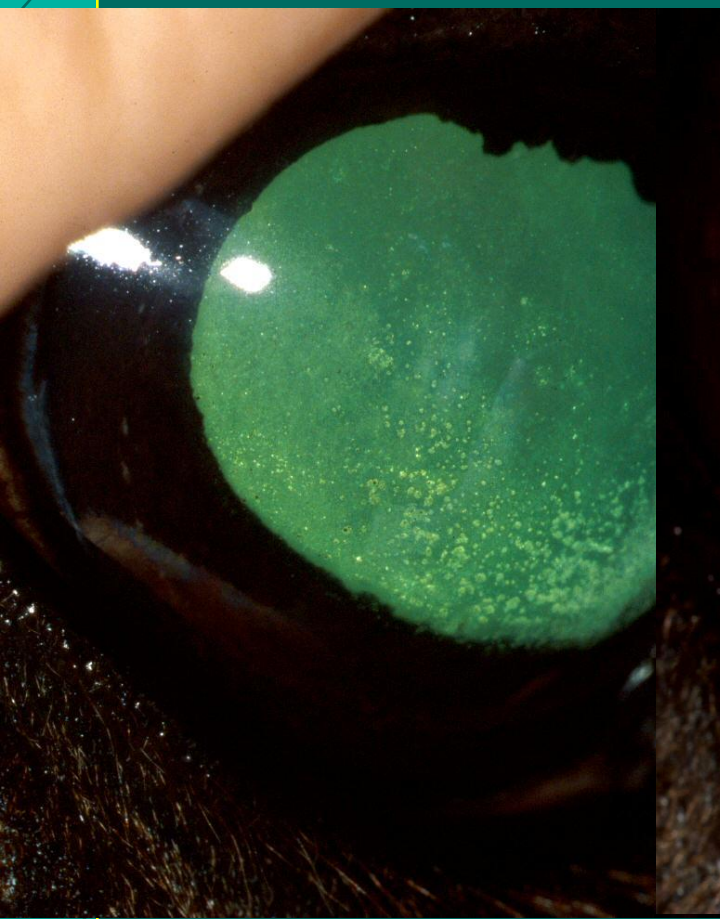
The more pigment, the less ERU, and the less CSNB!



Iris color changed to brown

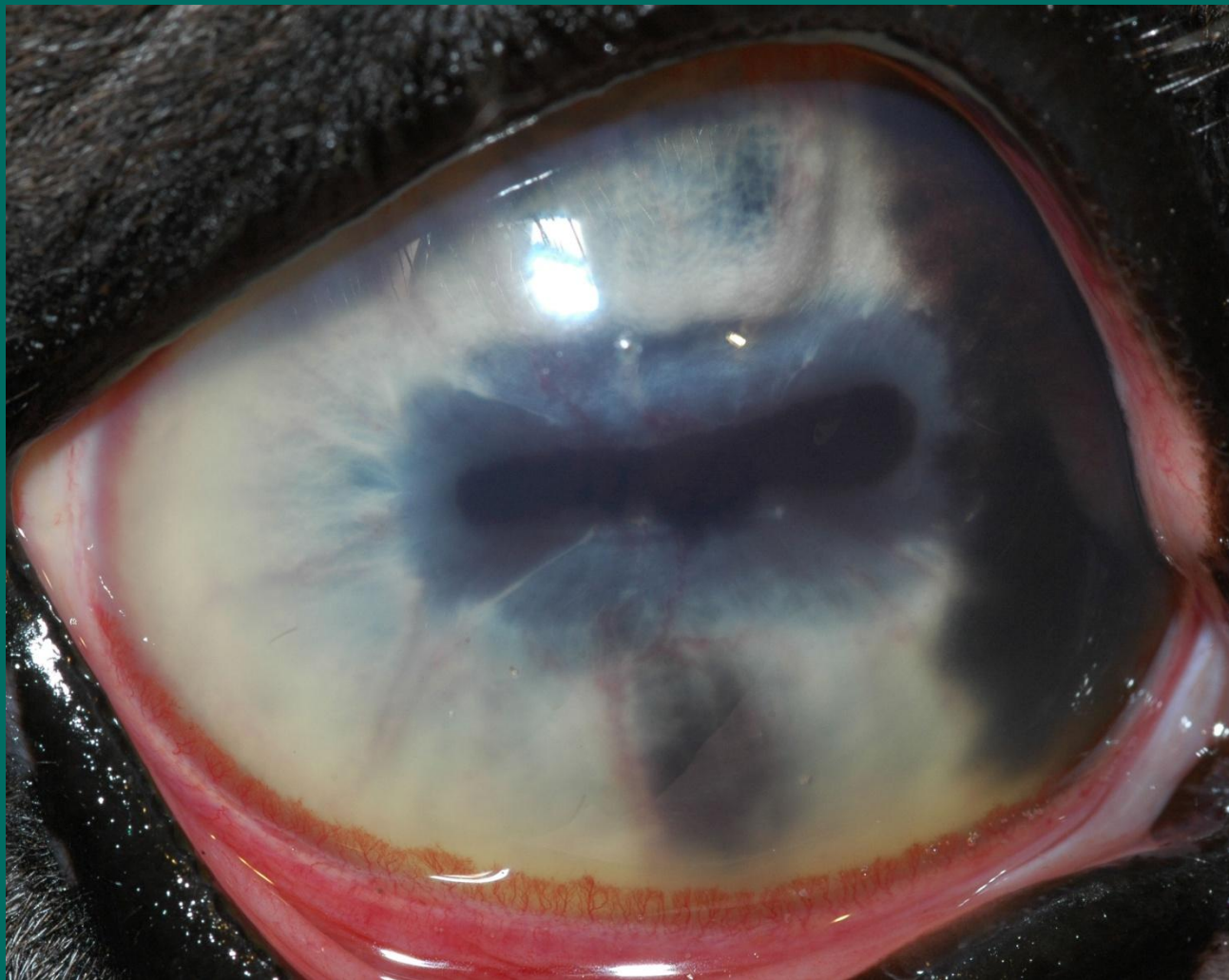


Keratic Precipitates (KPs)

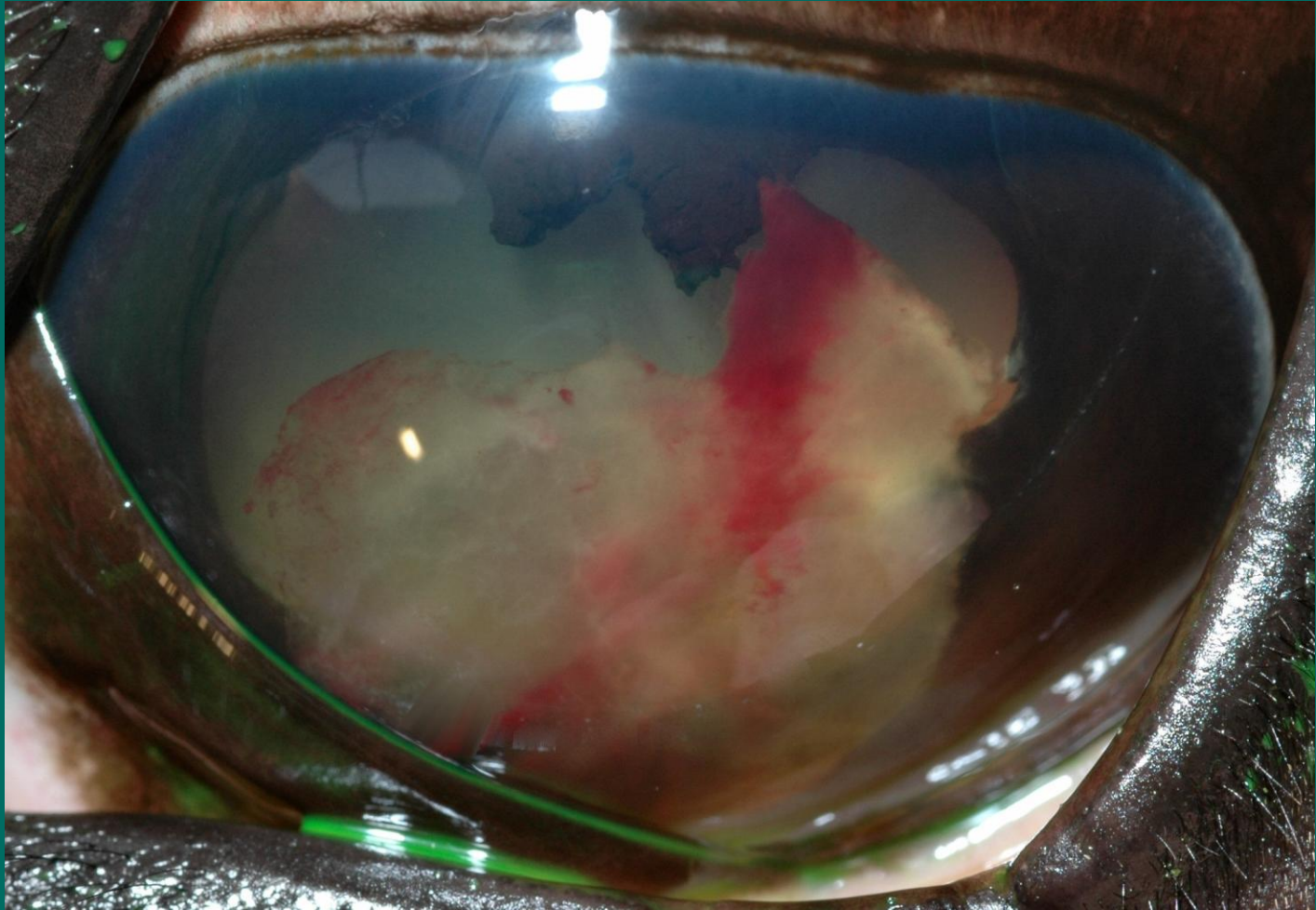




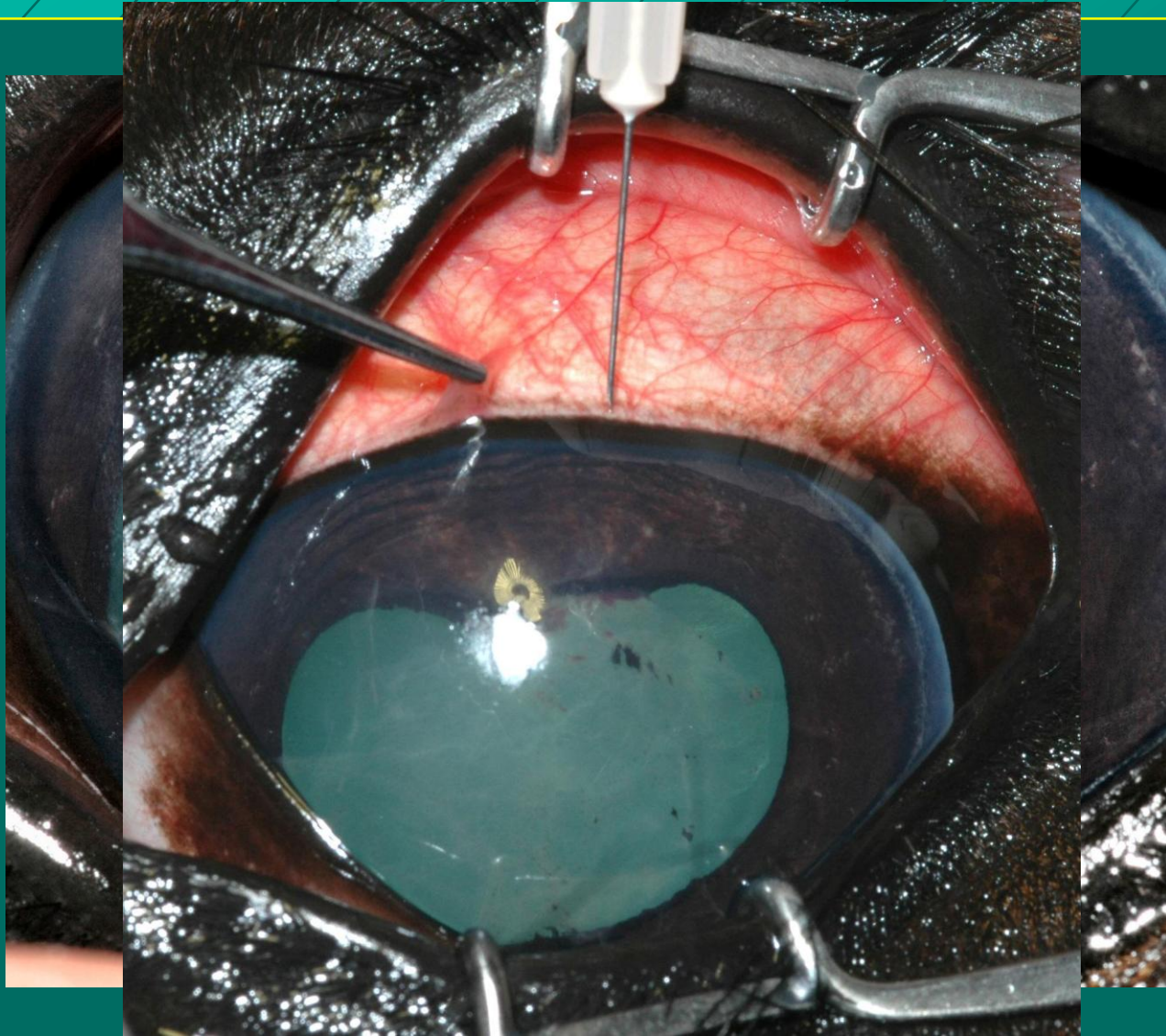
PMNs give a green appearance in ERU.



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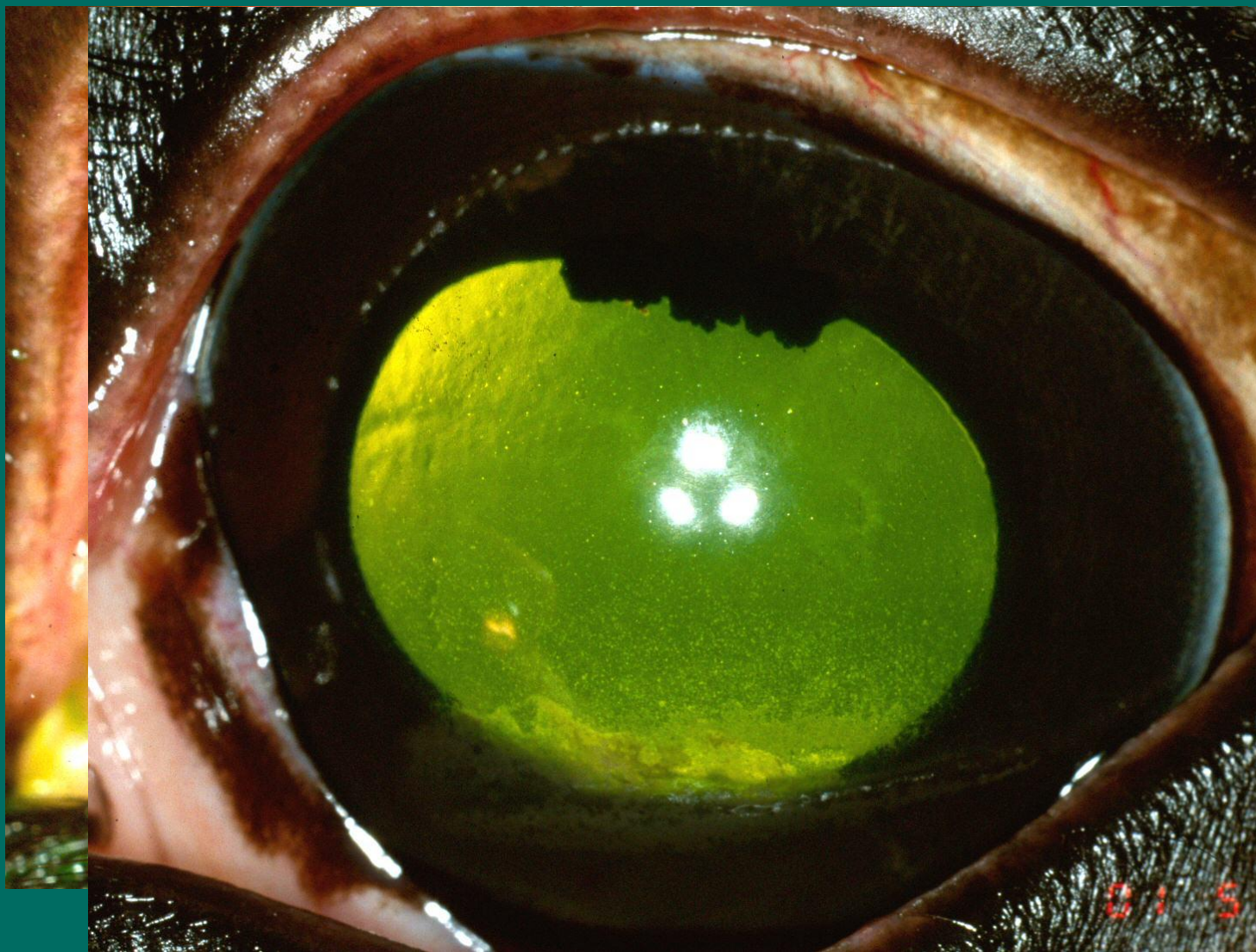
ERU and fibrin (Cookie)



Gypsy and Tissue Plasminogen Activator



Fibrin is removed by TPA

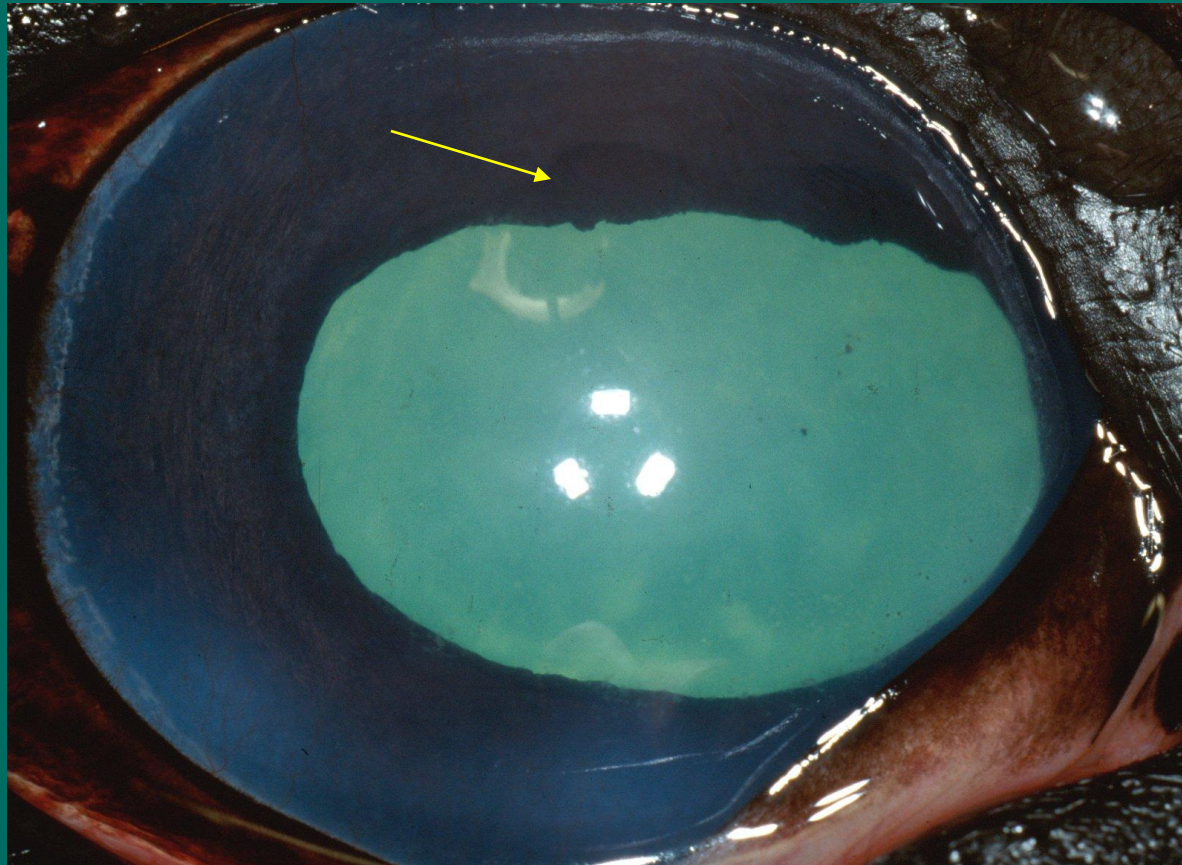


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Tissue Plasminogen Activator

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

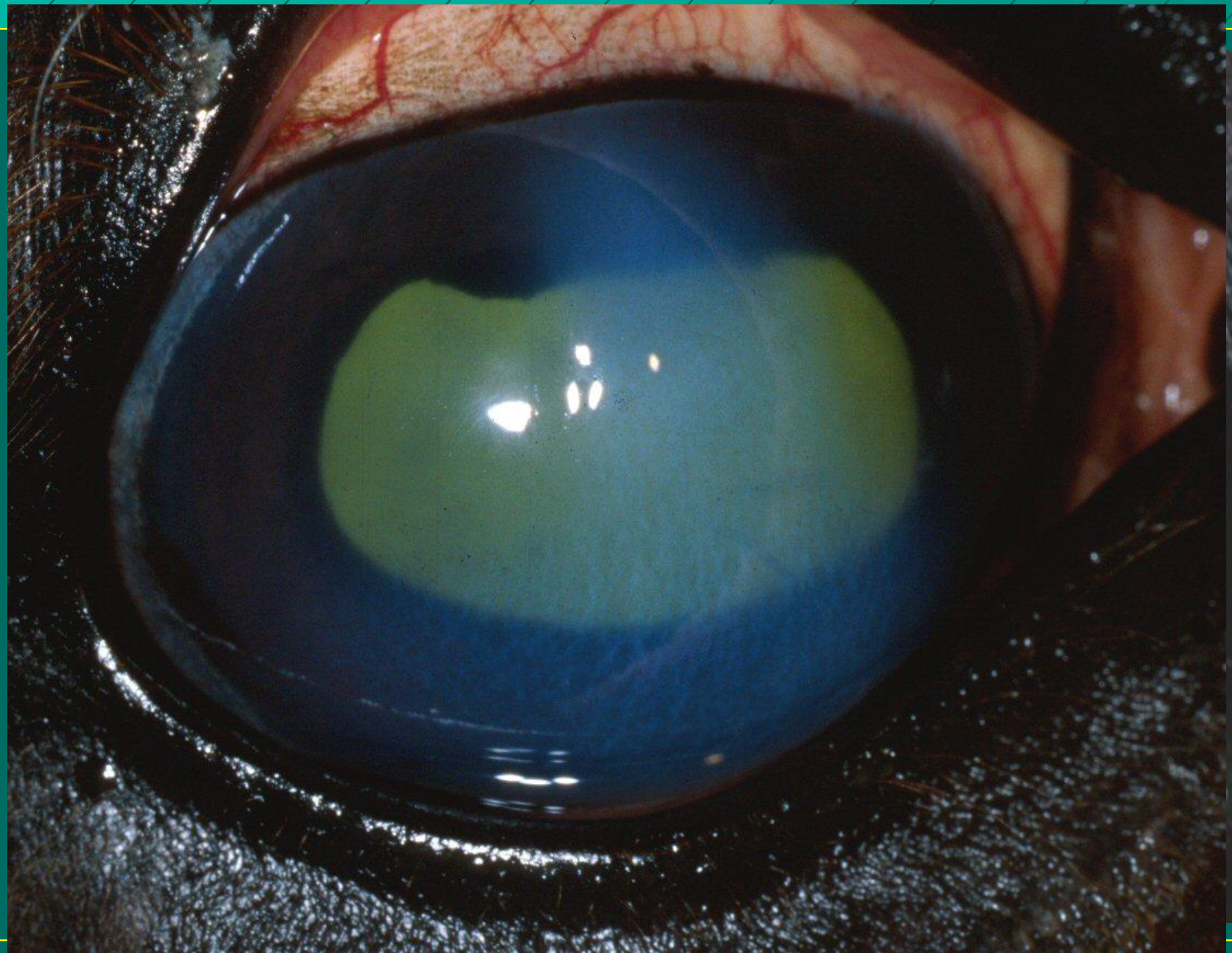


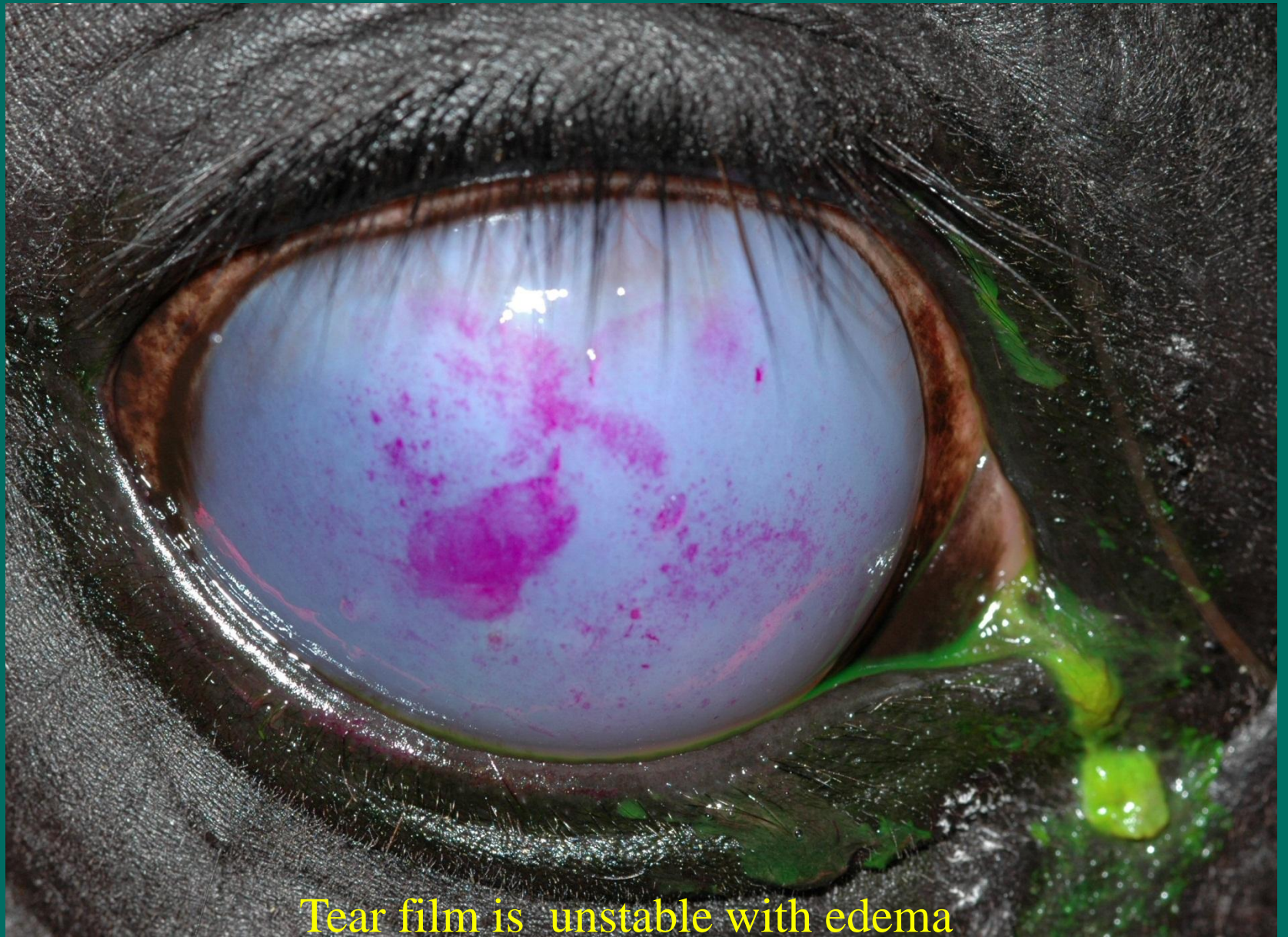


Corpora nigra atrophy in ERU

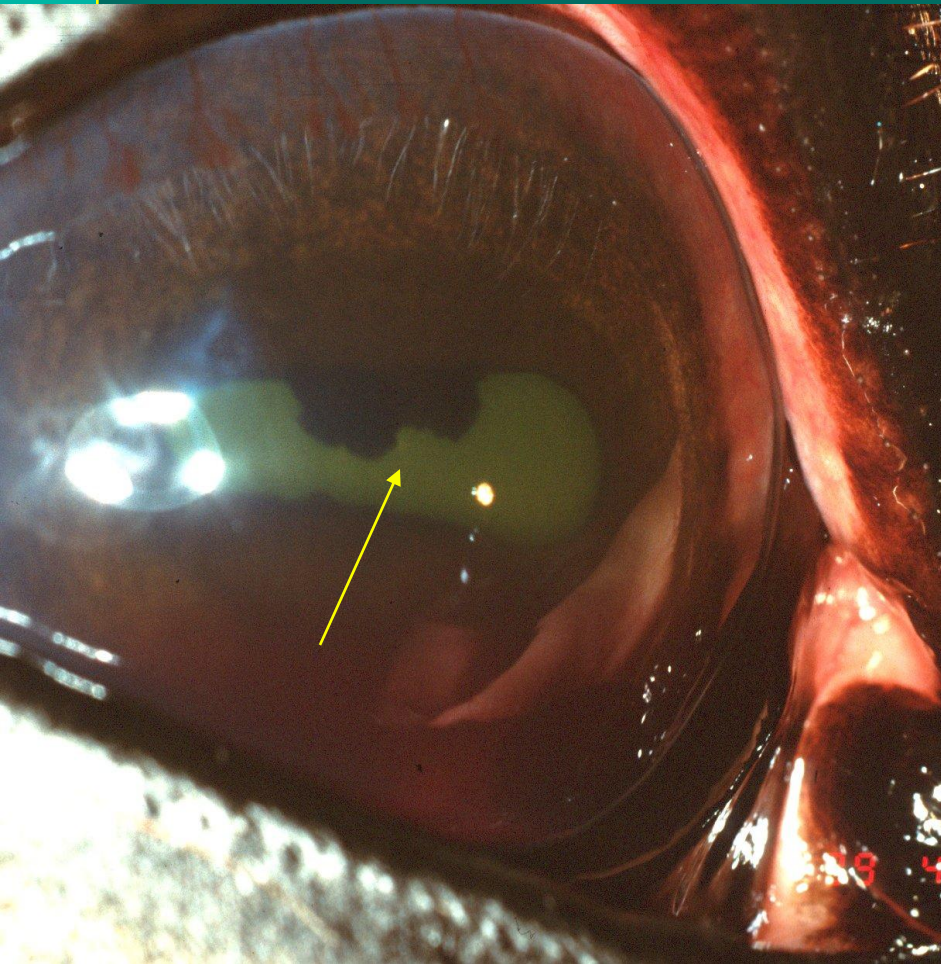


Endotheliitis: precursor of glaucoma??

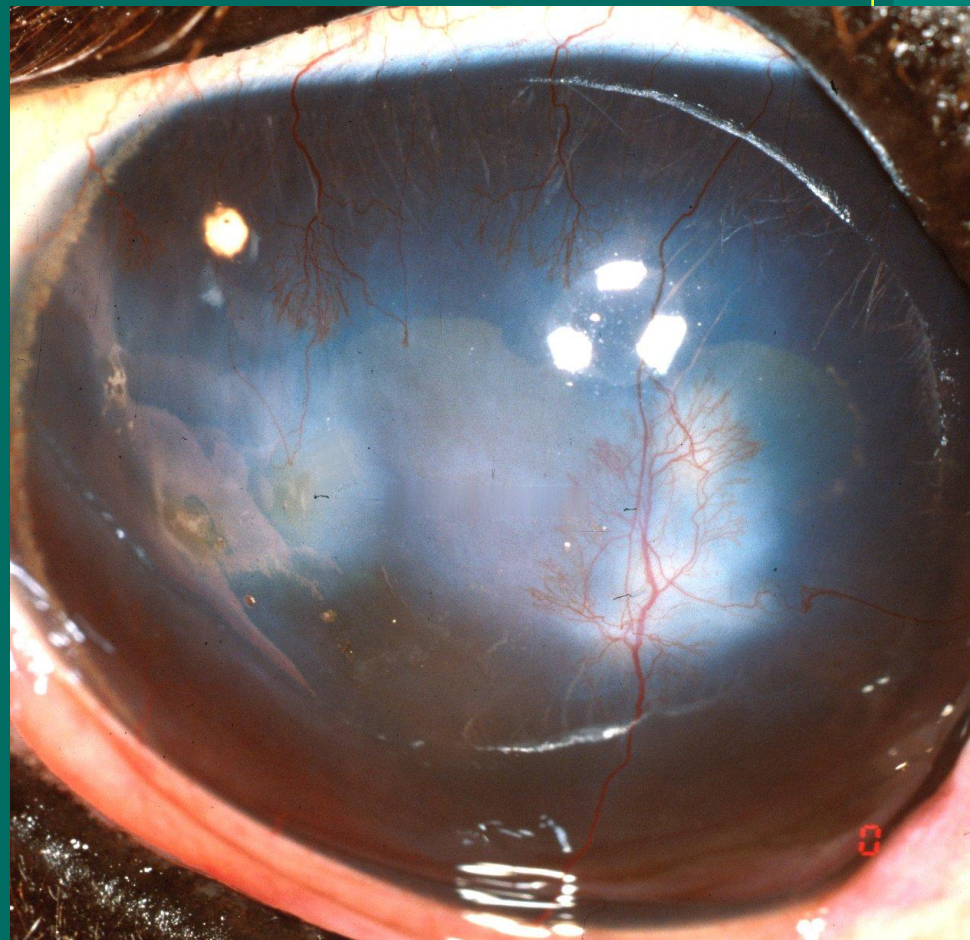




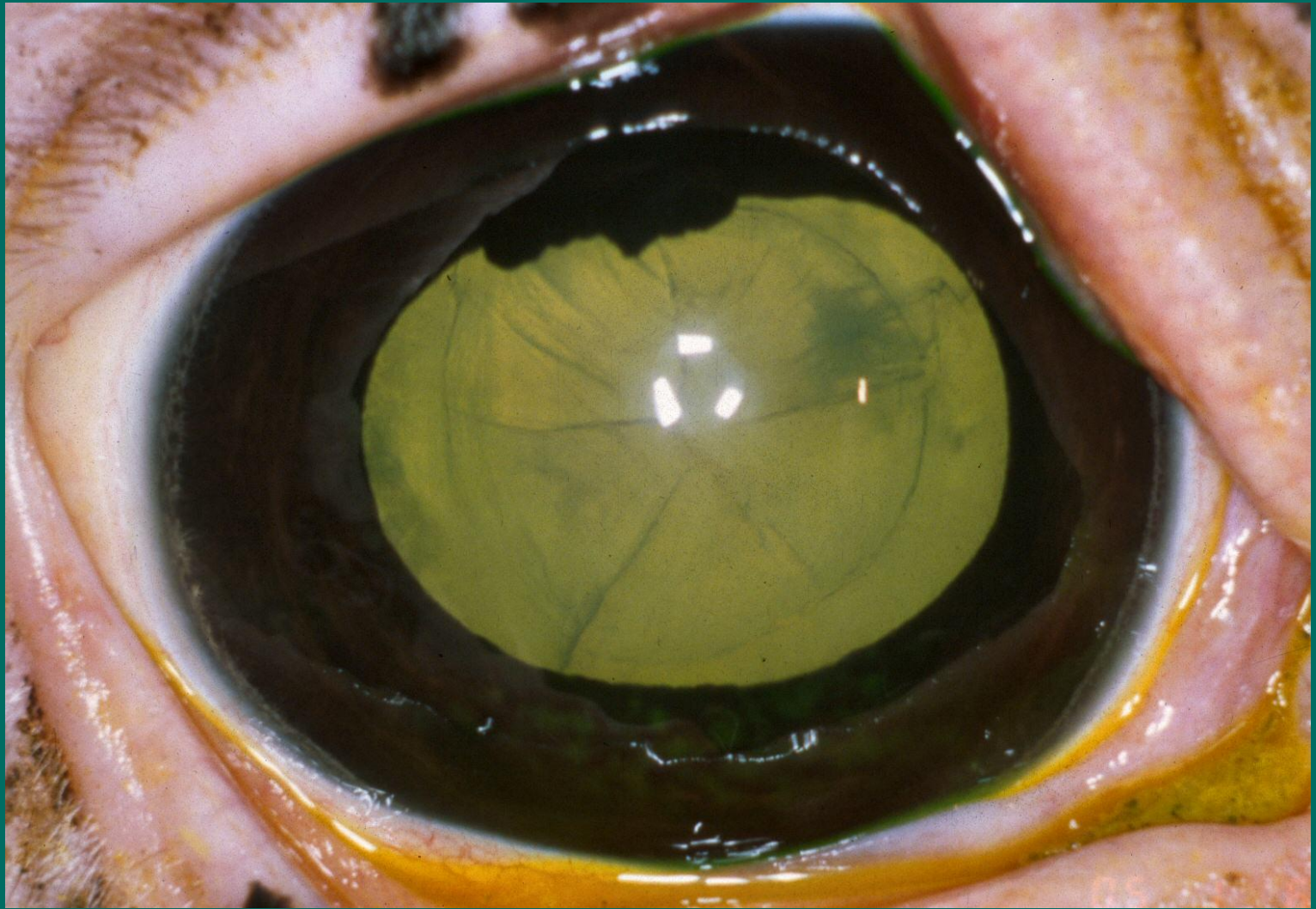
Tear film is unstable with edema

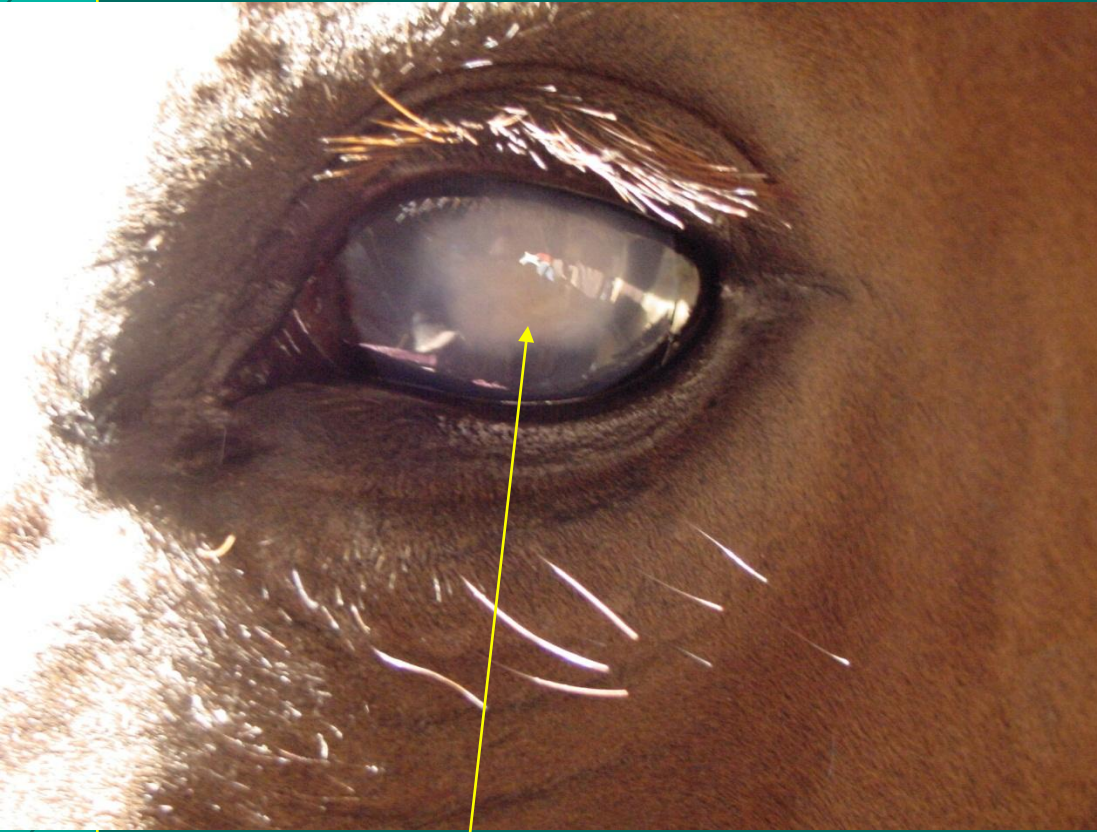


Miosis



Corneal scarring



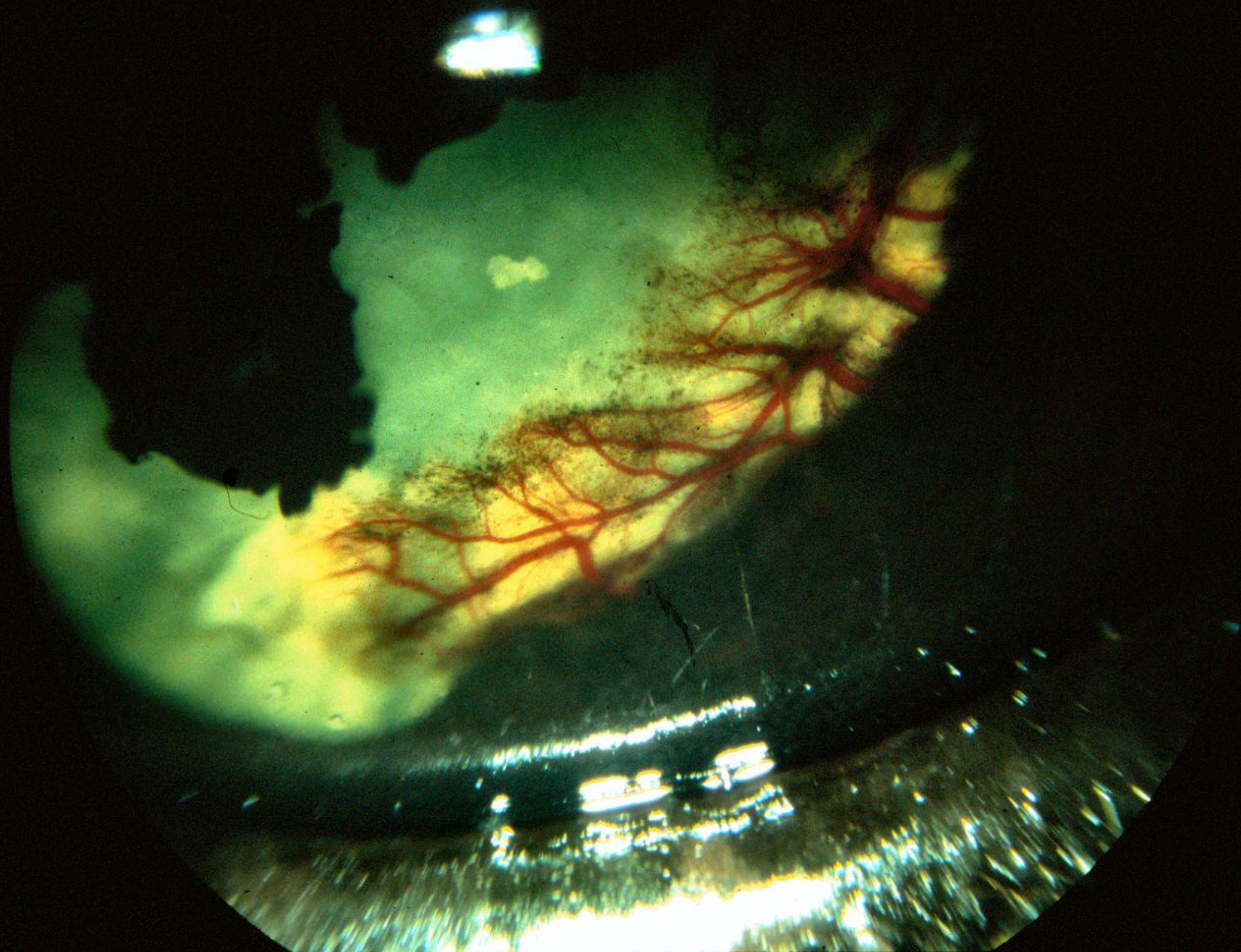


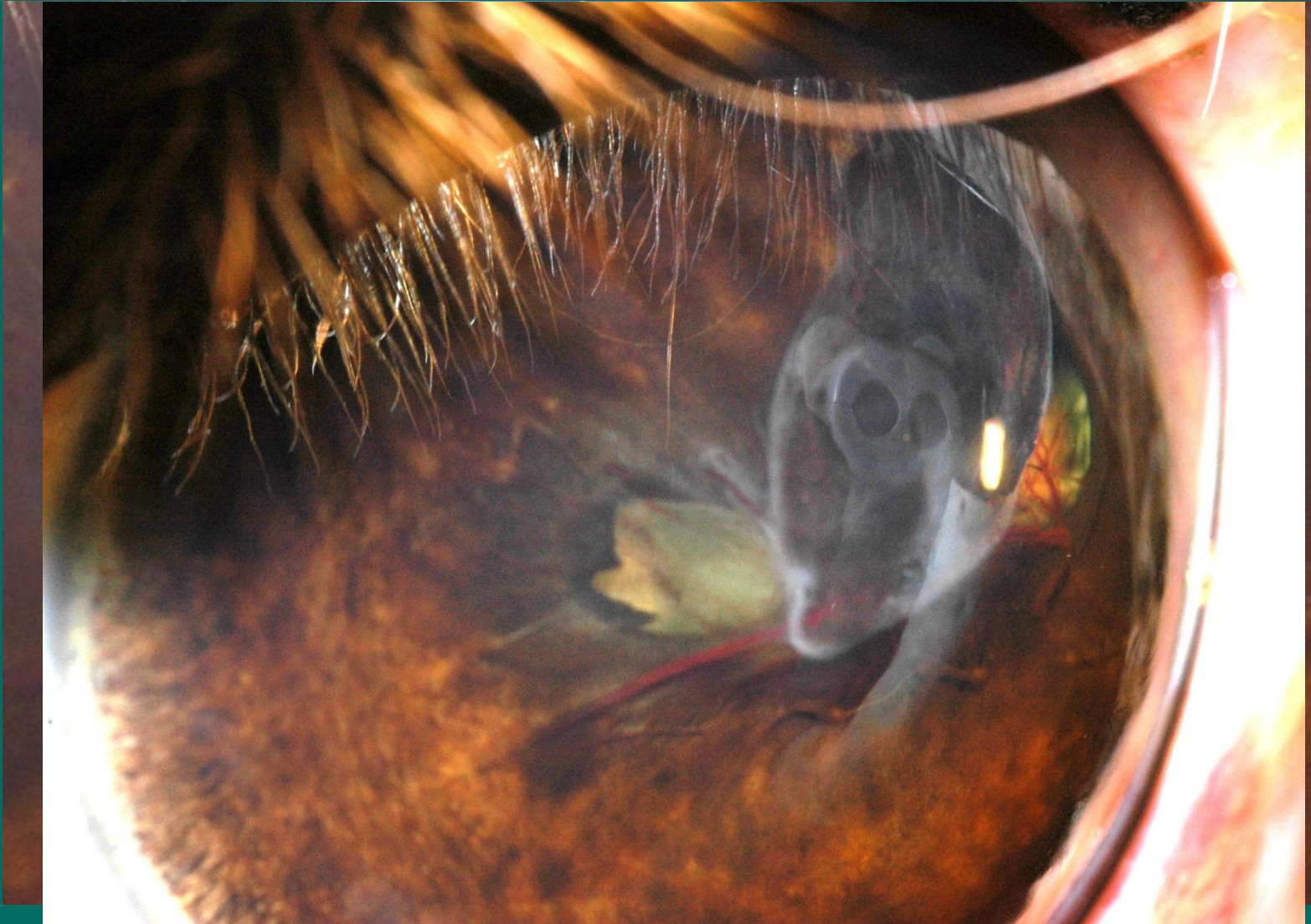
Fibrin plaque in pupil.



ERU causes cataracts. Some feel oral aspirin reduces this.

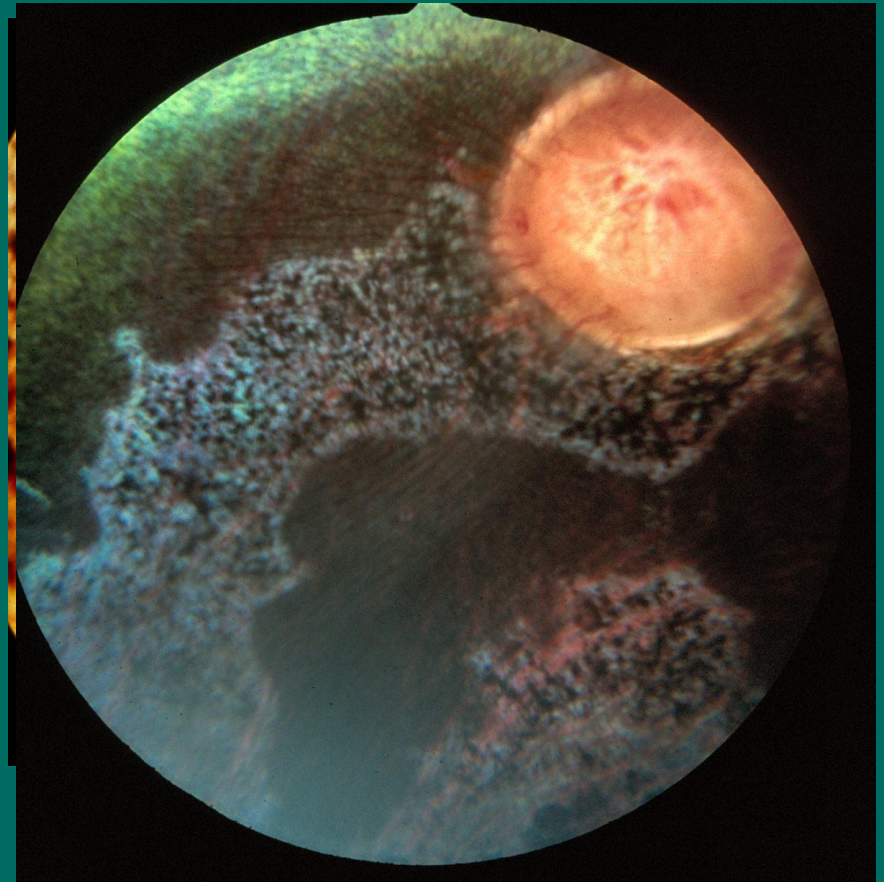
Why is the pupil dilated?



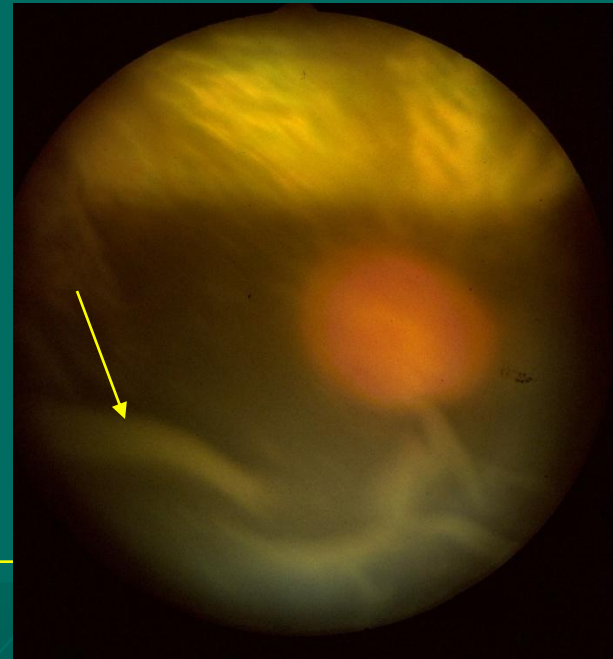
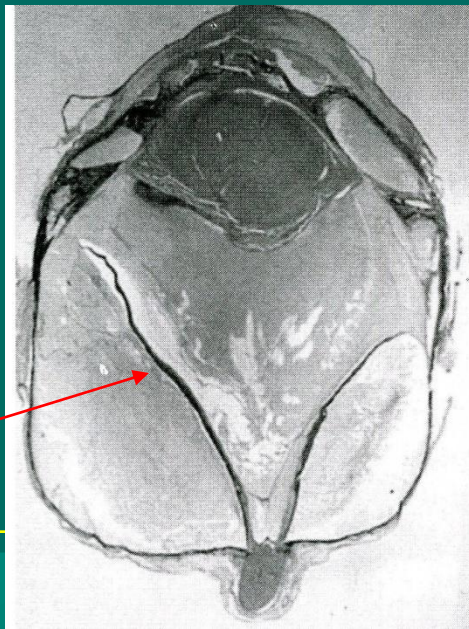
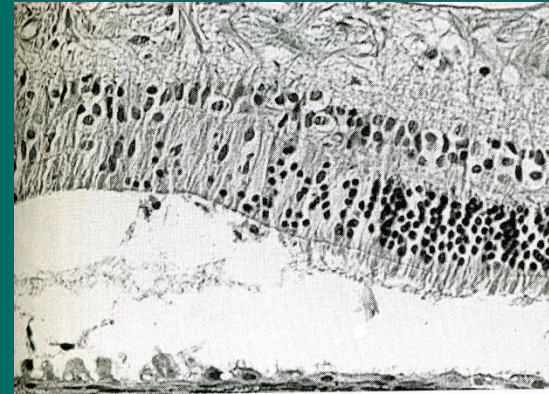
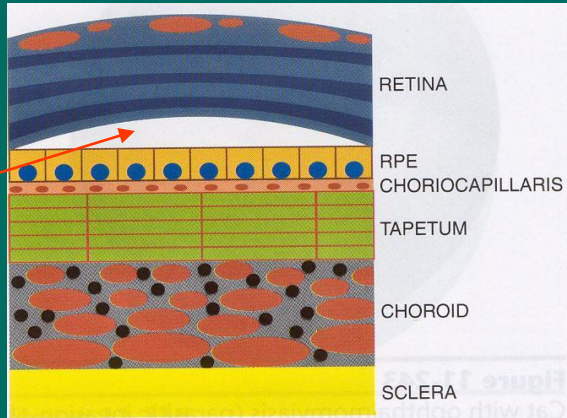


Chorioretinitis

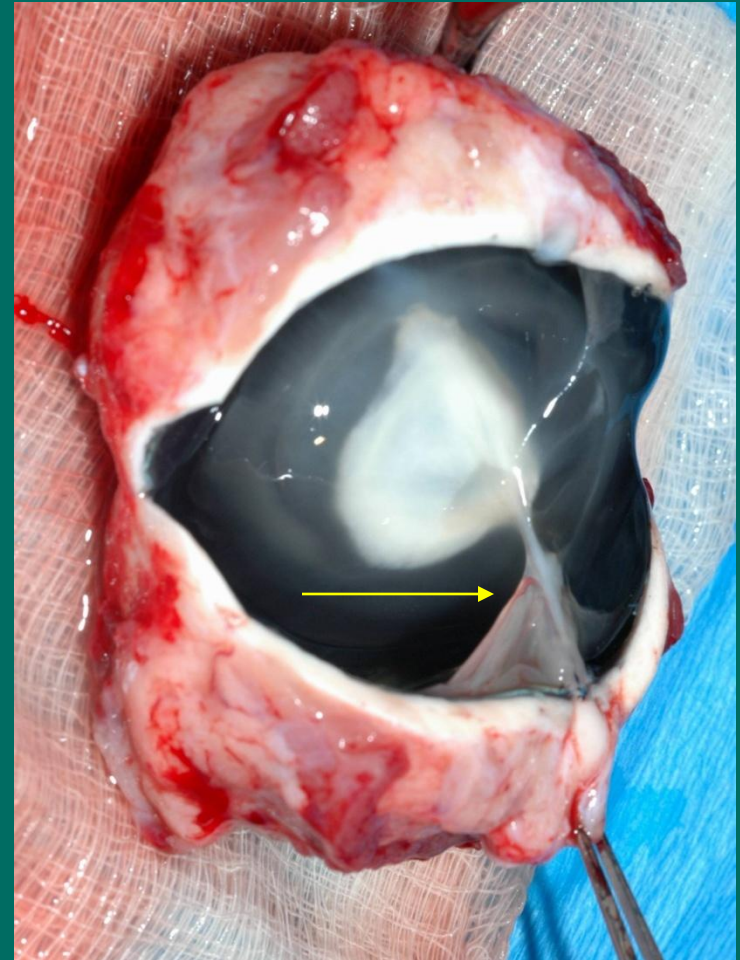
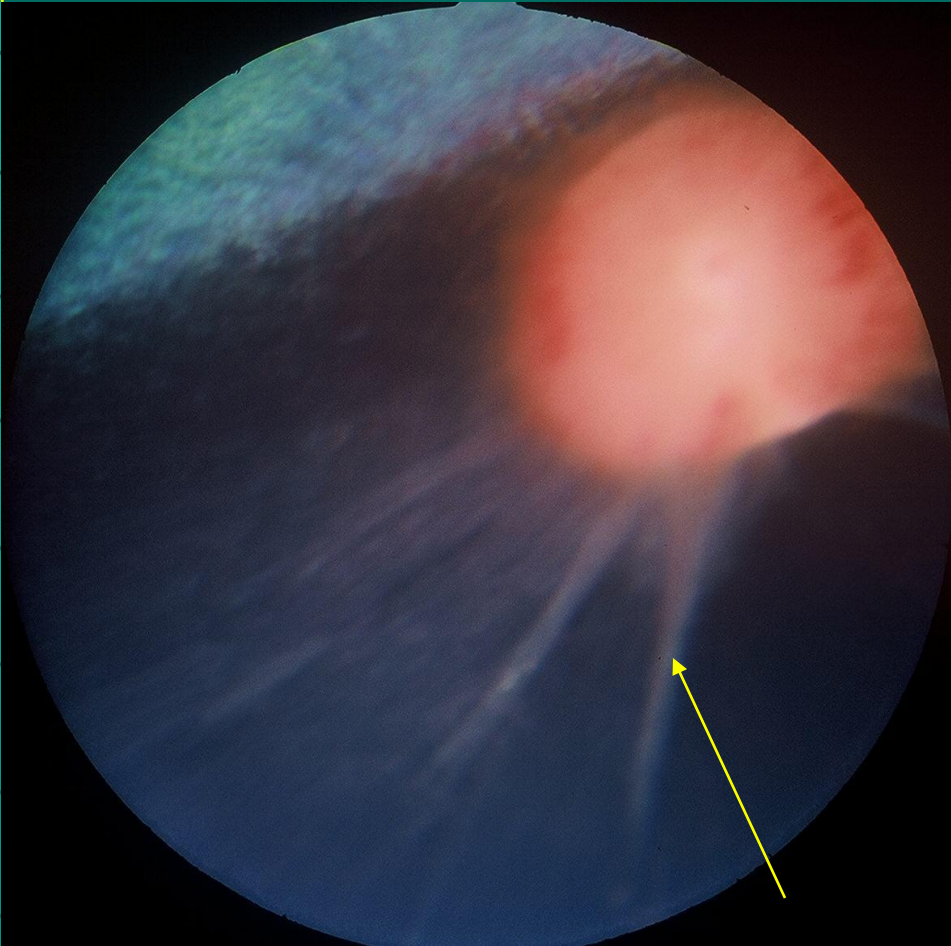
- Found at all stages of ERU!



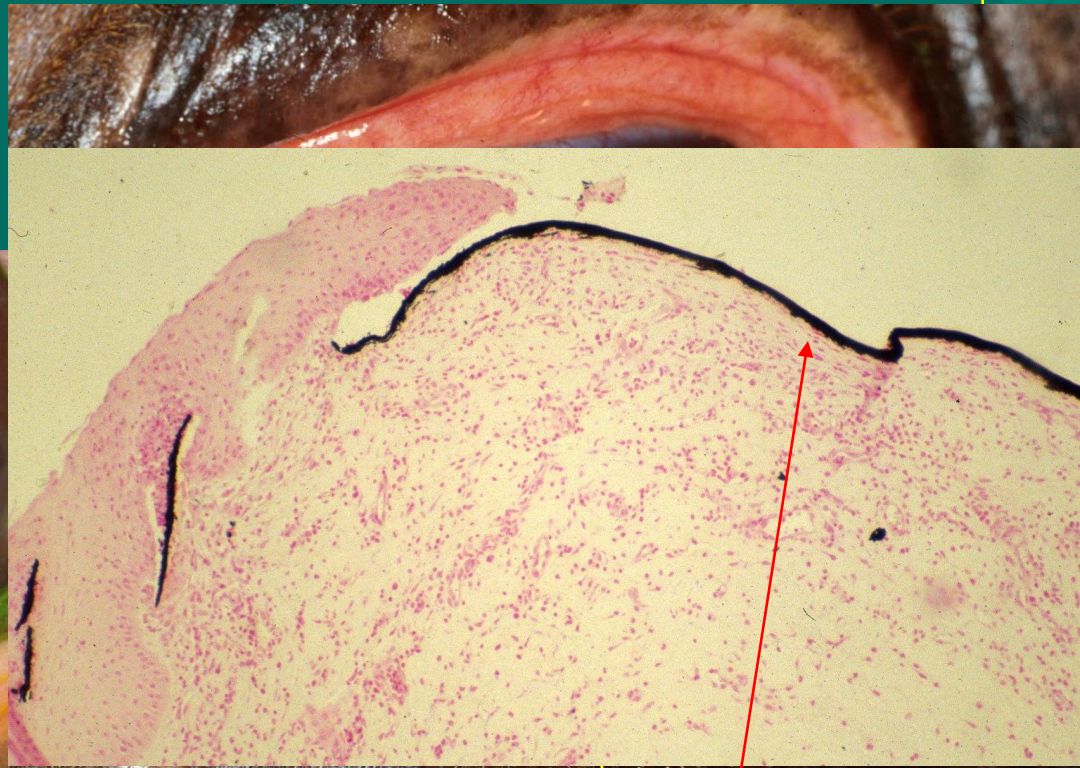
Detachment of Retina



Retinal Detachment

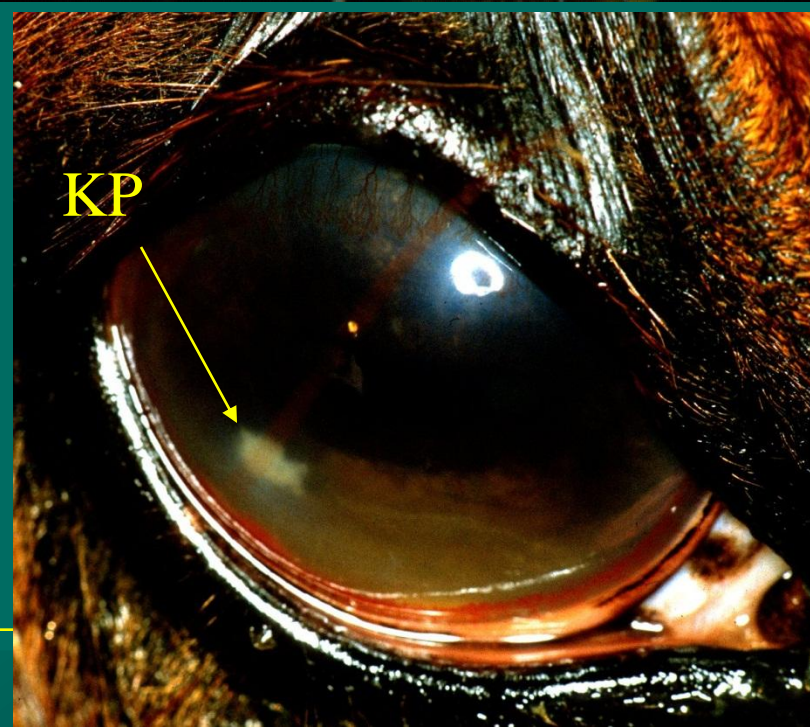
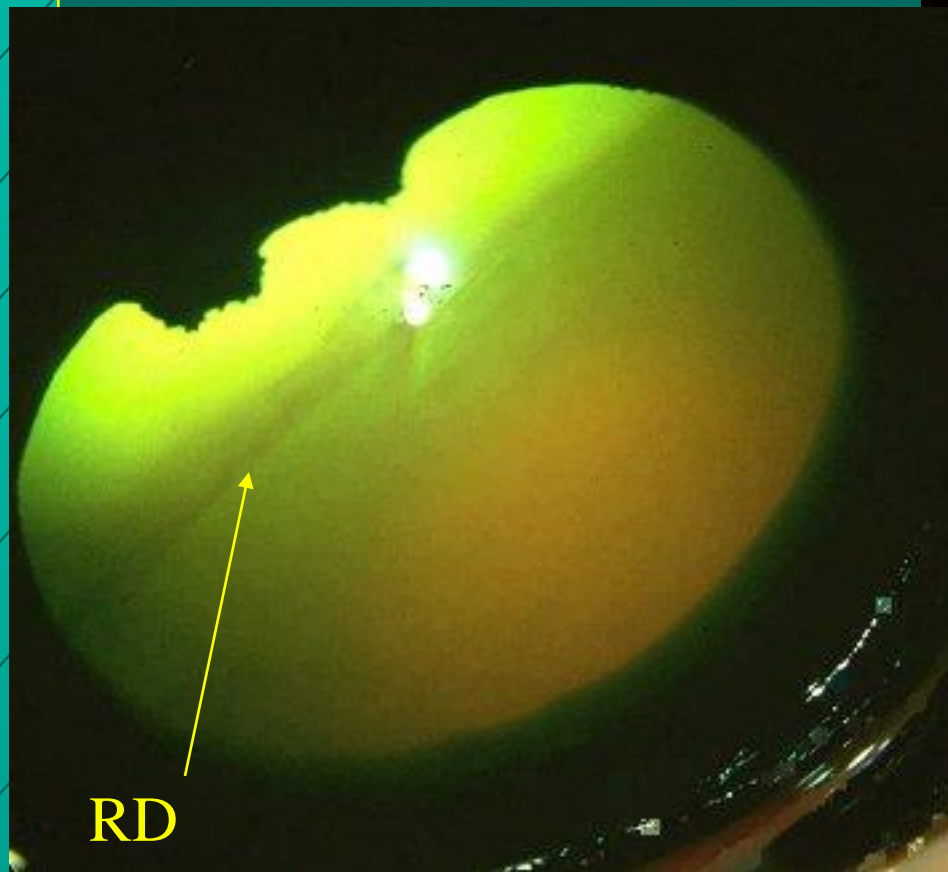


Band Keratopathy: chronic ERU- 6% of cases

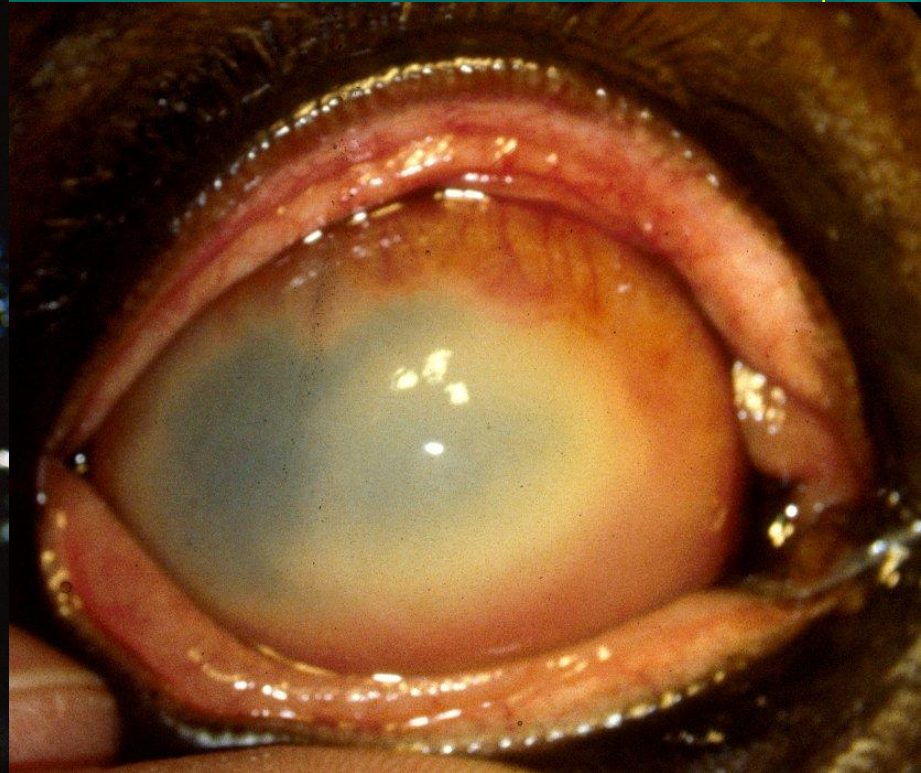
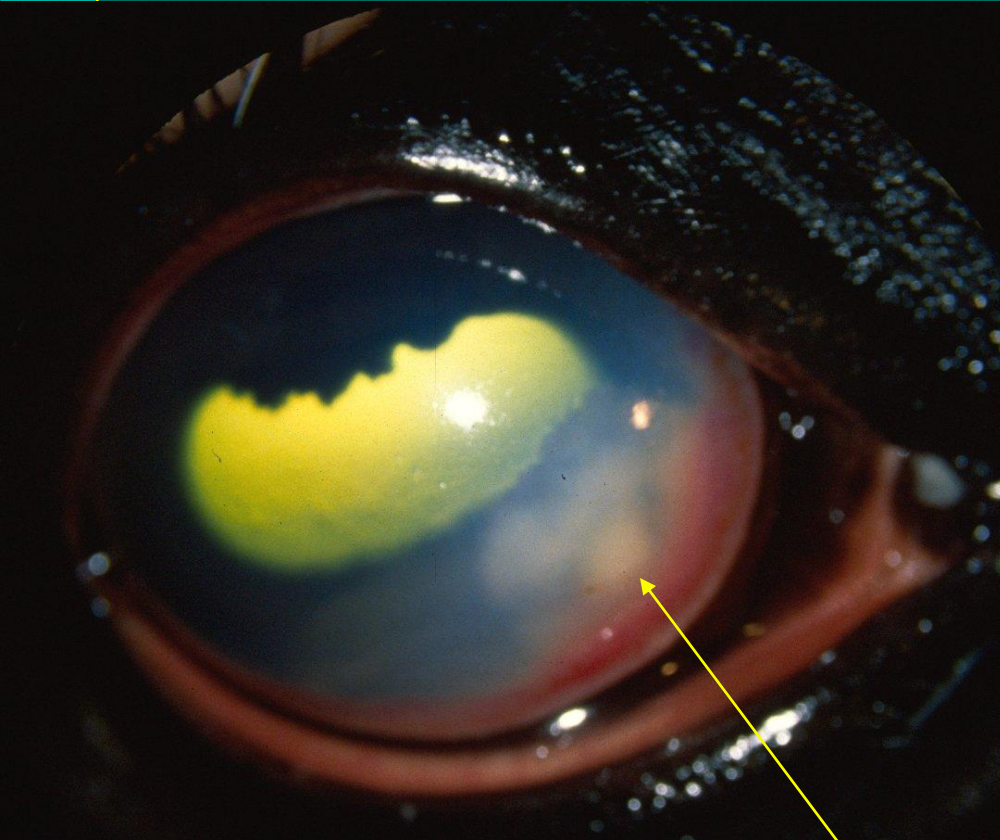


Treatment is EDTA topically.
BK occurs in treated horses??

calcium



Differentials for ERU



3 wks later

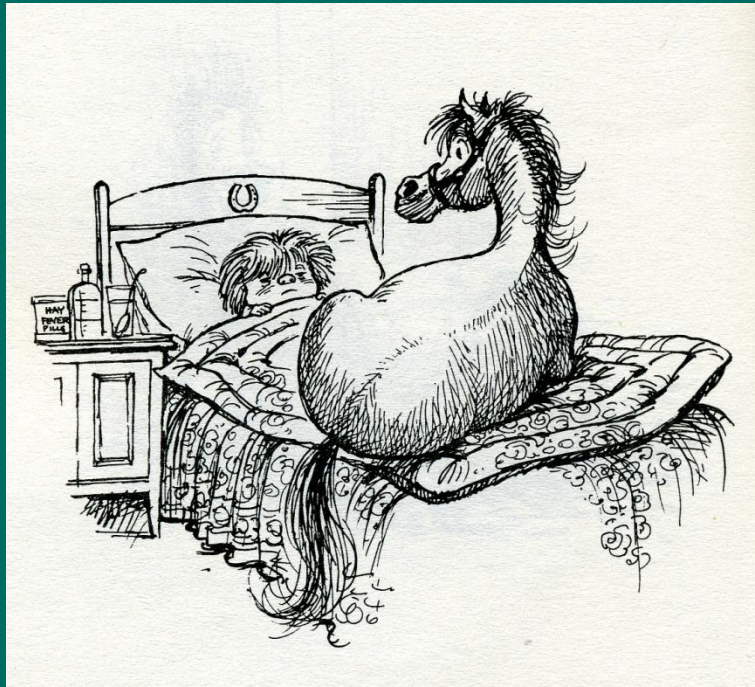
ERU resembles SA.

KEY POINTS: Treatment



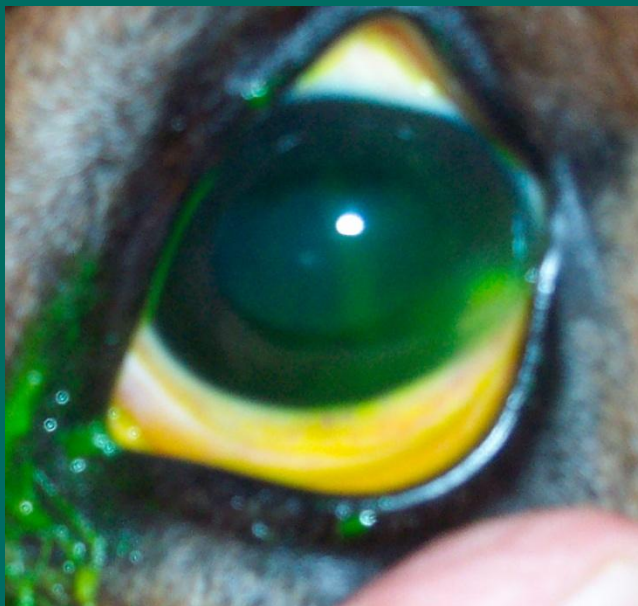
- Initially, owners may be very diligent about therapy
- Adherence to therapy is good

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

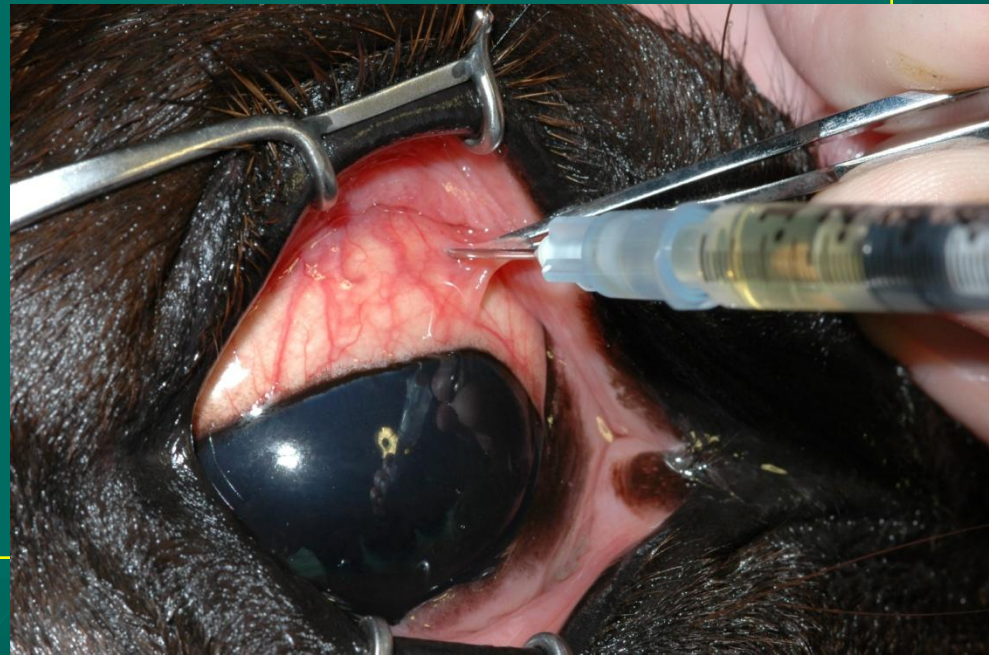
– Systemic NSAIDs:

- 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

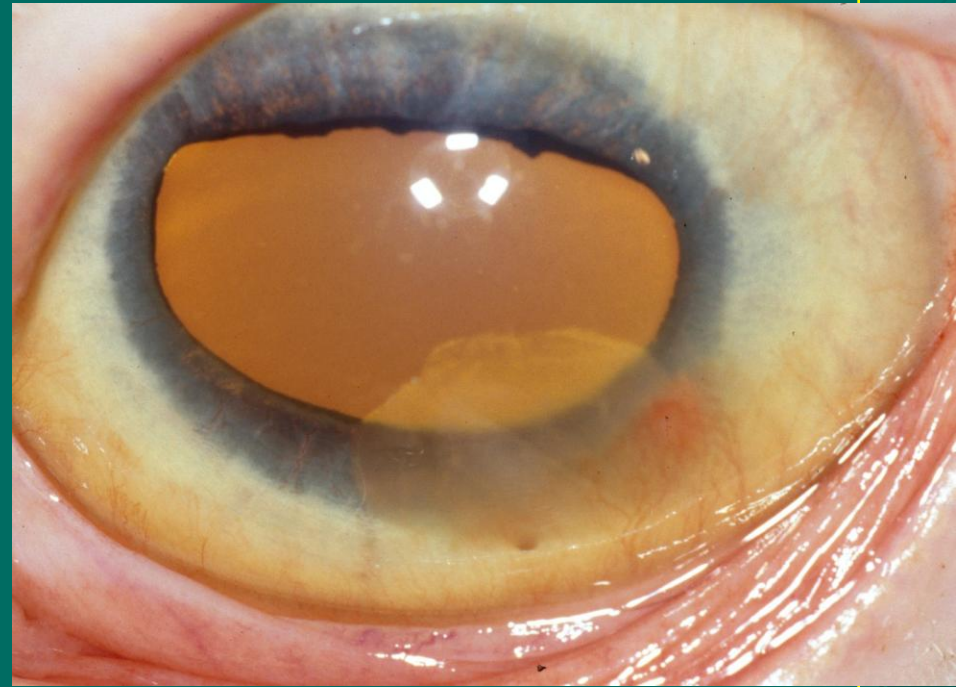


Fibrin and TPA

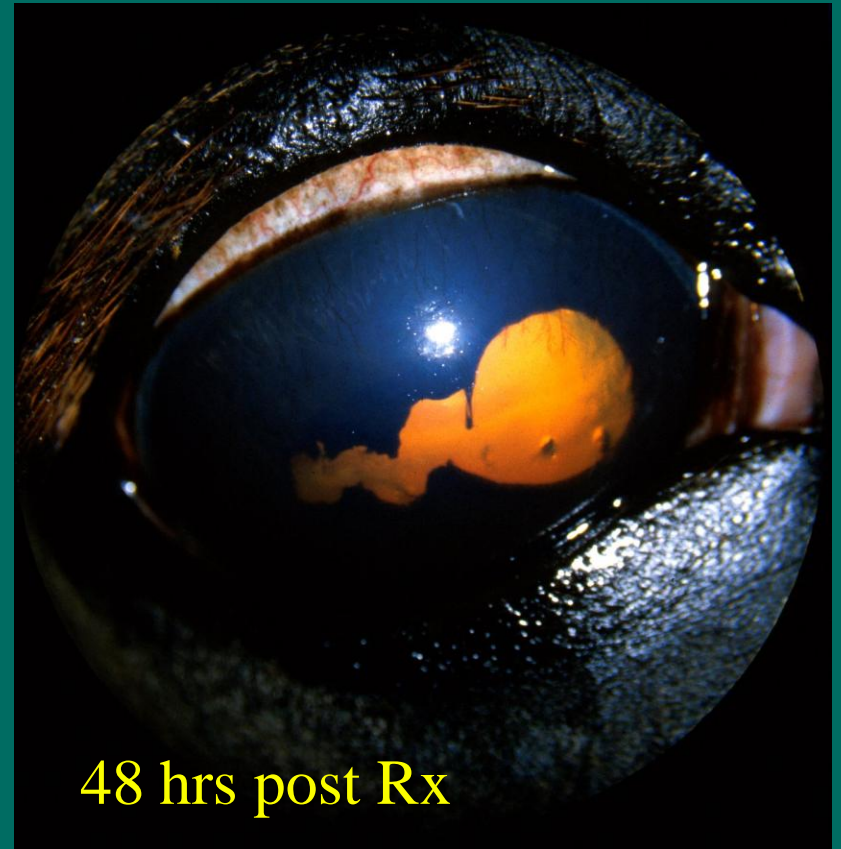
Medical Treatment “Works”



Miosis and fibrin



Pupil dilated and fibrin consolidating



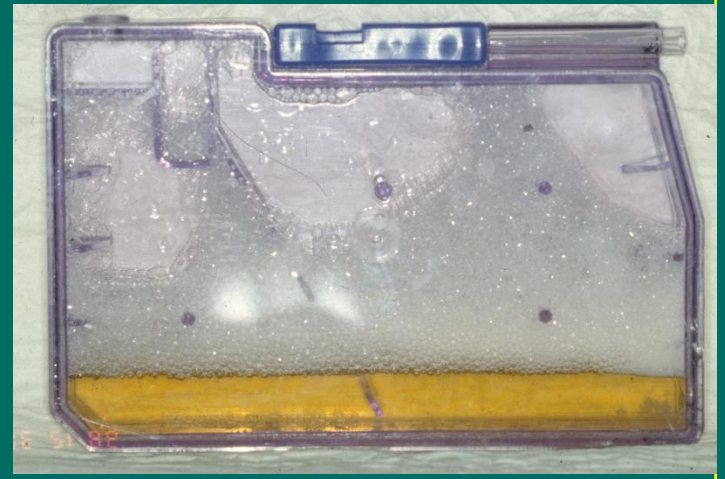
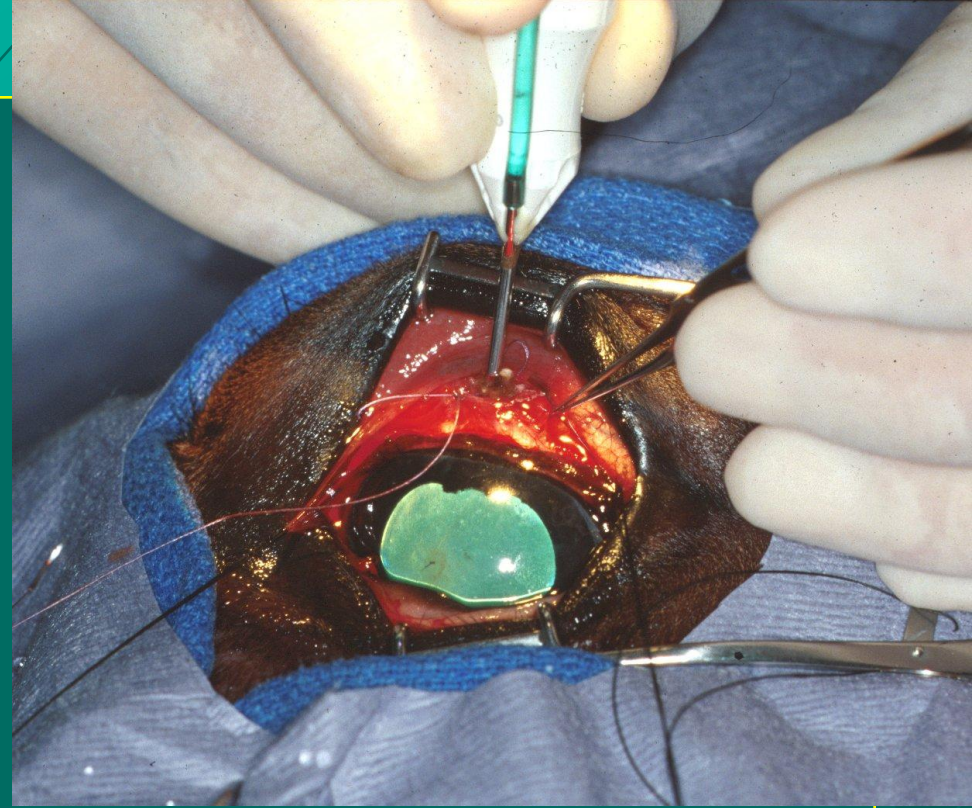
Surgical Vitrectomy for ERU



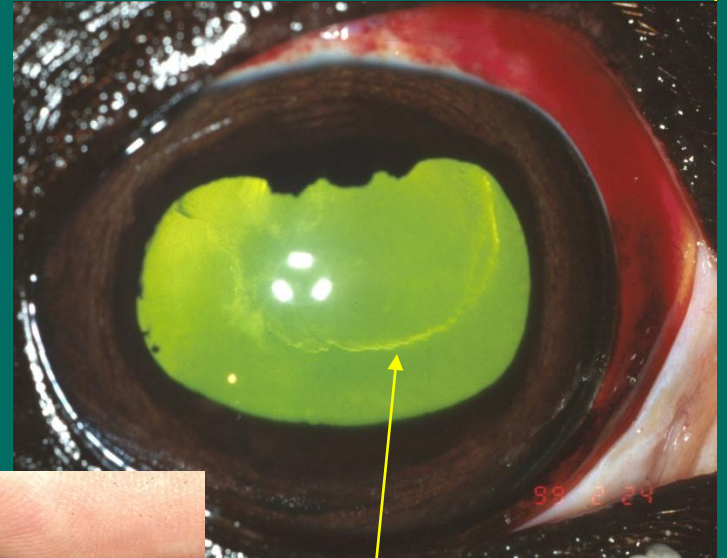
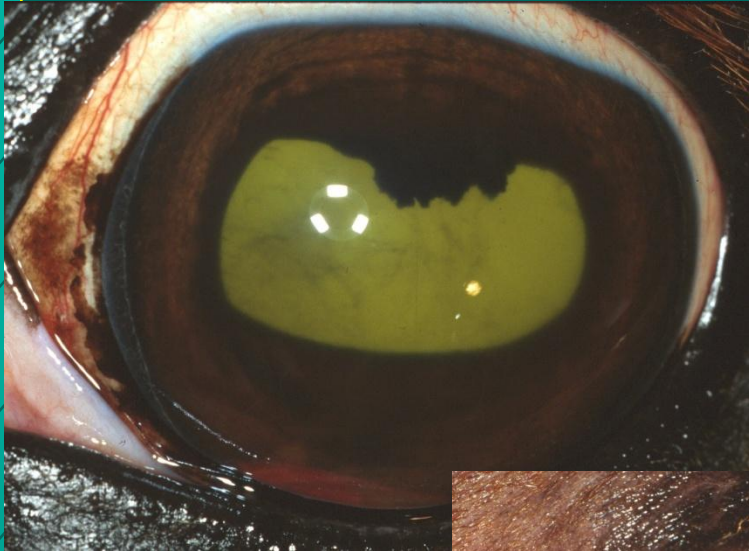
■ Vitrectomy

- 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 μ g/day for 5 years)
 - Intravitreal
 - Suprachoroidal
- 81% have less inflammation and attacks
- 87% visual at 14 months postop

CSA

