

# The SEVEN HABITS of Highly Effective Anterior Uveitis Management

**Paul Karpecki, OD, FAAO**

Director, Cornea Services & External Disease  
Kentucky Eye Institute  
Associate Professor, KYCO, UPIKE  
Chief Clinical Editor, Review of Optometry

**Paul M. Karpecki, OD, FAAO**

**Financial Disclosures:**

Aerie Pharmaceuticals  
Akorn  
Alcon Labs  
Aldeyra  
Allergan/Abbvie  
Allysta  
Amaros Medical  
Aurinia  
Avellino Labs  
Azura Pharmaceuticals  
Bausch Healthcare  
BioTissue  
BlephEx  
Bruder Healthcare  
Bruno Pharmaceuticals  
Cambium Pharma  
DGH Technology  
Dompe  
Enchroma  
Eyedetec  
Eyegate  
Eyepoint

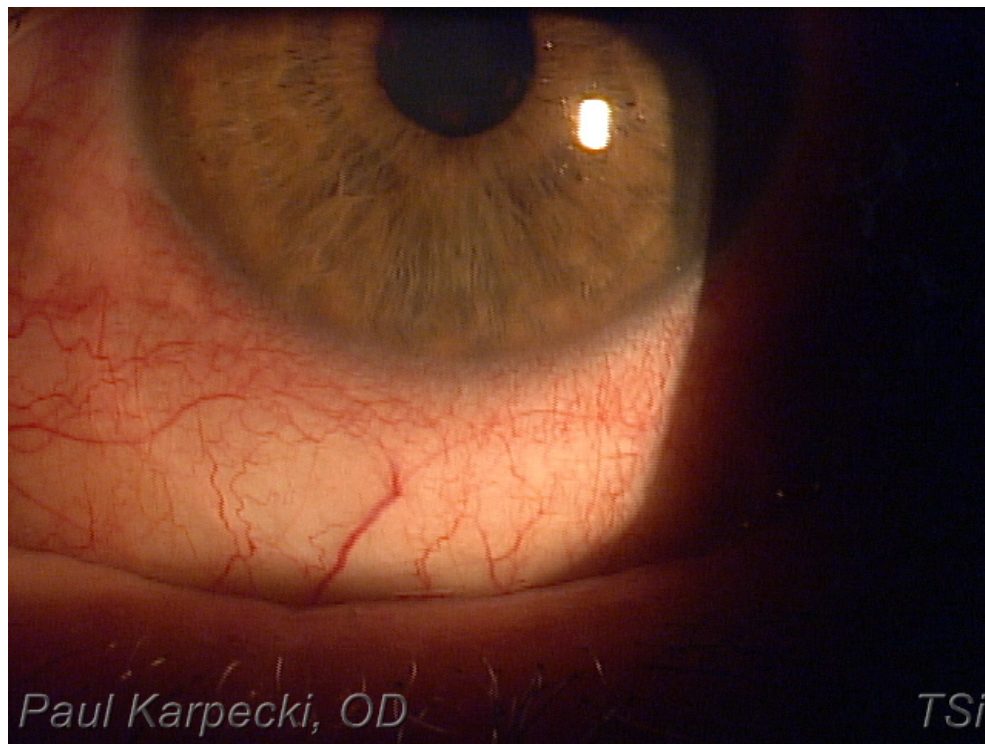
Eyevance  
Healthe  
Hue.AI  
iCare USA  
Imprimis  
Ivantis  
Jobson/Web MD  
Johnson & Johnson Vision  
Kala pharmaceuticals  
Keplr Vision  
Konan Medical  
LeGrande  
LenTechs  
Maculogix  
Mallinckrodt  
Mati Therapeutics  
Neurolens  
Novaliq  
Novartis  
Oasis Medial  
Ocuphire  
Ocular Sciences  
Ocular Therapeutix  
OcuSoft

Oculus  
OcuMedic  
Oyster Point  
Percept  
Quark Pharmaceuticals  
RegenerEyes  
Reichert  
Rendia  
RxSight  
Science Based Health  
Sentiss Pharma  
Sight Sciences  
Silk Technologies  
Sun Pharmaceuticals  
Surface  
Tarsus Medical  
TearClear  
TearLab  
TrueVision Systems  
Visant Medical  
Vital Tears  
Yolia

# Case History

68 y.o. Caucasian female  
Complains of photophobia and  
blurred vision  
As well as a headache over right  
eye for 2 days

SLEx findings:

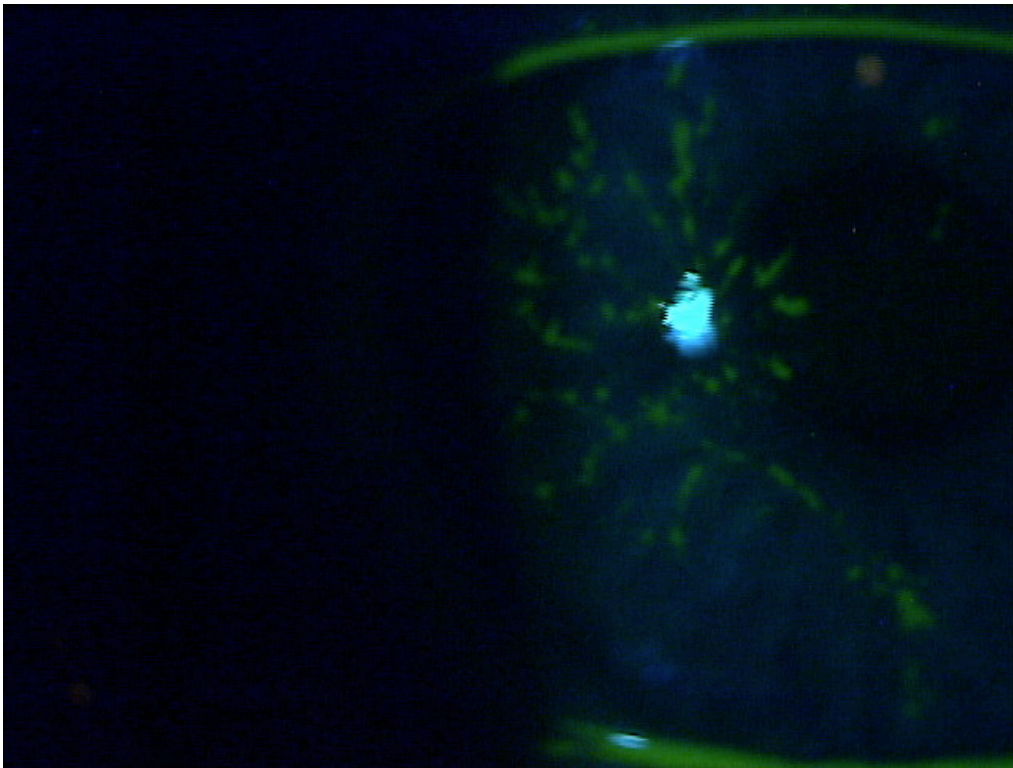


*Paul Karpecki, OD*

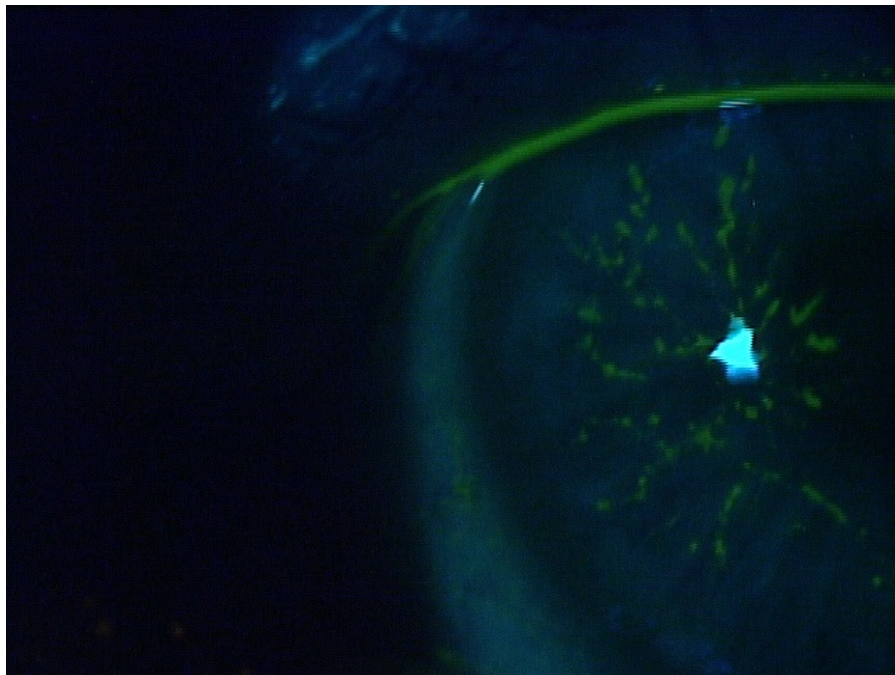
*TSi*

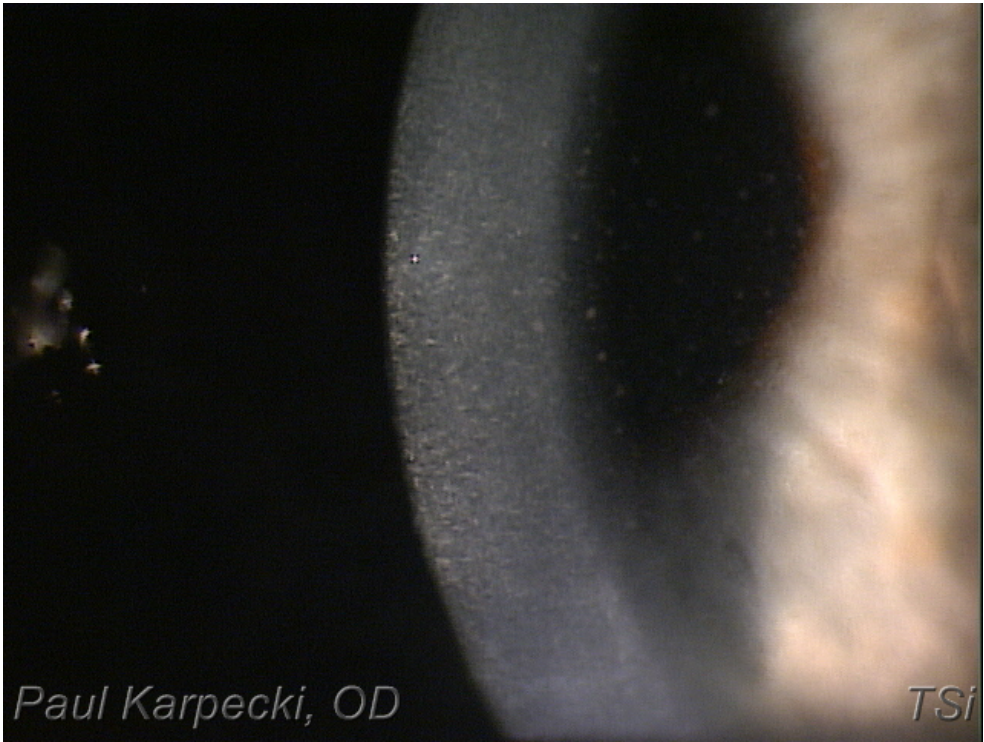


SLEx corneal findings:



SLEx corneal findings:





Diagnosis??



***Herpes Zoster  
Ophthalmicus***

# **Herpes Zoster**

Nearly 1 Million Americans develop  
herpes zoster each year

HZ ophthalmicus accounts for up to 25%  
of presenting cases

Over 50% incur ocular damage

# **Hutchinson's Sign:**

Lesion on the tip of the nose  
Nasociliary branch of ophthalmic  
division of trigeminal nerve (V)  
Nasal means possibly ciliary  
(ocular) involvement

**According to a study by Thean what was the most common complication associated with HZO?**

A. Iritis

B. Optic neuritis

C. Neurotrophic  
keratitis

D. Scleritis



## **Ocular findings:**

Conjunctivitis/Scleritis

Pseudodendrites

Neurotrophic keratitis

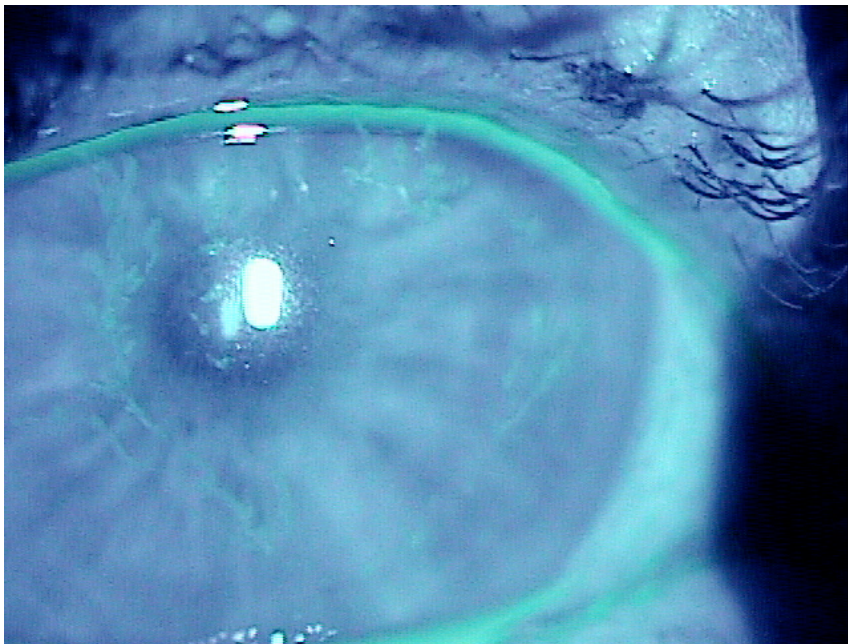
**Iritis**

Glaucoma

ION, vein or artery occlusion

Nerve Palsy

# Herpes Zoster Ophthalmicus



Pseudodendrites

# **Iridocyclitis and HZO**

Most common and most often  
overlooked ocular complication  
(43%)

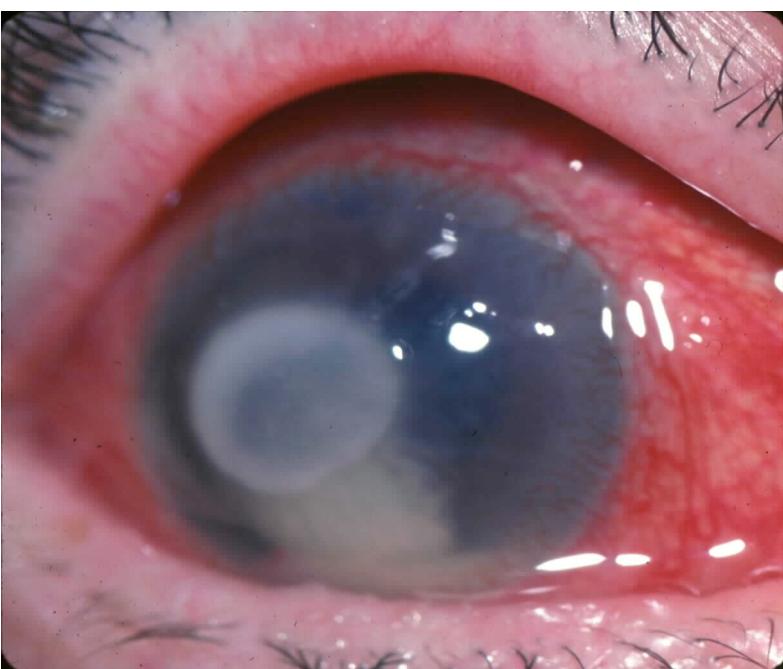
Highly elevated IOP

Study by Thean, Hall & Stawall  
*-clinical Ophthalmology Dec 2001*

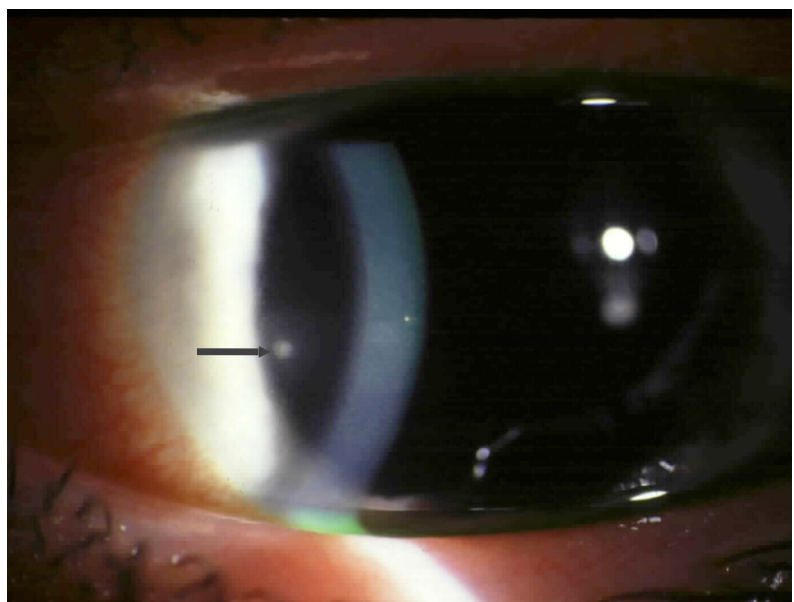
56% of patients developed  
glaucoma!!

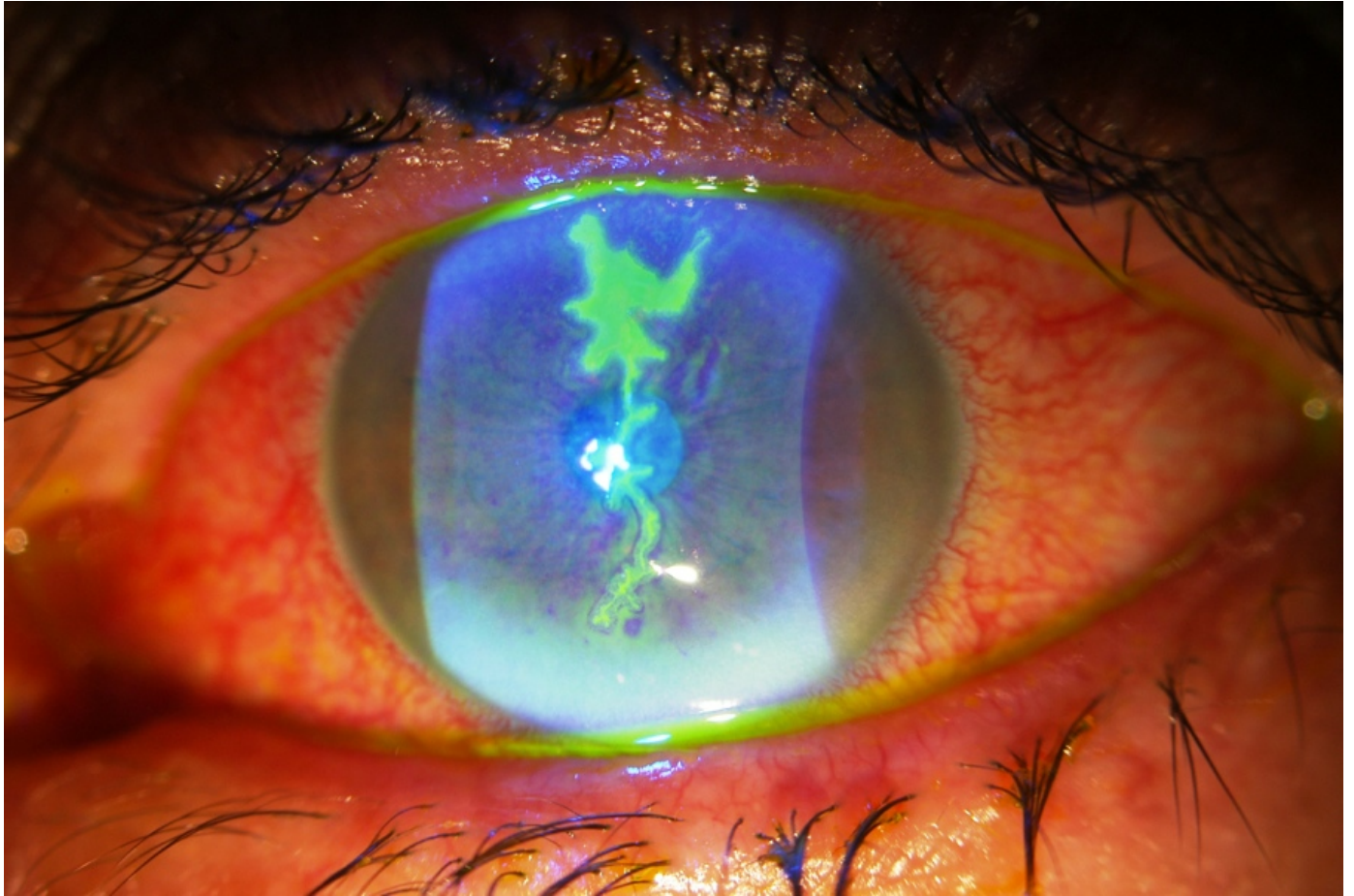
## **Seven Rules of Highly Effective Iritis Management**

1. Rule out keratouveitis
2. Check IOP
3. Rule out previous ocular surgery
4. Gauge severity – need for systemic work-up
5. Treat AGGRESSIVELY
6. Go beyond AC cell and flare (Restore the Blood-Aqueous Barrier)
7. Dilate and examine the posterior segment



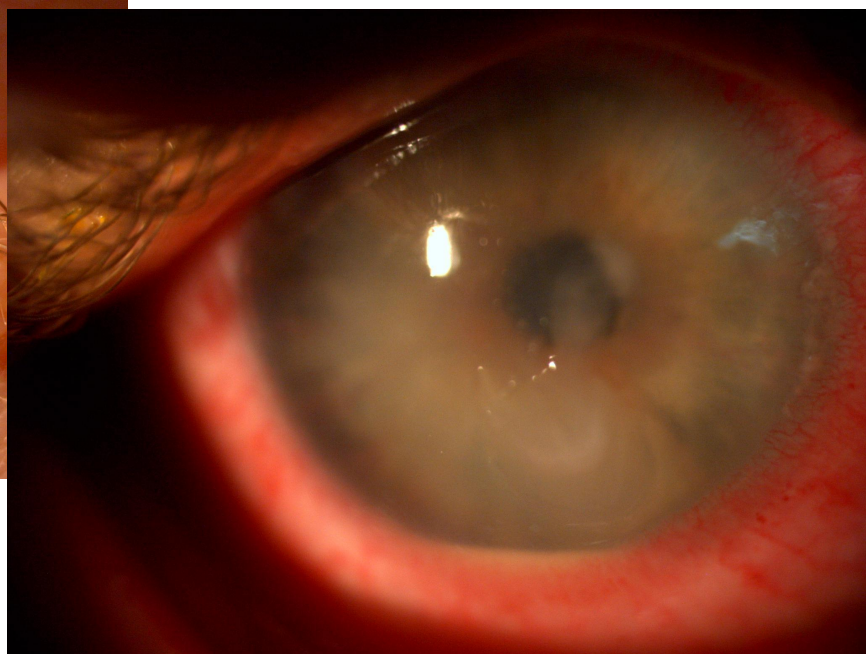
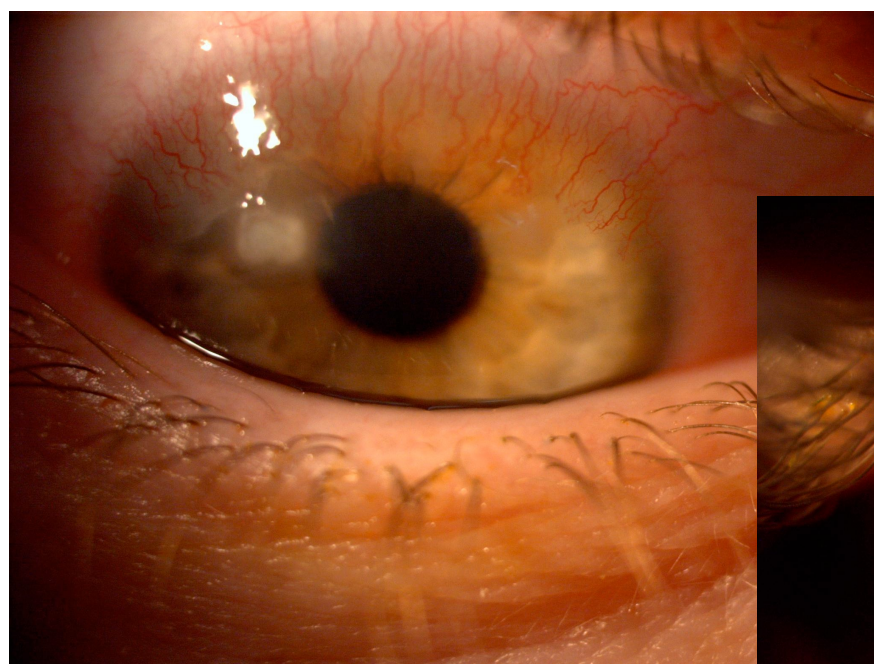
Rule out  
keratouveitis







Rule out keratouveitis



## **Check IOP**

Typically IOP will go down because of slowing of the ciliary body muscle

Can it go up?

Trabeculitis, fibrin in the AC

HZO case described earlier had an IOP of 56!

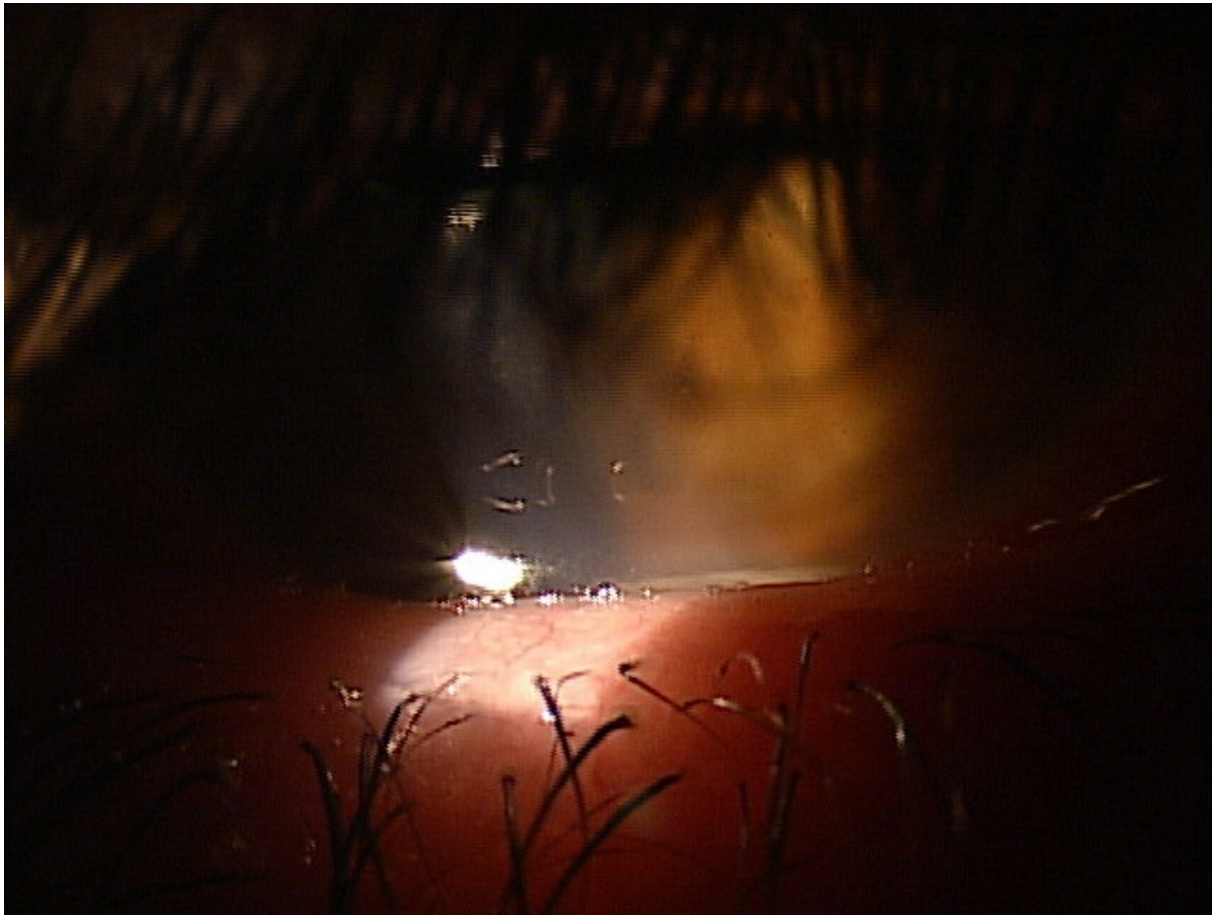


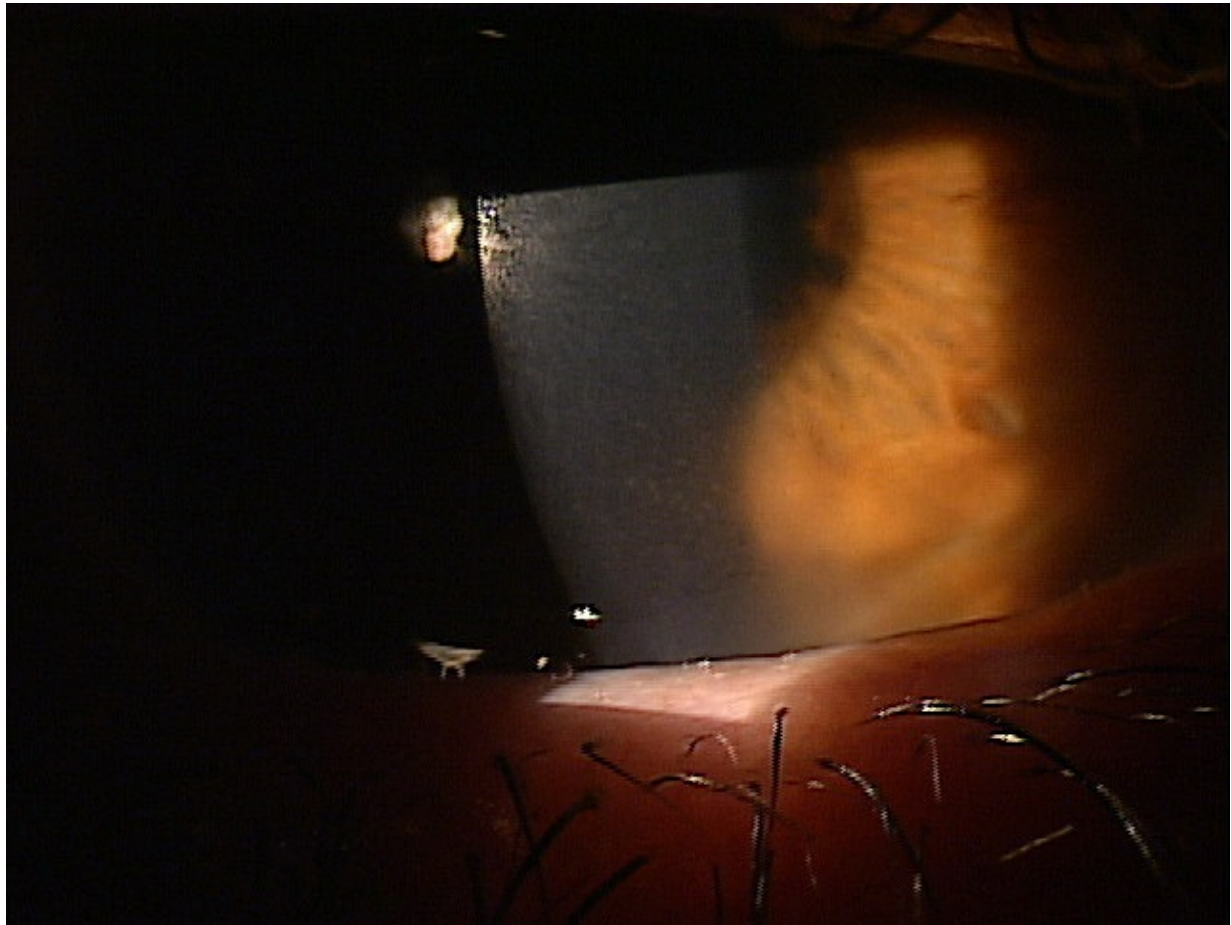
## **Rule out previous ocular surgery**

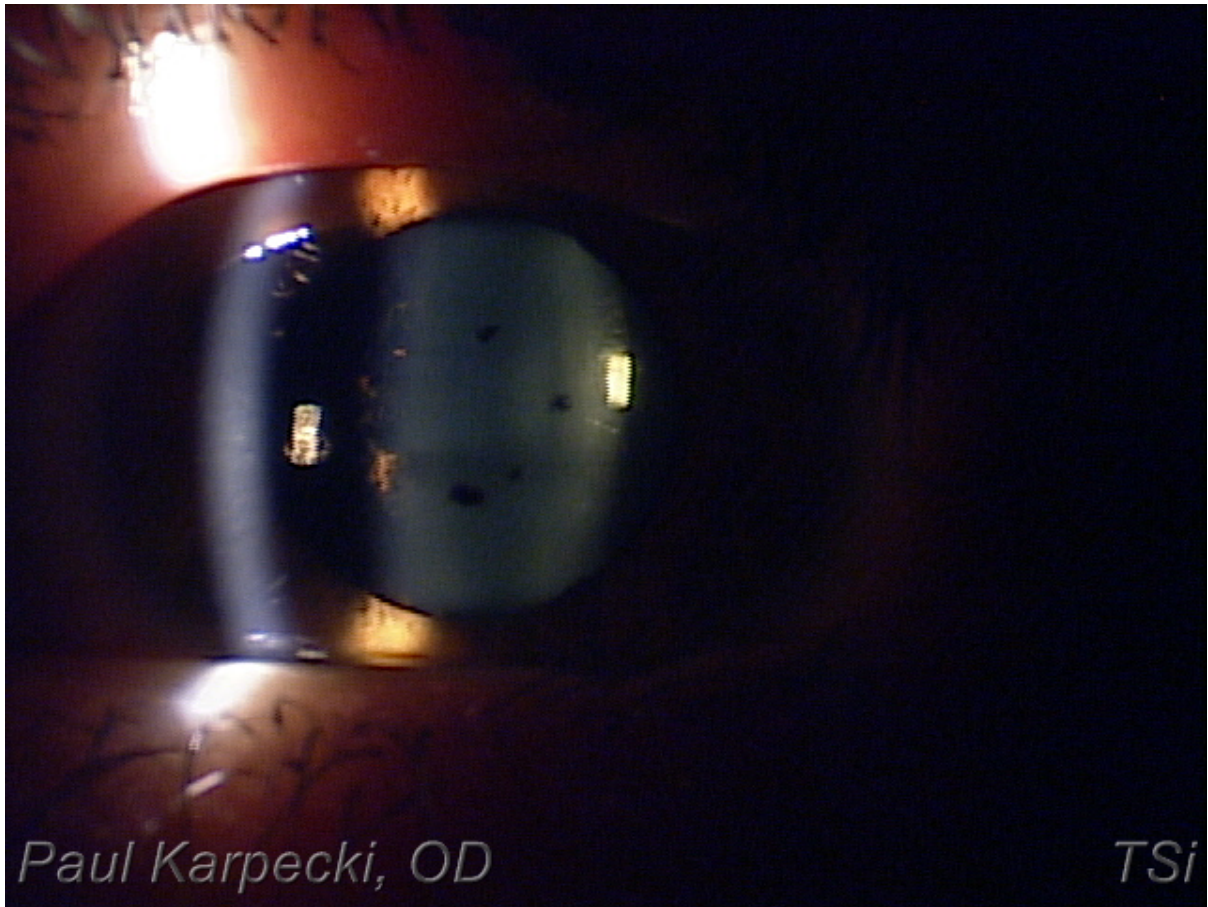
A significant iritis following a surgical procedure may be an endophthalmitis

According to the ASCRS 2009 & 2010 surveys the average time of diagnosis of endophthalmitis after cataract surgery was:  
9.2 days!

**Gauge Severity to  
determine if further  
testing is required**



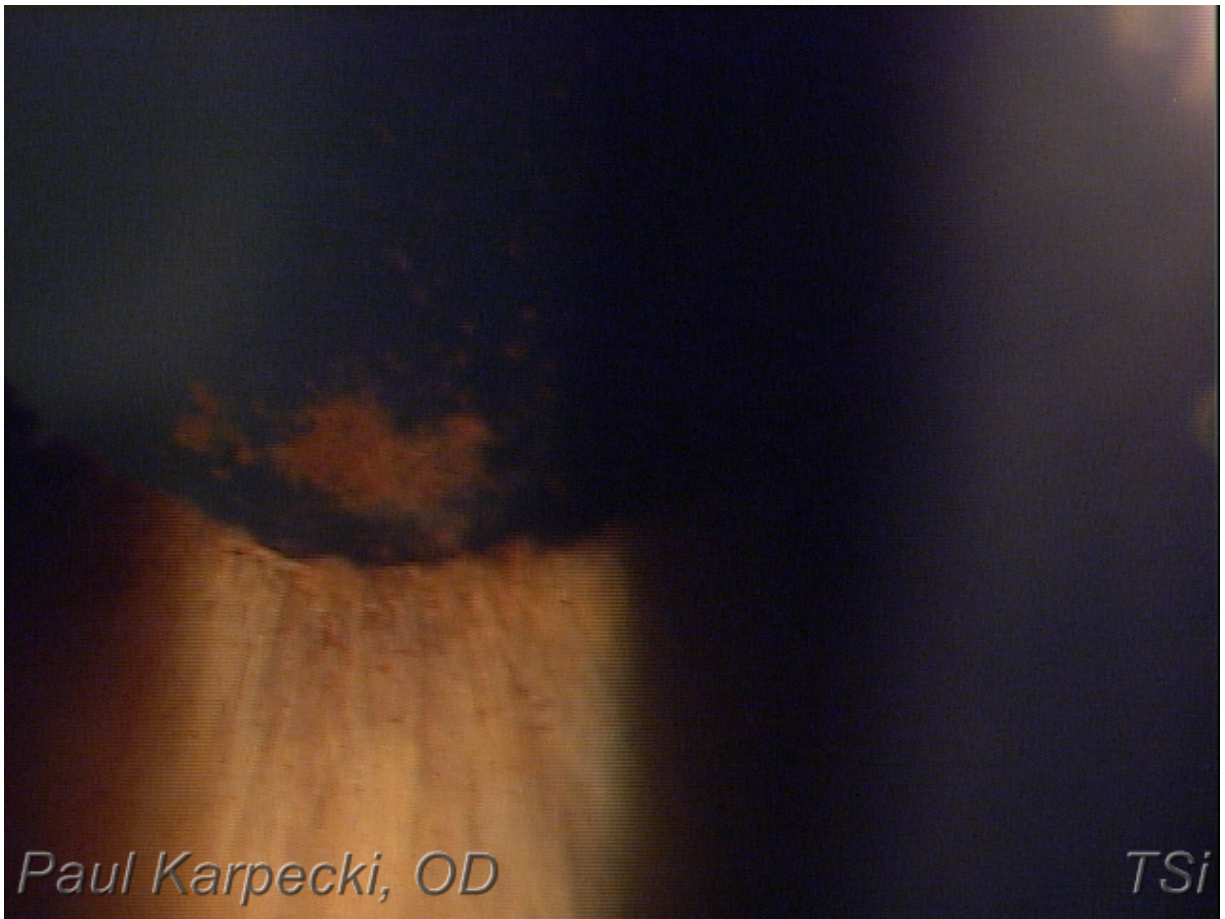




*Paul Karpecki, OD*

*TSi*





*Paul Karpecki, OD*

*TSi*

## **When would a systemic work-up be warranted?**

PS or PAS

KP's on endothelium

Hypopyon

Bilateral presentation

Recurrent presentation

In all cases?

Over 50% of iritis cases are HLA-B27 positive

## **Six Initial Tests to Run:**

1. CBC with Diff, and BMP (also check lymph nodes)
2. ESR/CRP
3. HLA-B27 antibody
4. RPR and FTA-ABS (fluorescent treponemal antibody absorption)
5. Quantiferon gold
6. VZV and HSV 1 and 2



## **HLA-B27 positive antibody:**

- Indicates a systemic predisposition
- Diseases include but are not limited to:
  - Juvenile rheumatoid arthritis  
(< age 16)
  - Rheumatoid arthritis  
Check the patients hand  
Ask about psoriasis i.e. psoriatic arthritis
  - Ankylosing spondylitis  
Young men  
Ask about lower back pain or stiffness
  - Reiter's Disease  
urethritis, tendonitis and polyarthritis
  - Crohns disease or ulcerative colitis  
ask about diarrhea and GI problems



## **Treat aggressively**

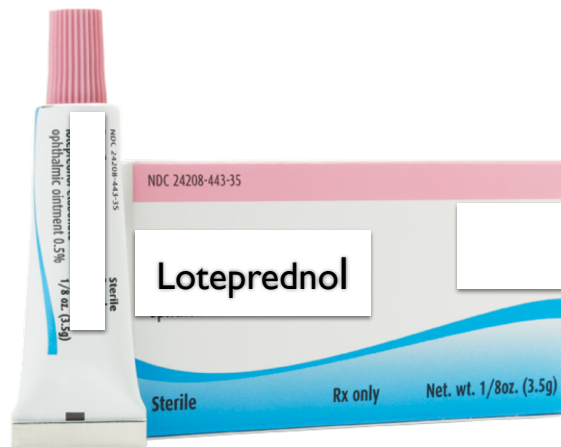
Never start an iritis treatment QID  
Must be Q2H or Q1H even for  
grade 1

Or consider stronger steroids:

**Difluprednate QID**

NEW: **LOTEPREDNOL UNG QHS**

Loteprednol ointment is a new **preservative-free** steroid ointment.



Loteprednol ointment is a corticosteroid indicated for the treatment of post-operative inflammation and pain following ocular surgery.

# Loteprednol ung attributes

- Established efficacy in post-operative inflammation and pain<sup>1</sup>
- Low risk of significant intraocular pressure (IOP) elevation seen in clinical studies<sup>2</sup>
  - <1% of patients experiences intraocular pressure elevation  $\geq 10$  mm Hg
  - If product is used 10 days or longer IOP should be monitored
- Preservative-free<sup>1</sup>
- As with other ophthalmic corticosteroids, LOTEMAX<sup>®</sup> ointment is contraindicated in most viral diseases of the cornea and conjunctiva including herpes simplex keratitis (dendritic keratitis), vaccinia, and varicella, and also in mycobacterial infection of the eye and fungal disease of the ocular structures<sup>1</sup>

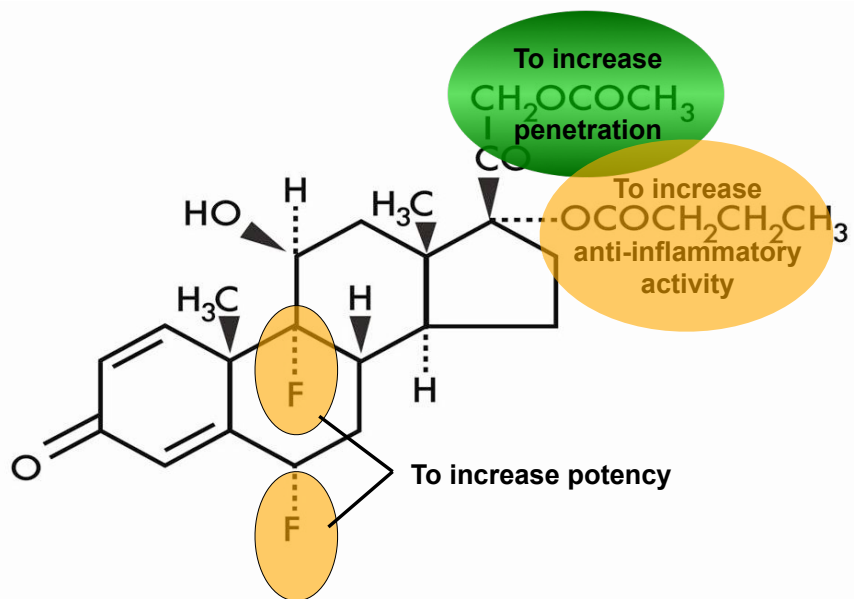
## **Difluprednate**

Developed by Mitsubishi as a dermatological preparation

- Categorized as a “very strong” steroid in dermatology

Developed by Senju as an ophthalmic emulsion

## Difluprednate Molecule



## **Difluprednate Formulation**

Developed as an emulsion

- No shaking required

BAK-free

- Uses sorbic acid as a preservative

Available in 5 mL bottle



Studied extensively in Japan for ophthalmic use  
In one preclinical pharmacokinetic study, the emulsion formulation was shown to have better ocular bioavailability than the suspension formulation<sup>1</sup>

In several preclinical studies, it was found to be

- Safe and well tolerated after repeated doses
- Effective at reducing inflammation in animal models of postoperative inflammation<sup>2,3</sup>

1. Inoue, J., et al. Preclinical pharmacokinetics of difluprednate ophthalmic emulsion. ARVO Annual Meeting, May 6–10, 2007, Ft Lauderdale, FL, poster B741, program 2651.

2. Okumura A, et al. Efficacy of difluprednate ophthalmic emulsion in preclinical studies of uveitis. ARVO Annual Meeting, May 6–10, 2007, Ft Lauderdale, FL, poster B742, program 2652.

3. Kida T, et al. Difluprednate emulsion inhibits postoperative inflammation in rabbit paracentesis model. ARVO Annual Meeting, May 6–10, 2007, Ft Lauderdale, FL, poster B745, program 2655

## Masking Scheme

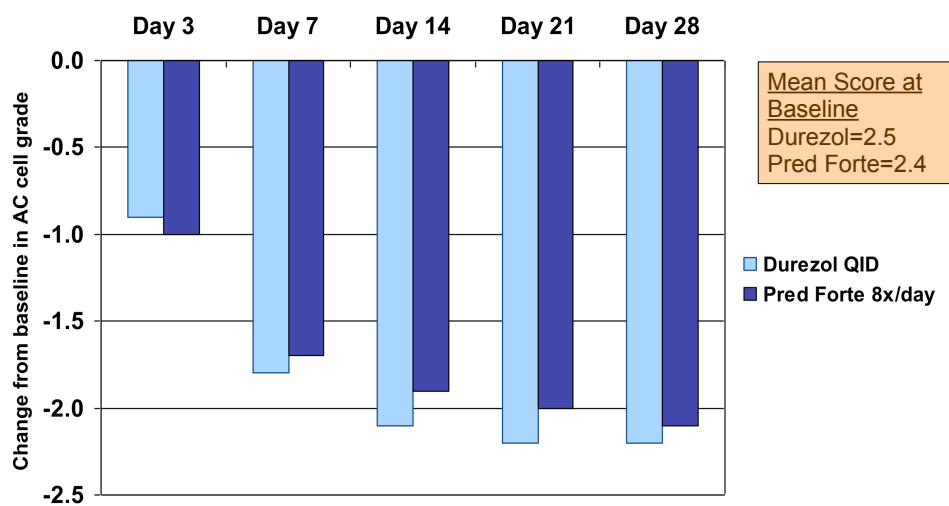
Patients were each given two bottles: Bottle A and Bottle B  
Each patient received 8 drops every day

In the Durezol group Bottle A contained Durezol and Bottle B contained vehicle

In the Pred Forte group, Bottle A contained Pred Forte and Bottle B contained Pred Forte

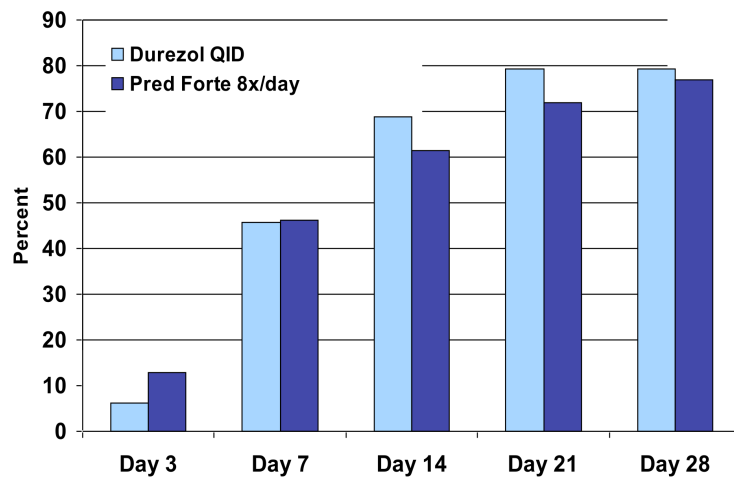


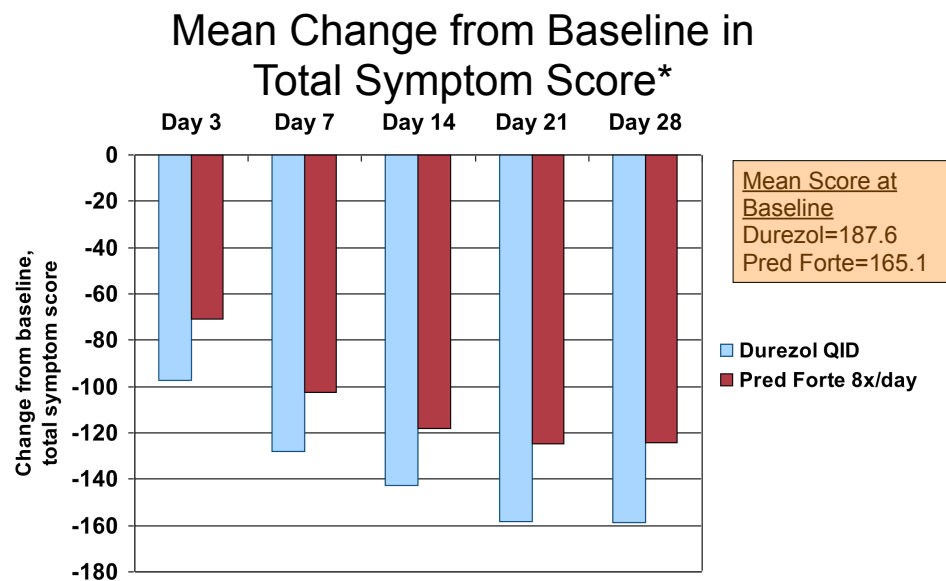
## Mean Change from Baseline in Anterior Chamber Cell Grade



\*At Day 14, the non-inferiority hypothesis was met, demonstrating that Durezol QID was not inferior to Pred Forte dosed eight times a day with a Confidence Interval of 95%

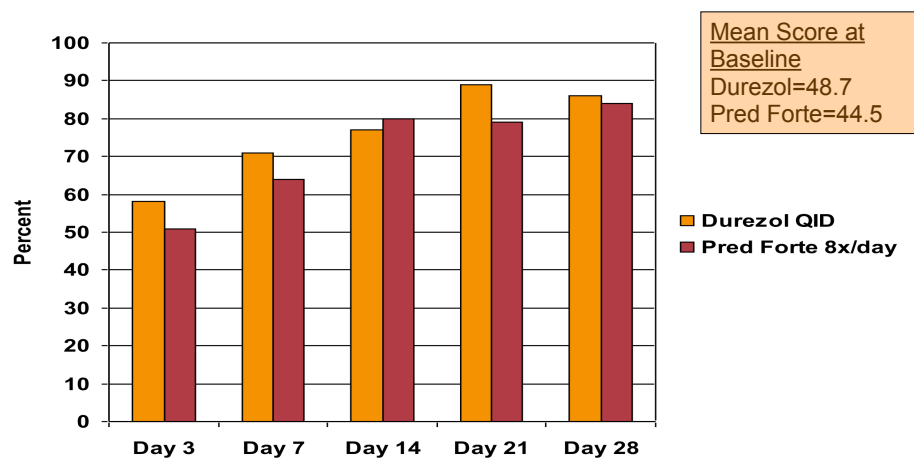
Percent of Subjects with Clearing of  
Anterior Chamber Cells  
(Grade 0 defined as  $\leq 1$  cell)



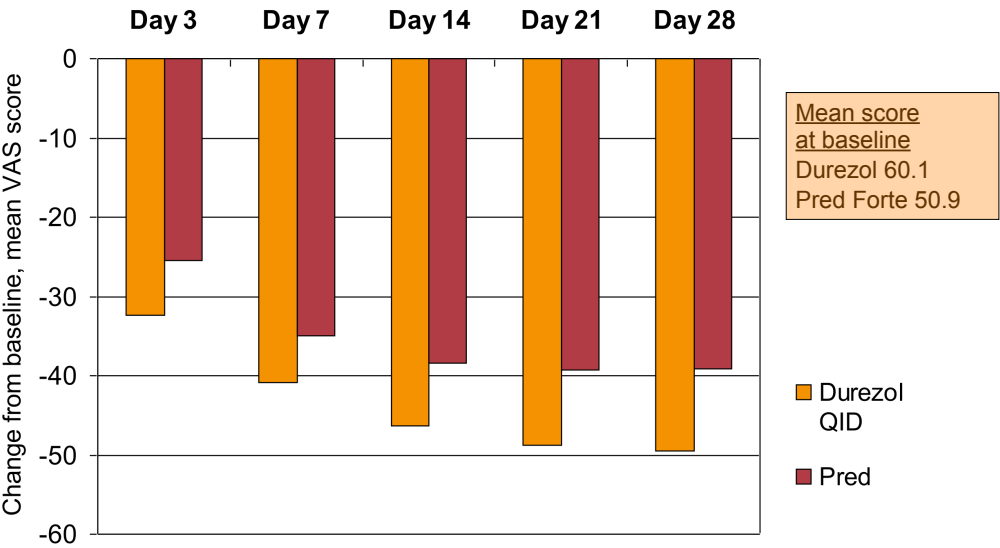


\*The total symptom score was the sum of pain/ocular discomfort, photophobia, blurred vision, and lacrimation. Each symptom was graded using a visual analogue scale that ranged from 0-100. Patients were asked to assess these symptoms by using a mark on a 100 mm line where 0 = absent, 100 = maximal.

## Percent Reduction in Mean Pain Score from Baseline



**Photophobia, Mean change from baseline**



## **Treatment: Iridocyclitis**

Prednisolone acetate 1% q1h or q2h

Difluprednate 0.05% QID

Loteprednol longer term or in  
Glaucoma patients

Cycloplegia

- Homatropine 5% bid
- Cyclopentolate 1% bid



# **The Importance of Cycloplegia**

1. Re-establish vascular permeability
2. Prevent synechiae
3. Pain Management

**AVOID:**

Atropine (synechiae lock)



*Paul Karpecki, OD*

*TSi*

# ACTH Gel in Uveitis Retrospective Chart Review

## Study Goal

To describe patient characteristics, treatment patterns with ACTH, and physicians' assessments of patients with uveitis treated with ACTH

## Study Design

- Ophthalmologists in the AMA physician and ACTH prescriber databases were contacted for cases of uveitis treated with ACTH in the past 12 months
    - 91 eligible patient charts were identified
  - Health care providers abstracted data using an electronic data collection instrument and responded to survey questions
    - Data were aggregated and reported using descriptive statistics
- 
- Retrospective data collection may be incomplete
  - Outcomes may be influenced by therapies not documented in the chart
  - Patient outcomes and safety were not quantified

# Patient Presentation

## Patient Demographics (n=91)

- Mean age, 41±14 years (range, 11-78 years)
- Women, n=56 (62%)
- Patients were primarily:
  - Caucasian (n=42; 46%)
  - African American (n=29; 32%)
  - Hispanic/Latino (n=8; 9%)
  - Asian, (n=5 ;5%)
- 69% of patients had 1 or more comorbidities typically associated with uveitis

## Uveitis Characteristics (n=91)

- Anatomic presentation
  - Anterior uveitis (n=38; 42%)
  - Intermediate uveitis (n=19; 21%)
  - Posterior uveitis (n=9; 21%)
  - Diffuse uveitis/panuveitis (n=15; 16%)
- Both eyes affected in 59% of cases
- Mean duration of uveitis diagnosis, 3.98 years
- Mean number of acute episodes, 3.5
- Symptom severity
  - Moderate (n=63; 69%)
  - Severe (n=23; 25%)

# Uveitis, Signs, Symptoms

Signs and Symptoms Present, n (%) (n=91)		Severity		
		Mild	Moderate	Severe
Blurred vision	81 (89)	10	52	19
Light sensitivity	41 (45)	9	22	10
Floaters	40 (44)	12	25	3
Visual loss/acuity	40 (44)	5	24	11
Eye pain	34 (37)	9	20	5
Eye redness	30 (33)	6	22	2

Visual Impairment, n (%)	1 Eye (n=37)	Both Eyes (n=54)
Mild or none (better than 20/70)	10 (27)	11 (20)
Moderate (worse than 20/70, better than 20/200)	18 (49)	30 (56)
Severe (worse than 20/200, better than 20/400)	9 (24)	12 (22)
Undetermined/unspecified	0	1 (2)

# Observations and Assessments

- ACTH was used for the first time by 83/91 (91%) of patients
- At the time of data collection, treatment was ongoing at the initial dose in 27 patients (30%), with a mean duration of 16.7 weeks

Physicians' response to:  
*What is the patient's current status?*

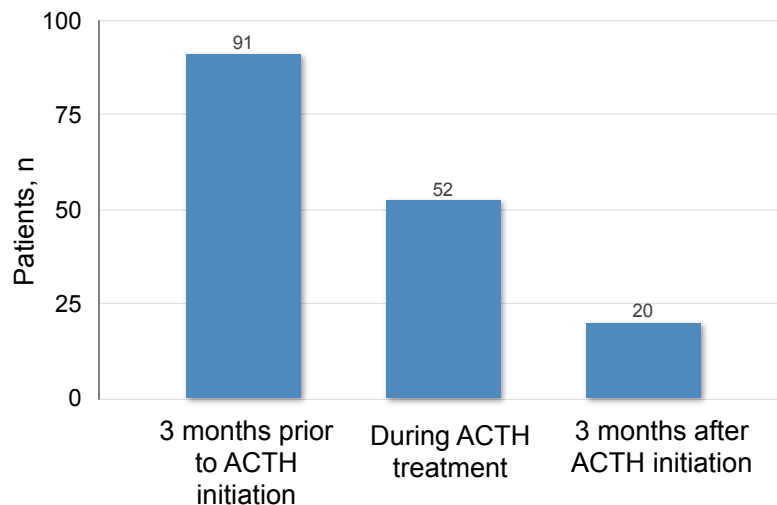
- Patients improved, n=76 (84%)
- Patients were same, n= 15 (16%)

Physician assessment in response to:  
*Please select the outcomes below that have improved as a result of ACTH treatment*

Respondents selected all options that apply	n (%)
Improvements in vision	78 (86)
Improvements in eye pain	25 (27)
Improvements in vitreous haze	24 (26)
Reduction of background medication use	22 (24)
Improvements in vitreous flare	21 (23)
Improvements in macular edema	16 (18)

# Additional Observations

## Concomitant Medication Use Before, During, and Following the Start of ACTH therapy



- Prior to ACTH initiation, all 91 patients were receiving concomitant medications for uveitis
- Concomitant medications used by  $\geq 20\%$  of patients in the 3 months prior to ACTH initiation included steroid eye drops, oral steroids, intraocular steroids, and nonsteroid eye drops
- The number of patients treated with concomitant medications decreased during ACTH treatment, and during the 3 months following the initiation of ACTH therapy

# ACTH Gel Storage and Handling for Administration

## **ACTH offers flexible dosing for patients and providers**

- ACTH (IM or SC) can be given by a caregiver or self-administered
- Typical dosing 80 mg SC two times per week for 3 months then taper
- ACTH Gel should be stored under refrigeration between 2°C and 8°C (36°F-46°F)
- Vials should be warmed to room temperature before using



## **Seven Rules of Highly Effective Iritis Management**

1. Rule out keratouveitis
2. Check IOP
3. Rule out previous ocular surgery
4. Gauge severity – need for systemic work-up
5. Treat AGGRESSIVELY
6. Go beyond AC cell and flare (Restore the Blood-Aqueous Barrier)
7. Dilate and examine the posterior segment

# Taper and extend

- Typical Example:
  - Difluprednate QID until significant improvement in AC reaction then TID x 1 week, BID x 1 week, QD x 1 week
  - No C & F noted, continue for 3-5 days

# Dilate

- Rule out other causes e.g. retinal tear or RD
- Examine the posterior pole for vitritis overflow, chorioretinitis etc.
- Systemic indications

Retinal Detachment 7654321

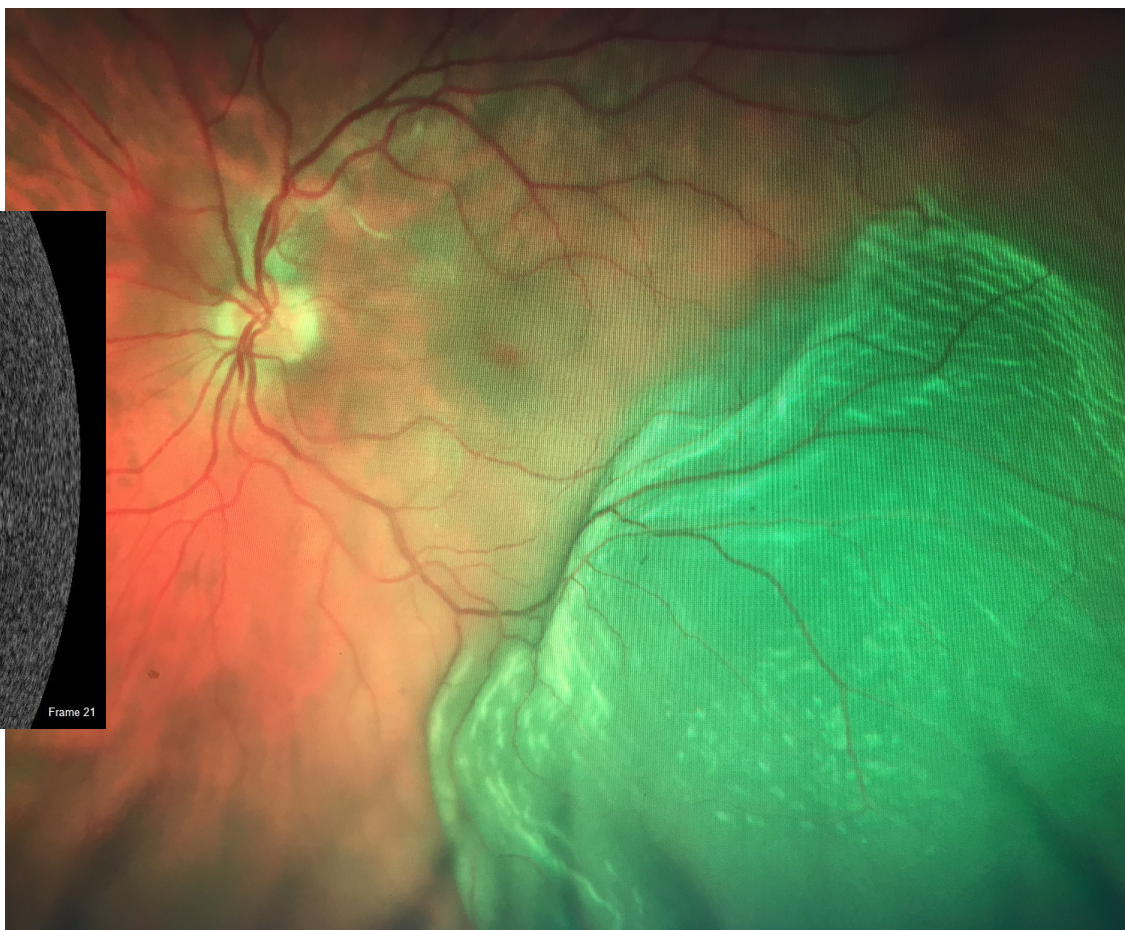
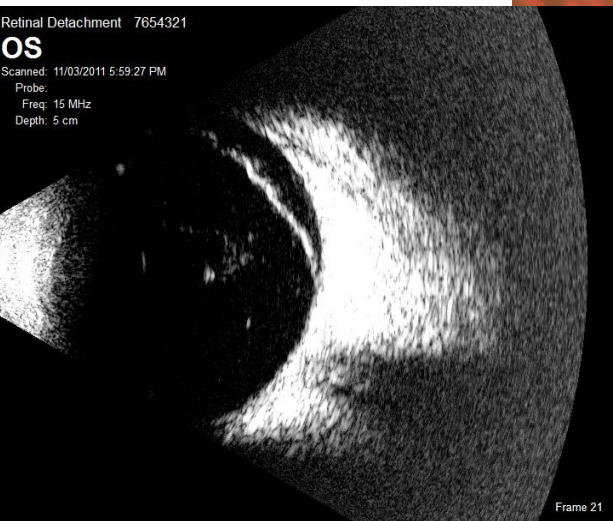
OS

Scanned: 11/03/2011 5:59:27 PM

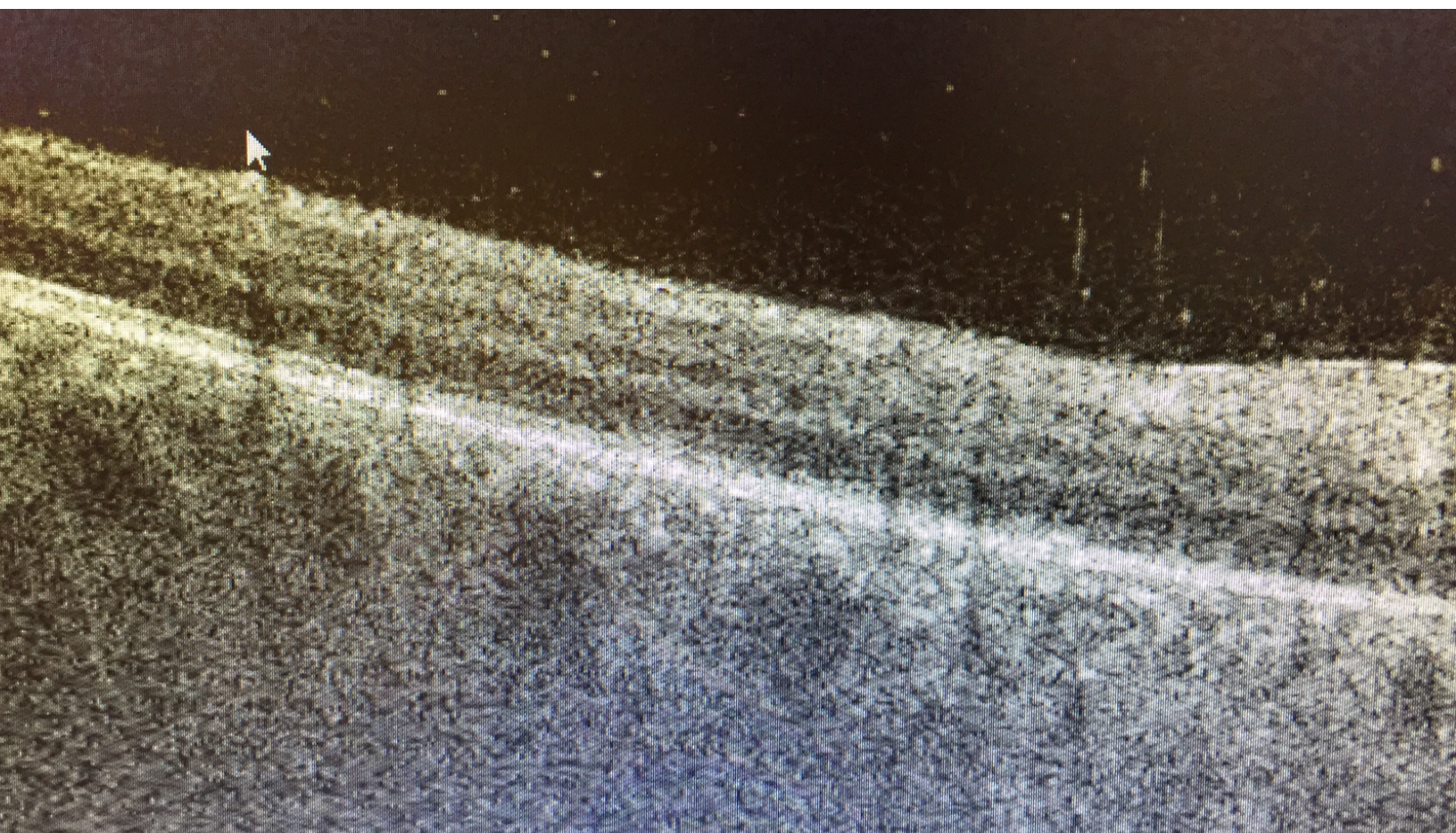
Probe:

Freq: 15 MHz

Depth: 5 cm





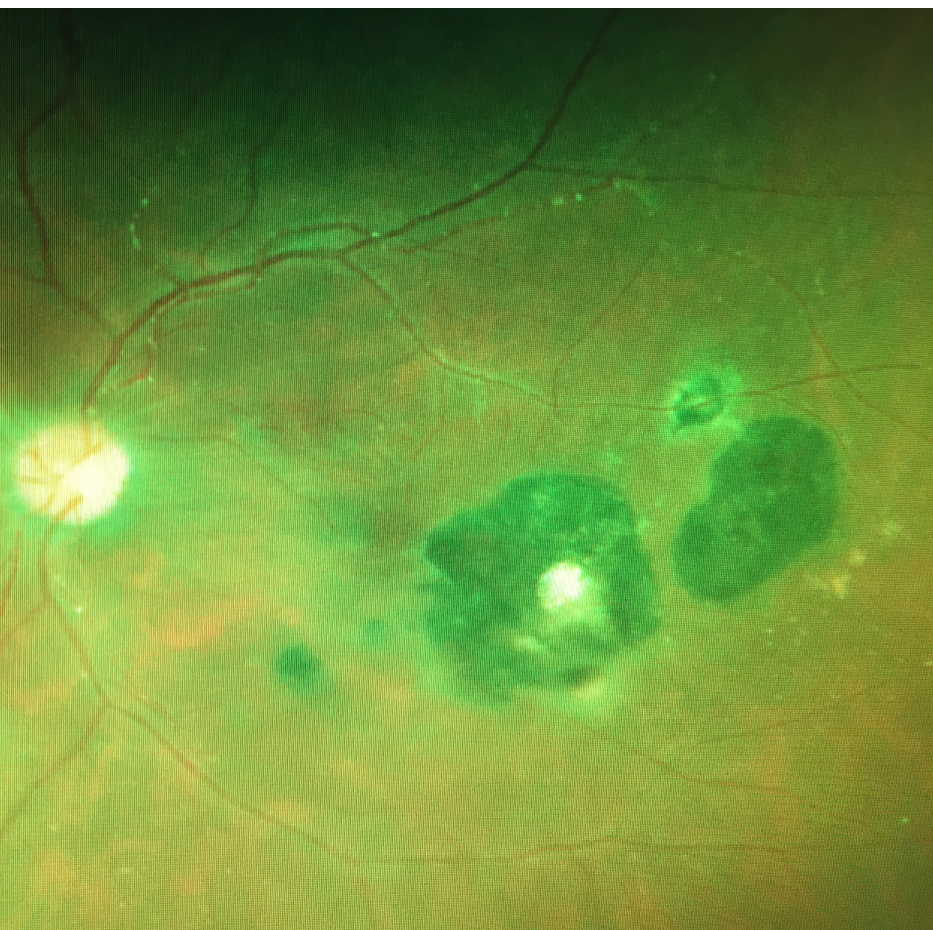


# Clinical triad

- Rapidly progressing circumferential retinal necrosis
- Vitritis
- Vasculitis (primarily occlusive arteritis, though phlebitis can occur)
- Kyrieleis Plaques may precede the vasculitis







## **Conclusions:**

- Iritis is a common condition diagnosed by optometry
- Following the seven rules will allow you to successfully manage these patients and keep you out of trouble
- Understand the importance of systemic disease in iritis and take appropriate measures to co-manage
- Keep advancing, iritis is a great area of ocular disease management



**THANK YOU**

[karpecki@Karpecki.com](mailto:karpecki@Karpecki.com)