Differential Diagnosis in Anterior Segment Disease

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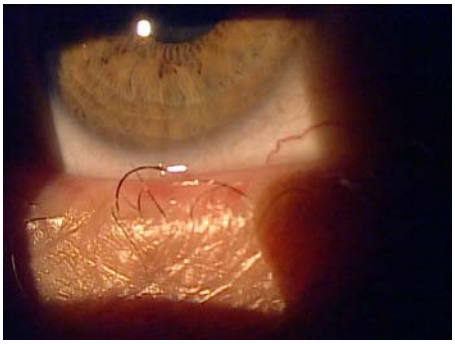
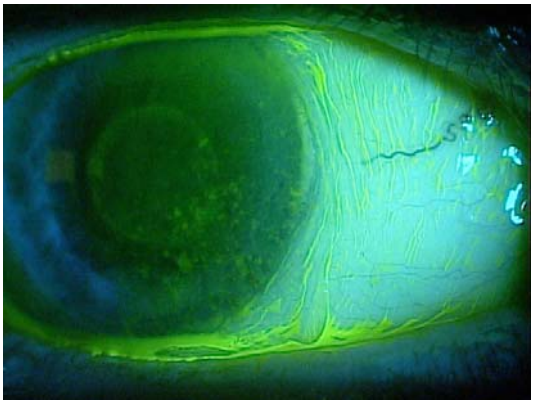
Case I

- 58 y.o. Caucasian female
- CC: F.B. sensation
- Slight blur (20/20 -2)
- Epiphora

Epiphora

- SLEx finding
  - e.g. conjunctivochalasis or trichiasis
- Nasolacrimal sac obstruction
- Lid Laxity conditions- ectropion
- Dry Eye





Back to Case I History

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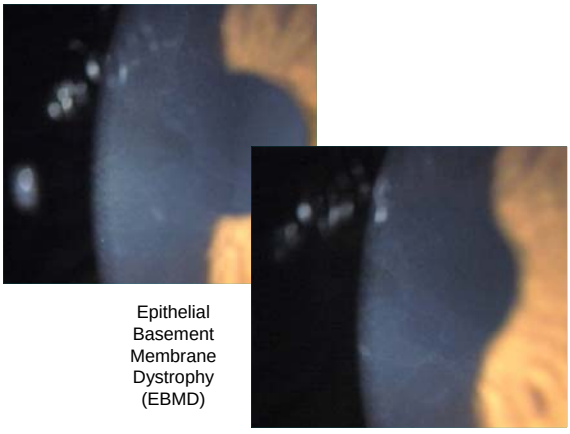
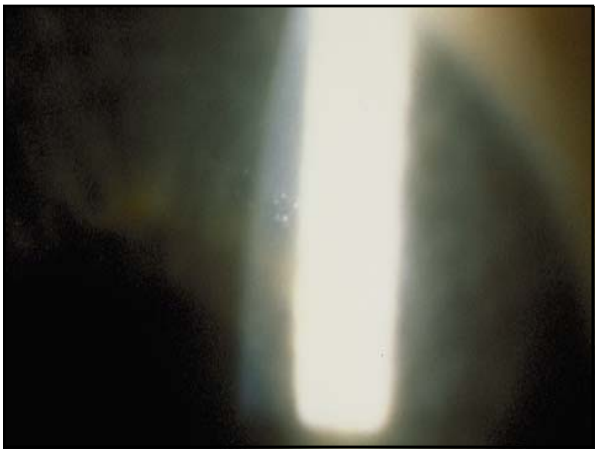


Epithelial Basement Membrane Dystrophy (EBMD)



87% of all recurrent erosion occurs in what region of the cornea?

A. Superior Cornea
B. Central Cornea
C. Inferior Cornea
D. Exposure areas of 3:00 and 9:00

Diagnosis:

Recurrent Corneal Erosion Syndrome

EBMD

Initial Treatments:

- Hyperosmotic agents
  - Muro 128 ung & gtts
- Bandage contact lens
  - Silicone hydrogel

Treatment:

- Daytime meds?
- What about hyperosmotic drops?
- FreshKote gtts up to QID (Behind the counter or in office)

Which of the following should be avoided in the treatment of RCE?

A. Steroid drops
B. Antibiotic drops
C. Oral tetracycline
D. Lubricating ointments

Treatment:

What medications should be avoided?

Bland Artificial Tear Ointments

Eke T et al Recurrent symptoms following traumatic corneal abrasion Eye 1999 June

Treatment level 2:

- Steroids such as Lotemax
  - Q.I.D. x 2 wks then BID x 6 wks
- P.O. Tetracycline
  - *Doxycycline 50 mg bid x 2 months*

- *Dursun D. et al. Treatment of recalcitrant recurrent corneal erosions with inhibitors of matrix metalloproteinase-9 doxycycline and corticosteroids Ophthal 2001 July*

Why does this work?

- Metalloproteinases which cleave Bowman's layer below the anchoring system (Hemidesmisones)
- MMP's Develop through the production of Leukotrienes

For how long should RCE therapy be maintained to obtain a clinical cure?

A. 1 week

B. 6 weeks

C. 2-4 weeks

D. Until the first sign of resolution of symptoms

New Treatment for Recalcitrant RCE:

- Muro 128 ung x 2 mo
- FreshKote drops tid x 2 mo
- Lotemax qid x 2 weeks then bid x 6 weeks
- Doxy 50 mg PO BID x 2 mo

Other Options for Recalcitrant Cases:

- Bandage Contact Lens
- Stromal Puncture
- Phototherapeutic Keratectomy
- Autologous serum
- Amniotic membrane

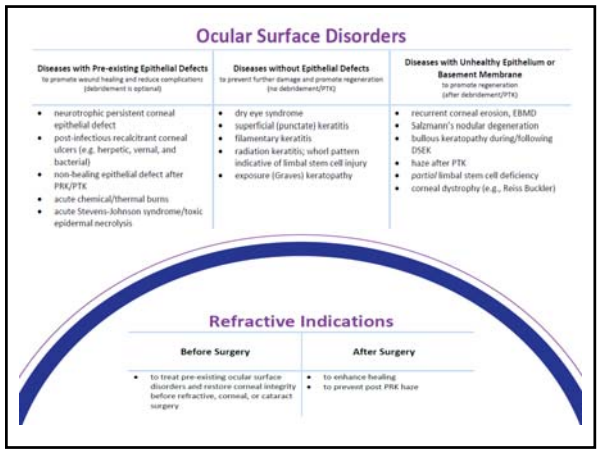
PROKERA® Amniotic Membrane

- Class II medical device comprising of CRYOTEK™ amniotic membrane into a thermoplastic ring set
- Combines the functionality of a symblepharon ring with the biologic actions of CRYOTEK™ amniotic membrane to create a unique treatment option for corneal and limbal wound healing

Clinical Evidence for PROKERA®

- A safe and effective method to promote healing of the corneal surface with minimal side effects[1]
- Inhibits abnormal angiogenic processes and inflammation, thus promoting scarless healing[1-7]
- Stimulates healthy re-epithelialization of the corneal wound without sutures[1,2,4-6,8]
- Provides pain relief and reduces haze, resulting in improved visual acuity by a mean (SD) of 2.5 (2.6) Snellen lines[2]

1. Pachigolla G, et al. *Eye Contact Lens.* 2009;35:72-75. 2. Sheha H, et al. *Cornea.* 2009;28:1118-1123. 3. Gomes JA, et al. *Curr Opin Ophthalmol.* 2005;16:233-240. 4. Shay E, et al. *Cornea.* 2010;29:359-361. 5. Kheirkhah A, et al. *Arch Ophthalmol.* 2008;126:1059-1066.
6. Shammas MC, et al. *Am J Ophthalmol.* 2010;149:203-213. 7. Shay E, et al. *Invest Ophthalmol Vis Sci.* 2011;52:2669-2678. 8. Lazarro DR. *Eye Contact Lens.* 2010;36:60-61.



PROKERA® Insertion

- Set patient expectations! Inform the patient they may experience some initial stinging and foreign body sensation
- Apply topical anesthesia
- Rinse the PROKERA® a with a sterile solution (saline, BSS etc…)
- Hold the upper eyelid
- Ask the patient to look down
- Insert the PROKERA® into the superior fornix, preferably using your fingers to hold the ring
- Slide the PROKERA® under the lower eyelid

46% of all patients in this study had EBMD

James Reidy et al. Recurrent erosions of the cornea: epidemiology and treatment. Cornea 2000 Nov; 19(6):767-71

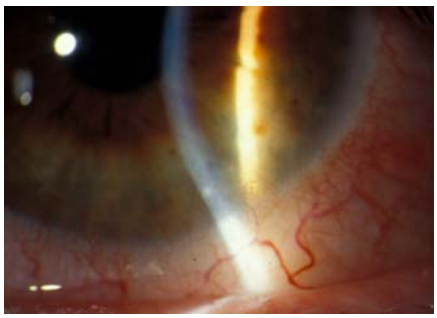
The remainder had trauma induced causes
Fingernail
Paper cut etc.

Patient RSJ

- 31 y.o. African American Male
- Presents after having seen 2 previous doctors with some improvement but no resolution of red eye
- Has been going on for 3-4 months

Patient RSJ

- Previous doctors diagnosed corneal infiltrates related to contact lens wear and tried antibiotics combination agents with little response
- Showed improvement but the condition returned after discontinuation even with a slow taper



Small peripheral infiltrates noted

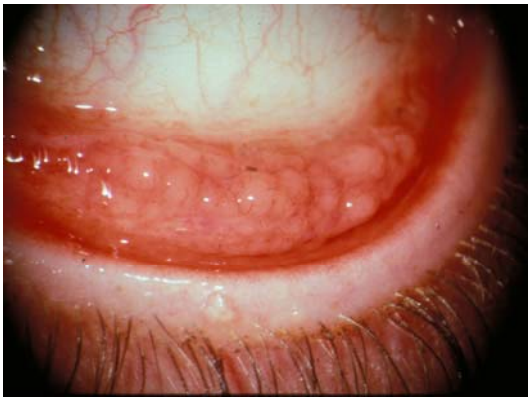
What is your diagnosis?

A. CL related sterile infiltrates

B. Adult Inclusion conjunctivitis (Chlamydia)

C. EKC or other viral keratitis

D. Toxic keratitis



What is your recommended treatment?

A. 1000mg Azithromycin once

B. 5 Day Z-Pack

C. 100 mg doxycycline x 3 weeks

D. Topical AzaSite

Treatment:

- 1000 mg Azithromycin (Zithromax)
- Four 250 mg tablets all at once
- What about a Z-pack?
- What about tetracycline?

Findings:

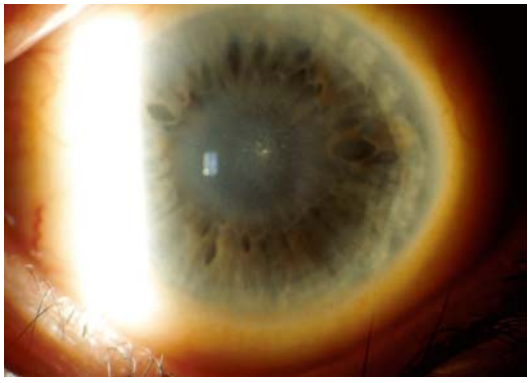
- Subepithelial infiltrates
- Neovascularization or micropannus
- Follicular conjunctivitis
- Preauricular lymph node on ipsilateral side
- Starts unilateral, if goes long enough could become bilateral

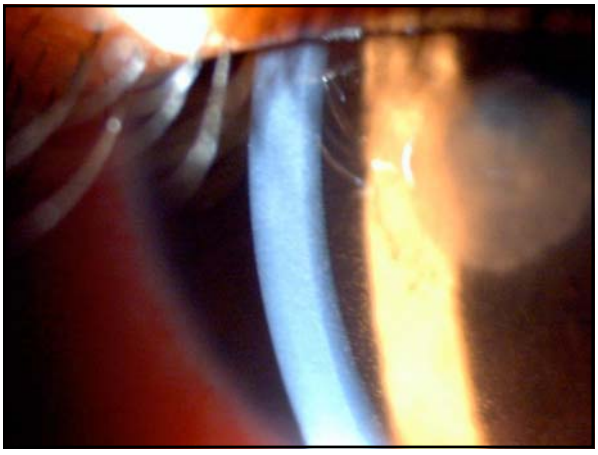
Psittacosis:

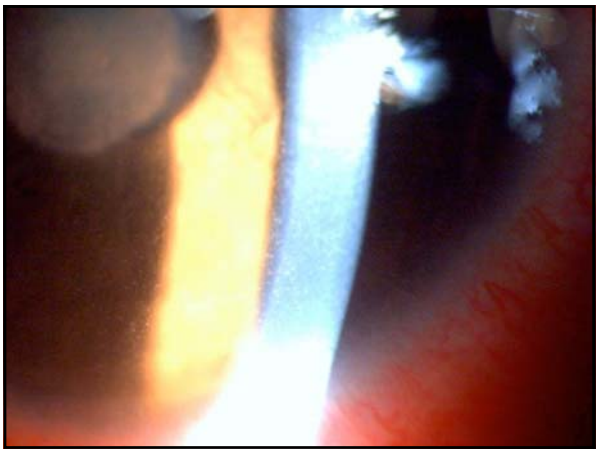
- Transmitted via the respiratory route from many avian species including Parakeets and Parrots, chickens etc.
- Follicular conjunctivitis
- Fever, dry cough
- Tx: Doxycycline 100mg BID x 3 weeks (pulmonologist/PCP)

Anterior Seg Case 3

- 38 y.o. African American Female
- Complaint of decreased vision for about 1 week
- Longstanding contact lens wearer
- Vision seems to be getting worse over last few days
- No significant pain
- No corneal staining







Testing???

Cotton Wisp or Dental floss
to measure corneal sensitivity

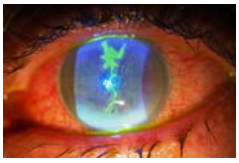
Diagnosis??

Herpes Simplex Virus (HSV) Endotheliitis

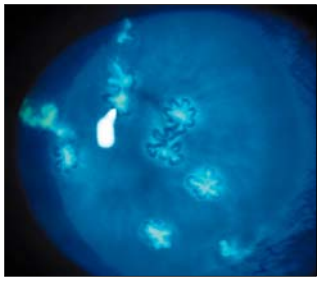
Infectious Epithelial Keratitis: Cornea Vesicles

Infectious Epithelial Keratitis: Dendritic Ulcer

- Branching linear ulceration
- Swollen epithelial borders
- Contain active virus
- Most common presentation for HSK



Dendritic Epitheliopathy

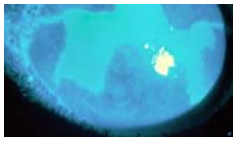


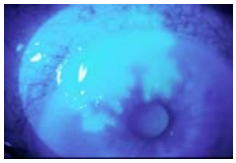
Infectious Epithelial Keratitis: Geographic Ulcer

Enlarged dendritic ulcer

Scalloped borders

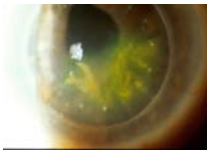
Contains active virus

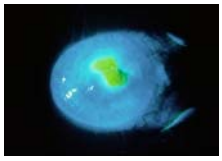




HSV Neurotrophic Keratopathy

- Clinical Appearance
- Punctate epithelial erosions
- Ulcer
- Dendritic epitheliopathy





Immune Stromal Keratitis (Interstitial Keratitis)

Clinical Findings

Stromal haze or infiltrate

Neovascularization

Immune ring

Intact epithelium

Endotheliitis

- Central or paracentral disc-shaped area of edema
- KP corresponding to edema
- Iritis
- Elevated IOP

Treatment: Epithelial Involvement

- In the past: trifluoridine - Viroptic q2h
- New replacement: **Zirgan** 5 x per day until ulcer disappears then TID x 1 week
- PO Valtrex 500mg TID
- PF artificial tears
- L-Lysine PO 1-3g per day?
- Follow-up (next day), day 3-4, day 7-10

Treatment: Stromal keratitis or Endotheliitis

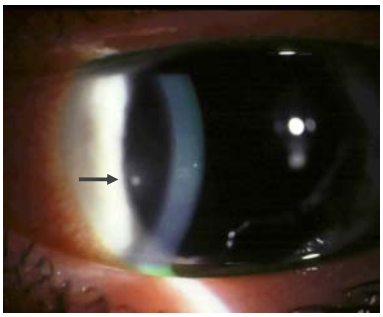
- Durezol QID
- Pred Forte Q2H
- Cover with PO Acyclovir (400 mg bid) or Valtrex (1000mg QD) or topical (Zirgan TID)

When to use Oral Therapy

- Toxicity of Viroptic requires lower dosing
- Patient with stromal keratitis
- Prevention of HSV stromal keratitis
- Children -primary HSV
- Prior to surgery
- In all cases?
  - Trigeminal ganglion suppression

CASE S.P. History

- 26 y.o. Caucasian male
- "Foreign body sensation" "light sensitivity" and "eye is red"
- Longstanding contact lens wearer
- Began this morning



Examination:

- 2+/3- conjunctival injection
- Slight lid edema
- Pupils normal
- Cornea –small peripheral infiltrate, SPK over infiltrate
- AC grade 2 cell and flare

What appears to be a sterile infiltrate but has an AC reaction…

Begin treatment with _____
Follow-up in one day

Symptoms

- Acute onset
- Pain
- Photophobia
- Discharge - mucopurulent
- Decreased vision

- Excessive tearing, lid edema, blepharospasm

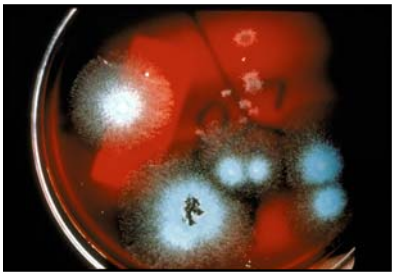
Signs

- Conjunctival hyperemia and ciliary flush
- Lid edema
- Tear film debris - thick & cells present
- Epithelial defect
- Grayish-white stromal infiltrate
- AC reaction
  - from few cells to hypopyon

When to culture?

- 1,2,3 Rule:
  - 1 mm from visual axis
  - 2 infiltrates (or more)
  - 3mm or greater in size

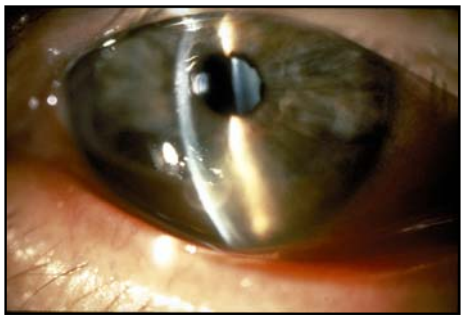
- Nosocomial infections
- Immuno-compromised patient
- Post-surgical
- Significant thinning
- Atypical



Mini-tip Culturette

Epley KD, Katz HR, Herling I, Lasky JB: Platinum spatula versus Mini-tip Culturette in culturing bacterial keratitis. *Cornea 1998;17(1):74-78.*

Sensitivity = 83.3%. - Specificity = 100%.



Therapeutic Treatment

- Fluoroquinolones
  - Zymar, Vigamox, Besivance
- Loading dose q 15 min x 1 hour
- Q1h while awake
- Q2h while at night or
- Ung – bacitracin or tobramycin

2009 ARMOR Surveillance
All S. aureus (n= 200)

Antibiotic	MIC Range	MIC_{50}	MIC_{90}
Vancomycin	0.25 – 2	0.5	1
Besifloxacin	≤0.008 – 4	0.03	1
Moxifloxacin	≤0.008 – 64	0.06	8
Ciprofloxacin	≤0.06 – 256	0.5	256
Tobramycin	≤0.06 – >256	0.5	256
Azithromycin	≤0.25 – >512	128	>512

39% of ocular *S. aureus* isolates were MRSA

38% of ocular *S. aureus* isolates were FQ-resistant

Haas et al. Presented at ARVO, Fort Lauderdale, FL, May 2-6, 2010. Abstract #D965, % resistance based on oxacillin and ciprofloxacin breakpoints.

Anti-bacterial Therapy

- **Besifloxacin 0.05% (Besivance)**
  - Fluoroquinolone FDA approved in July 09
  - MRSA and MRSE data is far superior to any other fluoroquinolone
  - Uses the DuraSite vehicle
  - No systemic form of the drug

What it the best form of pain management for a keratitis?

A. Cycloplegia

B. Steroids

C. Topical NSAIDs

D. Oral NSAID's

Therapeutic Treatment

- Other medications for severe keratitis:
- Systemic tetracycline
- Fortified Antibiotics
- Co-manage with a cornea specialist

Case History

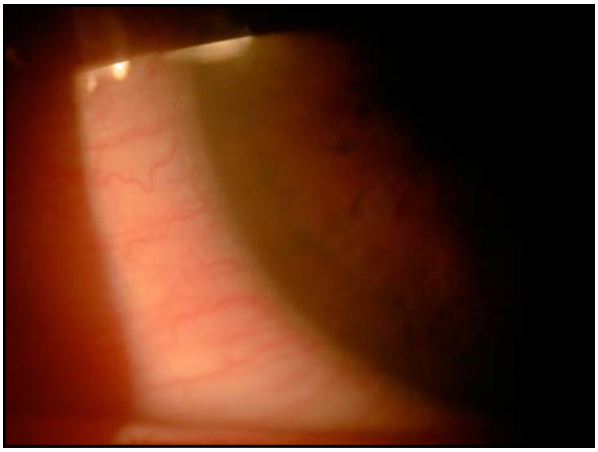
66 y.o. Caucasian female
Complains of pain and headache over eye and scalp area began 4 days ago
Feels very nauseated and getting worse “unbearable”
Significant loss of vision OD this morning

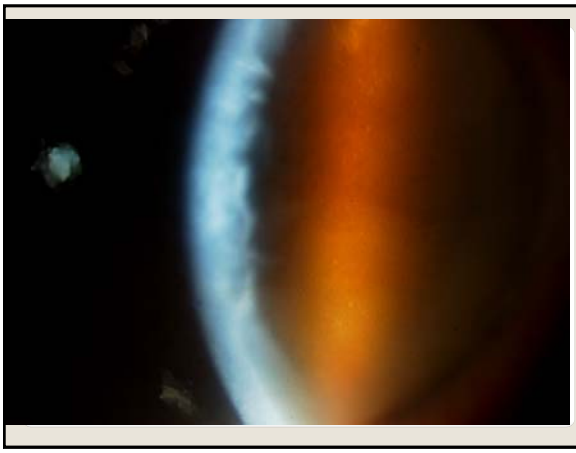
Primary testing:

- VA (BCVA): 20/400 OD, 20/20- OS
- Pupil testing: difficult to ascertain
- CF: little to no vision and difficulty

Slit lamp exam:

Grade 2+ conjunctival injection:
Cornea: 3+ corneal edema
AC: grade 3+ cell & flare





Differential Dx??
Systemic Disease

Systemic Disease DDx:

Herpes Zoster Ophthalmicus
Temporal Arteritis / Giant Cell Arteritis

HZO v. GCA

HZO: No lesions noted in scalp area, forehead etc.
Key questions related to temporal arteritis:
- Jaw pain or stiffness?
- Weight loss?
- Polymyalgia rheumatica?
- TIA in last 2 months?

Palpated temporal artery and patient did not mention any increased pain or sensitivity

Lab Testing:

SED RATE
C-Reactive Protein
CBC

Key Ocular Testing??

Key Testing??

IOP

56 mmHg OD
17 mmHg OS

Differential Dx for an elevated IOP??

A. Inflammatory glaucoma

B. Acute angle closure

C. Glaucomatocyclitic crisis

D. Neovascular glaucoma

Inflammatory Glaucoma

Best to Observe?

- Cell and flare in AC
- Miotic pupil, PS
- Ciliary flush and conj injection
- Angles open

FINAL DIAGNOSIS:

UVEITIS
Secondary to HZO

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

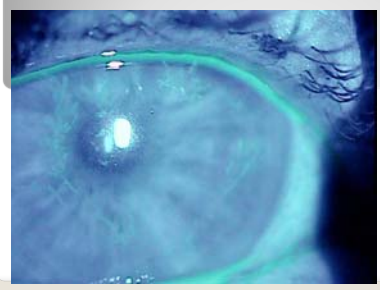
C. Neurotrophic keratitis

D. Scleritis

Ocular findings:

- Conjunctivitis/Scleritis
- Pseudodendrites
- Neurotrophic keratitis
- Iritis
- Glaucoma
- ION, vein or artery occlusion
- Nerve Palsy

Herpes Zoster Ophthalmicus



Pseudodendrites

Herpes Zoster Ophthalmicus

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 Iritis Management

- Rule out keratouveitis
- Check IOP
- Rule out previous ocular surgery
- Gauge severity – need for systemic work-up
- Treat AGRESSIVELY
- Go beyond AC cell and flare (Restore the Blood-Aqueous Barrier
- Dilate and check posterior segment

Treatment: Iridocyclitis

- Pred Acetate 1% q1 or q2h
- **Durezol** (Difluprednate) 0.05% QID
- Lotemax Long term
- Cycloplegia
  - Homatropine 5% bid
  - Cyclopentolate 1% bid

Also added medication to lower the IOP

- Diamox 500 mg (non-sequels) after asking about sulfa allergies and kidney problems
- Beta-blocker gtts (after asking about heart rate and breathing problems)
- Iopidine/Alphagan

Treatment for HZO:

Acyclovir 800 mg 5x/day
Famvir 500 mg 3x/day or **Valacyclovir** 1000 mg 3x/day
Advantages:

- Easier to take 3x Vs. 5x
- Decreased post-herpetic neuralgia, faster resolution of patient (Ormrod - *Drugs* June 2000)

Treatment for HZO:

When should you begin therapy?

Prior to 72 hours proven for Acyclovir (HE Kaufman)
Not as critical for Valacyclovir or Famvir* (Ormrod)

Treatment for HZO:

Duration?

7 days for most patients although newer studies (Zaal - Am J or Ophthal. Jan 2001) suggest
10 days for patients over age 66 due to shedding

Back to our patient: Full Blown Zoster

Significant Shingles in area of scalp and forehead

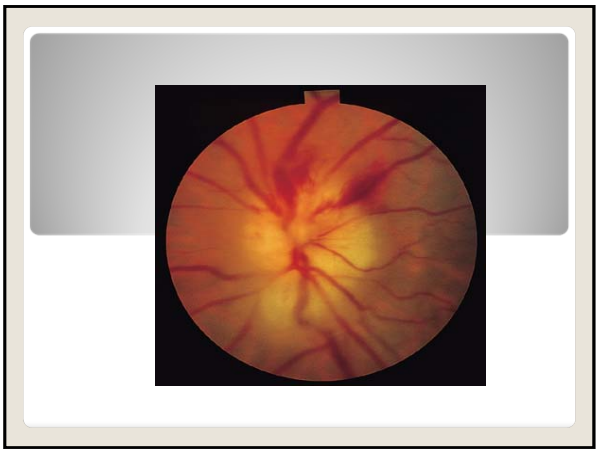
Back to our patient: Full Blown Zoster

- Therapy helped significantly
- IOP after glaucoma meds and Durezol were 28 in office, then 23
- Next day 14 and AC Reaction down to 2+ cell and 1+ flare
- No PAS

VA: 20/400 @ 1 week visit

What is the greatest concern with a highly elevated pressure?

A. Glaucoma
B. A hazy cornea
C. Patient comfort
D. Vascular Occlusion



Management of NAION

Previously no treatment, referral to PCP for Doppler, EKG and work-up

Now: www.EyeActNow.com

Quark NAION study QRK207

A Phase 2/3, Randomized, Double-Masked, Sham-Controlled Trial of QPI-1007 Delivered By Single or Multi-Dose Intravitreal Injection(s) to Subjects With Acute Nonarteritic Anterior Ischemic Optic Neuropathy (NAION)

Purpose of the study

- Determine the effect of QPI-1007 on visual function in subjects with recent-onset NAION.
- Assess the safety and tolerability of intravitreal injections of QPI-1007 in this population.
- Evaluate the structural changes in the retina following administration of QPI-1007.

Study Design

- This is a double masked, randomized, sham-controlled efficacy and safety study that will enroll approximately 530 subjects with recent-onset NAION.
- Subjects will be randomized into one of 5 groups in a 1:1:1:1:1 ratio, and assigned to receive QPI-1007 and/or a sham procedure. Subjects will have a one in five (20%) chance of receiving sham procedure (no active treatment).
- 5 cohorts: single low dose injection, single high dose injection, multiple low dose injections, multiple high dose injections, and sham injection procedure.
- Total study time involvement is approximately 12 months.

Key Inclusion Criteria

- Males and females 50-80 years old
- Positive diagnosis of first episode of NAION in the study eye with symptom onset within **14 days** prior to planned study drug administration/sham procedure
- Clear ocular media and able to undergo adequate pupil dilation to allow a good fundus examination

Go to **www.EyeActNow.com** for current sites

THANK YOU

paul@karpecki.com