Rapid Fire Referral Grand Rounds

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Disclosures - Walter O. Whitley, OD, MBA, FAAO has received consulting fees, honorarium or research funding from:

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**All financial relationships have been mitigated

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Triage Considerations

- Urgency vs. Emergency
- Acute vs. Chronic
- Mild vs. Severe
- Progressive vs. Stable
- Document all calls

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Emergency Immediately	Very Urgent Few Hours	Urgent Within a day
Retinal Artery Occlusions	***Perforation***	Orbital Cellulitis
Chemical Burns	***Ruptured***	***Orbital Injury***
	Acute Glaucoma	Corneal Ulcer
	Sudden Proptosis	***Corneal Abrasion***
		Hyphema
		Intraocular Foreign Body
		Retinal Detachment
		Macula Edema

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General Trauma Considerations

- Take care of the obvious
  - ABCDE's
  - Radiology
  - Concussion evaluation
  - Mental status of patient

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Importance of History

- Stop….. ***Emergency***… if chemical burns, proceed to provide copious irrigation before history and physical or exam is done
- Take your time with the history
- Nature of insulting object
  - Sharp, dull, big, small
- What was your vision before the injury?

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Evaluation of Ocular Trauma

- Visual acuity
- Pupil testing
- Confrontation visual fields
- EOMs
- Gross examination
- Slit lamp examination
- Tonometry*
- Dilation*
- B-scan ultrasonography*
- Color vision
- Imaging studies

7

Computerized Tomography

- If you suspect any of the following, a CT scan is indicated
  - History of loss of consciousness for more than 10 minutes
  - Alcohol intoxication
  - History of seizures
  - Unreliable history of the accident
  - Age less than 2 years
  - History of persistent vomiting
  - Bleeding from the nose, mouth or ear
  - Patient has serious facial injury
  - Penetrating injury to the skull
- No MRI for fear of metallic foreign body

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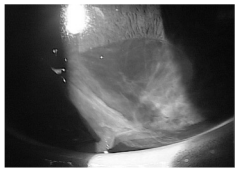
Open-Globe Injuries

- Full-thickness wound of the eye wall
- Rupture – Inside-Out
- Laceration – Outside-In
- Penetrating – Single entrance
- Perforating – Two wounds same object



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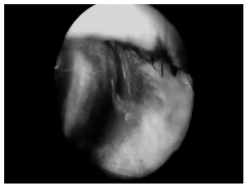
Open Globe

- Check VA - reduced
- Seidel's sign
- Displaced / peaked pupil
- Non-reactive pupil
- Low IOP
- Poor reflex
- Hyphema



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Weekend Call

- 64 yowm c/o decreased VA OS, watery eye, no pain
- Hit head on corner of the bed last night
- Went to sleep hoping it gets better
- Used ATs for relief
- Ocular Hx: Cataract surgery OU, PKP OS 2005

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Corneal Foreign Body

- Remove if visible and not completely penetrating
- Always document depth of FB
- Stain cornea with NaFl
- Anesthetize eye for patient comfort and to allow a better view.
- Dilate????

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IOFB Diagnosis

- Beware of metal on metal - **No MRI**
- Careful SLE
- Look at lens closely
- Look at corneal endothelium
- Siderosis
- Dilate
- Gonioscopy
- Transillumination
- B-scan, Plain Film, and/or CT scan

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IOFB Treatment

- Prompt Referral
- Traumatic Endophthalmitis
- Bacillus Cereus: kissin' cousin to Anthrax
- High risk of NLP and loss of eye
- Immediate Intravitreal Antibiotics and Vitrectomy within several days
- Chronic IOFB also requires prompt contact with specialist

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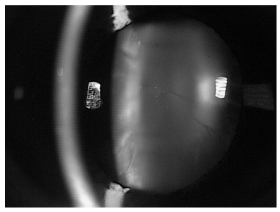
Case Example

- 65 YOWF Referred for Cataract Sx
  - Blurred VA X 6 months Dist / Near

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Stand-Alone vs. Combined Procedures

- Significance of the cataract
- Does the cornea need surgical intervention?
- Sequential versus triple procedure
- Convenience, cost, visual recovery

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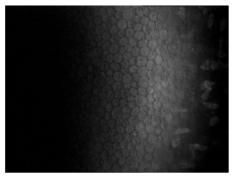
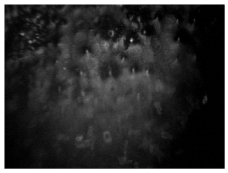
Background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ABC's of Corneal Transplants

- PK
- DALK
- PLK / DLEK
- DSEK / DSAEK
- DMEK / DMAEK

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DMEK

- Graft of Descemet's membrane and endothelium only
- Better optical outcome of 20/25 or 20/20
- Difficult to manipulate
- Early graft dislocation risk
- Decreased risk of rejection

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DSEK/DMEK Complications

- Caused by any of the following
  - Graft-recipient interface
  - Fragile graft tissue
  - Graft location
  - Glaucoma
  - Infection
  - CME
  - Retinal detachment

Miller, J. Accessed from http://www.revoptom.com/content/d/technology/c/16179/

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Long-term Maintenance DMEK and DSEK

- Long term topical steroid
  - Helps decrease rejection rate
  - Loteprednol, prednisolone acetate, fluoromethalone 1 gtt QD typically
- Unknown length of graft viability
  - No long term data since started approx 2003
  - In theory surpass PK ~20 years
- 5 year Graft survival similar at 93%[1]

1. Price DA, Kelley M, Price FW Jr, Price MO. Five-Year Graft Survival of Descemet Membrane Endothelial Keratoplasty (EK) versus Descemet Stripping EK and the Effect of Donor Sex Matching. Ophthalmology. 2018 Oct;125(10):1508-1514. doi: 10.1016/j.ophtha.2018.03.050. Epub 2018 May 3. PMID: 29731147.

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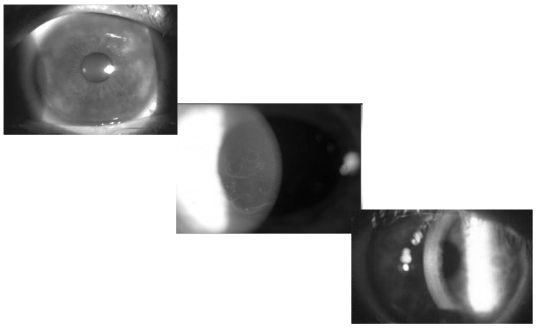
Corneal Dystrophies



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9/1/22
85yo AAF Presents for Blurry Vision OD

- 7-10 day cornea / OCT-M / BCL removal
- Oc Hx:
  - K abrasion 8/23/22
  - OTHN
  - ERM OD
  - CME OD
  - Phaco OD 7/28/22
  - RD Repair OD, Cataract OS
- Oc Meds: Moxifloxacin TID OD, Difluprednate QID OD, ketorolac QID OD, timolol BID OD, Brimonidine BID OD
- Med Hx: HTN, Bladder cancer
- Meds: acetaminophen, fexofenadine HCL, ASA, sucralfate, doxcycycline 100mg qd, piroxicam, fluticasone propronate, gabapentin, indapamide, nifedipine, omeprazole, valacyclovir, Vit C

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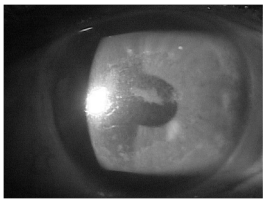
- BCVA OD: 20/80-2
  PH: NI
- SLE:
  - 1+K edema / 2mm V x 5mm H epi defect
  - Rare cell
  - PCIOL – 1+ PCO
- What's Next?



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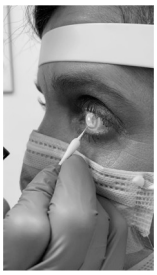
Corneal Sensitivity Testing



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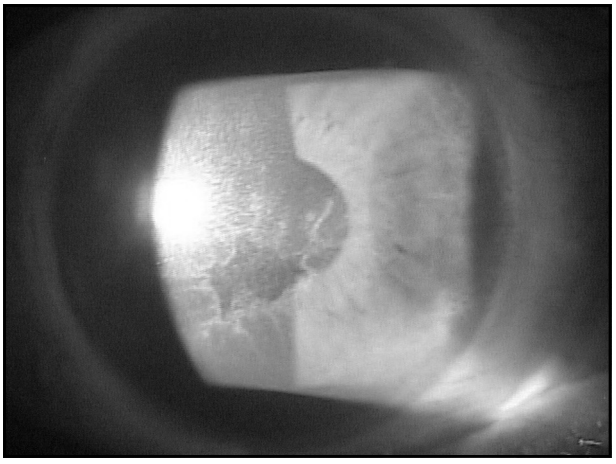

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Case Example

- The 84 year old, AA female presents for 3-4 month DES check (no touch) and MMP-9 testing. Pt has a h/o DES and POAG mild OU. Pt states OS>OD has some itching. Pt states she has only been using her cyclosporine 0.05% and AT's. She never picked up fluoromethalone drops and is not using AT's ointment or a heat mask.

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- Ocular Hx:
  - Dry eye syndrome – 10+ yrs
  - Herpes stromal keratitis OS
    - Inactive – Last episode 2020
  - Anterior scleritis OS
    - Inactive
  - POAG - Mild OU
  - Pterygium sx OU
  - Phaco / istent OU
  - Previous treatments
    - Amniotic membrane OS (2019, 2020)
    - Punctal cautery (2011) OU
- Med Hx:
  - NIDDM 15 yrs
  - Osteoarthritis
  - Hypothyroid
  - Seasonal allergies
- Meds:
  - Ceterizine
  - Lactulose
  - Levothyroxone

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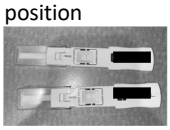
Clinical Exam

- Lids / Lashes – Clear and good position
- Conjunctiva – tr injection OU
- Cornea
  - OD 2+ Inf SPK
  - OS Dense SPK, 1+ K edema
- A/C – Deep and Quiet
- PCIOL OU
- IOP – 11 mmHg OU
- K Sensitivity – OD Normal OS Reduced



Anything else we should add???

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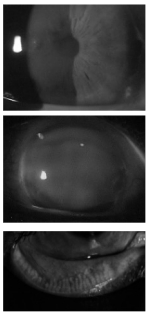
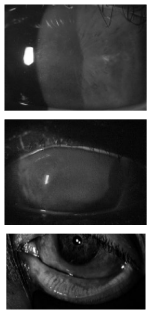
OD



OS



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Differentials??

Treatments??

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Neurotrophic Keratitis: Classification

Mackie classification

- Stage I is characterized by hyperplasia and/or irregularity of the epithelium, evolving to punctate keratopathy, corneal edema, neovascularization, stromal scarring.
- Stage II is defined by a recurrent or persistent epithelial defects or a PED without stromal thinning.
- Stage III: stromal involvement leads to corneal ulcer, melting and perforation

Mackie IA. Neuroparalytic keratitis. Current Ocular Therapy. Philadelphia, PA: WB Saunders; 1995:452-4.

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Neurotrophic Keratitis: Etiology

1. Infectious: HSV, VZV, leprosy
2. CN V palsy
   - Surgery for trigeminal neuralgia, neoplasia (acoustic neuroma), aneurysm, facial trauma, congenital, familial dysautonomia (Riley-Day syndrome), Goldenhar-Gorlin syndrome, Möbius syndrome, familial corneal hypesthesia

- Topical medications: anesthetic abuse
- Iatrogenic: LASIK/PRK, corneal incisions (RK, AK), contact lens wear, scleral bands, vitrectomy and photocoagulation to treat diabetic retinopathy[1,2]
- Chemical and physical burns
- Systemic: DM, multiple sclerosis, Vit A deficiency
- Increasing age, chronic DED[3]

1. Banerjee PJ. JAMA ophthalmology 2014;132:750-2.
2.Tinley CG, Eye 2009;23:1819-23
3. Ocul Surf. 2007 Apr;5(2):75-92.

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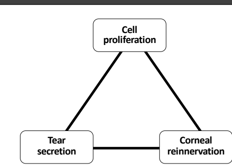
Endogenous nerve growth factor (NGF) and its role in NK:

impaired trigeminal corneal innervation	Endogenous NGF maintains corneal integrity by three mechanisms

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



Nerve damage ➡ loss of corneal sensitivity ➡ NK

Mastropasqua et al. (2017) J Cell Physiol 232:717-24

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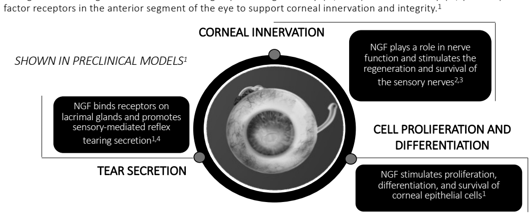
Endogenous NGF Maintains Corneal Integrity By Three Mechanisms

Endogenous Nerve growth factor acts through specific high-affinity (ie, TrkA) and low-affinity (ie, p75NTR) nerve growth factor receptors in the anterior segment of the eye to support corneal innervation and integrity.[1]



1. Mastropasqua L, Massaro-Giordano G, Nubile M, Sacchetti M. Understanding the pathogenesis of neurotrophic keratitis: the role of corneal nerves. *J Cell Physiol.* 2017 Apr;232(4):717-724. 2. Müller LJ, Marfurt CF, Kruse F, Tervo TM. Corneal nerves: structure, contents and function. *Exp Eye Res.* 2003 May;76(5):521-42. 3. Sacchetti M, Lambiase A. Diagnosis and management of neurotrophic keratitis. *Clin Ophthalmol.* 2014;8:571-9. 4. Muzi S, Colafrancesco V, Sornelli F, et al. Nerve Growth Factor in the Developing and Adult Lacrimal Glands of Rat With and Without Inherited Retinitis Pigmentosa. *Cornea.* 2010;29:1163–1168.

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Severity-Based Therapy

Stage	Therapy
1	• Preservative-free artificial tears formulations • Punctal occlusion • Hydrogel contact lens (consider large diameter) • Recombinant human NGF (rhNGF, cenegermin) • Serum/plasma/platelet rich plasma
2	Supportive therapies plus: • rhNGF • Scleral lens (± serum/plasma) • Amniotic membrane • Botulinum induced ptosis, Tarsorrhaphy
3	• rhNGF • Keratoplasty + scleral lens, tarsorrhaphy, neurotization

Sacchetti M, Lambiase A. Diagnosis and management of neurotrophic keratitis. *Clin Ophthalmol.* 2014;8:571-579. Sheha H, Tighe S, Hashem O, Hayashida Y. Update on cenegermin eye drops in the treatment of neurotrophic keratitis. *Clin Ophthalmol* .2019;13:1973-1980. Published Oct 7, 2019.

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Serum/Plasma Therapy

- Serum / plasma have reported efficacy as primary or adjunct therapy
- Reported success of serum alone (20-50% concentration) ranges from 71 to 100% within 90 days (Guadilla et al. Arch Soc Esp Offalmol 2013; Jeng and Dupps Cornea 2009; Pflugfelder *AJO* 2006)
- Umbilical cord serum may be more effective and has higher concentrations of substance P and NGF than peripheral blood serum (Yoon KC et al. *Ophthalmology* 2007)
- Epithelial defect healed in 97.4% of stage 2-3 NK after 11 weeks of plasma rich in growth factors (PRGF) (Sanchez-Avila RM et al. *Int Ophthalmol* 2018)
- Serum can be used safely in combination with SiH CL. No inflammation or CL deposits were observed (Choi JA *ECL* 2011)

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Autologous Serum

- Blood drawn via 18 gauge needle – 40 mL blood collected into blood tubes
- Blood set aside to clot at room temperature for two hours, then centrifuged at 5600 rpm for 10 minutes
- Serum filtered to remove fibrin strands before mixing with saline
- Typically start with 20% AS up to 50%
- Unopened bottles stored in freezer up to 3 months; open bottles in refrigerator for 48 hours
  - Potential for safe refrigerator storage for up to 1 month

Vital Tears???

Source: Review of Optometry

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Benefits and Pitfalls of Autologous Serum

Benefits
- Preservative free and innately allergy free
- Adverse events rare
- Improvement in symptomology
- Demonstrated improvement in staining (Tsubota – SS pts)

Complications
- Cost – no insurance coverage
- Frequent blood draw
- Availability of labs to make ASED
- Strict handling

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Amniotic Membrane

- Randomized clinical trial reported healing of refractory neurotrophic ulcers with conventional therapy (lubrication plus BCL or tarsorrhaphy) or amniotic membrane transplant (AMT). Healing rates were similar in the 2 groups: 67% with conventional therapy and 73% with AMT (Khokhar S et al. Cornea 2005)
- AMT was also equivalent to autologous serum (AS) in healing neurotropic ulcers: 70% for AS and 73% for AMT (Turkoglu E et al. Semin Ophthalmol 2014)
- Multilayer AMT recommended for deep ulcers and Descemetoceles (Kruse F et al. Ophthalmology 1999)

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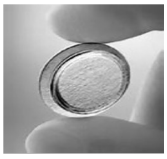
Amniotic Membranes / Amniotic Membrane Extract Eye Drop (AMEED)



Cryopreserved Membranes

Dry Membranes

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Pros and Cons of Amniotic Membrane Modalities

Cryopreserved
- Self-retaining on cornea
- Higher levels of regenerative complex HC-HA/PTX3
- Shorter storage life – requires refrigeration
- Potential discomfort from symblepharon ring
  - Avoid with filtering procedures

Dehydrated
- Longer storage life – room temperature
- No ring = better comfort
- Frequent slippage
- Requires bandage lens to maintain position

*****For all amniotic membranes, RCTs limited**

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Hindawi
Journal of Ophthalmology
Volume 2017, Article ID 6404918, 10 pages
https://doi.org/10.1155/2017/6404918

Clinical Study

Corneal Nerve Regeneration after Self-Retained Cryopreserved Amniotic Membrane in Dry Eye Disease

Thomas John,[1,2] Sean Tighe,[3,4] Hosam Sheha,[3,4,5] Pedram Hamrah,[6,7] Zeina M. Salem,[6,7] Anny M. S. Cheng,[3,4] Ming X. Wang,[8] and Nathan D. Rock[8]

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[2] *Loyola University at Chicago, Maywood, Chicago, IL, USA*
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[5] *Research Institute of Ophthalmology, Cairo, Egypt*
[6] *Boston Image Reading Center, Tufts Medical Center, Tufts University School of Medicine, Boston, MA, USA*
[7] *Center for Translational Ocular Immunology, Department of Ophthalmology, Tufts Medical Center, Tufts University School of Medicine, Boston, MA, USA*
[8] *Wang Vision Institute, Nashville, TN, USA*

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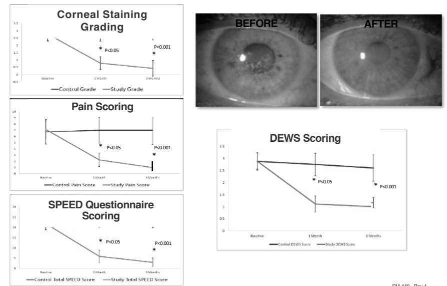
Improvements in Clinical Signs and Symptoms



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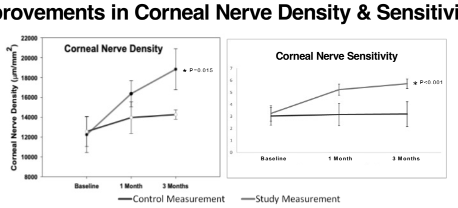
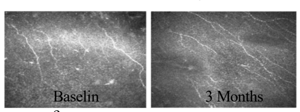
Improvements in Corneal Nerve Density & Sensitivity





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Scleral Lenses

- Use of fluid filled scleral contact lenses for treatment of NK initially reported decades ago (Romero-Rangel et al. *AJO* 2000)
- Non-healing corneal epithelial defects with BCL healed without recurrence in all 9 eyes treated with PROSE scleral lens (Ling J et al. *Am J Ophthalmol* 2013)
- Overnight wear (with close monitoring) may accelerate healing (Lim P et al. *AJO* 2013)

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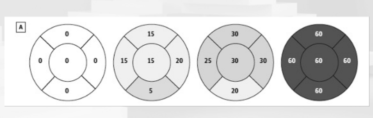
Corneal Neurotization

- Corneal sensitivity restored after sural nerve grafts (Elbaz et al. *JAMA Ophthalmol* 2014)
- Free sural nerve graft was coapted end-to-side with supratrochlear nerve and the distal portion of the nerve was separated into fascicles that were distributed around the limbus
- Corneal sensitivity, measured pre- and post-op with the Cochet-Bonnet esthesiometer, returned to normal after 5 months



PRE POD 91 POD 161

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cenegermin-bkbj 20 mcg/ml was approved by FDA in August 2018

AMERICAN ACADEMY OF OPHTHALMOLOGY®

Phase II Randomized, Double-Masked, Vehicle-Controlled Trial of Recombinant Human Nerve Growth Factor for Neurotrophic Keratitis

*Stefano Bonini, MD,[1] Alessandro Lambiase, MD, PhD,[2] Paolo Rama, MD,[3] Francesco Sinigaglia, MD,[4] Marcello Allegretti, PhD,[4] Wendy Chao, PhD,[4] Flavio Mantelli, MD, PhD,[4] for the REPARO Study Group**

Purpose: To evaluate the safety and efficacy of topical recombinant human nerve growth factor (rhNGF) for treating moderate-to-severe neurotrophic keratitis (NK), a rare degenerative corneal disease resulting from impaired corneal innervation.
Design: Phase II multicenter, randomized, double-masked, vehicle-controlled trial.
Participants: Patients with stage 2 (moderate) or stage 3 (severe) NK in 1 eye.
Methods: The REPARO phase II study assessed safety and efficacy in 156 patients randomized 1:1:1 to rhNGF 10 μg/ml, 20 μg/ml, or vehicle. Treatment was administered 6 drops per day for 8 weeks. Patients then entered a 48- or 56-week follow-up period. Safety was assessed in all patients who received study treatment, whereas efficacy was by intention to treat.
Main Outcome Measures: Corneal healing (defined as <0.5-mm maximum diameter of fluorescein staining in the lesion area) was assessed by masked central readers at week 4 (primary efficacy end point) and week 8 (key secondary end point) of controlled treatment. Corneal healing was reassessed post hoc by

- Approved for the treatment of neurotrophic keratitis in adults and children age 2 and older
- Available for ordering since January 2019
- Developed by Dompé pharmaceuticals, available through specialty pharmacy

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.

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Dosing and Administration

2 — Every 2 hours instill 1 drop of (cenegermin-bkbj) ophthalmic solution 0.002% in the affected eye(s)

6 — Apply 6 times daily

8 — Continue for 8 weeks

OXERVATE Prescribing Information, 2018.

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Treatment

- Continue:
  - Cyclosporine 0.05% BID OU
  - Heat Mask
- Stop
  - Oral ceterizine
- Order
  - Cenegermin 20 mcg/mL – Patient to call once meds come in to review meds / demo proper usage
  - Ceterizine ophth sol BID OU
  - Taped tarsorrhaphy OD
- Follow Up
  - 3-4 months glaucoma / Dilate OCT - G

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Somebody Help Me

- NP 29 yowf presents for significant dry eyes. Eyes are always in pain, burning, gritty and feels like sand paper. Currently using serum tears 50% qid ou and would like to get serum tears 75%.
- Oc Hx: 8 years
- Med Hx: ADHD, Hypothyroid
- Meds: Nortriptyline, levothyroxine
- What questions do you want to ask?

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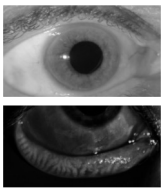
Previous Treatments

- Omega III – stopped on her own – NI
- Cyclosporine BID OU – stopped after 1 month / made eyes worse
- Prednisolone QID OU – stopped due to NI
- Plugs – 3 month plugs all puncta / NI
- Lifitegrast BID OU – stopped after 2 mos / made eyes worse
- Loteprednol 0.2% - NI
- Doxycycline 100 mg BID po – stopped after 2 weeks
- Erythromycin ung – NI
- Neomycin/polytrim/dexamethasone ung – NI
- Multiple preservative free drops

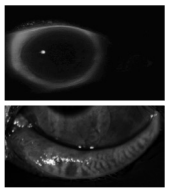
52

Neuropathic Corneal Pain

- Normal eye



- Nafl Normal eye



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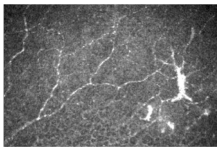
Causes of NCP



Microneuroma
Photo Courtesy of Scott Hauswirth, OD

- Trauma
- Chemical exposures
- Previous infection
- Eye surgery
- Systemic disease
  - Autoimmune or inflammatory conditions
  - Diabetes
  - Fibromyalgia
- Other neurological disease
  - Trigeminal neuralgia
  - Migraine

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Diagnosis of NCP

- No universal criteria for dx
- Case history
- Initial triggers for pain
- Time course
- Alleviating and exacerbating factors
- Treatment history
- Symptoms - Topical lubricants provide no / minimal relief
- Clinical Exam
  - Pain without stain
  - Topical anesthetic relief
- Confocal Microscopy

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Neuropathic Pain

- Treatment to either:
  - Regenerate nerves
  - Reduce inflammation that makes nerves more sensitive
- Treatment Options
  - Serum tears
  - Steroids
  - Amniotic membrane
  - Neurostimulation
  - Blue filter glasses
  - Systemic neuro-modulatory therapies
  - Biologics

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Gabapentin

- Used for suppressing exaggerated pain and seizures
- Glutamate is also involved in transmitting pain signals in the brain and nervous system
- Gabapentin reduces the release of glutamate
- Recently failed study for ocular pain control after PRK (JCRS)
- Dosage 300 mg BID to QID

57

Gabapentin and NCP

- Ongun N, Ongun GT. Is gabapentin effective in dry eye disease and neuropathic ocular pain? Acta Neurol Belg. 2021 Apr;121(2):397-401. doi: 10.1007/s13760-019-01156-w. Epub 2019 May 27. PMID: 31134508.
- Yoon HJ, Kim J, Yoon KC. Treatment response to gabapentin in neuropathic ocular pain associated with dry eye. J Clin Med. 2020;9(11):3765.
- Dario Rusciano, Massimo Dal Monte, Maurizio Cammalleri, Melania Olivieri, Salvatore Pezzino, Paola Bagnoli; EFFECTS OF TOPICAL GABAPENTIN ON OCULAR PAIN AND TEAR SECRETION. *Invest. Ophthalmol. Vis. Sci.* 2021;62(8):1288.

58

Efficacy and tolerability of Nortriptyline in the management of neuropathic corneal pain

- **Purpose**: Off-label use of Nortryptyline has been used successfully in the management of non-ocular neuropathic pain – helpful in the management of neuropathic corneal pain (NCP)?
- **Methods**:
  - Retrospective cohort study at the New England Eye Center, Tufts Medical Center, Boston, Massachussetts from July 2015-March 2019
    - 54 patients with NCP with centralized component who were treated with Nortryptyline
    - Centralized NCP:
      - Discordance in clinical signs and symptoms
      - Persistent ocular discomfort/pain after 90s of instillation of 0.5% proparacaine hydrochloride
    - Nortryptilline dosed at 10mg initially and tapered upward to 100mg based on response and tolerability
  - Response to treatment measured using Ocular Pain Assessment Survey (OPAS)

Ozmen et al. 2020

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- **Results**:
  - 30 patients included in final efficacy analysis:
    - 40% (n = 12) reported 50% or greater reduction in overall pain score (table 5)
    - Statistically significant reduction in all pain level dimensions (table 6)
    - Statistically significant reduction in many quality of life dimensions (table 7)
  - 19 of 54 discontinued due to side effects:
    - 8 of 19 were included in final analysis and discontinued despite reduction in pain score by 22.4%
    - Lethargy, dry mouth, constipation, nausea, headache, tachycardia, unspecified
- **Conclusion**:
  - Noteworthy pain decrease in patients with centralized component of NCP

Table 6
Results from the questions in pain level dimension of the Ocular Pain Assessment Survey.

OPAS #	Eye Pain Question	First Visit Score	Last Visit Score	Percent Change in Pain Score	p
4	Most in 24 h	7.3 ± 2.2	5.5 ± 2.7	−8.5 ± 83.3	**0.028**
5	Least in 24 h	3.8 ± 2.8	2.4 ± 2.9	−16.7 ± 76.3	**0.013**
6	Average in 24 h	5.7 ± 2.1	3.6 ± 2.1	−37.4 ± 32.6	**<0.0001**
7	Most in 2 w	7.7 ± 1.7	5.9 ± 2.9	−25.0 ± 35.0	**0.003**
8	Least in 2 w	4.6 ± 2.8	2.8 ± 3.2	−34.1 ± 46.4	**0.002**
9	Average in 2 w	6.3 ± 2.0	4.2 ± 3.1	−30.5 ± 39.9	**0.001**

Table 7
Results from the questions in quality of life dimension of the Ocular Pain Assessment Survey.

OPAS #	QoL dimension: pain effecting,	First Visit Score	Last Visit Score	Percent Change in QoL Score	p
13	Reading/computer use	6.8 ± 3.3	4.3 ± 2.4	−29.2 ± 55.5	**0.007**
14	Driving/watching tv	5.3 ± 3.5	3.9 ± 3.5	−11.5 ± 107.7	0.247
15	General activity	5.3 ± 2.8	3.9 ± 3.1	−26.8 ± 62.9	0.051
16	Mood	6.7 ± 2.9	4.8 ± 3.1	−14.0 ± 89.8	**0.029**
17	Sleep	3.8 ± 4.0	1.5 ± 2.7	−61.1 ± 52.7	**0.011**
18	Enjoying life	6.5 ± 3.2	4.6 ± 3.5	−26.4 ± 63.5	0.066
19	Time spent thinking about pain	7.6 ± 3.3	5.2 ± 3.5	−23.9 ± 57.6	**0.041**

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Future Insights on Neuropathic Corneal Pain

- Antiepileptics
  - Topiramate
  - Lamotrigine
  - Carbamazepine
- Analgesics
  - Mexiletine
  - Naltrexone
- Transcutaneous electrical nerve stimulation (TENS)
- Botulinum toxin type A

61

What About Botox?

- Cross-sectional retrospective study evaluated the effect of BoNT-A on photophobia and dry eye symptoms in individuals with chronic migraine (CM) and evaluate factors predictive of a positive treatment response.
- 90 patients had chronic migraine (≥ 15 per month) and had failed a trial of at least 2 migraine drugs or had contrain-dications to these medications.
- Symptom scale from "0" for no photophobia and "10" for the worst photophobia imaginable

Diel RJ, Kroeger ZA, Levitt RC, Sarantopoulos C, Sered H, Martinez-Barrizonte J, Galor A. Botulinum Toxin A for the Treatment of Photophobia and Dry Eye. Ophthalmology. 2018 Jan;125(1):139-140.

62

- Symptom Improvement
  - The investigators found that the intensity of all 3 sensations—migraine pain, photophobia, and dryness
  - 72.5% of patients reporting improvement in photophobia
  - 29.3% reporting improvement in dry eye symptoms
  - >33% with photophobia improvement rated it as "much better"
  - Older patients reported more relief in eye pain symptoms.
- Inflammatory action - researchers believe that calcitonin gene-related peptide (CGRP) may be central to study results.
  - One of the proposed mechanisms in migraine is excessive CGRP release, which leads to neurogenic inflammation, recruitment of inflammatory cells to the site, and an inflammatory environment that does further damage to nerves

63

Take the Holistic Approach!!

- Consider neurologic and psychiatric collaboration
- Pain specialist
- Primary care physician

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Case Study

- 2/13 ROV: 52 YO Asian Female / Follow up 4 month dry eye check. Intermittent foreign body sensation and fogged vision over 1 year
- Ocular Hx: DES, LASIK 12.08.11
  - Ocular Medications: Restasis BID OU
- Medical Hx: Allergies, Borderline Diabetes, Acid Reflux
  - Systemic Medications: Multivitamin, Iron

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Slit Lamp Examination

- BCVA
  - OD 20/25-
  - OS 20/20-
- MR
  - OD pl – 0.75 x 005
  - OS -0.50 DS
- External: normal OU
- Conjunctiva: 2+ injection
- Cornea: 1+ Diffuse SPK OU
- Tear Eval:
  - 4 sec NIBUT
  - Schirmer 8/9
- Iris: flat OU
- A/C: deep & quiet OU
- Lens: clear OU

66

Diagnostic Testing

- Clinical history
- Symptom questionnaire
- Tear film break up time
- Ocular surface staining
  - Nafl / Lissamine Green
- Schirmer / Red Thread Test
- Lid and meibomian morphology
- MG Expression
- Tear meniscus
- Tear film osmolarity

67

Superior Limbic Keratitis

- Definition
  - Uncommon chronic disease
  - Superior bulbar and tarsal conjunctiva and limbus
  - Bilateral
  - Middle aged women
  - Abnormal thyroid function
  - Symptoms worse than signs
  - Remission occurs spontaneously
- Pathogenesis
  - Blink-related trauma
  - Tear film insufficiency
  - Excess of lax conjunctival tissue
  - Inflammatory process
  - Self-perpetuating cycle

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SLK and Treatment

- Lubrication
- Acetylcysteine
- Mast cell stabilizers
- Steroids
- Cyclosporine A
- Soft contact lens
- Silver nitrate
- Autologous serum
- Botulinum toxin
- Supratarsal steroid injection
- Resection
- Conjunctival ablation
- Consider thyroid evaluation

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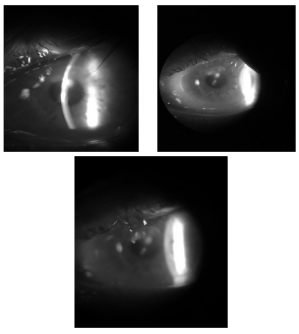
Culture Club

- 51 y/o Caucasian male referred for corneal ulcer
- Patient complains of blurry and foggy vision, discomfort, and redness OS
- H/o soft contact lens wear
- Drops: OTC anti-histamine

70

Ulcer Case

- VA: 20/200
- Conjunctiva: 2+ injection
- Cornea: central ulcer with multiple (8) infiltrates, 3mm x 1.4 mm epithelial defect
- Cultures obtained including blood, chocolate and fungal



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Bacterial Keratitis: Risk Factors

- Contact lens wear - #1
- Nonsurgical trauma
- Surgical trauma
- Lid dysfunction
- Ocular surface disease
- Corneal epithelial abnormalities
- Systemic diseases
- Topical medications

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Indications for Cultures

- Hyperacute conjunctivitis
- Neonatal conjunctivitis
- Post-operative infections
- Chronic conjunctivitis
- Central corneal ulcers
- Membranous / Pseudoconjunctivitis
- Preseptal / Orbital cellulitis
- Post-traumatic infections
- Marginal infiltration / ulceration
- Atypical external disease
- Severe dry eye
- Bullous keratopathy
- Axial and severe keratitis

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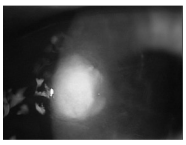
Work-up

- History
- Slit lamp examination
- Photodocumentation
- Culture - Rules of 1-2-3
  - Within **1** mm of visual axis
  - Ulcers with **2** or more infiltrates
  - **3** mm or more in diameter



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Equipment

- Slit lamp
- Sterile Kimura spatula
- #15 Blade, sterile
- Calcium alginate swab
- Culture media
- Microscopy slides
- Alcohol lamp

75

Procedure

- Anesthetize the cornea
  - Preservative-free tetracaine
- Scrape ulcer base / leading edge of infiltrate
- Place specimen on slide, then culture media
  - Smears – fixing organisms to be stained / observed
  - Culture – microbial growth
- Sterilize spatula over flame between slides / cultures

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Slides / Stains

- Multiple slides
  - Bacterial
  - Fungal
  - Acanthamoeba if suspected
- Routine
  - Gram stain – bacteria, yeasts
  - Giemsa stain – cytology, bacteria, fungi, chlamydia
  - Calcofluor white – acanthamoeba, fungi
- Optional
  - Acid-fast, KOH wet mount, etc.

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Medium

- Routine
  - Blood agar – all-purpose, grows most bacteria
    - Except for Neisseria and Haemophilus
  - Chocolate agar – Haemophilus, Neisseria
  - Sabouraud's agar – fungal isolation
- Optional
  - Lowenstein-Jensen – mycobacteria, Nocardia
  - Non-nutrient agar w/E. coli overlay – acanthamoeba
  - Thayer-Martin agar – gonococcal isolation

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Example of Culture Report

- Hold for
  - Bacteria 1 week
  - Viral 2 weeks
  - Fungal 1 month
- Test for all sensitivities


28-JUL-2008 14:21 Page 2/2

SENTARA BAYSIDE HOSPITAL	800 Independence Blvd	Va Beach, VA	23455	757-363-6156
SENTARA LEIGH HOSPITAL	830 Kempsville Road	Norfolk, VA	23502	757-261-6650
SENTARA NORFOLK GENERAL HOSPITAL	600 Gresham Drive	Norfolk, VA	23507	757-388-3530
SENTARA REFERENCE LABORATORY	600 Gresham Drive	Norfolk, VA	23507	757-388-3621
SENTARA CAREPLEX	3000 Coliseum Drive	Hampton, VA	23666	757-736-0100
SENTARA VA BEACH	1060 First Colonial Rd	Va Beach, VA	23454	757-395-8200
SENTARA MEDICAL GROUP	816 Kempsville Road	Norfolk, VA	23502	757-261-5920
SENTARA WILLIAMSBURG COMMUNITY	100 Sentara Circle	Williamsburg, VA	23188	757-984-7990

Name: [redacted] Doctor: SHEPPARD, J JR MD Client: VIRGINIA EYE CONSUL-CORP
ID#: 7202 / [redacted] Assoc: 241 CORPORATE BLVD
Age: 57 YRS Sex: F Race: NORFOLK
SSN: [redacted] VA235020000
FINAL

---ROUTINE CULTURES AND SMEARS---

Accession: 08-206-10042 Specimen Collected: 24JUL082006
Test Name: EYE CULTURE Specimen Received: 24JUL08 2006
Source: EYE Testing Began: 24JUL082006
SEN TO ALL STAPH/HOLD 1 W

----Final Report----
28JUL08 1255
STAPHYLOCOCCUS AUREUS FEW ; *****MRSA-review isolation precautions.***** Resistance may develop rapidly to monotherapy with Clindamycin, Tetracycline or Rifampin. CONTACT MICROBIOLOGY LAB FOR FURTHER TESTING IF CLINDAMYCIN IS CONSIDERED FOR TREATMENT

----Susceptibility Results----

	STA AUR INTERP
CEFAZOLIN-D	R
GENTAMICIN	S
LINEZOLID	S
OXACILLIN	R
PENICILLIN	R
RIFAMPIN	S
TETRACYCLINE	S
TRIMETH/SULFA	S
VANCOMYCIN	S

MRSA

SRL PT#: (05536)030026099 Doctor: SHEPPARD, J JR MD Print Date/Time: 28JUL08 1401
Name: [redacted] Page #: 1 (last page:)
ID #:7202 / [redacted] Assoc:
Age: 57 YRS Sex: F Race: DOB: [redacted] Location: POPE

07/28/2008 MON 13:26 [TX/RX NO 5804] 002

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Polymerase chain reaction (PCR)

- Rapid diagnostic test
- Results within hours vs days to weeks (culture)
- Procedure
  - Obtain sample via cotton swab, metal spatula, or recently developed FTA filter paper
  - DNA of micro-organisms is extracted and amplified
  - DNA compared to DNA in literature using software

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Polymerase chain reaction (PCR)

- High sensitivity
- Unacceptable specificity
  - Low specificity = high false positives
    - High amounts of unnecessary treatment
    - Increased corneal toxicity
- Ongoing studies to improve sensitivity

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Confocal Microscopy

- Historically used for endothelial cell evaluation
  - Fuch's dystrophy
  - Post-surgical bullous keratopathies
- Recently, studied for use in diagnosing infectious keratitis
  - Acanthamoeba
  - Fungal keratitis

82

82

Confocal Microscopy & Fungal Keratitis

- Studies show
  - Sensitivities: 80-94%
  - Specificities: 78-93%
- Procedure
  - Thick fluid-coupling agent on cornea
  - Scans all layers

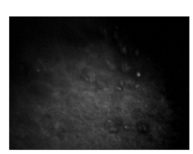
83

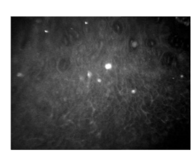
http://www.nidektechnologies.it/ProductsCSIntro.htm

83

Dx: Acanthamoeba Ulcer

- Monitored daily
  - Day #2: epithelium debridement and subconj. Gentamicin injection
    - Added Bactrim DS 1 PO BID along with Polyhexamethyline Biguanide/PHMBG 9-11x/day





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Acanthamoeba

- Parasitic infection
  - *A. castellanii* and *A. polyphaga*
- Typically pain is out of proportion to findings
- Culture on dish of E. coli plated over non-nutrient agar

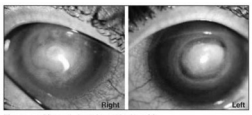

Figure 1 - Bilateral *Acanthamoeba* keratitis

http://eyewiki.aao.org/Acanthamoeba_Keratitis

Picture accessed from: http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0004-27492008000300025

https://www.reviewofophthalmology.com/article/acanthamoeba-a-dangerous-pathogen

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Acanthamoeba

Symptoms
- Decreased vision
- Pain
- Light sensitivity
- Redness
- Foreign body sensation
- Lid edema

Signs
- Epithelial irregularities
- Epithelial or subepithelial infiltrates
- Satellite lesions
- Stromal infiltrates (ring-shaped, disciform)
- Anterior uveitis
- Scleritis
- Chorioretinitis

http://eyewiki.aao.org/Acanthamoeba_Keratitis

https://www.reviewofophthalmology.com/article/acanthamoeba-a-dangerous-pathogen

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Differential Diagnoses of Acanthamoeba

- Herpes Simplex Virus Keratitis
- Recurrent Corneal Erosion
- Bacterial Keratitis
- Fungal Keratitis
- Contact Lens Associated Keratitis
- Dry Eye Syndrome

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Treatment and Management of Acanthamoeba

- Early stages- topical antibiotics
- Cationic antiseptics- polyhexamehtylene biguanide (PHMB) and Chlorhexidine
- Combination therapy with a diamidine
- Debridement of tissue
- Penetrating keratoplasty
- Steroids?

https://www.reviewofophthalmology.com/article/acanthamoeba-a-dangerous-pathogen

Lorenzo-Morales, Jacob et al. "An update on Acanthamoeba keratitis: diagnosis, pathogenesis and treatment" *Parasite (Paris, France)* vol. 22 (2015): 10.

88

Back to Patient…

- All satellite lesions healed ~15 days following initial evaluation
- Prokera was inserted at 1 month visit
- Patient continued to improve; PHMG was tapered weekly (7x/week, 6x/week,5x/week, 4x/week, etc.)

89

When the Lights Go Out

- 70YOWF presents to clinic with sudden unilateral painless vision loss in the left eye last night with slight dull pain
  - Noticed flashes and black spots every now and then
  - Cloud doesn't move when she moves her eye around
- Ocular Hx: Dry eye, cataracts
- Medical Hx: NIDDM, Throat cancer, heart disease, sarcoid,
- Meds: Many

90

DDx of Decreased Vision

Transient Visual Loss

- Seconds
  - Papilledema
- Minutes
  - Transient ischemic attacks
  - Vertebrobasilar artery insufficiency
- > 10 Minutes
  - Migraine

VA Loss > 24 Hours

- Sudden, Painless
  - RAO / RVO
  - Optic neuropathy / neuritis
- Gradual, painless
  - Cataract
  - Retinal disease
- Painful loss
  - Angle closure
  - Uveitis
  - Hydrops

91

Exam Findings

- Vision
  - OD 20/30 PH 20/25
  - OS 20/HM PH NI
- Entrance Testing - 4+ APD OS, CVF: unable to see fingers OS
- IOP: 18/14
- SLE – 1+NS OU, PVD OS, See fundus photos
- BP: 176/101

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Differential Diagnosis??

- Retinal artery or vein occlusion
- Ischemic optic neuropathy
- Vitreous hemorrhage
- Retinal detachment
- Optic neuritis

93

CRAO

- Ocular emergency
  - Cerebral Stroke
- Significant sudden unilateral vision loss
  - 94% CF to LP
- Retinal whitening in posterior pole and cherry red spot in macula
- (+) APD
- Arteriolar attenuation, box-carring, segmentation of blood vessels
- *If VA is LP or worse: ophthalmic artery occlusion

94

Risk Factors/Etiology

- **Atherosclerotic: uncontrolled high blood pressure
- **Diabetes
- Hyperlipidemia
- Obesity
- Smoking
- TIA events
- Collagen-vascular disease: SLE, PAN
- Hypercoagulation disorders (OCP, polycythemia)
- Sickle Cell
- Embolus, thrombosis

95

Assessment/Plan

- Central Retinal Artery Occlusion, left eye
  - BP in office today 176/101
  - Patient sent to ER/PCP for work up stroke workup
    - Rule out GCA - CBCw/diff, ESR, CRP
    - Carotid artery evaluation
    - Cardiac evaluation
    - Consider IVFA, ERG or both

96

Treatment

- Treatment has not proven to be effective
  - Improvement if initiated within 90-120 min of event
- Ocular massage
- Carbogen inhalation
- Acetazolamide infusion or AC paracentesis
  - Lower IOP and increase gradient across ONH
- Vasodilators
- tPA: clot lysis
  - Within 6 hours
- If embolus: YAG

97

Fluorescein Angiography

- High percentage of vision threatening ocular disease has leaking vessels
- Healthy retinal vessels don't leak
- Healthy choriocapillaris vessels leak freely
- Abnormal Fluorescein Patterns
  - Hypofluorescence: no perfusion, blocked
  - Hyperfluoresence: leakage, abnormal vessels

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Fluorsecein Angiography

Choroidal filling (Prearterial phase)	10-12 sec (young) 12-15 sec (older)
Arteriovenous phase	1-3 sec after choroidal filling AV transit time - first appearance of dye within the retinal arteries of the temporal arcade until the corresponding veins are completely filled
Recirculation phase	After 30 sec, recirculating fluorescein
Late phase	10 min post injection

99

Aftermath

- Vision usually still poor
- Neovascularization
  - 20% of patients
  - 4 weeks after onset
  - PRP
- Follow up monthly for 4 months

100

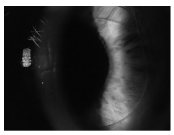
So Impersonal

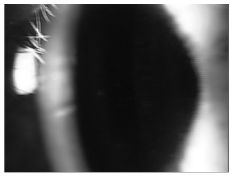
- 74 YOWM presents for evaluation of a fog like vision and increased floaters OS since an intravitreal injection of bevacizumab two days prior
- Ocular History: Dry AMD OD, wet AMD OS, pseudophakic OU, macular edema OD
- Systemic Disease: Arthritis, HTN, hypercholesteremia, atrial fibrillation, hypothyroidism,
- Medications: Toprol XL, Omeprazole, Lyrica, Crestor, Synthroid, Co Q-10 and Klonopin.

101

Case Example - KS

- BCVA: OD 20/20-2 OS 20/60+2 NI with pinhole.
- Pupils: Irregular pupil OS, (-) APD
- SLE:
  - Tr injection OS
  - Fine KP and trace edema OS
  - Iris: PI @ 4:00 OS.
  - AC: 3+ cell OS
  - Lens: ACIOL in good position OS
  - 2+ Cells in PC





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Diagnosis

- Acute postoperative endophthalmitis
  - Staphylococcus epidermidis accounts for nearly 60% of cases
  - Staphylococcus aureus accounts for another 20%
  - Incidence after intravitreal injection between 1/1300 to 1/10,000

103

Work Up

- Complete ocular history and examination
- Consider a B-Scan which may confirm marked vitritis and establishes a baseline against which success of therapy can be measured
- Perform culture and sensitivity studies on aqueous and vitreous samples
- TAP vs. PPV???

104

Treatment

- Intravitreal antibiotics
- Consider intensive topical steroids and intensive topical fortified antibiotics
- Atropine 1%
- Immediately pars plana vitrectomy if LP or worse
- IV antibiotics are not routinely used
- Some oral antibiotics may be considered an alternative

105

Role of Antibiotics

- Yin et al. Abx resistance of ocular surface flora with repeated use of topical abx after intravitreal injection JAMA opht. Apr 2013.
- Bascom Palmer ARVO 2011 - Topical Abs pre/post provided no benefit for reduced endophthalmitis

106

Follow-Up

- Monitor q12h
- Relief of pain is a useful early sign of response to therapy. After 48 hours patients should show signs of improvement
- Consider oral steroids
- If patient is responding well, topical fortified antibiotics may be slowly tapered after 48 hours and then switched to regular strength antibiotics
- Fortunately, endophthalmitis after intravitreal injection is rare, but clinicians should maintain a low threshold for treatment.

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Routine Cat Sx

- CC: Decreased VA OD, > 2 yrs, progressive, affects near and far, Glare OD>OS
- BCVA OD 20/70-2 PH 20/60
  OS 20/25-2 BAT 20/50-
- SLE: Cataracts OD>OS
- 12/02/08 – Unremarkable Cataract Sx OD

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Postoperative Day 1

- Pain last night, today better
- UCVA OD: 20/40 PH 20/30
- IOP - 18 at 1:55pm
- SLE:
  - Wound secure
  - 2+ SPK
  - AC well formed with about 1+ cell
  - IOL well centered in pupil

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Postoperative Medication

- Review medications
- No restrictions on physical activity
- Remind patient that it is normal for vision to be blurry and eyes out of balance
- F/U 1 week
- Fax results to surgeon if co-managed

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Weekend Emergency

- CC: VA decreased and foggy, no pain
- BCVA: OD 20/200 PH/NI
- IOP: 10 mmHg
- SLE: 3-4+ cells / deep / PVD / 3+ Vitritis / Dot hemes / whitening throughout periphery
- A: Increased post op inflammation OD
- P: Prednisolone acetate q1h OD, nepafanac TID, moxifloxacin TID / F/u tomorrow

111

Thoughts???

- Sudden decrease in vision
- Increase in inflammation
- No PVD noted previously
- No pain / discomfort
- Dot hemorrhages in the periphery

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What is the Most Common Organism Found in Bacterial Endophthalmitis?

A. S. aureus
B. S. epidermidis
C. S. pneumonia
D. H. influenza

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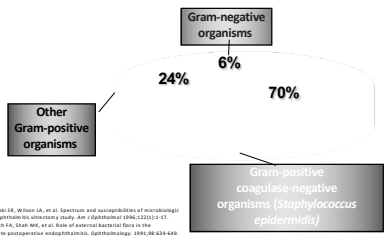
Endophthalmitis Vitrectomy Study

- **69% of patients with bacterial endophthalmitis were culture-positive**



1. Han DP, Wisniewski SR, Wilson LA, et al. Spectrum and susceptibilities of microbiologic isolates in the endophthalmitis vitrectomy study. *Am J Ophthalmol* 1996;122(1):1-17.
2. Speaker MG, Milch FA, Shah MK, et al. Role of external bacterial flora in the pathogenesis of acute postoperative endophthalmitis. *Ophthalmology* 1991;98:639-649.

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Endophthalmitis Vitrectomy Study

		VA Outcomes			
Presenting VA		20/40 or better	20/100 or better	Les than 5/100	Recommend Treatment
HM or better	TAP	62%	84%	3%	TAP
	PPV	66%	86%	5%	
Light Perception	TAP	11%	30%	47%	PPV
	PPV	33%	56%	20%	

PPV = pars plana vitrectomy and intravitreal injection of antibiotics
TAP = vitreous tap and intravitreal injection of antibiotics

http://www.nei.nih.gov/neitrials/viewstudyweb.aspx?id=29#Results

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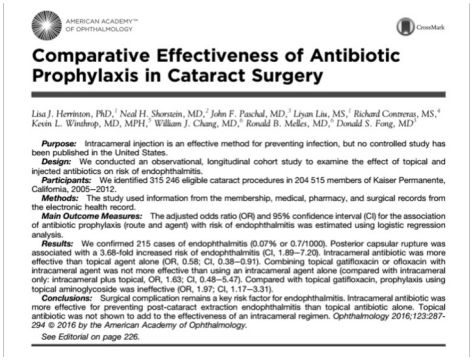

AMERICAN ACADEMY OF OPHTHALMOLOGY

Comparative Effectiveness of Antibiotic Prophylaxis in Cataract Surgery

Lisa J. Herrinton, PhD,[1] Neal H. Shorstein, MD,[2] John F. Paschal, MD,[3] Liyan Liu, MS,[1] Richard Contreras, MS,[4] Kevin L. Winthrop, MD, MPH,[5] William J. Chang, MD,[6] Ronald B. Melles, MD,[6] Donald S. Fong, MD[7]

Purpose: Intracameral injection is an effective method for preventing infection, but no controlled study has been published in the United States.
Design: We conducted an observational, longitudinal cohort study to examine the effect of topical and injected antibiotics on risk of endophthalmitis.
Participants: We identified 315 246 eligible cataract procedures in 204 515 members of Kaiser Permanente, California, 2005–2012.
Methods: The study used information from the membership, medical, pharmacy, and surgical records from the electronic health record.
Main Outcome Measures: The adjusted odds ratio (OR) and 95% confidence interval (CI) for the association of antibiotic prophylaxis (route and agent) with risk of endophthalmitis was estimated using logistic regression analysis.
Results: We confirmed 215 cases of endophthalmitis (0.07% or 0.7/1000). Posterior capsular rupture was associated with a 3.68-fold increased risk of endophthalmitis (CI, 1.89–7.20). Intracameral antibiotic was more effective than topical agent alone (OR, 0.58; CI, 0.38–0.91). Combining topical gatifloxacin or ofloxacin with intracameral agent was not more effective than using an intracameral agent alone (compared with intracameral only: intracameral plus topical, OR, 1.63; CI, 0.48–5.47). Compared with topical gatifloxacin, prophylaxis using topical aminoglycoside was ineffective (OR, 1.97; CI, 1.17–3.31).
Conclusions: Surgical complication remains a key risk factor for endophthalmitis. Intracameral antibiotic was more effective for preventing post-cataract extraction endophthalmitis than topical antibiotic alone. Topical antibiotic was not shown to add to the effectiveness of an intracameral regimen. *Ophthalmology 2016;123:287-294 © 2016 by the American Academy of Ophthalmology.*

See Editorial on page 226.

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Next Day Visit

- Increase in pain today
- OD VA: 20/400 NI w/ Pinhole
- SLE: Central K stain w/ Dendritic appearance / 2+ Cells in AC / 3 + Cells in Vitreous / Dot hemorrhages / Retinal whitening

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What's She Have????

- Possible Acute Retinal Necrosis
  - Foscarnet 2.4 mg/ 0.1cc injected intravitreally
  - Vicodin 5/325 1 tab every 4-6 hrs PRN
  - Valtrex 1000mg every 8 hrs for 10 days
  - Ordered blood cultures, fungal, PCR for VZV, HSV I, HSV 2, gram stain, CBC, Chem 7, ESR, and C-reactive protein
- Cannot r/o bacterial endophthalmitis
  - Recommend intravitreal injections of Vancomycin 1mg/0.1cc and Ceftazidime 2.25 mg/ 0.1 cc.
  - Vitreous specimen sent to lab
  - Monitor very closely

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Lab Reports

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Acute Retinal Necrosis

- Definition
  - Necrotizing herpetic retinitis. May present unilaterally or bilaterally (20%)
- Epidemiology
  - Usually occurs in young, healthy adults.
  - Less common are elderly and immunocompromised
  - Caused by infection with HZV or HSV
- History
  - Iritis or episcleritis
  - Rapid decline in VA with intense vitritis

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Acute Retinal Necrosis

- Important Clinical Signs
  - Vitritis with peripheral retinal whitening that coalesces
- Associated signs
  - Iridocyclitis, photophobia, vitritis, optic neuritis, and retinal arteriolitis

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Acute Retinal Necrosis

- Diagnosis
  - Diagnosis based on clinical exam
  - Polymerase chain reaction
  - Retinal biopsy
- Management
  - Systemic antiviral treatment
  - IV acyclovir 10mg/km tid for 7 to 10 days
  - Followed by 3 month course of acyclovir po
    - 800mg five times per day
  - Risk of RD is 8 to 12 weeks
  - Laser photocoagulation
  - Pars Plana Vitrectomy

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Clinical Pearls

- If patient calls with symptom of sudden decrease VA or pain during the first week: the doctor *must* see the patient
- Treat as infectious until proven otherwise
- Importance of communicating with surgeon

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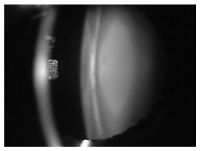
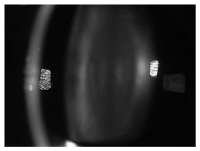
My Vision is Worse

- CC: Referred for cataract evaluation, blurred VA OD>OS
- BCVA:
  - OD -5.50+1.25X015 20/50
  - OS -1.25+1.50X180 20/20-1

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Post-Operative One Month Follow-up

- OD phone consult – Reports decreased VA OD
- Reported VA at 1 week was uncorrected 20/20
- No observable inflammation/swelling
- Recommended f/u to clinic for OCT and start NSAIDs/Steroids

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2nd Opinion Post Surgery

- VA OD was blurry, compliant w/ drops
- BCVA OD 20/40-1 PH/NI
- SLE: 2+SPK OD / PCIOL – 1+ PCO / (+) Macula edema
- Recommended OCT OD

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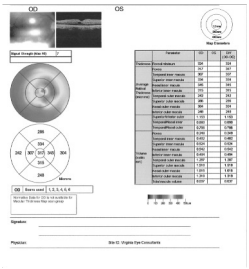
Cystoid Macular Edema

- OCT Findings
- Fluorescein Angiography
  - If OCT findings unclear
- Assessment
  - CME OD
  - PCO OD
  - DES OD
- Plan
  - PF QID / NSAID QID
  - Refer for intravitreal kenalog injection



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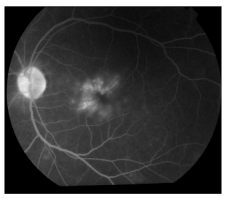
Cystoid Macular Edema

Courtesy of University of Pittsburgh Visual Imaging

- CME is the most frequent cause of visual decline following *uncomplicated* cataract surgery
- Late on-set (*4 to 6 weeks* post-operatively) [1]
- Estimated to occur in 1-3% of low-risk cataract cases
- CME development is due in part to prostaglandin-mediated breach of blood-retinal barrier[3]



1. Samiy N, Foster CS. The role of nonsteroidal antiinflammatory drugs in ocular inflammation. *Int Ophthalmol Clin*. 1996;36(1):195-206.
2. 2. Mishima H, Masuda K, et al. The putative role of prostaglandins in cystoid macular edema. *Prog Clin Res* 1989;31:251-264.

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Risk Factors for CME

- Pre-existing ocular inflammation
- Diabetic retinopathy
- Any ocular vascular disease
- Cardiovascular disease
- Epiretinal / vitreoretinal membrane

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Cystoid Macular Edema

- Self-limiting for the first several weeks
- Diagnosis: SLE, OCT, IVFA
- Treatment: *treat aggressively*
  - Steroids / NSAIDS qid X 1-3 months
    - 50% recover in 6 mos
  - Consider oral steroid, periocular steroid injection, pars plana vitrectomy
  - Acetazolamide po

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Spider Bite

- 63YOWM Referred by PCP for sudden decrease VA OD and swelling of eyelids OD>OS for 1 week
  - Pressure from forehead to cheek
  - Worse in evenings
  - Mild seasonal allergies
  - Some tearing and redness OD
- Bitten 3 weeks ago on top of the head while working in the yard which become swollen that evening
- Went to PCP and given oral ABX which finished yesterday

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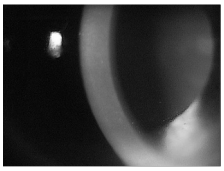
Examination

- Non-healing scab on R forehead
- Conjunctiva: 2+ injection OD
- Cornea: 2+SPK, 2+ MCE, 1+ KPs, No dendrites OD
- AC: 2+ Cells OD
- Lens: 2+ NS OD / 1+NS OS
- IOP: 31/13



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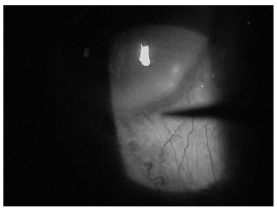
What About IOP?



- Angle closure
- Postoperative
- High IOP in non-seeing eyes
- HSV/HZV Trabeculitis

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Diagnosis???

- Considerations
  - PCP told him he had an infection not shingles
  - Episode started 3 weeks prior
- Treatment
  - Valacyclovir 1000mg TID po
  - Difluprednate QID OD
  - Timolol 0.5% QAM OD
  - F/u 1 week

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Herpes Varicella-Zoster Virus

- Primary infections: Chicken pox
  - Remains latent in dorsal root or other sensory ganglia after primary infection
  - May lie dormant for years to decades
- Later infections: Shingles
  - Virus specific cell-mediated immune responses decline
  - Localized cutaneous rash erupting in a single dermatome
  - HZO accounts for 10-25% of all cases of shingles

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Herpes Zoster Ophthalmicus

- 90% of U.S. population infected with VZV by adolescence
- 100% of U.S. population by 60 years of age
- 1.5-3.4 cases per 1,000 individuals

http://emedicine.medscape.com/article/783223-overview#aw2aab6b4

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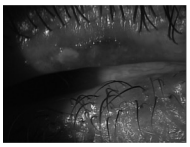
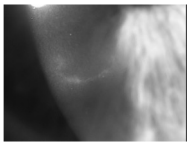
Herpes Zoster Ophthalmicus

- Conjunctivitis
- Scleritis
- Pseudodendrites
- Keratic precipitates
- Iritis
- Synechiae
- Neurotrophic keratitis
- Elevated IOP
- Potential vascular occlusion
- Nerve palsies
- Glaucoma (longer-term)





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HZO: Signs and Symptoms

- Prodromal phase: fatigue, malaise, low-grade fever
- Unilateral rash over the forehead, upper eyelid, and nose
  - 60% of patient have dermatomal pain prior to rash
  - Erythematous macules to papules to vesicles to pustules to crusts
  - Other symptoms: eye pain, conjunctivitis, tearing, decrease VA, eyelid rash
  - Hutchinson's sign
- Post-herpetic neuralgia: >12 months for 50%

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HZO: Treatment

- Local wound care
- Analgesia
- Antivirals
  - Valtrex 1g TID
- Antibiotics??
- Oral corticosteroids
- Post-herpetic neuralgia
  - Tricyclic antidepressants
  - Topical capsaicin ung
  - Gabapentin

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Oral Antivirals

- Inhibit viral DNA polymerase without inhibiting normal cellular activity
- Works best if treatment initiated within 72 hours
- Pregnancy category B
- Caution in patients with renal disease

Antiviral Drug	HSV	HZO
Acyclovir	400 mg 5x/day for 1 week	800 mg 5x/day for 1 week
Valacyclovir	500 mg TID for 1 week	1000 mg TID for 1 week
Famciclovir	250 mg TID for 1 week	500 mg TID for 1 week

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Vaccines for HZO – Shingrix (GSK)

- Vaccine indicated for prevention of herpes zoster (shingles) in adults aged 50 years and older
- 2 IM doses (0.5 mL each) at 0 and 2 to 6 months
- Reduced risk of developing HZ from 85 – 97%
- Efficacy against PHN 85.5%

Data available from Shingrix PI

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Last Saturday On Call

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82 yowf Sudden Loss of VA OD

- Ocular history:
  - Primary open angle glaucoma OU
  - Epithelial basement membrane dystrophy OU
  - Pseudophakia OU
  - Early Dry ARMD OU
- Medical history:
  - Arthritis
  - Hypertension
  - High Cholesterol
  - Peripheral Neuropathy
  - Restless leg Syndrome
  - GERD

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- Ocular Medication
  - Combigan BID OS
  - Travatan Z QHS OU
- Systemic Medication
  - Crestor 5mg
  - Amlodipine-Benazepril 5/10mg
  - Pramipexole 0.125mg
  - Tramadol HCL
  - Nexium 40mg
  - Lidoderm patch
  - Gabapentin 300mg
  - Celebrex 200mg
  - Iron supplement
  - Krill oil supplement

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Case Example

- VAcc:
  - OD: LP
  - OS: 20/50 +2
- Pupils
  - OD: 1+ APD
  - OS: round and reactive
- EOM
  - Full OU
- CVF
  - OD: constricted inferior 180
  - OS: Full to finger counting
- IOP: 18mmHg/18mmHg by Goldmann

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PW-GCA

- Assessment
  - Ischemic Optic Neuropathy OD
    - Pt denied any jaw pain, headaches, shoulder or hip pain, change in weight and malaise
- Plan
  - Labs ordered: ESR, CRP, CBC w/diff
  - Medication: Prednisone 20mg 3 PO
  - Meds are not to be started before having blood drawn
  - Follow up in 1 week pending lab results

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PW - GCA

- Lab Results:
  - ESR: 95 (High)
  - CRP: 7.09 (High)
  - Platelet: 465 (High)
- Temporal artery biopsy scheduled in 2 weeks

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PW -GCA

- Temporal Artery Biopsy Result
  - Active arteritis with rare giant cells, consistent with temporal arteritis
  - Mild arteriosclerosis
  - Disruption and focal loss of internal elastic lamina
- Informed the patient that her PCP will monitor her labs from now on and adjust her oral prednisone dose accordingly. She is to continue on the 60mg/day dosing for right now until he instructs her otherwise
- Follow up in 1 month

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Prednisone

- Suppresses inflammatory cascade and immune response
- Optic neuritis
  - Methylprednisolone 1g/day i.v. for 3 days
  - 60-100mg qd p.o. for 11 days
  - Only after initial IV steroid treatment per ONTT to decrease risk of recurrence
- AION: 60-100mg qd
- Scleritis/Uveitis
  - Not responding to topical treatment
  - 40-80 mg as an initial dose with taper

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Prednisone

- Side Effects/Contraindications:
  - Increased IOP
  - Cataract formation
  - Fluid retention (moon face, buffalo hump)
  - Increase blood sugar levels in diabetics
  - Gastric ulcers
  - Not to be used if pregnant
  - Mood changes
- Advantages:
  - Widely available
  - Inexpensive

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Oral Corticosteroid Considerations

- Accurate diagnosis is essential
- Indicated for acute inflammatory eye, orbital and eyelid conditions
- Pregnancy category C
- Dosepaks available
  - 24 mg, 30 mg, 60 mg with taper
- Best taken with meals
- Short term rarely has ocular side effects

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Non-arteritic Ischemic Optic Neuropathy

- Localized ischemic event at junction of optic nerve
- May be younger in age than AION (40-60 YOA)
- Signs and symptoms
  - Sudden painless vision loss
    - 30-2 severe defect
    - VA decreased
      - Less severe than AION
  - APD
  - Pale disc swelling
  - Flame shaped heme

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NAION

- Diagnosis of exclusion
  - Normal MRI
    - May find chronic microvascular changes on MRV
  - Normal ESR/CRP
- 40% show some improvement in vision over the next 6 months
  - Monitor with visual fields
- Optic nerve edema will resolve within 8 weeks
  - Can monitor with OCTG
- Risk of contralateral eye involvement

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NAION Treatment

- It has been suggested in a study by Foulds in the 1970's that the patients may benefit long term visual recovery from the use of 40-60mg of oral prednisone for 1 month.
  - 85% of patients treated with 60mg oral prednisone showed visual acuity improvement compared to those untreated

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NAION Treatment

- More recent study, 2008, Hayreh and Zimmerman 696 eyes
  - Treated within 2 weeks of onset with 70mg oral prednisone tapered
  - 69.8% of eyes treated had an improvement in visual acuity
    - Only 40.5% of eyes untreated had an improvement in visual acuity

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Graefes Arch Clin Exp Ophthalmol. 2016 Apr;254(4):757-64. doi: 10.1007/s00417-015-3191-z. Epub 2015 Oct 20.

Levodopa as a possible treatment of visual loss in nonarteritic anterior ischemic optic neuropathy.

Lyttle DP[1], Johnson LN[2,3], Margolin EA[4], Madsen RW[5].

Author information

Abstract

PURPOSE: To determine the clinical effectiveness and potential neuroprotection of levodopa in improving visual acuity, visual field, and retinal nerve fiber layer (RNFL) thickness in eyes affected by NAION.

METHOD: Retrospective cohort study involving 59 eyes of 59 participants with NAION who were evaluated within 15 days of NAION onset. Participants received 25 mg carbidopa/100 mg levodopa three times daily with meals for 12 weeks (levodopa group) or were untreated (control group). Best-corrected visual acuity converted to logMAR, mean deviation (MD) threshold sensitivity on automated perimetry, and mean RNFL thickness on optical coherence tomography (OCT) were assessed. The primary outcome was the categorization of eyes into improved visual acuity (by 0.3 logMAR difference), worsened visual acuity (by 0.3 logMAR difference), or no change in visual acuity. The proportions in each category were compared between the levodopa and control groups.

RESULTS: Among participants with 20/60 or worse initial visual acuity, levodopa-treated participants had significant improvement ($P < 0.0001$) in the mean change from initial to final logMAR visual acuity of -0.74 ± 0.56 (95 % CI, -0.98 to -0.50), while the mean change for the control group at -0.37 ± 1.09 (95 % confidence interval estimate, -1.00 to +0.26) was not significant ($P = 0.23$). A significant difference between groups was observed ($P = 0.0086$) such that 19/23 (83 %) in the levodopa group improved and none got worse, as compared with 6/14 (43 %) in the control group improving while four (29 %) worsened. The change in visual field MD and RNFL thickness on OCT showed no significant difference at $P = 0.23$ and $P = 0.75$ respectively. No levodopa-treated participant had any adverse event from the levodopa.

CONCLUSIONS: Treatment within 15 days of onset of NAION with levodopa improved central visual acuity by an average of 6 lines on Snellen acuity chart. Levodopa may promote neuroprotection of the maculopapular retinal ganglion cell fibers in NAION.

KEYWORDS: Dopamine; Levodopa; NAION; Neuroprotection; Nonarteritic anterior ischemic optic neuropathy; Optic nerve

PMID: 26483145 DOI: 10.1007/s00417-015-3191-z

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Levodopa for NAION

- 59 patients within 15 days of onset NAION
  - Either untreated or given 25mg carbidopa/100mg levodopa PO TID
  - 19/23 in the levodopa group BCVA improved and none got worse
  - 6/14 in control group BCVA improved and 4/14 got worse

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Clinical Pearls

- All visual fluctuations are related to ocular surface disease
- Consider time course of events
- Benefit of prophylactic NSAIDs
- Communication between surgeon / referring OD

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Thank You!!!

- wwhitley@cvphealth.com

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