



Oral Meds in Anterior Segment Disease

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Disclosures

- B+L SVP
- BostonSight
- Dompe
- Nordic Pharma
- Tarsus
- Medical Advisory Board, International Keratoconus Academy
- Scleral Lens Education Society
- Editorial Board, Journal of Dry Eye and Ocular Surface Disease



"I didn't experience any of the side effects listed in the enclosed literature. Should I be concerned?"

Indications for Oral Medications

- If topical agents are ineffective/inappropriate
- Systemic ocular conditions
- Limit your treatment to **eye/adnexa!**
- Know what to Rx, but more importantly what NOT to Rx!
- Be sure you have the correct diagnosis

Prescribing Considerations

- Know your medications!
- Top 10 list
- Check cost/formularies
- Use judiciously
- **Resources:**
 - Epocrates
 - Drugs.com
 - Good Rx
 - Friendly pharmacist





Prescribing Considerations

- Allergic to any meds?
- What meds are they currently taking? (Rx and OTC, herbal)
- What systemic medical conditions do they have?
- Immunocompetent?
- Liver and Kidney status/ Pulmonary/cardiac
- Age- may need to change dosage if child or elderly (polypharmacy)
- Insurance status- how much is it going to cost?
- Birth control?

Antibiotic and oral contraceptive drug interactions: Is there a need for concern?

[George G Zhanel](#)^{1,2,3,✉}, [Shannon Siemens](#)²,
[Kathryn Slayter](#)⁴, [Lionell Mandell](#)⁵

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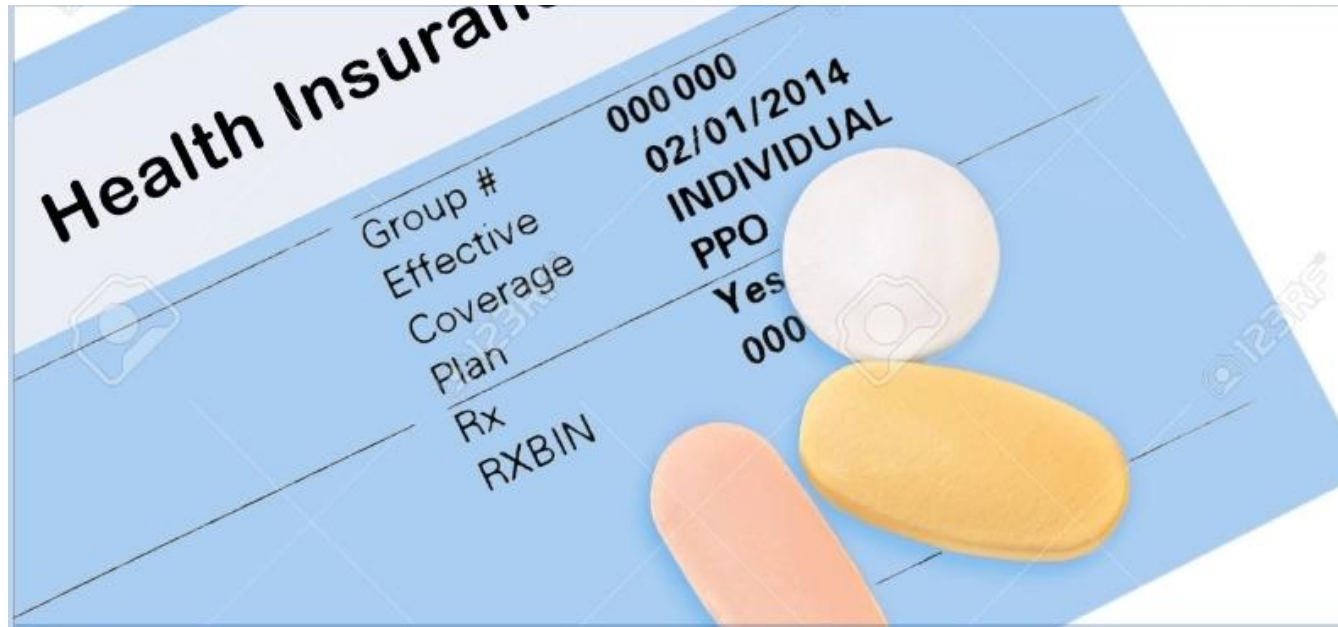
CONCLUSIONS:

Rifampin is the only antibiotic to date that has been reported to reduce plasma estrogen concentrations. Oral contraceptives cannot be relied upon for birth control while taking rifampin.

Keywords: Antibiotics, Drug interactions, Oral contraceptives, Pregnancy



Polypharmacy



BUT I'M ALLERGIC TO GENERIC!

*PHARMACY
MEME*

**WHAT? \$400 FOR BRAND?
OH LOOK MY ALLERGY WENT AWAY**

Prescribing Considerations

- Pregnancy
- Nursing
- True Allergy vs side effects
- Call OB/GYN if necessary
- Consult w/ other specialists (i.e. PCP/nephrologist/hepatologist)



Causes of Failure of Therapy

- Inaccurate Diagnosis
- Inadequate dosing
- Resistant Organisms
- Non compliance
- Toxicity
- Allergy



Meds that are OK to use in Pregnancy

- Amoxicillin
- Amoxicillin/Clavulanate (Augmentin)
- Azithromycin
- Acyclovir
- Valacyclovir
- Acetaminophen
- Cephalexin

Allergic Reactions

- Hypersensitivity reaction- mediated by IgE
- 10-15% of population allergic to PCN?
- True Allergic Reactions
 - Breathing difficulty/wheezing/skin rash/hives
 - Swelling of lips/face/throat
- D/C use immediately and consult physician
- If SEVERE- immediate EMERGENCY CARE



“I am allergic to antibiotics”

- Ask the patient: “What exactly happens when you take them?”
- Stomach upset- not a true allergy
- Sometimes it is difficult distinguish side effects from allergy
- Allergy testing- **10%** of US population reports a PCN allergy, but less than 1% are actually allergic after testing



Oral Antibiotics

- Is an oral antibiotic truly needed?
- Check allergy history
- Most are available as low cost generics
- Take full course of therapy to avoid resistance
- GI/ thrush- take yogurt/probiotics????- take with food
- Always be aware of Pseudomembranous colitis/ *C. difficile*

Clostridium difficile and Antibiotics

Virtually ALL antibiotics can increase CDI. They alter the normal intestinal flora

Greatest risk- 3rd and 4th generation Cephalosporins

Fluoroquinolones

Clindamycin

Amoxicillin

Risk is highest during administration of antibiotics and up to 3 months afterwards

Doxycycline may be protective? Active against *C. difficile* growth in the gut

Pseudomembranous Colitis

Severe inflammation of the lining of the large intestine caused by *C. difficile*

Usually treated with Vancomycin or fidaxomicin (Dificid)

Another treatment option is metronidazole (Flagyl)

FMT (fecal microbiota transplantation)

Probiotic supplementation during antibiotic treatment is unjustified in maintaining the gut microbiome diversity: a systematic review and meta-analysis

[Anna Júlia Éliás](#)^{1,2}, [Viktória Barna](#)³, [Cristina](#)

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This is the first meta-analysis and the most comprehensive review of the topic to date using high quality methods. The limited number of studies and low sample sizes are the main limitations of our study. Moreover, there was high variability across the studies regarding the indication of antibiotic therapy and the type, dose, and duration of antimicrobials and probiotics.

Conclusions

Our results showed that probiotic supplementation during antibiotic therapy was not found to be influential on gut microbiome diversity indices.

Defining appropriate microbiome diversity indices, their standard ranges, and their clinical relevance would be crucial.

Antibiotic-associated Diarrhea in Adults

A Meta-Analysis of Randomized Placebo-Controlled Trials

[Wanqian Liao](#) ^{*,†}, [Chongxiang Chen](#) ^{*,†}, [Tianmeng Wen](#) [‡], [Qingyu Zhao](#) ^{*,†,§}

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PMCID: PMC8183490 PMID: [33234881](#)

Objective:

This meta-analysis aims to combine the latest research evidence to assess the effect of probiotics on preventing antibiotic-associated diarrhea (AAD) in adults.

Conclusions:

This updated meta-analysis suggested that using probiotics as early as possible during antibiotic therapy has a positive and safe effect on preventing AAD in adults. Further studies should focus on the optimal dosage and duration of probiotics to develop a specific recommendation.

Oral Antibiotics

- **Dacryocystitis**
- Dacryoadenitis
- Chalazia/Hordeola
- Preseptal Cellulitis
- Chlamydia
- Orbital trauma/blow out fractures
- MGD/Dry eye
- RCE/corneal ulcers
- Ocular Rosacea





eyeWiki

Case #1

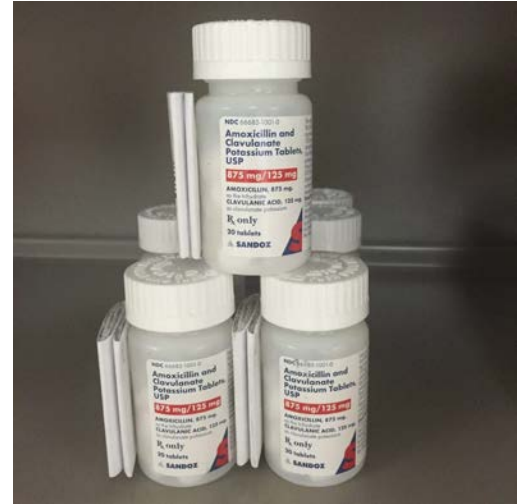
- Patient presents w/ swollen left lower lid x 3 days. Noticed a small bump that was tender to the touch- has gotten more red and larger in size. Now encompasses most of the lower lid. Warm to the touch
- VA 20/20
- Pupils nml
- No pain on EOMs. No diplopia
- Temp 99.1 degrees
- Medical history unremarkable
- NKDA

Case #1

- Hordeola vs Preseptal Cellulitis vs Orbital Cellulitis
- **Preseptal Cellulitis:**
- Usually caused by hordeolum or adjacent infection (insect bite. scratch)
- Usually upper eyelid involvement-lid swelling
- No pain on EOMS, no diplopia. VA normal. Normal temperature
- Infection /inflammation ANTERIOR to the orbital septum- limited to the superficial periorbital tissues
- If **MRSA** possibility- consider Bactrim/Septra if no sulfa allergy
- **Orbital Cellulitis-** EMERGENCY. EOM pain/restrictions. Pupils affected. Typically ethmoid sinus infection
- +febrile

Case #1

- AUGMENTIN
- Amoxicillin/Clavulanic acid
- **Clavulanic Acid** protects amoxicillin from beta lactamases- not an antibiotic
 - Fixed at 125 mg
- Can use in pregnancy (category B)
- Comes in liquid form (pediatrics) H. Influenza
- Generic available
- Gram + and some gram -



Case #1 - Augmentin

- Cannot use if PCN allergy
- Good for human and animal bites(anaerobic organisms)
- Skin and soft tissue infections staph/strep
- Take w/ food (probiotics)
- Adult dosage 500 mg TID or 875 mg BID

What to use if Allergic to Penicillin?

- Cephalosporins? Literature suggests up to 10-15% of patients have cross sensitivity with Cephalosporins
- According to American Academy of Pediatrics- OK to use Omnicef (3rd generation) if no history of cephalosporin allergy, atopic conditions or severe allergic reactions

would increase the overall number of diabetic patients requiring intervention being identified.

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The authors declare no conflicts of interest.

References

1. Van der Heyden AA, Abramoff MD, Verbraak F, Van Hecke MV, Leim A, Nijpeis G. Validation of automated screening for referable diabetic retinopathy with the Dx-CPI device in the Hoom Diabetes Care System. *Acta Ophthalmol*. 2017; 96(1): 63-68. [STEP 2]
2. Abramoff MD, Folk JC, Han DP, et al. Automated analysis of retinal images for detection of referable diabetic retinopathy. *JAMA Ophthalmol*. 2013; 131(3):351-357. [STEP 2]

Is it safe to use cephalosporins in patients who are allergic to penicillin?

EVIDENCE-BASED ANSWER

It may depend on the cephalosporin. There is a 4- to 5-fold increased risk of cross-allergy reactions with first-generation cephalosporins and penicillin, but there is no increased risk of cross-reactivity seen with second-generation and third-generation cephalosporins (SOR: B, meta-analysis with methodologic limitations).

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A 2007 meta-analysis of nine studies (individual trial designs and patient characteristics not described) assessed cross-reactivity to cephalosporins among patients with and without penicillin allergy by history alone (six studies) and by penicillin allergy history confirmed with skin testing (four studies); one study presented data with both comparisons.¹ In the six studies of patients with (N=2,387) and without (N=44,879) a penicillin allergy reported by history alone, there was an increased risk of reaction to first-generation cephalosporins and cephalexin but not to second- or third-generation

cephalosporins (see TABLE). In the four studies comparing patients with a history of penicillin allergy who had a positive (N=451) versus a negative (N=1,380) skin test reaction to penicillin, there was a nonsignificant increased risk of cross-reaction to first-generation cephalosporins and cephalexin but not to second- or third-generation cephalosporins (see TABLE). Limitations included the lack of relevant information about the trials (eg, study design, patient demographics, study local) and no assessment of the risk of biases (eg, completeness of outcome reporting, selective reporting), as well as a reliance on patient history to determine penicillin allergy status. Furthermore, of the nine studies, eight were published between 1964 and 1993, and only one was published after 2000.

A 2018 prospective cohort study evaluated cephalosporin challenges in 252 patients with a history of 319 immediate reactions to penicillin-based antibiotics (71.8% anaphylaxis and 28.2% cutaneous reactions or angioedema); these individuals also had at least one positive skin test to penicillin reagents.² The patients were between 14 and 80 years old (mean age, 47.7 years) seen in three separate allergy clinics in Italy. In all patients, the researchers measured serum Immunoglobulin E (IgE) levels to cefaclor (a second-generation cephalosporin) and assessed skin test reactions to the following antibiotics: three aminoccephalosporins (the first-generation agent cephalexin and the second-generation agents cefaclor and cefadroxil); the second-generation agents cefamandole and cefuroxime; the third-generation agents ceftazidime, ceftriaxone, and cefotaxime; and the fourth-generation agent cefepime. Of the 252 patients with documented penicillin allergy, 99 (39.3%) also had an allergic reaction to one or more cephalosporin drugs when assessed by skin test, IgE levels, or direct challenge. The rate of positive skin test reaction to ampicillin was higher in those with versus without an allergic reaction to cephalosporins (80.8% vs 62.7%, respectively, odds ratio, 2.5; 95% CI, 1.4-4.5). A total of 244 patients with negative allergy testing to cefuroxime, ceftazidime, ceftriaxone, cefotaxime, and cefepime were challenged with oral cefuroxime and intramuscular ceftriaxone, and none experienced allergic reactions. Among patients with negative allergy testing to the three aminoccephalosporins, 170 were challenged with oral cefaclor and three (1.8%) experienced allergic reactions (one case each of erythema, urticaria, and anaphylaxis), whereas 167 were challenged with oral cefadroxil, and four (2.4%) experienced allergic reactions (one case of erythema and three cases of urticaria). The study was limited by reliance

Penicillin Allergy

- OK to use:
 - Macrolides (erythromycin/azithromycin/clarithromycin)
 - Fluoroquinolones
 - Tetracyclines
 - Sulfa

Cephalexin (Keflex)

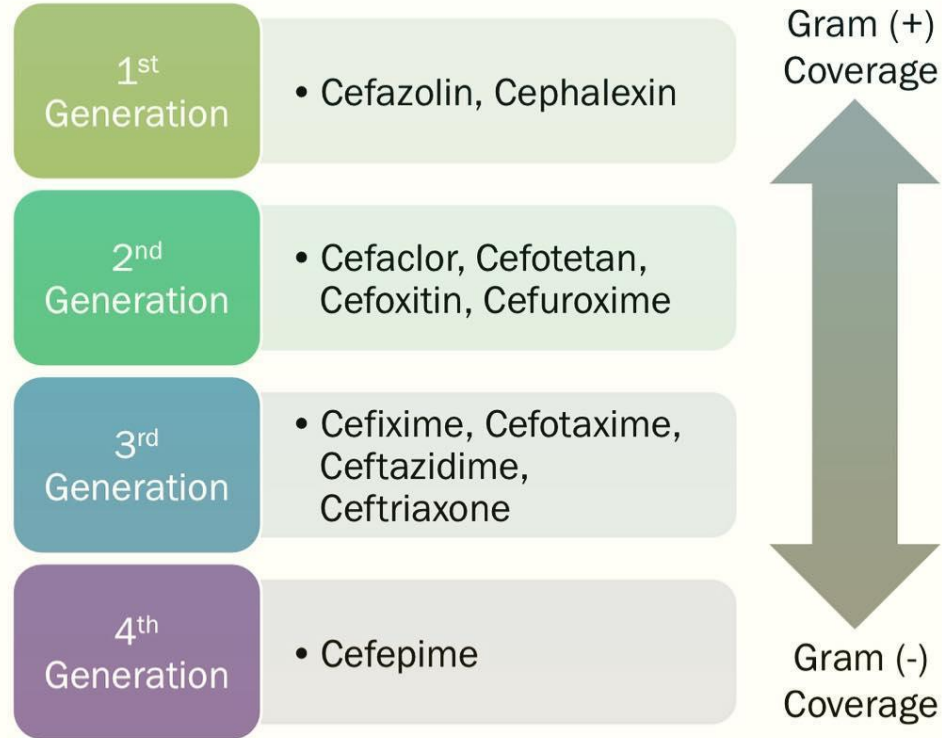
- 1st generation cephalosporin
- Good for soft tissue infections
- Good gram + coverage (Staph/Strep)
- Drug of choice for orbital blow out fractures
- Cheap/generic
- Category B
- 5-10 % cross sensitivity w/ PCN?
- Caution with renal insufficiency
- Typical dosage 500 mg TID or 750 BID



Cephalosporins

- 1st to 5th generation
- Eye care usage typically 1st through 3rd generation
- 4th and 5th generation: use by infectious disease docs. More gram - coverage
- Example of 2nd generation- Ceclor/Ceftin
3rd generation- Omnicef
- Category B

CEPHALOSPORIN COMPARISONS



Ceftaroline: “5th generation” or “advanced generation”
Similar to 3rd generation, but added MRSA coverage

Cephalosporins

Cephalosporins are bactericidal beta-lactam antibiotics derived from the fungus *Acremonium* — they disrupt peptidoglycan formation in the cell wall.

They have no activity against **LAME**: Listeria, Atypicals (Mycoplasma/Chlamydia), MRSA and Enterococci. (Only MRSA exception being 5th Generation drugs: Ceftobiprole etc.)

1 st Gen	2 nd Gen	3 rd Gen	4 th Gen	5 th Gen
Cefadroxil Cefalexin Cefazolin Cefazedone	Cefaclor Cefuroxime Cefotetan Cefprozil	Cefixime Ceftriaxone Cefdinir Cefodizine Cefotaxime Ceftazidime	Cefepime Cefquinome	Ceftobiprole Ceftaroline Ceftolozane

General Rule

1st Gen are predominantly active against gram-positives, with succeeding generations progressively more active against gram-negative strains (often with reduced gram-positive activity, except 4th, which are extended spectrum agents).

Adverse Effects

Nausea, diarrhoea, rash, pain and inflammation at injection site.

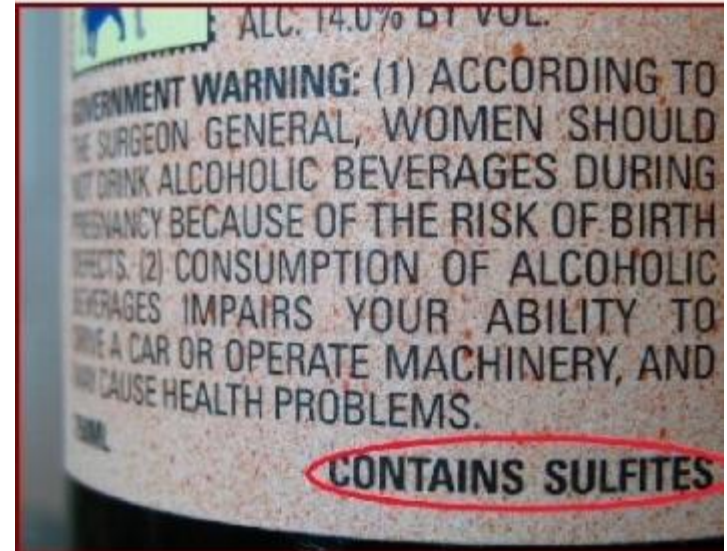
Those allergic to penicillins may show cross-sensitivity with some cephalosporins, but the figure is thought to be considerably less than the 10% commonly cited.

Sulfa Antibiotics

- Limited use- MRSA
- Contraindicated in pregnancy and sickle cell disease
- Category C
- “Triple Sulfa” for toxoplasmosis
- High Incidence of Stevens Johnson Syndrome
- Watch cross reaction with other sulfa based meds:
 - CAI’s (acetazolamide), Celebrex and Thiazide diuretics
- Metallic taste/tingling and burning in hands/feet
- Aplastic anemia risk

Sulfa Allergies

- Not SULFUR (or sulfites)
- Rash is a common sign
- Septra/Bactrim
- Diamox (IOP) -post PKP
- Neptazane (IOP)
- No concern w/ Polytrim gtts



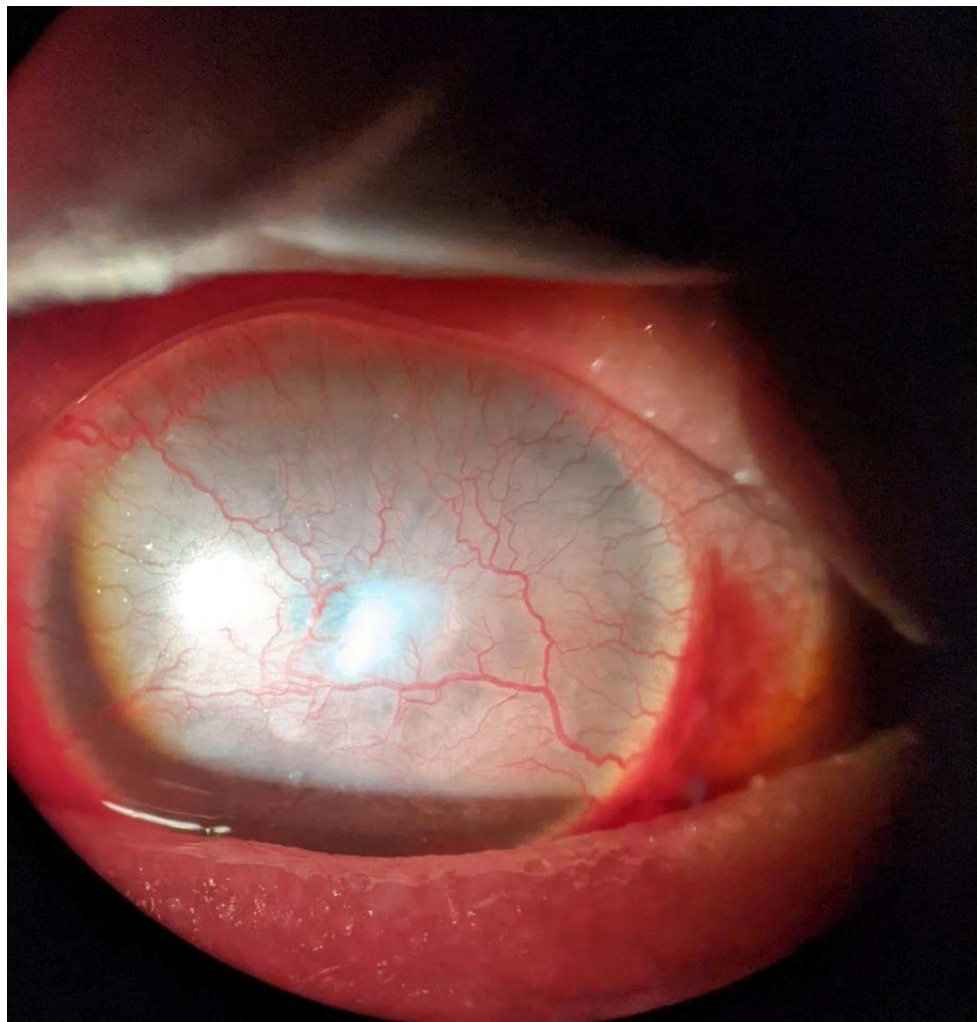
Stevens Johnson Syndrome

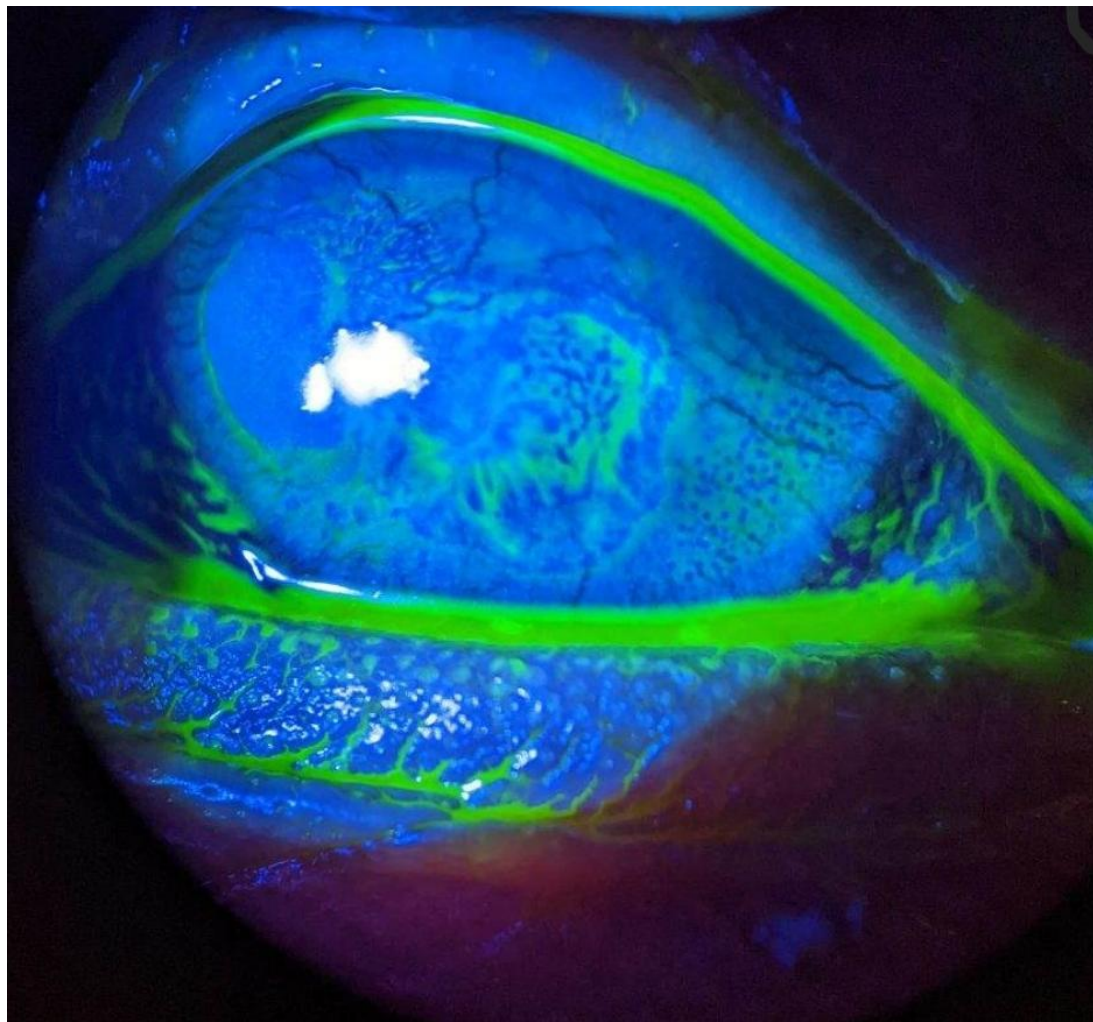
- Rare, serious disorder of the skin and mucous membranes
- Fewer than 20,000 US cases/year
- Starts with flu-like symptoms , followed by a rash and then blisters
- Requires hospitalization- burn unit
- Can take weeks/months to recover
- More severe form is called TEN (Toxic Epidermal Necrolysis)
- Anti gout meds, anticonvulsants, antipsychotics, sulfonamides, pain relievers

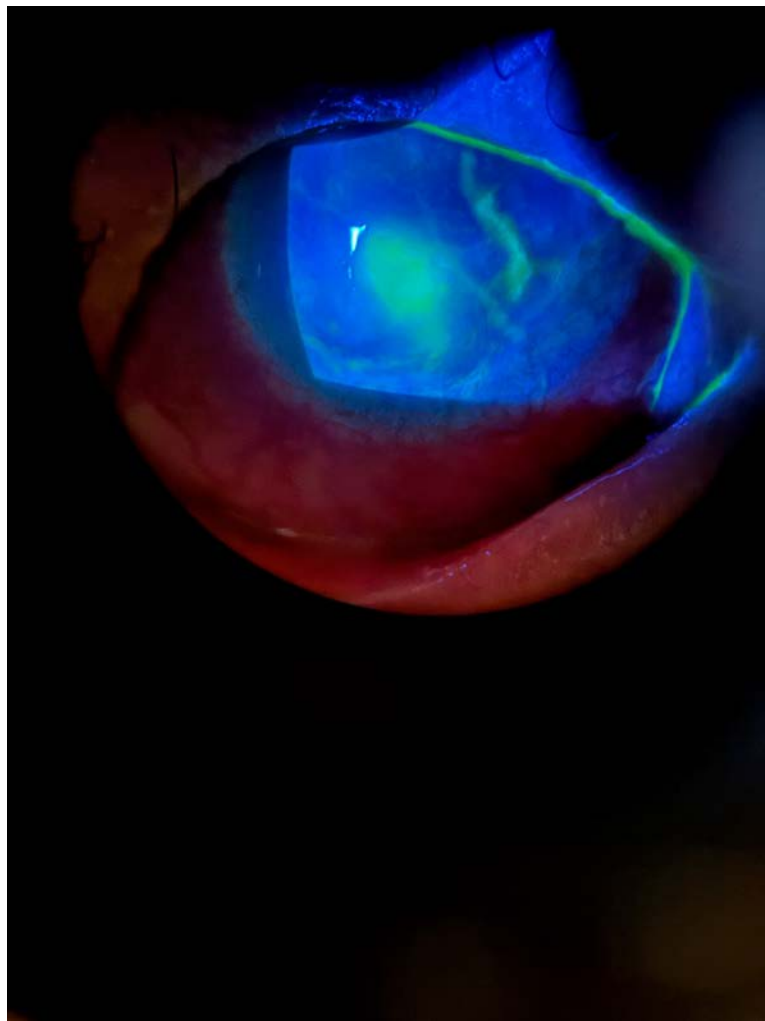
Stevens Johnson Syndrome (SJS)

- Ocular Sequelae:
- Eyelid margin keratinization
- Symblepharon
- Corneal neovascularization/scarring/opacification
- Loss of limbal stem cells
- Use of large diameter scleral lenses
- Poor outcomes in corneal grafts/Limbal Stem cell grafts
- Boston KPro



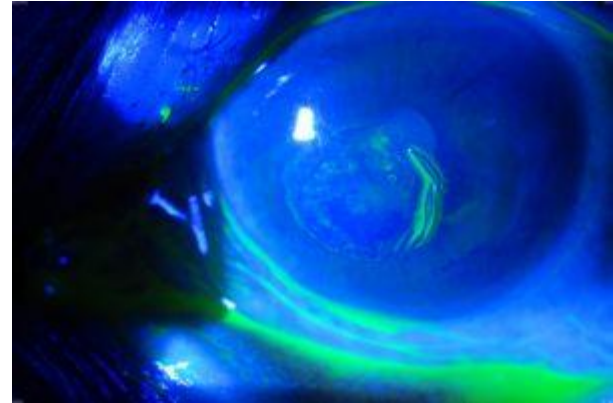






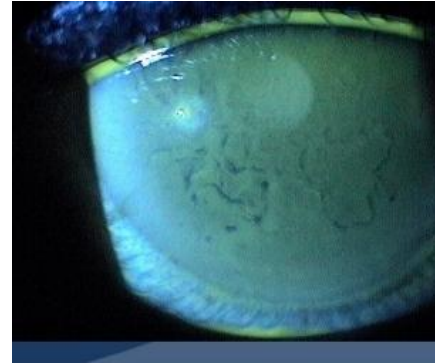
Case #2

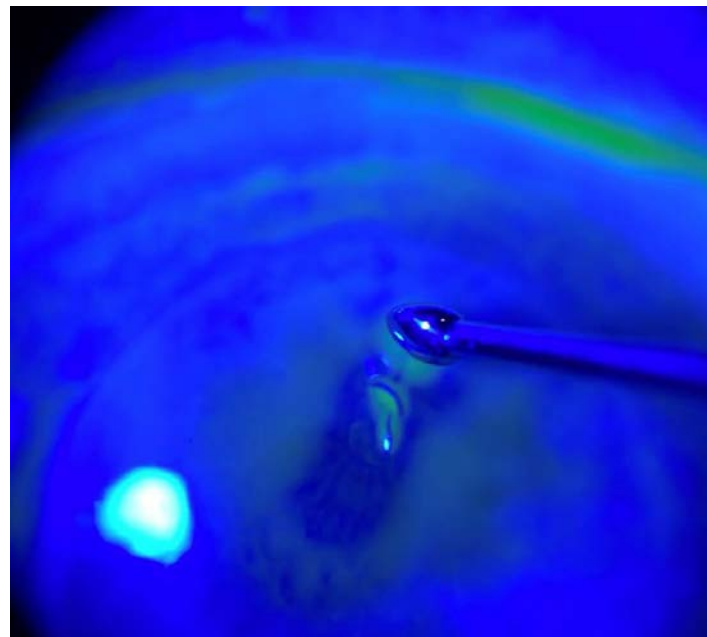
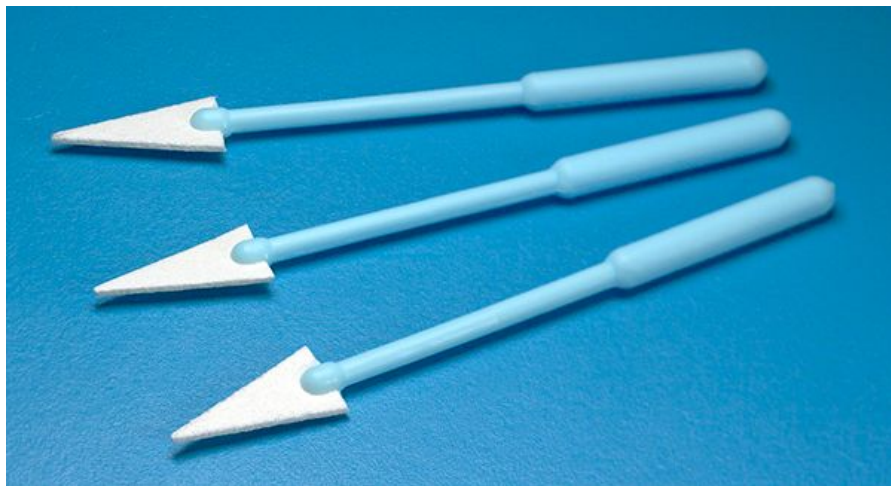
- 33 yo pt presents after waking w/ acute pain, tearing and redness OD.
- Prev Hx of “paper cut to same eye” years earlier.
- VA 20/25
- Epithelial defect noted inferiorly in the cornea.
- A/C clear. Mild hyperemia.



Case #2

- **Recurrent corneal erosion (RCE)**
- Weak attachment between corneal epithelium and basement membrane
- Hx of mechanical trauma
 - Corneal dystrophies
 - Corneal surgery
- Use a weck-cel sponge to test for areas of weak epithelium.
- Cornea sweep-Dr Brian Kim





Recurrent Corneal Erosions

- Treatment for **acute RCE**:
 - Lubrication(AT)
 - Pain control: cycloplegia
 - APAP/Ibuprofen
 - Topical NSAID
 - BCL
 - Topical Antibiotics- avoid gels (Besivance, Moxeza)
 - Amniotic Membranes-dry vs cryopreserved
 - Punctal plugs

Recurrent Corneal Erosions

- **Recalcitrant cases:**
- Muro ung 5% QHS
- Fresh Kote TID
- Autologous Serum gtts
- Amniotic Membranes-FLO
- Long term BCL



Topical Steroids (Lotemax/FML/Flarex) QID x 1 mo then BID x 1 mo

Doxycycline 50 mg BID x 1 mo then QD x 1 mo

- Azasite if concurrent MGD
- Scleral lenses

American Journal of Ophthalmology

Volume 132, Issue 1, July 2001, Pages 8-13

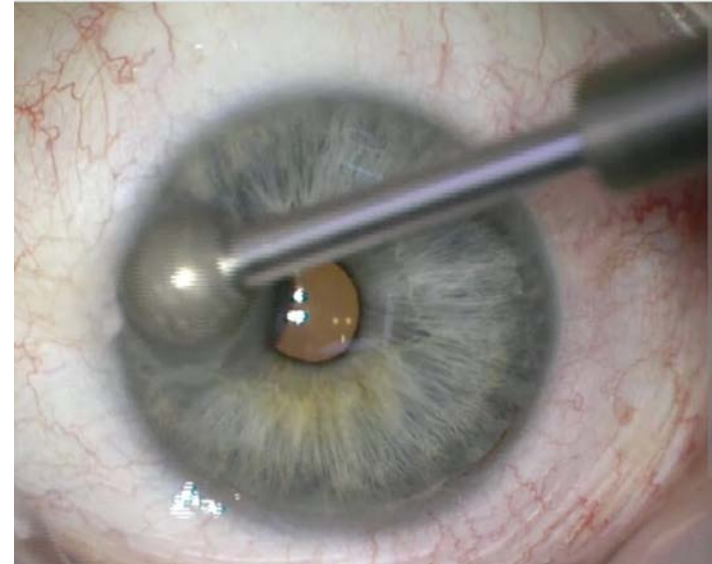
Treatment of recalcitrant recurrent corneal erosions with inhibitors of matrix metalloproteinase-9, doxycycline and corticosteroids ☆

Dilek Dursun MD ^a, Michael C Kim MD ^a
, Abraham Solomon MD ^a, Stephen C Pflugfelder MD ^a 

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Eye Institute, Department of Ophthalmology,
University of Miami School of Medicine, Miami,
Florida, USA

Recurrent Corneal Erosions

- Surgical treatments:
- ASP-anterior stromal puncture
- PTK
- Diamond Burr polishing
- Debridement



Tetracycline

- Category D
- Cannot use in children under age 8-12-teeth discoloration
- Cannot use in pregnancy/nursing
- Used in eye care mostly for anti inflammatory properties
- QID dosing 250-500 mg QID
- Must take on empty stomach
- No dairy products, antacids
- Crosses blood brain barrier readily -IIH (psuedotumor cerebri)
- Can cause photosensitivity
- Minocycline commonly used by dermatology





Tetracycline

- Ocular uses:
- MGD/Posterior blepharitis
- Hordeola
- Dry eye
- RCE
- Acne Rosacea



Doxycycline

- Less side effect profile than tetracycline
- QD to BID dosing
- Can take with food
 - No dairy within 2 hours of taking doxy
- Cannot take with antacids
- GI upset
- Vertigo- more common w/ minocycline
- Esophageal irritation- take at least 2 hrs prior to lying down



Doxycycline

- **Dosage forms:**
- 50 mg /100 mg capsule or tablet
- Hyclate vs monohydrate
- Periostat-20 mg
- Oracea-sustained release





Doxycycline

- Inhibits **collagenase** activity
- **MMP-9** (matrix metalloproteinase)inhibitor
- Alters sebum content
- Adjunct use in RCE
- Adjunct use in corneal ulcers- can help prevent perforation
- Significant bacterial resistance
- Alternative treatment of chlamydia









Dry Eye Treatment

- Omega 3 fish oil
- Ethyl ester vs triglyceride form
- Krill oil-crustacean
- Dosage? 2,000 mg/day
- EPA vs DHA in dry eye disease
- Vitamin E- causes fish burps and GI upset- necessary in EE fish oil to prevent spoilage
- Vegan/vegetarian formulations





Can omega-3s help reduce the risk of heart attacks and CHD?



The Vitamin D and Omega-3 Trial (VITAL) studied the impact of EPA & DHA omega-3s on 25,000 healthy subjects

28% reduced risk of **HEART ATTACKS***

17% reduced risk of **CORONARY HEART DISEASE (CHD)****

The results strengthen the argument that **omega-3s may reduce the risk of heart attack and CHD** in those without cardiovascular disease.

Findings at <http://bit.ly/VITALresults>

*statistically significant secondary outcome **statistically significant



About the VITAL Study
Study Findings
VITAL-Related Publications
VITAL in the News
Ancillary Studies
Study Q&A
VITAL Signs
Download Photos of our researchers
Contact Us
Brigham and Women's Hospital
Mass Division of Preventive Medicine
For Healthcare Providers
For VITAL Investigators

Welcome to the VITAL Study

Welcome to the Web site of the VITamin D and Omega-3 Trial (VITAL) at Brigham and Women's Hospital, an affiliate of Harvard Medical School, in Boston, Massachusetts. VITAL is an ongoing research study in 25,871 men and women across the U.S. investigating whether taking daily dietary supplements of vitamin D3 (2000 IU) or omega-3 fatty acids (Omacor® fish oil, 1 gram) reduces the risk for developing cancer, heart disease, and stroke in people who do not have a prior history of these illnesses. Please click on Study Q&A to learn more about this important research endeavor.



JoAnn Manson, MD

The website is updated regularly to keep participants informed about the study's progress, as well as health topics that we hope are of interest. We also answer frequently asked questions from participants on this website.



Julie Buring, ScD

Thank you for your interest!
JoAnn Manson, MD
Julie Buring, ScD
VITAL Study Directors

VITAL Researchers Answer Your Findings!

Please visit us on Facebook, Twitter, and YouTube to see a summary of the results.

Participant Perspectives: What does VITAL mean to you?

We are interested in hearing what motivated you to join VITAL, and why you think it is important to continue participating until the study ends. Please go to our new video at www.vitalstudy.org

Click here to watch a sampling of participant responses recorded to date.

Click here to see an interactive video created by your fellow VITAL participants.

Click here to view a brief overview by Dr. JoAnn Manson (VITAL Director).



Brief Summary:

The VITamin D and OmegA-3 Trial (VITAL; NCT 01169259) is a randomized clinical trial in 25,875 U.S. men and women investigating whether taking daily dietary supplements of vitamin D3 (2000 IU) or omega-3 fatty acids (Omacor fish oil, 1 gram) reduces the risk of developing cancer, heart disease, and stroke in people who do not have a prior history of these illnesses. This ancillary study is being conducted among participants in VITAL and will examine whether omega-3 fatty acids or vitamin D3, compared to placebo, reduce the incidence and/or progression of dry eye disease.

Detailed Description:

This ancillary study to VITAL will examine the efficacy of omega-3 fatty acids and vitamin D3 in prevention of dry eye disease. The primary aims are to test whether omega-3 fatty acid supplementation (1) reduces the incidence of dry eye disease, and (2) improves the natural history of dry eye disease by relieving symptoms and other impacts on quality of life. Secondary aims are to estimate the incidence of dry eye disease in the US, prospectively examine the natural history of dry disease, explore factors that could modify or influence the impact of omega-3 fatty acid supplementation, evaluate the interrelationship of dry eye disease and depression, and test for possible independent or joint effects of vitamin D3 supplementation in the incidence and natural history of dry eye disease.



MENU



July 05, 2022 | 1 min read

SAVE 

Marine omega-3 fatty acid supplements show no benefit in preventing dry eye disease

By [Michela Cimberle](#)

Perspective from [John D. Sheppard, MD, MMSc](#)

[+ Source/Disclosures](#)

Long-term supplementation with marine omega-3 fatty acid has no effect on incident clinically significant dry eye disease or reported severe symptoms of the disease, according to a study.

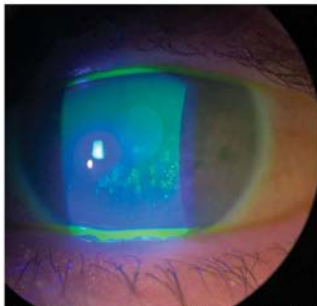
The VITAL-Dry Eye was an ancillary study of VITAL, a large nationwide trial conducted in the U.S. to assess the potential effects of vitamin D (2,000 IU daily) and omega-3 fatty acids (fish oil, eicosapentaenoic acid and docosahexaenoic acid), 1 mg daily, in the prevention of cancer and cardiovascular disease. VITAL Dry-Eye included 23,523 adults with no signs and symptoms of dry eye disease at baseline. There was a similar number of participants in the treatment and placebo groups.

Primary endpoint of the study was incident clinically diagnosed DED. Secondary endpoint was incident clinically diagnosed DED plus reported severe and persistent DED symptoms. Investigators defined DED as comprehensive of all subtypes (aqueous deficient and evaporative dry eye) and etiologies (contact lens wear, intensive computer use and meibomian gland dysfunction).

Omega Fatty Acid Supplementation Does Not Prevent Dry Eye

These findings add to the skepticism about such an intervention that followed the DREAM study's failure to find a treatment effect.

By Staff



This study found no difference in dry eye severity between those who supplemented with omega fatty acids and those who didn't. Photo: Pam Theriot, OD. [Click image to enlarge.](#)

While several small randomized studies have suggested that marine ω -3 fatty acid supplementation may aid the treatment of dry eye disease (DED)—and one prominent trial, the DREAM study, found no evidence—questions also remain regarding whether these supplements can prevent the condition.

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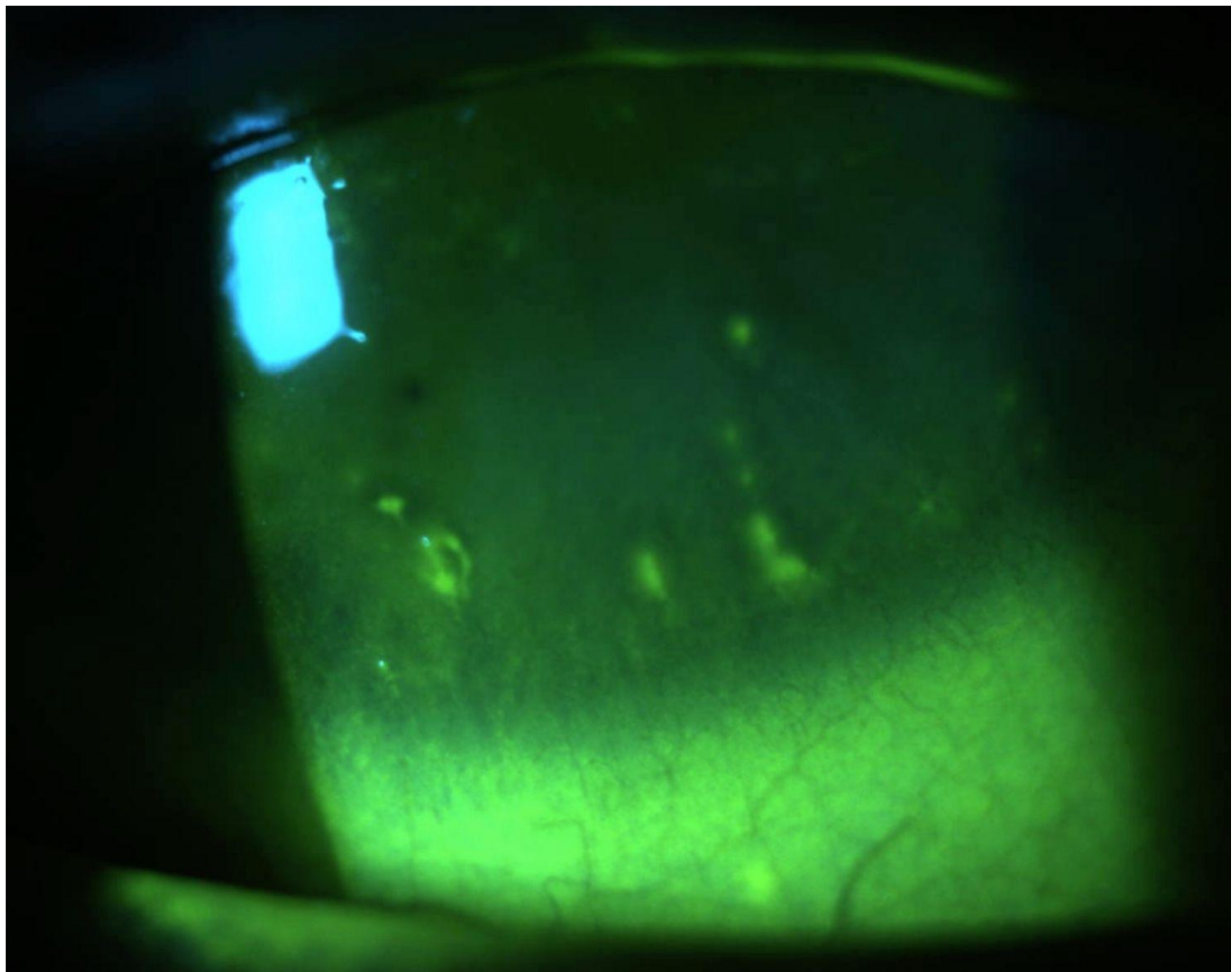
Results of the 12-month [Dry Eye Assessment and Management \(DREAM\) study](#) showed that dietary supplementation with oral omega-3 fatty acids is no better than placebo in relieving signs and symptoms of dry eye disease (DED).

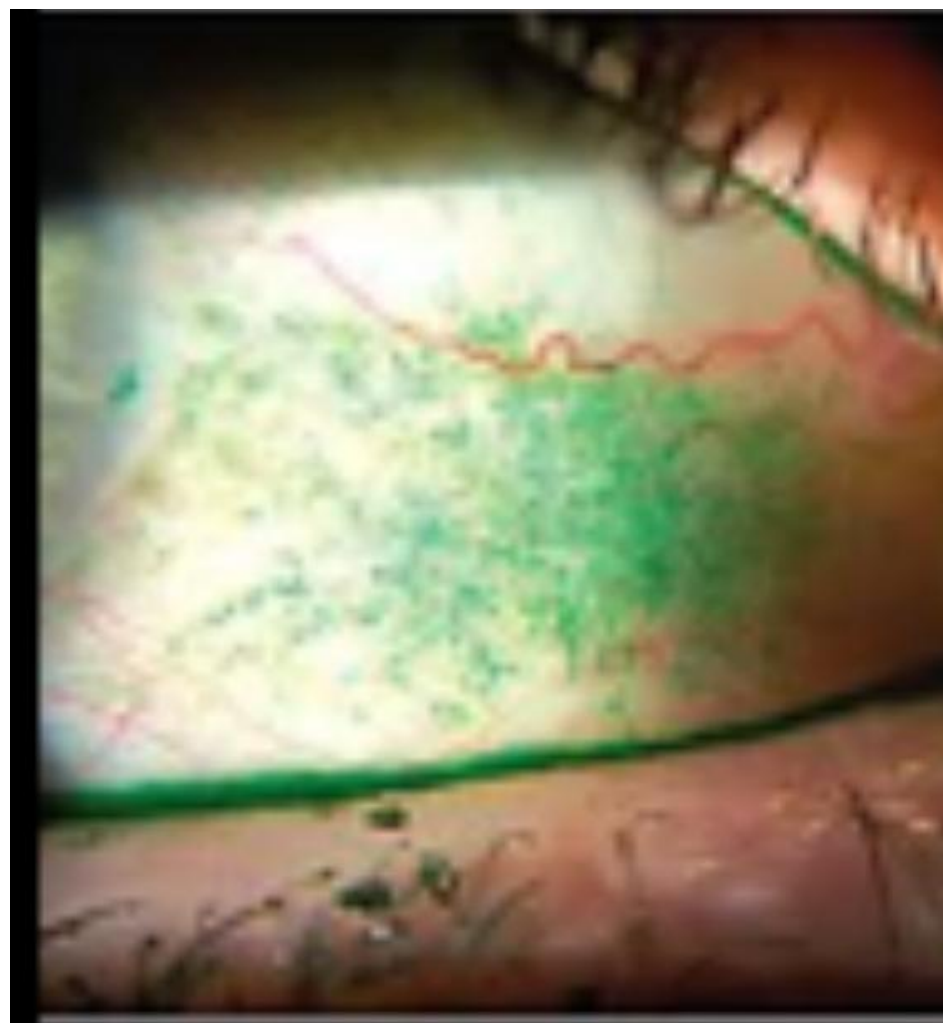
Results from the 12-month DREAM Extension study are consistent with the findings of the primary trial, according to [Penny A. Asbell, MD, MBA](#), study chairperson for the DREAM research group, and Barrett G. Haik Endowed Chair, chairperson and professor of ophthalmology, [University of Tennessee Health Science Center, Memphis, TN](#).

Selected Highlights

- The DREAM study tested fish oil versus olive oil (placebo) for addressing dry eye.
- Dry eye symptoms and signs improved in both fish oil and olive oil users during the study, though improvement was not significantly different between the groups.
- The study's design allowed users to continue with or change their dry eye therapies during the study, an approach with both benefits and potential drawbacks.
- While a placebo other than olive oil might have been less controversial, the reason for improvement in the placebo group is difficult to know with certainty.
- The DREAM study findings do not apply to GLA (used in ScienceBased Health's supplement, HydroEye) since GLA is not found in fish or olive oils.
- Other clinical research suggests possible benefits of GLA for dry eye.

From eyedolatry.com





Sjögren's Syndrome

- Sjögren's Syndrome is a multisystem chronic autoimmune disorder of the exocrine glands with associated lymphocytic infiltrates in affected glands.
- Involvement of the lacrimal and salivary glands leads to the classic symptoms of dryness of the eyes and mouth.
- Joint Pain, fatigue
- Associated with RA, sarcoidosis, SLE, Raynaud's phenomenon, increased dental damage, peripheral neuropathy, dry skin, reflux esophagitis
- 10% risk of lymphoma

Sjögren's Syndrome: Testing

- Sjögren-specific antibody A (SS-A) and Sjögren-specific antibody B (SS-B)
- Rheumatoid factor (RF) and antinuclear antibody (ANA- not disease-specific)
- SP-1 Salivary protein
- CA-6 Carbonic anhydrase 6
- PSP Parotid secretory Protein

Treatment Options

- Systemic treatments-biologics
- Evoxac/Salagen
- Topical treatments immunomodulators
- Topical cyclosporines: newly FDA approved: .1% Cyclosporine drop Vevye
- Punctal occlusion
- Topical steroids
- Bandage contact lenses
- Mucomyst
- Amniotic membranes
- Autologous serum/PRP
- Scleral lenses

Sjogren's Syndrome

- **Pilocarpine** (Salagen) 10 mg TID- titrate dose over 1 month. Start at 5 mg/day. Do not exceed 30 mg/day total
- **Cevimeline** (Evoxac) 30 mg TID
- Both stimulate the lacrimal gland (and salivary glands) to produce tears and saliva
- Side effects: diarrhea, irregular heartbeat, nausea, vomiting, stomach cramps, difficulty breathing
- Contraindicated in narrow angle glaucoma and asthma



NDC 0713-0883-01

Evoxac[®]
(cevimeline HCl) 30 mg
Capsules

Rx only

100 Capsules

C
Cosette
PHARMACEUTICALS

Cosette Pharmaceuticals, Inc.
South Plainfield, NJ 07080
NDC 0713-0883-01

Case #3

- Pt presents with red bump left lower lid. Slightly painful to touch x 1 week. Lid is slightly swollen. No recent ocular trauma. Slit lamp exam shows inspissated meibomian glands OU.
- + PCN allergy.



Case #3

- Treatment?
- Hot compresses
- Topical antibiotic/steroid combo gtts/ung
- Oral antibiotics?

- **Internal hordeolum**- infection of the meibomian glands
- **External hordeolum**- glands of Zeis and Moll
- **Chalazion**

Case #3

With a history of TRUE PCN allergy, what would be your preferred antibiotic?



Macrolides

- Erythromycin, Azithromycin, Clarithromycin
- Inhibits bacterial protein synthesis
- Use with caution in liver disease and myasthenia gravis
- Category B
- Erythromycin high dosage at QID- GI upset
- Clarithromycin (Biaxin)- not used much in eye care

Macrolides - Drug Interactions

- Dilantin/Depakote/Tegretol (epilepsy)
- Digoxin
- Coumadin
- Lipitor
- Theophylline



► Br J Clin Pharmacol. 2009 Sep;68(3):427–434.

doi: [10.1111/j.1365-2125.2009.03473.x](https://doi.org/10.1111/j.1365-2125.2009.03473.x) 

Rhabdomyolysis a result of azithromycin and statins: an unrecognized interaction

[Johanna Strandell](#)^{1,2}, [Andrew Bate](#)^{1,3}, [Staffan](#)

[Hägg](#)², [I Ralph Edwards](#)¹

► [Author information](#) ► [Article notes](#)

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PMCID: PMC2766483 PMID: [19740401](#)

In general, 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors (statins) are well tolerated by most users [1, 2]. However, the clinical syndrome rhabdomyolysis has been demonstrated to be a rare but potentially life-threatening adverse effect of statins [3]. The mechanism of rhabdomyolysis with statins is poorly defined, but the occurrence is known to increase with dose/concentration [4]. Consequently, the risk increases when drugs that exclusively can cause rhabdomyolysis are used concomitantly with other drugs that can increase their effects via interactions. The macrolides erythromycin, clarithromycin, troleandomycin and telithromycin have been mentioned as potential interacting agents with statins in standard drug references [5, 6] since they are cleared through the same metabolic pathway.

Azithromycin (Zithromax)

- More user friendly - dosing regimen increases compliance
- Easiest medication to Rx!
- Pregnancy Category B- OK for children and pregnancy
- Less GI side effects than erythromycin
- Chlamydia treatment- 1 g dose
- **Most commonly prescribed antibiotic** 55 million Rxes/year in US
- Generic availability
- **Long half life**
- Pediatric suspension

Azithromycin (Zithromax)

- Z pack- 500 mg first day (2 pills)
then 250 mg (pill) day 2-5
 - **Improves compliance**
- Also available as Tripack (500 mg for 3 days)
- Used for URI- watch for resistant organisms
- Topical gtt- Azasite (Thea)



Azithromycin (Zithromax)

- FDA warning in 2013- increases risk of cardiac arrhythmias and sudden death



COMMENTARY

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Mass Medical School, Mount Lebanon School,
and the Mass Medical Science Training
Program, Mount Lebanon, MA

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Azithromycin and risk of sudden cardiac death: Guilty as charged or falsely accused?

A MARCH 2013 WARNING by the US Food and Drug Administration that azithromycin (Zithromax, Zmax, Z-pak) may increase the risk of sudden cardiac death does not mean we must abandon using it. We should, however, try to determine if our patients have cardiovascular risk factors for this extreme side effect and take appropriate precautions.

■ AZITHROMYCIN: THE SAFEST OF THE MACROLIDES?

Azithromycin, a broad-spectrum macrolide antibiotic, is used to treat or prevent a range of common bacterial infections, including upper and lower respiratory tract infections and certain sexually transmitted diseases.

In terms of overall toxicity, azithromycin has been considered the safest of the macrolides, as it neither undergoes CYP3A4 metabolism nor inhibits CYP3A4 to any clinically meaningful degree, and therefore does not interfere with the array of commonly used medications that undergo CYP3A4 metabolism.

Also, *in vitro*, azithromycin shows only limited blockade of the potassium channel *hERG*. This channel is critically involved in cardiomyocyte repolarization, and if it is blocked or

otherwise malfunctioning, the result can be a prolonged QT interval, ventricular arrhythmias, and even sudden cardiac death.¹⁻⁴ Therefore, lack of blockade, as reflected by a high inhibitory concentration (table 1), boded well for the safety of azithromycin in terms of QT liability. However, we should be cautious in interpreting *in vitro* data.

With its broad antibiotic spectrum and perceived favorable safety profile, azithromycin has become one of the top 15 most prescribed drugs and the best-selling antibiotic in the United States, accounting for 55.4 million prescriptions in 2012, according to the IMS Institute for Healthcare Informatics.

■ THE FDA RECEIVES 203 REPORTS OF ADVERSE EVENTS IN 8 YEARS

However, beginning with a report of azithromycin-triggered torsades de pointes in 2001,⁵ a growing body of evidence, derived from postmarketing surveillance, has linked azithromycin to cardiac arrhythmias such as prolonged QT interval prolongation and associated torsades de pointes (which can progress to life-threatening ventricular fibrillation). Other, closely related macrolides such as clarithromycin and erythromycin are also linked to these effects.

Furthermore, in the 8-year period from 2004 to 2011, the US Food and Drug Administration (FDA) Adverse Event Reporting System (FAERS) received a total of 203 reports of azithromycin-associated QT prolongation, torsades de pointes, ventricular ar-

Compelling evidence exists that azithromycin is not free of the QT-prolonging and torsadogenic effects long associated with other macrolides

¹Dr Ackerman is a consultant for Vangaur, intellectual property derived from the research program awarded to license agreements in 2004 between Mount Sinai Medical Center (formerly Mount Sinai Medical Center) and Vangaur (formerly Vangaur Pharmaceuticals and now Vangaur). Funding sources: This work was supported by the Mount Sinai South Campus Comprehensive Cardiac Care Program. Dr Guidicelli is supported by a National Heart, Lung, and Blood Institute Academic Medical Institution Physician Scientist (AMPS) Fellowship (F30 HL096012) and the Mount Sinai Medical Science Training Program.

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CLINICAL COURSE JOURNAL OF MEDICINE VOLUME 116 NUMBER 9 SEPTEMBER 2013 539

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Oral azithromycin versus doxycycline in meibomian gland dysfunction: a randomised double masked open label clinical trial.

Kashkouli MB¹, Fazel AJ¹, Kiavash V¹, Nojomi M², Ghiasian L³.

⊕ Author information

Abstract

BACKGROUND/AIMS: To assess the efficacy and safety of oral azithromycin compared with oral doxycycline in patients with meibomian gland dysfunction (MGD) who had failed to respond to prior conservative management.

METHODS: 110 patients (>12 years old) with MGD were randomly assigned to receive either oral 5-day azithromycin (500 mg on day 1 and then 250 mg/day) or 1-month doxycycline (200 mg/day). They also continued eyelid warming/cleaning and artificial tears. A score comprising five symptoms and seven signs (primary outcome) was recorded prior to treatment and at 1 week, and 1 and 2 months after treatment. Total score was the sum of both scores at each follow-up. Side effects were recorded and overall clinical improvement was categorised as excellent, good, fair or poor based on the percentage of change in the total score.

RESULTS: Symptoms and signs improved significantly in both groups ($p=0.001$). While improvement of symptoms was not different between the groups, bulbar conjunctival redness ($p=0.004$) and ocular surface staining ($p=0.01$) were significantly better in the azithromycin group. The azithromycin group showed a significantly better overall clinical response ($p=0.01$). Mild gastrointestinal side effects were not significantly different between the groups except for the second visit, when the doxycycline group had significantly more side effects ($p=0.002$).

CONCLUSIONS: Although both oral azithromycin and doxycycline improved the symptoms of MGD, 5-day oral azithromycin is recommended for its better effect on improving the signs, better overall clinical response and shorter duration of treatment.

TRIAL REGISTRATION NUMBER: NCT01783860.

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**ONLINE FIRST**

Original Investigation

March 23, 2023

Pulsed Oral Azithromycin vs 6-Week Oral Doxycycline for Moderate to Severe Meibomian Gland Dysfunction A Randomized Clinical Trial

Phit Upaphong, MD¹;



Question Are the adverse effects of a 3-week course of weekly oral azithromycin equivalent to that of the 6-week course of oral doxycycline in treating moderate to severe meibomian gland dysfunction (MGD)?

Findings In this randomized clinical trial that included 137 eyes, at the 6- and 8-week follow-ups, the mean differences in total MGD scores between azithromycin and doxycycline were -0.33 and 0.13 , respectively. At both time points, the differences were within the prespecified equivalence margin of 2.

Meaning A 3-week course of weekly oral azithromycin was equivalent to a 6-week course of oral doxycycline in treating moderate to severe MGD.

Design, Setting, and Participants This double-masked randomized clinical trial was conducted at a referral center in Thailand from September 2018 to May 2022. Participants with moderate to severe MGD judged unresponsive to conservative management were included.

Interventions Patients were randomized 1:1 to receive oral azithromycin (1 g once per week for 3 weeks) or oral doxycycline (200 mg daily for 6 weeks).

Conclusions and Relevance These data support an equivalency of effects of azithromycin as compared with doxycycline for MGD score and OSDI score at both follow-up times. The study did not show more gastrointestinal AEs in the azithromycin group. The reduced dosing and potentially fewer gastrointestinal AEs associated with azithromycin support its use as an alternative to doxycycline for at least 6 weeks.

RCT: Pulsed Oral Azithromycin vs 6-Week Oral Doxycycline for Moderate to Severe Meibomian Gland Dysfunction

POPULATION

46 Men, 91 Women



Adults with moderate to severe meibomian gland dysfunction (MGD) unresponsive to conservative care

Mean age, 62 y

SETTINGS / LOCATIONS



1 Tertiary medical center in Chiang Mai, Thailand

INTERVENTION

137 Eyes from 137 participants randomized



68 Azithromycin

Oral azithromycin, 1 g/wk for 3 wk



69 Doxycycline

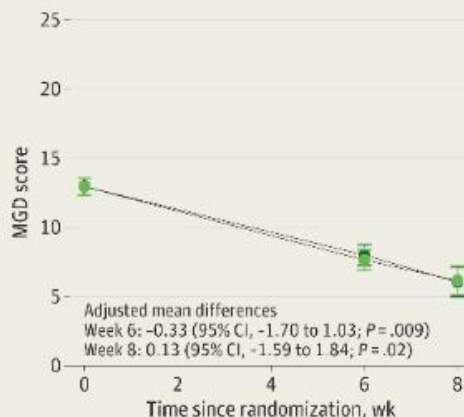
Oral doxycycline, 100 mg twice daily for 6 wk

PRIMARY OUTCOME

Total score on the 11-item MGD scale (range, 0-33) at 6 wk; equivalence margin between the 2 groups was ± 2 in the MGD scores

FINDINGS

There was no significant difference between the 2 groups in MGD score at 6 wk



AzaSite

- AzaSite (azithromycin 1% ophthalmic)
- Off label use for ocular rosacea/ MGD



Fluoroquinolones

- Category C
- Inhibit bacterial DNA synthesis
- Significant overuse/resistance in medicine (livestock)
- Mainly used for Gram (-) UTI's
- Cannot use in patients less than 18 -bone/cartilage formation
- Cannot use in pregnancy/nursing
- Contraindicated in renal disease and myasthenia gravis
- Tendonitis/achilles tendon rupture **BLACK BOX WARNING** for Levaquin



WARNING: SERIOUS ADVERSE REACTIONS INCLUDING TENDINITIS, TENDON RUPTURE, PERIPHERAL NEUROPATHY, CENTRAL NERVOUS SYSTEM EFFECTS AND EXACERBATION OF MYASTHENIA GRAVIS

Fluoroquinolones, including CIPRO®, have been associated with disabling and potentially irreversible serious adverse reactions that have occurred together including tendinitis and tendon rupture, peripheral neuropathy, and central nervous system effects.

Discontinue CIPRO immediately and avoid the use of fluoroquinolones, including CIPRO, in patients who experience any of these serious adverse reactions.

Fluoroquinolones, including CIPRO, may exacerbate muscle weakness in patients with myasthenia gravis. Avoid CIPRO in patients with known history of myasthenia gravis.

Because fluoroquinolones, including CIPRO, have been associated with serious adverse reactions, reserve CIPRO for use in patients who have no alternative treatment options for the following indications: acute exacerbation of chronic bronchitis, acute uncomplicated cystitis, acute sinusitis.

Disabling, Potentially Irreversible Serious Reactions

fluoroquinolones assoc. with tendinitis/tendon rupture, peripheral neuropathy, and CNS effects that may occur together; tendinitis/tendon rupture may occur during tx or months after tx D/C; incr. tendinitis/tendon rupture risk in all ages; risk further incr. in older pts >60 yo, pts taking corticosteroids, and pts w/ kidney, heart, or lung transplant

Avoid in Myasthenia Gravis

fluoroquinolones may exacerbate muscle weakness in pts w/ myasthenia gravis

Reserve Fluoroquinolone Use

for pts w/ no alternative tx options for acute bacterial sinusitis, acute bacterial exacerbation of chronic bronchitis, or uncomplicated UTI

FLUOROQUINOLONE ANTIBIOTICS

Cipro (ciprofloxacin), Levaquin (levofloxacin), Avelox (moxifloxacin), Factive (gemifloxacin)

FDA WARNINGS

2008

FDA issued warnings about increased risk of tendinitis and tendon rupture.

2013

FDA issued warnings about peripheral neuropathy (damage to the nerves that travel to your arms and legs).

2016

FDA issued warnings about disabling side effects of the tendons, muscles, joints, nerves and central nervous system.

2018

FDA issued warnings about significant decreases in blood sugar and certain mental health side effects.

FDA issued warnings about increase in the occurrence of rare but serious events of ruptures or tears in the main artery of the body, called the aorta.



[Case Rep Ophthalmol Med.](#) 2020; 2020:
8843182. Published online 2020 Nov 24.
doi: [10.1155/2020/8843182](#)

PMCID: PMC7710430 | PMID: [33299626](#)

Binocular Diplopia: A Possible Adverse Effect of Fluoroquinolone Therapy

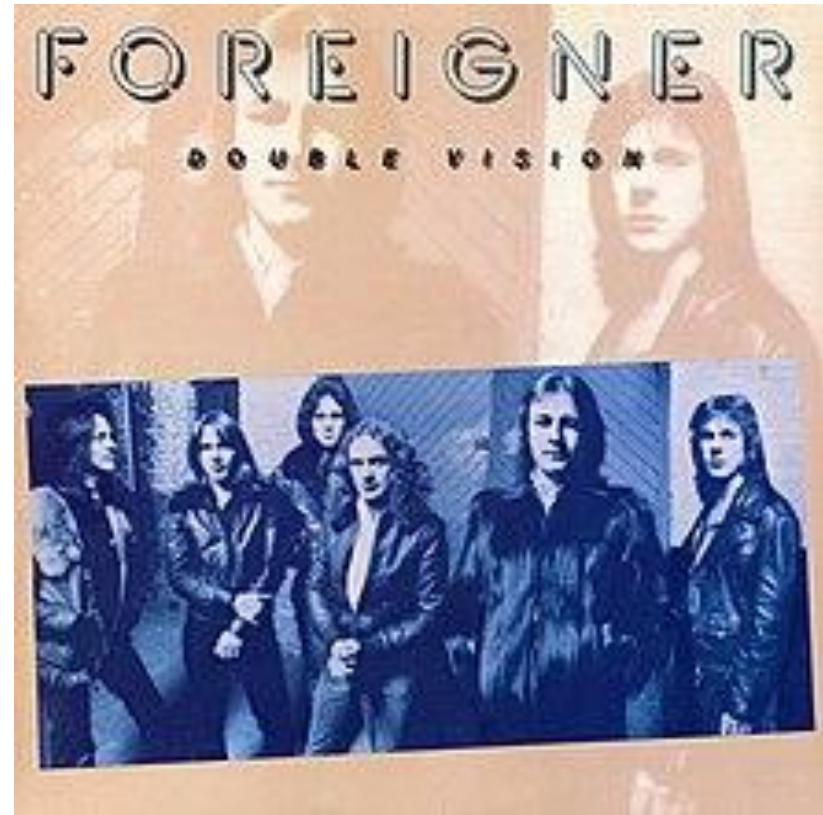
[Mariama Touray](#),¹ [Victoria Ando](#),¹
[Erwin Samutelela](#),² and [Jean-Philippe Zuber](#)¹

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Abstract

[Go to:](#) ►

The adverse effects of fluoroquinolones are yet to be fully elucidated. We present an interesting case of a 41-year-old male with binocular diplopia most likely induced by the use of a fluoroquinolone antibiotic.



ADRs & 3 P's of Fluoroquinolone Toxicities

Created by Brooke & Ashlee Barlow
@brookebarlow @ashleebbarlow

ACHILLES TENDON RUPTURE

A

What patients are at highest risk?
Elderly, solid organ transplant, corticosteroids, renal insufficiency, α/β

Counseling Pearls
Avoid vigorous physical activity




ACUTE AORTIC RUPTURE

What patients are at highest risk?
Elderly, HTN, aortic aneurysms, connective tissue disorders (Marfan-Danos or Marfan syndrome)

Counseling Pearls
Avoid smoking, monitor blood pressure




BLOOD GLUCOSE ALTERATIONS

What patients are at highest risk?
Elderly, renal insufficiency, diabetes, insulin, or oral anti-diabetic medications

Counseling Pearls
Check blood sugar more frequently, carry glucose tablets, eat consistent, well-balanced meal




B

CENTRAL NERVOUS SYSTEM

What patients are at highest risk?
Elderly, renal insufficiency, epilepsy, severe cerebral atherosclerosis

Counseling Pearls
Avoid driving or operating heavy machinery, Limit alcohol intake, Avoid NSAIDs (↑ seizure risk)




DIARRHEA (CLOSTRIDIODIES DIFFICILE)

What patients are at highest risk?
Elderly, immunocompromised, concurrent broad-spectrum antibiotic, PPI or H2RA use

Counseling Pearls
Eat a diet rich in probiotics (e.g. yogurt), Wash hands with soap & water if you develop diarrhea, avoid OTC anti-diarrheals & report to your doctor immediately




D

EXACERBATIONS OF MYASTHENIA GRAVIS

CONTRAINDICATED

PERIPHERAL NEUROPATHY

What patients are at highest risk?
Fluoroquinolone naive patients

Counseling Pearls
Screen and treat alternative etiologies of neuropathy: vitamin B12 intake, diabetes




P

PHOTOSENSITIVITY

What patients are at highest risk?
Excessive sun exposure, fair skin

Counseling Pearls
Wear protective eye-wear, clothing, Wear sunscreen minimum SPF 15, Avoid tanning beds, & excess sun exposure.




P

PROLONGATION OF THE QTC

What patients are at highest risk?
Elderly, female, bradycardia, $\downarrow$ K⁺, $\downarrow$ Mg²⁺, heart failure, concurrent QTc prolonging medications

Counseling Pearls
Optimize K⁺ and Mg²⁺ intake, Inform your doctor if you have any abnormal heart rhythms or if you take anti-arrhythmics




P

WARNING SIGNS: DISCONTINUE IF YOU EXPERIENCE:

- Pain, bruising, or swelling of the joints
- Increasing stool frequency
- Numbness, tingling, or in the extremities
- Confusion, seizures, or mood changes
- Sunburn or skin eruptions
- Symptoms of hypoglycemia: nervousness, dizziness, confusion, sweating, tremors
- Palpitations, chest pain, pain that radiates to your back

STOP! CALL YOUR DOCTOR & SEEK URGENT MEDICAL CARE

Case #4

- 67 yo pt w/ crusting/blisters on right upper lid. Also seen right side of forehead x 2 days. First noticed some tingling on forehead. VA not affected.



Herpes Zoster

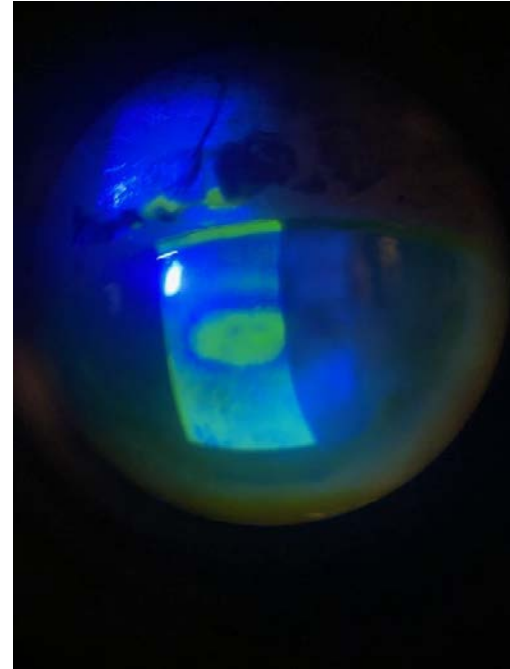
- ~ 1,000,000 Americans develop “shingles” every year
- Ocular involvement up to 25% of cases- many have long term ocular damage
- **Primary infection** - “Chicken pox”- varicella
- **Reactivation** - “shingles” becoming more common in younger patients
- 97% of people develop chicken pox by age 20
- **HZO** - Herpes Zoster Ophthalmicus- CN V dermatome (~20% of zoster cases)
 - Rash/vesicles/crusting that respects the midline
 - Hutchinson’s sign

Herpes Zoster

- Symptoms:
- Malaise, fever, headache
- Tingling on side of scalp or forehead before rash develops
- Photophobia/redness and eye pain if eye is involved

Herpes Zoster - Ocular Signs

- Pseudodendrite - epithelial keratitis
- Conjunctivitis
- Stromal (Interstitial)keratitis
- Endothelitis
- **Neurotrophic keratitis**
- Episcleritis (scleritis)/uveitis
- Retinitis/Choroiditis
- CN palsies



Herpes Zoster

- Start therapy within **72 hours** of symptom onset
- Acyclovir 800 mg 5 x day
- Valtrex 1000 mg 3 x day
- Famvir 500 mg 3 x day
- Topical Ab ung (erythromycin/bacitracin)
- ZEDS study-prophylaxis recently released!

Herpes Zoster

- **Zostavax vaccine** -live attenuated vaccine- no longer available
- **Shingrix**- non live vaccine in 2 doses
- ~97 % effective in preventing shingles
- ~90 % effective in preventing PHN - PKP considerations?
- POST HERPETIC NEURALGIA- up to 25% of patients with Zoster
- Chronic pain lasting longer than 3 months after disease onset
- Cold compresses
- Topical capsaicin or lidocaine ung
- Analgesics/Amitriptyline/Neurontin- pain management specialist



NDC 58160-823-11

Rx only

gsk

NOTICE: One vial of lyophilized powder and
one vial of liquid suspension MUST BE
COMBINED BEFORE USE

Zoster Vaccine Recombinant, Adjuvanted SHINGRIX

For 50 Years of Age and Older

1 + 2

Contents (10 doses of SHINGRIX):

10 Vials containing Lyophilized gE Antigen Component

10 Vials containing Adjuvant Suspension Component

After reconstitution, a single dose of SHINGRIX is 0.5 mL

SHINGRIX

CLINICAL SCIENCE

Zoster Eye Disease Study: Rationale and Design

Cohen, Elisabeth J. MD^{*}; Hochman, Judith S. MD[†];
Troxel, Andrea B. ScD[‡]; Colby, Kathryn A. MD, PhD^{*};
Jeng, Bennie H. MD[§]; on behalf of The ZEDS Trial
Research Group

[Author Information](#) 

Cornea 41(5):p 562-571, May 2022. | DOI:
10.1097/ICO.0000000000002743

OCTOBER 19, 2024

Long-Term, Low-Dose Antiviral Treatment Benefits Patients with Eye Disease & Pain from Shingles



After partially losing her vision to the disease, Dr. Elisabeth J. Cohen led a multiyear study on a new way to treat shingles that affects the eye.

NYU LANGONE HEALTH

ZEDS- Zoster Eye Disease Study

- Modeled after HEDS Study
- Multicenter, double-masked placebo-controlled randomized clinical trial
- 18 years of age or older. Immunocompetent. Hx of HZO within one year of enrollment
- Randomly assigned to 1000 mg oral valacyclovir daily or placebo for 1 year
- Participants are observed for 6 months after end of study to see if there is a persistent treatment benefit
- Enrollment ended December 31, 2022.
- Results published in 2024



Purpose of ZEDS

- To find out whether or not 12 months of low dose valacyclovir treatment, compared with placebo, delays time to development of new or worsening of specific eye disease manifestations of Herpes Zoster Ophthalmicus (HZO)
- Secondary objective: To find out whether there is persistent treatment benefit at 18 months, 6 months after cessation of treatment
- Participants were randomly assigned to valacyclovir or placebo in 4 groups
 - Age of onset of HZO: younger < 60 years vs older $\geq$ 60 years
 - Time since onset at enrollment: recent < 6 months vs chronic $\geq$ 6 mos
- Rationale for groups
 - Expected ~50% < 60, disease manifestations vary by age
 - Expected greater benefit in recent onset disease

Second Aim: Postherpetic Neuralgia

- To find out if low dose treatment for 12 months with oral valacyclovir reduces the chronic pain syndrome called post herpetic neuralgia (PHN) compared to placebo at 12 and 18 months in patients with HZO

Baseline Characteristics at Enrollment

Prescott, Cohen, Hochman et al. *Cornea* 2024 Feb 27 online (2024; 00:1-8)

- 50% of randomized participants were female
- Both sexes represented in each of the 4 groups (strata)
- 87% of participants were White
- 5% of participants were Hispanic or Latino
- Median age at randomization: 60 years
- 91% had received acute recommended antiviral treatment
- 79% of participants did not receive zoster vaccine prior to enrollment

ZEDS Guidance for Evidence-based Clinical Practice

- Evidence supports suppressive valacyclovir treatment 1000 mg daily for one year to reduce new or worsening keratitis or iritis in immunocompetent, non pregnant adults with good renal function
 - Pre-specified analysis of primary endpoint did not show overall benefit at 12 months, but did at 18 months (secondary endpoint)
- Evidence supports suppressive valacyclovir treatment to reduce multiple episodes of keratitis or iritis

Second Aim: Postherpetic Neuralgia (PHN)

- Zoster Brief Pain Inventory (ZBPI) score of worst pain in last 24 hours of 3/10 or more occurring 3 or more months after HZO onset was used to define PHN
- The effect of valacyclovir treatment on medication usage for pain was also analyzed
- At enrollment 14% of participants had PHN
- PHN was significantly more common in participants with HZO onset age 60 or older (20%, $p=0.007$)
 - But PHN also occurred in younger participants (9%)

ZEDS Guidance for Evidence-based Treatment of PHN/Pain

- Recommend 1 year of suppressive valacyclovir in HZO patients
 - HZO Onset < 60 years, chronic stratum
 - Significantly lower pain scores at 12 (p=0.05), 18 months (p=0.02)
 - HZO Overall
 - Significant decrease pain duration at 18 months (p=0.05)
- Why is benefit greater at 18 months?
 - Speculation: takes injured nerves time to heal??

ZEDS Guidance for Evidence-based Treatment of PHN

- Recommend one year of suppressive valacyclovir to significantly reduce dose of neuropathic pain meds at 12 and 18 months (p=0.006, p=0.012)
- Comments
 - Valacyclovir safe and better tolerated than neuropathic pain meds
 - Treatment benefit for PHN due to zoster in other locations merits study

Baseline Characteristics at Enrollment

Prescott, Cohen, Hochman et al. *Cornea* 2024 Feb 27 online (2024; 00:1-8)

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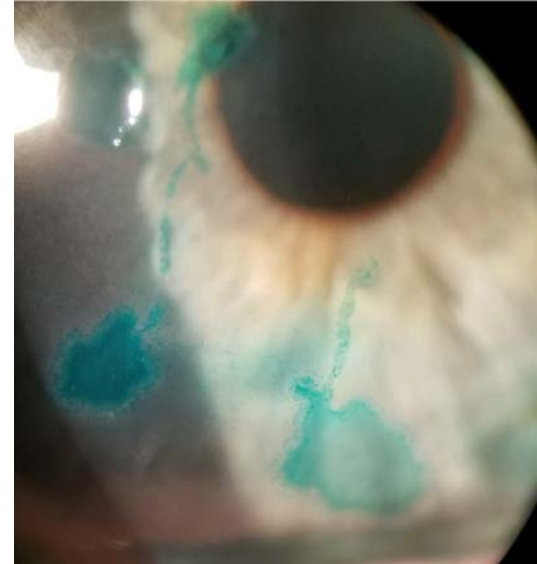


Herpes Simplex

- Double stranded DNA virus (HSV type 1 and 2)
- Most common virus found in humans(up to 99% infected by age 21)
- Primary infection occurs in childhood- typically subclinical
- Recurrent HSV after dormant in a dermatome
- Ocular recurrence 10% at 1 yr and 50% at 10 yrs

Herpes Simplex

- % redness/tearing/photophobia/blurred VA
- Epithelial keratitis- dendrites
- Subepithelial haze
- Reduced corneal sensitivity
- **Herpes Provocative test?**



Herpes Simplex - Treatments

- Topical - both are Pregnancy category C
- **Viroptic** (trifluridine)
9 x day - corneal toxicity
- Difficult to get- must be refrigerated by pharmacy
- **Zirgan** (ganciclovir gel) high cost. 5 x day
- Acyclovir ointment now available

Herpes Simplex - Treatments

- Oral antivirals
- Acyclovir 400 mg 5 x day
- Valtrex 500 mg TID
- Famvir 250 mg TID
- Few side effects - nausea
- Caution in patients with reduced kidney function
- Valtrex is **lactose** free





Advanced User Guide

Clinical Trial

Herpetic Eye Disease Study. A controlled trial of oral acyclovir for herpes simplex stromal keratitis

B A Barron et al. Ophthalmology. 1994 Dec.

Herpetic Eye Disease Study

- Showed benefit of adding steroid to oral acyclovir in treatment of herpetic stromal keratitis and HSV uveitis
- Acyclovir reduced by approximately 50 % recurrence of HSV keratitis after 1 year
- Communicate w/ PCP if on prophylactic dose to monitor BUN/creatinine levels
- Resistance?

HEDS Key Clinical Questions and Studies

QUESTION	FINDINGS	REFERENCE
Are topical steroids beneficial in treating HSV stromal keratitis?	Yes. Topical steroid significantly reduced stromal inflammation and duration of keratitis.	Wilhelmus KR et al., for the Herpetic Eye Disease Study Group. Herpetic eye disease study: A controlled trial of topical corticosteroids for herpes simplex stromal keratitis. <i>Ophthalmology</i> . 1994;101(12):1883-1895; discussion 1895-1896.
Does the addition of oral acyclovir to a regimen of topical steroid and trifluridine improve the clinical outcome in stromal keratitis?	No treatment benefit was seen in nonnecrotizing stromal keratitis; too few patients with necrotizing stromal keratitis to assess benefit.	Barron BA et al., for the Herpetic Eye Disease Study Group. Herpetic eye disease study: A controlled trial of oral acyclovir for herpes simplex stromal keratitis. <i>Ophthalmology</i> . 1994;101(12):1871-1882.
Is oral acyclovir helpful in treating iridocyclitis?	Too few patients to attain statistical significance, although the trend favored treatment with oral acyclovir.	A controlled trial of oral acyclovir for iridocyclitis caused by herpes simplex virus. The Herpetic Eye Disease Study Group. <i>Arch Ophthalmol</i> . 1996;114(9):1065-1072.
Does oral acyclovir prevent development of stromal keratitis in patients with epithelial keratitis?	No difference was apparent between the acyclovir and placebo groups.	A controlled trial of oral acyclovir for the prevention of stromal keratitis or iritis in patients with herpes simplex virus epithelial keratitis. The Herpetic Eye Disease Study Group. <i>Arch Ophthalmol</i> . 1997;115(6):703-712.
Does prophylaxis with oral acyclovir reduce recurrence of HSV?	Yes. Recurrence was reduced by 45% in the acyclovir group compared with placebo.	Wilhelmus KR et al., for the Herpetic Eye Disease Study Group. Acyclovir for the prevention of recurrent herpes simplex virus eye disease. <i>N Engl J Med</i> . 1998;339(5):300-306.
What triggers HSV recurrence?	None of the factors studied were confirmed as triggers as recorded by patients in weekly logs.	Psychological stress and other potential triggers for recurrences of herpes simplex virus eye infections. The Herpetic Eye Disease Study Group. <i>Arch Ophthalmol</i> . 2000;118(12):1617-1625.

Adapted from: BCSC Section 8, *External Disease and Cornea*, 2020-2021, Table 9-6.

Case #5

- Pt had Hx of painful bump on the eyelid with swelling 2 months ago
- Redness and pain have resolved
- Treated with hot compresses only
- VA slightly reduced in that eye
- No drug allergies
- Now presents with hard nodule on eyelid. No change in size.

Case #5

- Treatment?
- Topical antibiotics/steroids?
- Gtts vs ointment?
- Thermal pulsation?
- IPL/RF/LLLT?
- Oral antibiotics?

Case #5

- Doxycycline
- 50-100 mg BID po
- Duration?
- Intralesional kenalog-watch skin discoloration
- I+D- Incision and drainage/curettage
- Recurrent chalazion- r/o sebaceous carcinoma

Chalazion

- Most common inflammatory lesion of the eyelid (13.4%)
- Painless bump/swelling of eyelid
- History of hordeola/rosacea/ chronic blepharitis. Occasionally viral conjunctivitis
- Granulomatous inflammatory response
- **Not** infectious-antibiotics **not** indicated

Chalazion

- **Conservative Treatment:**
 - Hot compresses/gel masks
 - Eyelid massage
 - Lid scrubs
 - Topical steroids? Gtts vs ung. Combo steroid/antibiotics
 - Antibiotics- doxycycline /azithromycin
 - Omega 3 fish oil- ethyl ester vs triglyceride form
- **Thermal treatments**
 - Miboflow/Lipiflow/ Tear Care/ iLux- use in chalazia?
 - IPL/RF/ LLLT
- **Surgical management-chronic > 2 mo duration**
 - Intralesional Triamcinolone
 - Incision and Drainage





NDC 0003-0293-28

KENALOG[®]-40
(Triamcinolone
Acetonide Injectable
Suspension, USP)

400 mg per 10 mL

40 mg per mL

10 mL Multiple Dose Vial

Rx only

Read all sides



Bristol-Myers Squibb



The association of demodex infestation with pediatric chalazia

[Jing Huang](#)^{1,2}, [Meng-Xiang Guo](#)², [Dao-Man Xiang](#)², [Li-Feng Yan](#)², [Ying Yu](#)², [Ling Han](#)², [Jian-Xun Wang](#)², [Xiao-He Lu](#)^{1,✉}

► [Author information](#) ► [Article notes](#)

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PMCID: PMC8925234 PMID: [35291979](#)

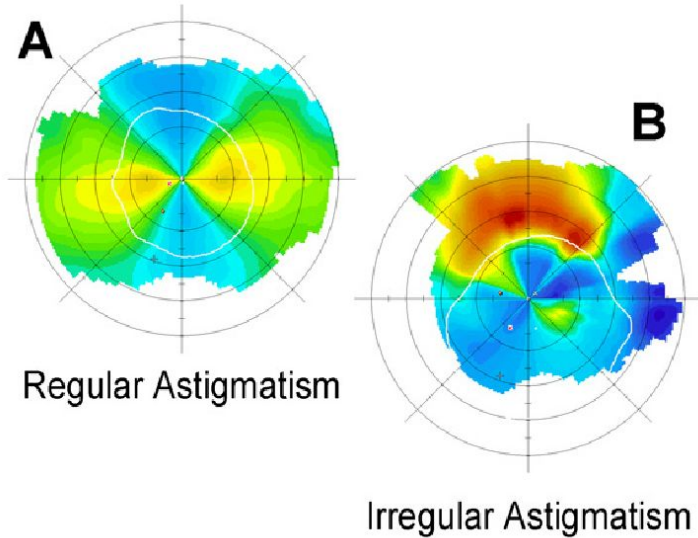
Abstract

Purpose

This study aimed to investigate the association of *Demodex* infestation with pediatric chalazia.

Case #5

Chalazia can induce irregular astigmatism



The News Feed



Published July 20, 2022 • By Staff
EYELIDS, NEWS

Study Identifies Risk Factors for Chalazia-induced Astigmatism

**Location, size and number of masses matter.
Researchers recommended prompt treatment
to avoid affecting visual acuity.**



**Chalazion in children may increase
risk of associated astigmatism.**

Photo: Joseph Sowka, OD. [Click image to
enlarge.](#)

Ouyang L, Chen X, Pi L, et al. Multivariate analysis of the effect of chalazia on astigmatism in children. BMC Ophthalmol. July 17, 2022. [Epub ahead of print].

- Incidence: The middle-upper eyelid was 50% (the highest) and the medial-upper eyelid was 42%.
- Type: There were more medium (54.5%) and large (54.7%) chalazia than in the control group (27.2%).
- Astigmatism: With multiple chalazia, the astigmatism incidence with two masses was 56%. The difference wasn't significant in chalazion with ≥ 3 masses. "Astigmatism vector analysis can intuitively show the differences between groups," the researchers noted in their paper. "The results are the same as refractive astigmatism."
- Refractive mean: The medial-upper, middle-upper and medial-lower eyelid were higher than the control group. The 3mm to 5mm and >5 mm groups were higher than the control group and <3 mm group. The >5 mm group was larger than the 3mm to 5mm group. The researchers pointed out that this suggests "that the risk of astigmatism was higher when the size of the masses was >5 mm."

Case # 6

- Pt with Hx of SLE- Lupus
- Prev used Plaquenil 200 mg BID po x 1 year. Recently D/C due to leg pain
- Scleral lens wearer x 2 years
- Presents w/ recent onset of eye soreness, tearing and redness x 1 week. VA not affected
- D/C scleral lens wear 2 days prior . No change in symptoms
- No current systemic meds
- Using PF artificial tears and lifitegrast BID OU



Case #6

- Cornea clear
- No A/C reaction
- DFE normal
- IOP 12
- OS clear
- VA 20/20- with glasses

Case #6

- Rx'd Loteprednol gtts QID x 1 week/Cold compresses QID
- Pt returned in 4 days with minimal improvement- redness slightly better but the eye still aches.
- IOP unchanged
- Next treatment option?
- Instilled 2.5 % phenylephrine gtt into the eye and waited 10 min



Case # 6

- Episcleritis vs Scleritis
- Episcleritis is usually a self limiting condition
- Simple (diffuse) vs nodular episcleritis
- Scleritis is categorized as diffuse, nodular and necrotizing
- Causes- idiopathic, autoimmune, surgically induced and infectious (HZV)
- Systemic disease workup -CBC/ CMP/ESR/CRP/HLA B27/RF/ANA/ACE/Chest X ray/FTA ABS/TB/Lyme

Case #6

- Rx Ibuprofen 800 mg TID po x 1 week
- Pt returned in 1 week with complete resolution
- Other treatment options:
- Flurbiprofen 100 mg TID
- Indomethacin 100 mg daily
- Naproxen (Aleve) 220 mg 6 x day OTC or Rx 500 BID
- Celebrex 100-200 mg BID

Case #6 Oral Steroids

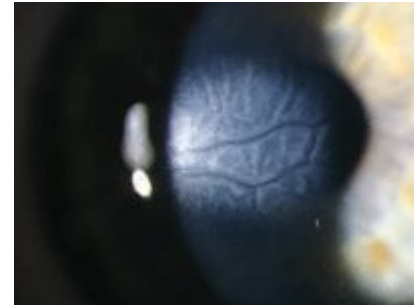
- Body weight calculations
- Category B
- Relatively safe for short duration
- Caution in patients with diabetes, GI issues, stomach ulcers and active infections

Case #6 Oral Steroids

- Side effects:
- Increased blood glucose levels
- HTN
- Osteoporosis
- GI pain, ulcers
- Bruising
- PSC/Increased IOP

Case #6 Oral Steroids

- Ocular Indications:
- Eyelids: Contact dermatitis, allergy, insect bites, poison ivy
- CME
- Uveitis, Scleritis
- TED/Graves
- GCA
- DLK



Case #6 Oral steroids

- Medrol Dose pack (methyl prednisone)- self tapering dosage
- 4 mg 6 x day first day
- Prednisone tablets
- Use in eye care is for short term treatment



Case #6

- NSAID contraindications:
- Hypersensitivity to NSAIDS
- Hx of allergic reactions to NSAIDs- urticaria/asthma
- GI bleeding issues/ulcers/H Pylori/ platelet dysfunction/ renal disease/cirrhosis
- Caution w/ anticoagulants
- Can increase risk of HTN, MI, cardiac ischemia
- Avoid in third trimester of pregnancy

Use of Pain Meds in Eyecare

- Short Duration
- Corneal Abrasions/RCE
- Trauma
- Neuropathic pain-Zoster “pain without stain” gabapentin/neurontin-Pain management
- Severe corneal ulcers?
- Post surgical especially PKP and PRK/PTK/CXL
- Most times topical NSAIDs/BCLs are sufficient -cycloplegia



Ibuprofen Plus Acetaminophen Equals Opioid Plus Acetaminophen for Acute Severe Extremity Pain

 PDF  Print  Comments

DAVID SLAWSON, MD, Director of Information Sciences University of Virginia Health System Charlottesville, Va.

 *Am Fam Physician.* 2018;97(5):348

Clinical Question

What oral analgesic combinations are effective for reducing the pain of an acute extremity injury in adults in the emergency department?

Bottom Line

In adults presenting to the emergency department with acute extremity pain severe enough to warrant radiologic investigation, ibuprofen plus acetaminophen was equally effective in reducing pain intensity at two hours compared with three different opioid and acetaminophen combination analgesics. In a similar study (Friedman BW, et al. *JAMA.* 2015;314(15):1572–1580), naproxen alone was as effective as naproxen plus oxycodone/acetaminophen or naproxen plus cyclobenzaprine (Flexeril) for reducing pain from acute musculoskeletal low back pain. It is time we stopped believing that opioids are superior to nonsteroidal anti-inflammatory drugs for acute pain control. We would save a lot of lives. (Level of Evidence = 1b)

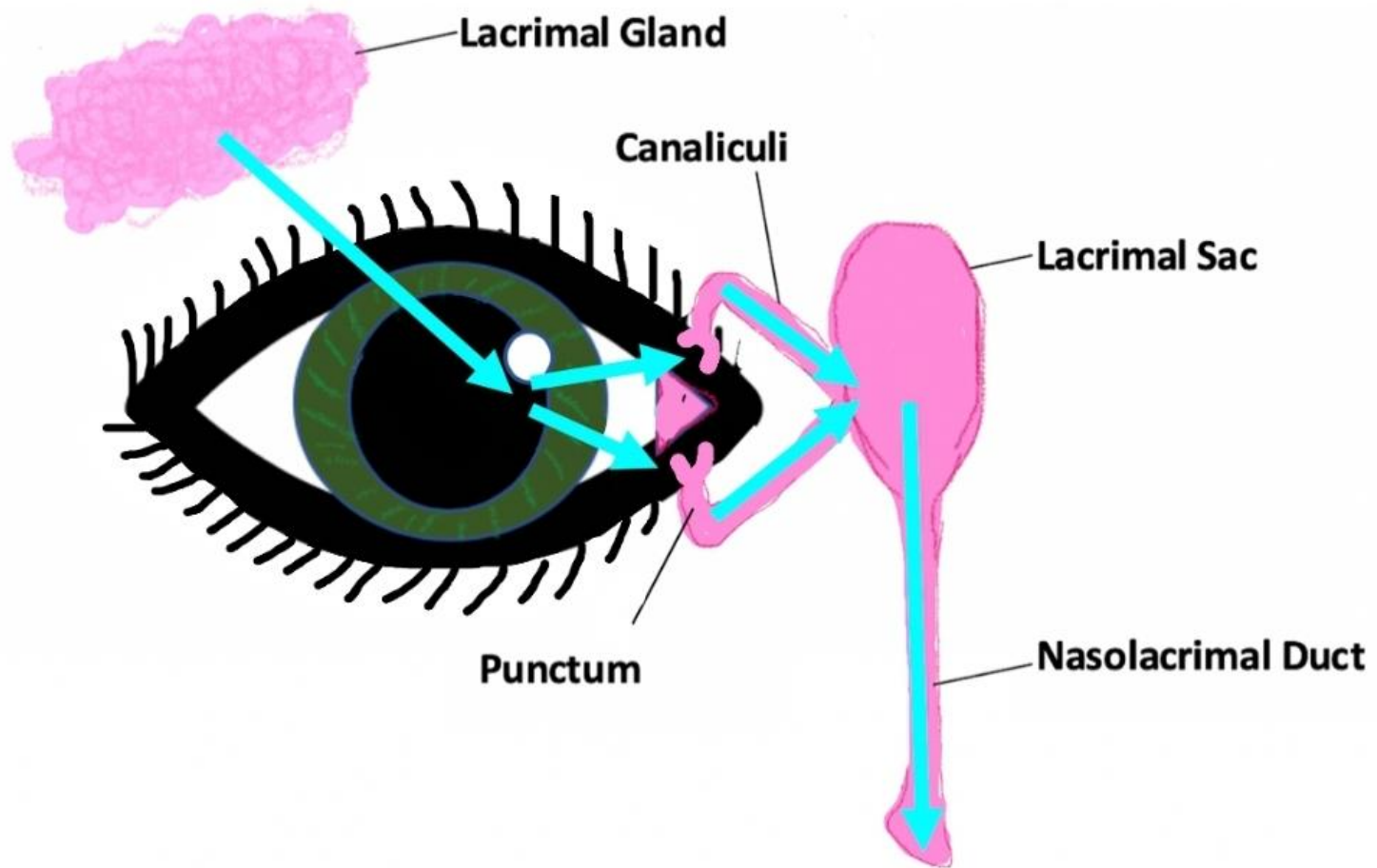
Case #7

- Pt presents with swollen inner corner of eye x 3 days. Noticed some crusting and tearing.
- Area is tender to the touch.
- Contralateral eye is fine
- No recent ocular trauma
- No pain on EOMS. VA normal. Temperature is normal.
- Hx of intra canalicular plug placed >10 years prior
- No drug allergies
- No liver/kidney dysfunction



Case #7

- Dacryocystitis
- Topical meds?
- Inflammation of the lacrimal sac
- Obstruction within the nasolacrimal duct causing backup and stagnation of tears within the lacrimal sac



Case #7

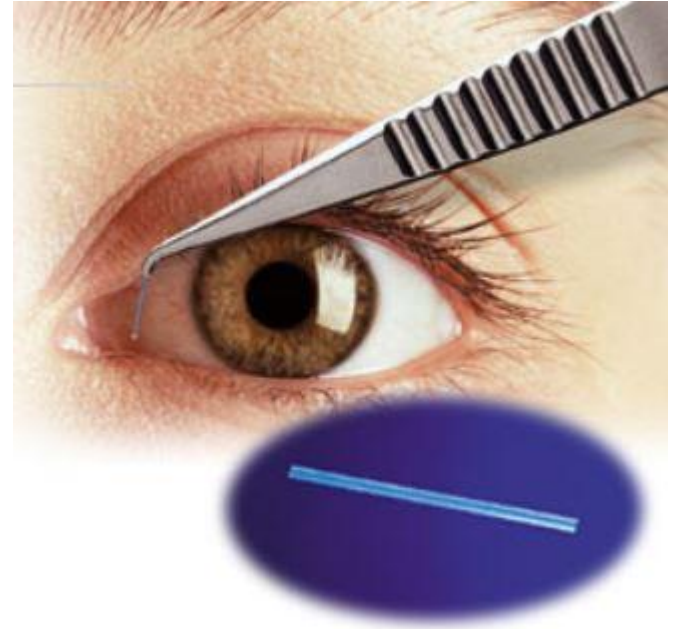
- NLDO- Nasolacrimal Duct Obstruction
- Acute vs Chronic
- Congenital (Valve of Hasner) 6 % of newborns vs Acquired - Involutional changes/Trauma/Surgery/Medications- Timolol/Pilocarpine/trifluridine
- Acute causes- duration less than 3 months
 - Infectious- Staph/Strep/H flu
 - Requires oral antibiotic therapy
- Chronic- requires surgical treatment (DCR)
- Dacryoliths- treat with Dilation and irrigation

Case #7

- Typically gram positive organisms
- Keflex 500 mg TID x 10 days
- If no improvement- refer to oculoplastics for evaluation and treatment
- Watch for development of orbital cellulitis- IV antibiotics

Case #7

- Punctal plugs can lead to pyogenic granulomas
- Treatment:
 - Antibiotic /steroid combo gtts
 - Timolol gtts 0.5% BID
 - Surgical treatment



ORIGINAL ARTICLE | [VOLUME 113, ISSUE 10, P1859-1862.E2, OCTOBER 2006](#)

 [Download Full Issue](#)

Management of Complications after Insertion of the SmartPlug Punctal Plug

A Study of 28 Patients

SmartPlug Study Group * • [Show footnotes](#)

Published: August 18, 2006 •

DOI: <https://doi.org/10.1016/j.opthta.2006.05.032>

Conclusions

Canaliculitis, acute dacryocystitis, and tearing may be seen in patients who have had SmartPlugs and may be managed by removal of the plug. A trial of topical and oral broad-spectrum antibiotics followed by retrograde massage of the plug through the canaliculus may be helpful should plug removal be deemed appropriate. If conservative measures fail, canaliculotomy with removal of the plug may be considered; DCR may be necessary. Although lacrimal irrigation may resolve the problem, irrigation also may dislodge the plug from its canalicular position and cause permanent obstruction of the lacrimal drainage system.

Just FDA approved: Lacrifill canalicular gel

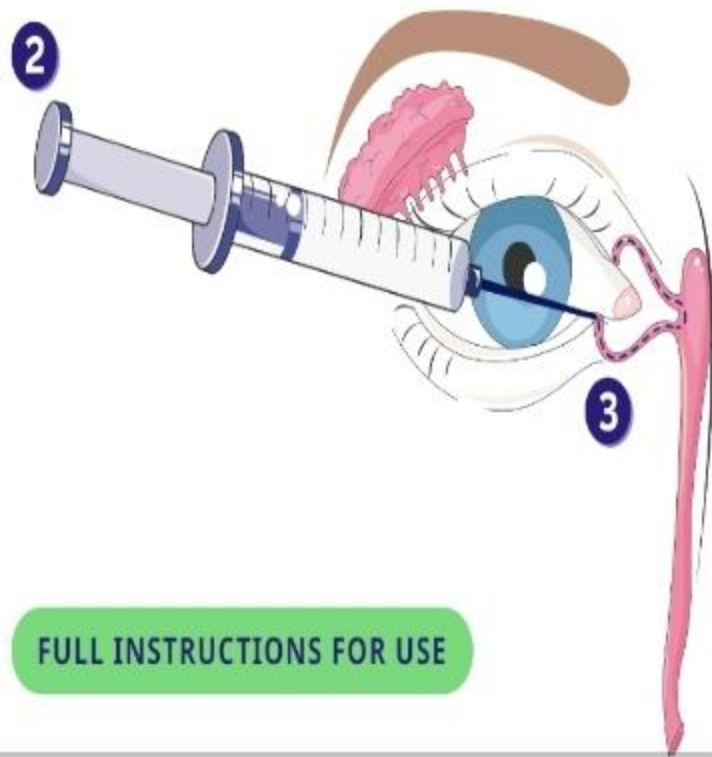
- The gel is a cross-linked hyaluronic acid derivative
- 6 month duration
- The gel treatment is customized for each patient to ensure the canalicular system is fully filled.

CPT code 68761



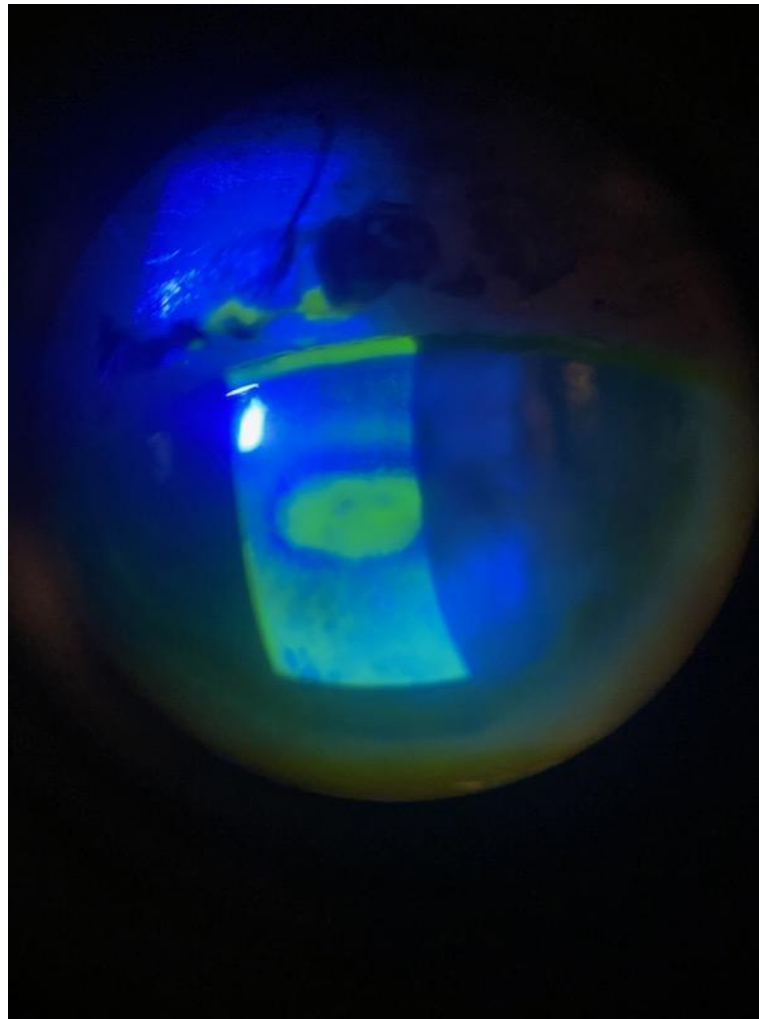
<https://www.nordicpharma.com/nordic-group-b-v-through-its-subsiary-nordic-pharma-inc-u-s-announces-the-launch-of-lacrifill-canalicular-gel-a-novel-therapy-for-dry-eye/>

- 1 LACRIFILL comes in a pre-filled injector with enough gel to treat the lower and upper canaliculi.
- 2 A cannula tip** is placed in the punctum and the LACRIFILL gel is inserted.
- 3 The gel flows through the punctum into the lacrimal sac.
- 4 If you see the gel extruding from the upper punctum, you know that both the upper and lower puncta have been blocked.



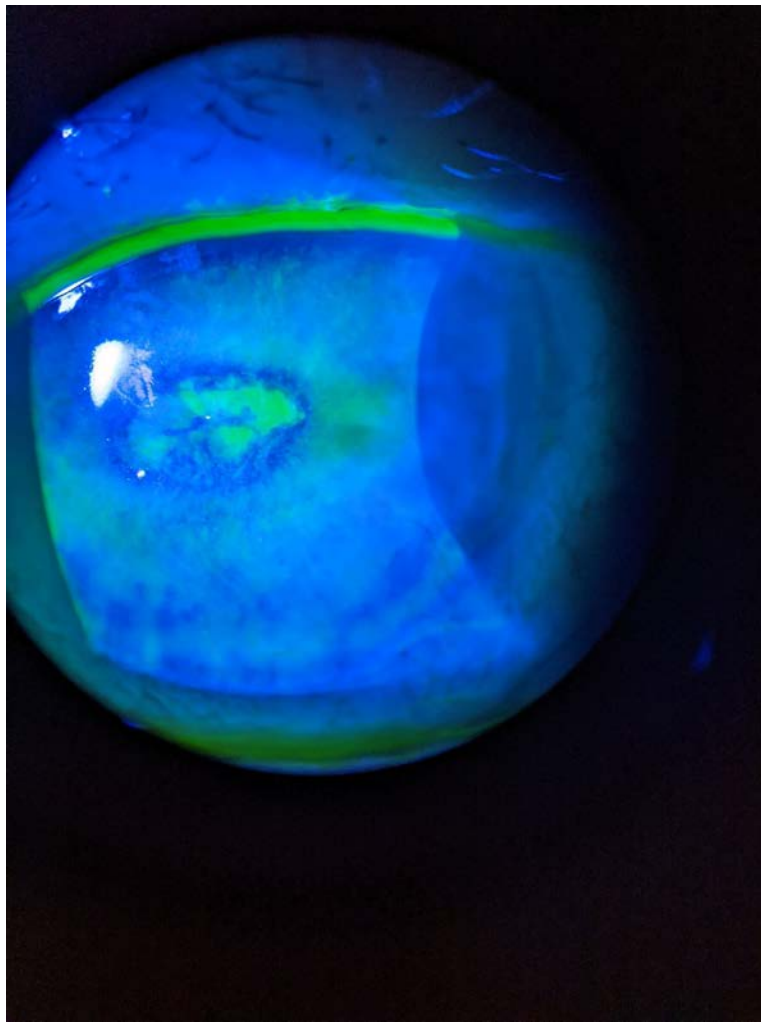
Case #8

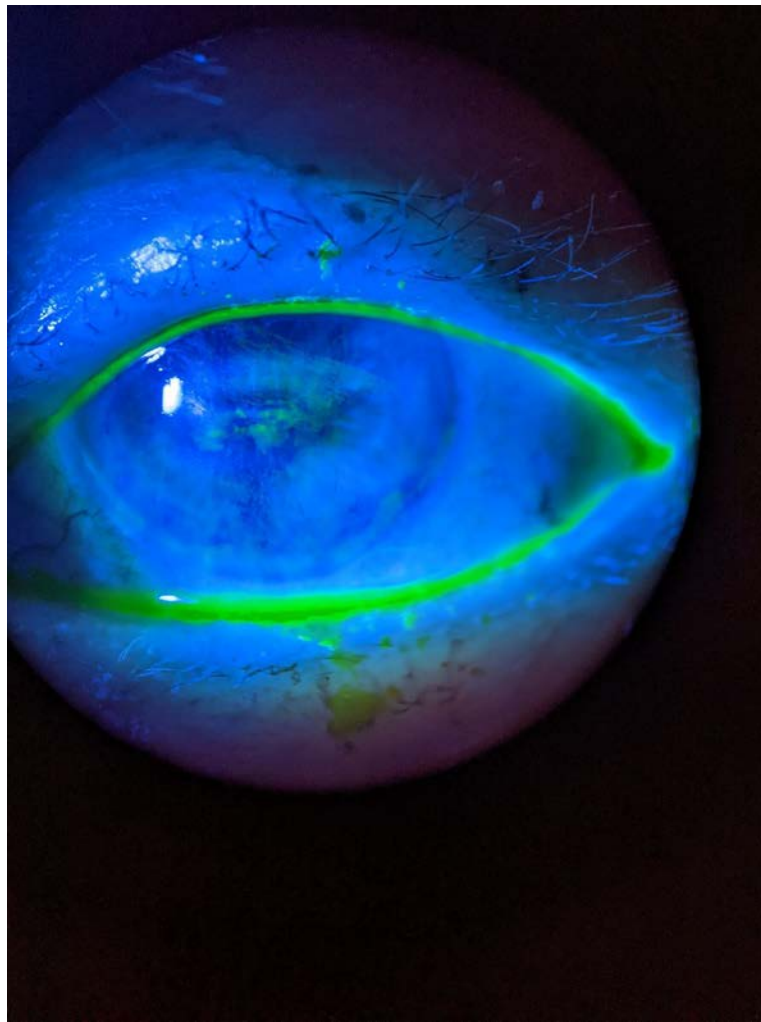
- 80 yo female
- Hx of recurrent HZO w/ corneal scarring OS. Prev RGP wearer -BCVA 20/50
- Referred by OMD for evaluation/treatment
- Treatment with multiple amniotic membranes, bandage contact lens, oral valacyclovir and topical ofloxacin/ Viroptic
- Uncorrected VA 20/200- PH 20/100
- Slit lamp evaluation- Dense HZO scarring centrally w/ area of pooling. No active dendrite/infiltrate. Anterior chamber clear IOP 10
- Area of pannus superiorly into lesion
- Started patient on moxifloxacin QID OS
- Corneal sensitivity absent



Case #8

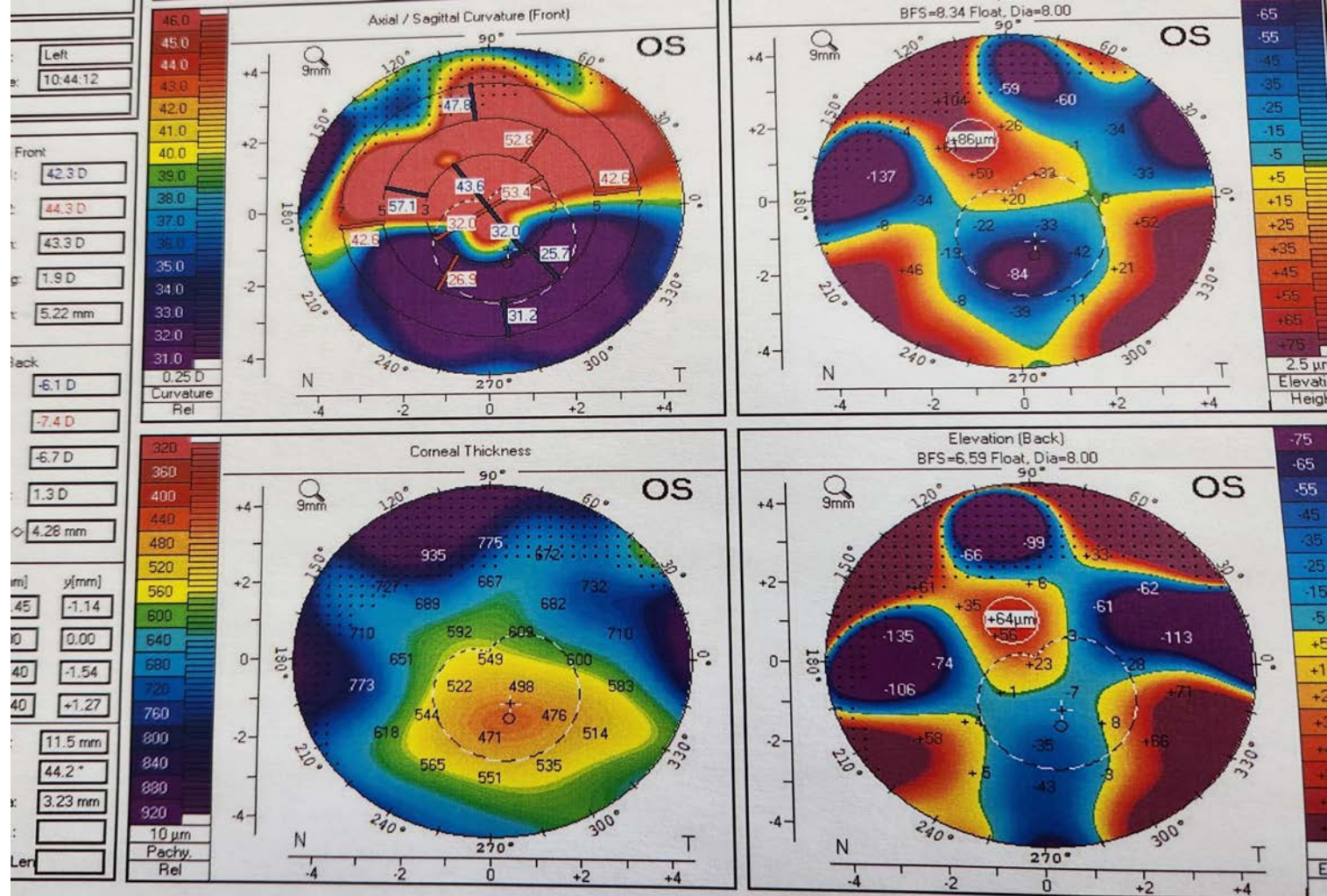
- Ordered cenergemmin- awaiting approval
- Maintenance dose of Valtrex 500 mg daily
- Follow up 2 weeks later
- Central pooling improved to previous. VA unchanged.
- Cenegermin approved and shipped to pt.
- Pt started meds and returned 2 weeks later.
- Continued improvement. Re-epithelialization over the next month

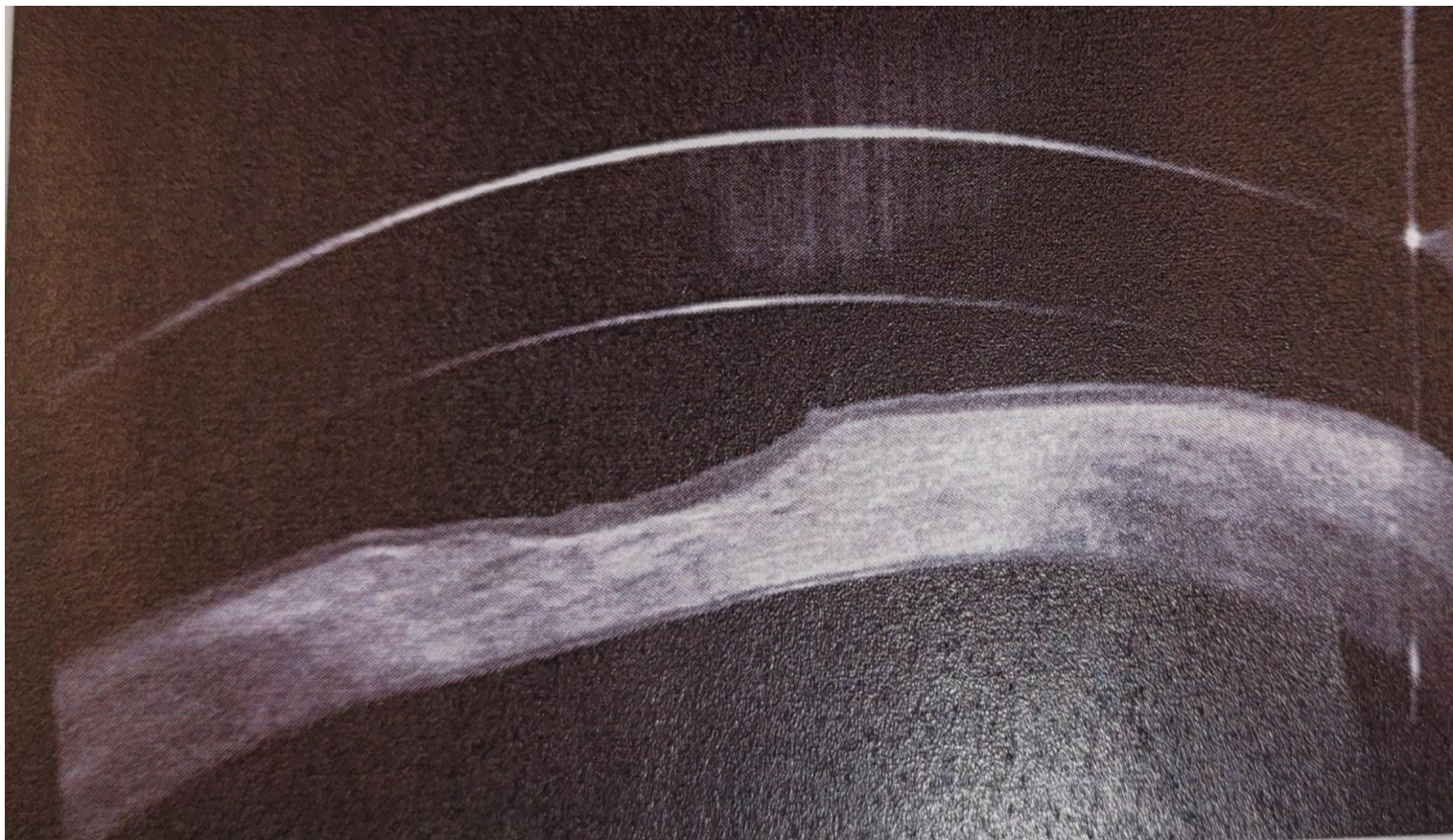


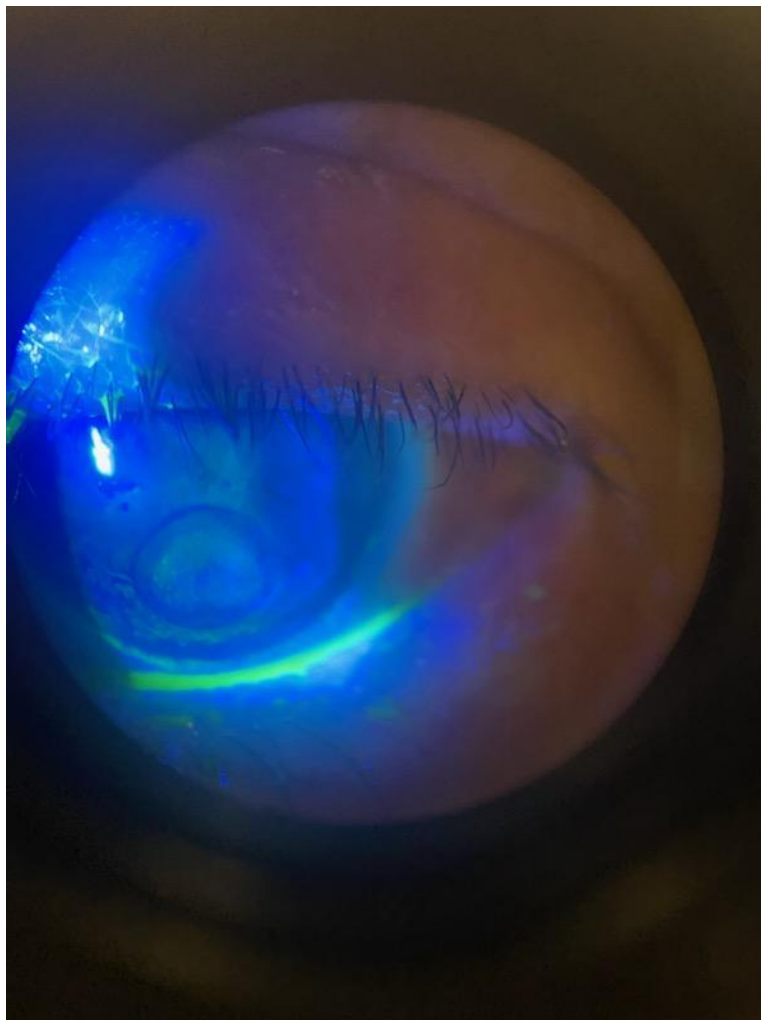


Case #8

- After re-epithelialization, Diagnostic scleral lens yielded 20/50 VA
- Discussed PKP with patient- other systemic medical issues made patient not a good candidate at this time
- Pt subsequently fit w/ scleral lens. Doing well. BCVA 20/40

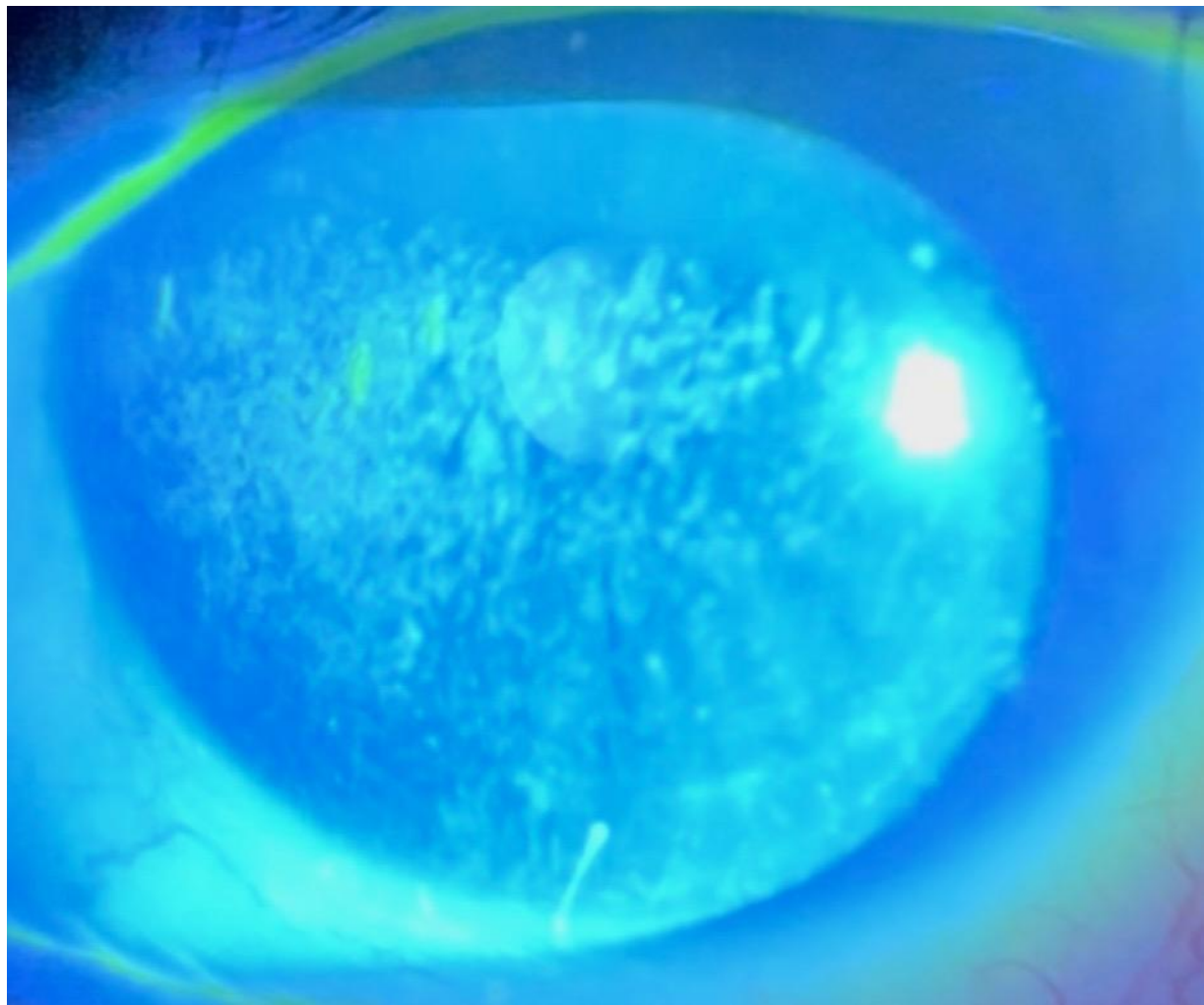


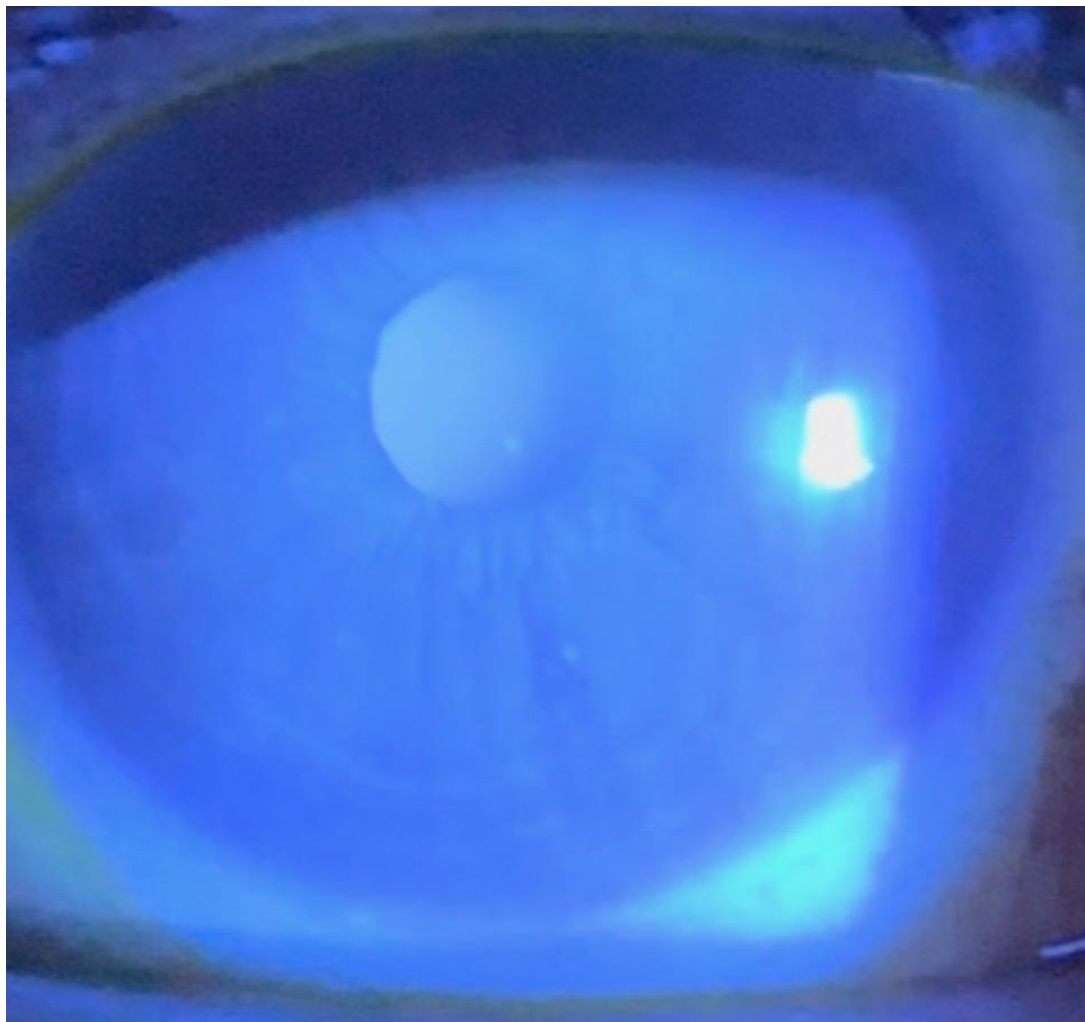


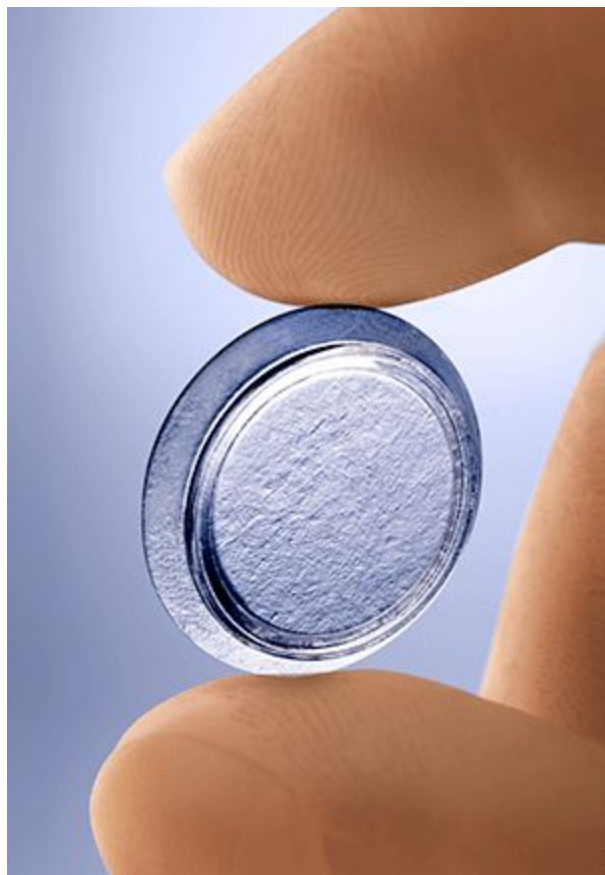


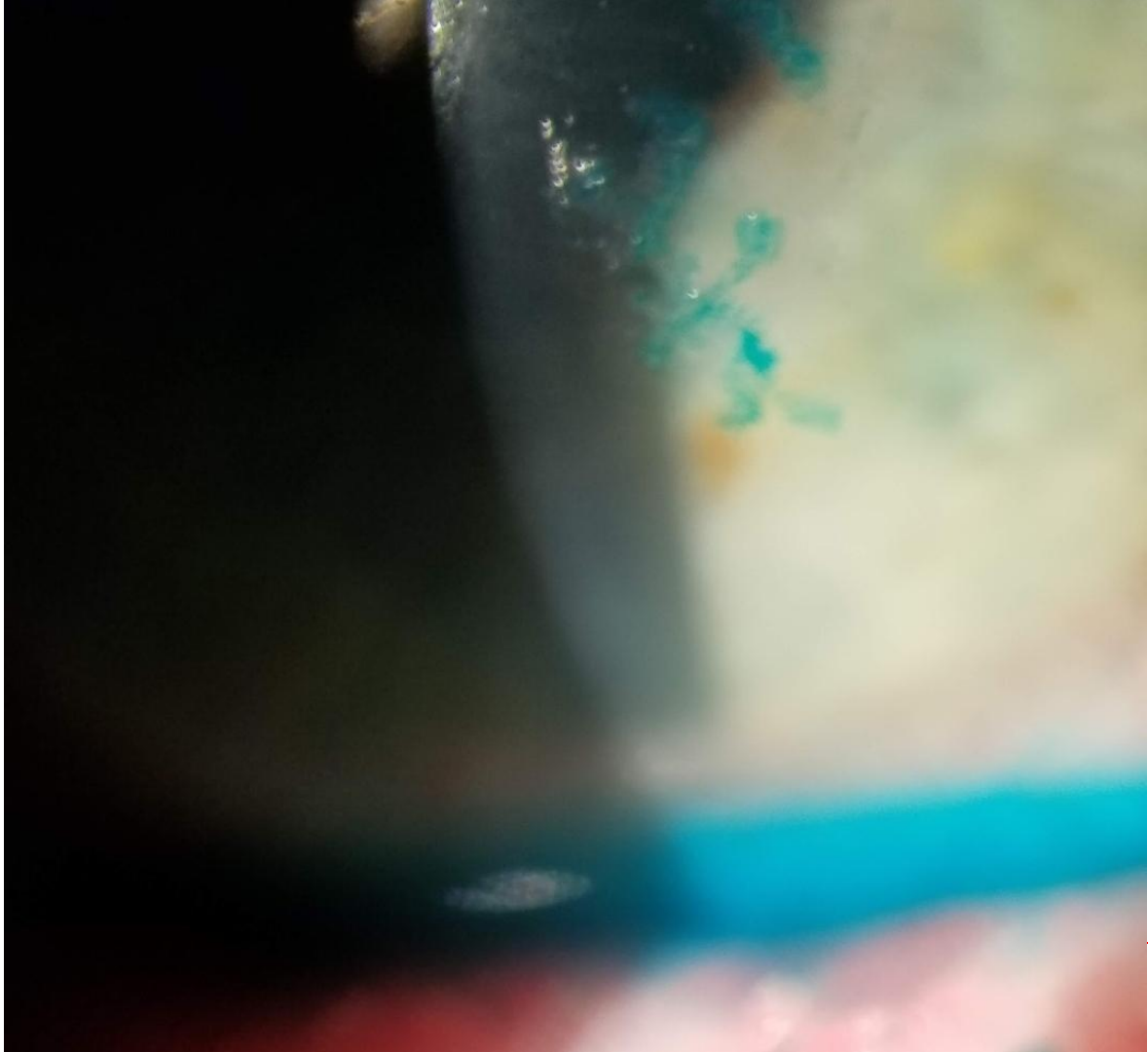
Neurotrophic Keratitis

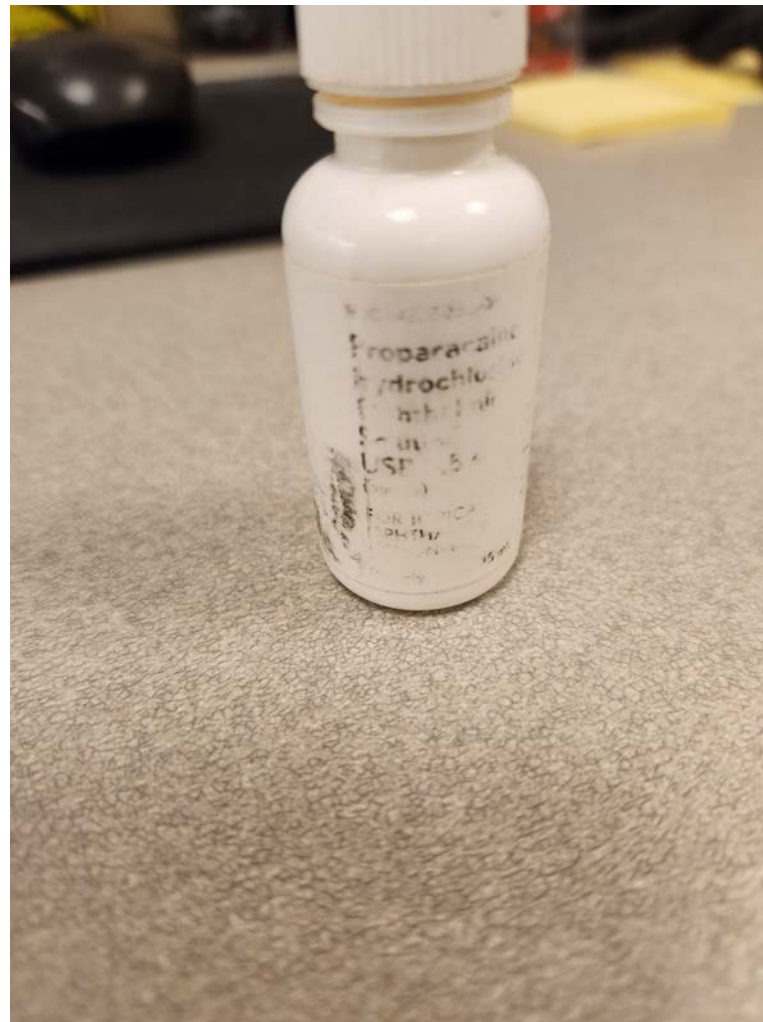
- **H. Simplex/Zoster**
- Cranial Nerve V palsy- neoplasia (**acoustic neuroma**), facial trauma, trigeminal neuralgia
- **LVC** (LASIK/PRK/AK) (also RK)
- Vitrectomy or PRP/retinal surgery
- Chemical burns/ **topical meds toxicity** (glaucoma meds). Anesthetic abuse
- Systemic disease- **DM**/Leprosy/Vitamin A deficiency/MS
- OSD- chronic DES- Mackie Stage 1. Persistent SPK











Neurotrophic Keratitis

- Reduction in corneal sensitivity causes breakdown in corneal epithelium and impaired corneal healing.
- Affects corneal homeostasis
- Corneal innervation from CN V



How do we test?



- Fine wisp of a cotton-tip applicator
- Dental floss (non- flavored)
- Cochet-Bonnet Esthesiometer
 - Contains a thin, retractable, nylon filament that extends up to 6 cm in length
 - The longer the filament, the more flexible it is, indicating that more corneal sensation is present
 - Check superior, temporal, inferior, nasal, central
- The Corneal Esthesiometer Brill (CEB) produces constant-pressure pulses of air at 5 levels of intensity, using a pressure range of 2 mbar (level 1) to 10 mbar (level 5).
- It can be handheld or placed in the slit lamp.



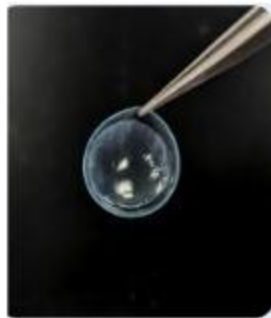
A noncontact handheld esthesiometer from BSI Systems.
Design and photo courtesy of Thomas L. Sabers, MD, PhD.

Neurotrophic Keratitis

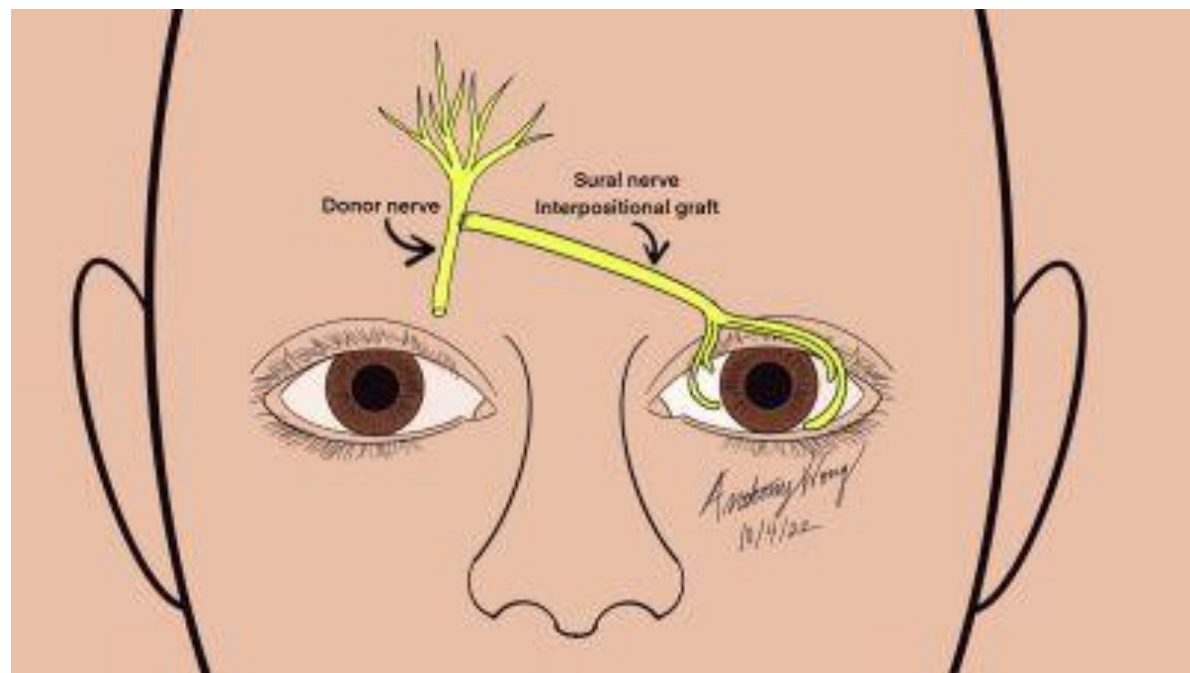
- Sutureless Amniotic membranes-
NEOX FLO
- Cryopreserved vs dehydrated
- Antiviral meds - HEDS/ZEDS
- ASED-Cost/blood draw/ Dilution
20-50% typically
- Scleral lenses
- Tarsorrhaphy
- Cenegermin- dosage 6 x day x 8 weeks
- Varenicline study?
- Surgical treatments- corneal
neurotization



CAM360 AmnioGraft



- BioTissue: (CAM360 AG), hydrated, shelf-stable cryopreserved amniotic membrane (CAM) solution that has been developed for the treatment of ocular surface disease and disorders.
- Ringless CAM that does not require refrigeration and includes adhesive properties so the CAM stays in place under a bandage contact lens (BCL).
- The solution instead has CryoTek and SteriTek preservation methods that retain HC-HA/PTX3 found in fresh tissue, which is in part responsible for amniotic membrane's therapeutic benefits



Topical Recombinant Human Nerve Growth Factor (Cenegermin) for Neurotrophic Keratopathy

A Multicenter Randomized Vehicle-Controlled Pivotal Trial

Stephen C. Pflugfelder, MD,¹ Mina Massaro-Giordano, MD,² Victor L. Perez, MD,³ Pedram Hamrah, MD,⁴ Sophie X. Deng, MD, PhD,⁵ Ladan Espandar, MD, MS,^{6,7} C. Stephen Foster, MD,^{8,9} John Affeldt, MD,¹⁰ John A. Seedor, MD,¹¹ Natalie A. Afshari, MD,¹² Wendy Chao, PhD,¹³ Marcello Allegritti, PhD,¹⁴ Flavio Mantelli, MD, PhD,¹⁵ Reza Dana, MD, MPH^{1,14}

Purpose: To evaluate the efficacy and safety of topical cenegermin (recombinant human nerve growth factor) in patients with neurotrophic keratopathy.

Design: Multicenter, randomized, double-masked, vehicle-controlled trial.

Participants: Patients with neurotrophic persistent epithelial defect with or without stromal thinning.

Methods: The NGF0214 trial, conducted among 11 sites in the United States, randomized 48 patients 1:1 to cenegermin 20 µg/ml or vehicle eye drops, 6 drops daily for 8 weeks of masked treatment. Follow-up was 24 weeks. Safety was assessed in all patients who received study drug. Efficacy was assessed by intention to treat.

Main Outcome Measures: The primary end point was healing of the neurotrophic lesion (persistent epithelial defect or corneal ulcer) after 8 weeks of masked treatment. Masked central readers measured neurotrophic lesions in randomized clinical pictures, then assessed healing status conventionally (<0.5 mm of fluorescein staining in the greatest dimension of the lesion area) and conservatively (0-mm lesion staining and no other residual staining). Secondary variables included corneal healing at 4 weeks of masked treatment (key secondary end point), overall changes in lesion size, rates of disease progression, and changes in visual acuity and corneal sensitivity from baseline to week 8.

Results: Conventional assessment of corneal healing showed statistically significant differences at week 8: compared to 7 of 24 vehicle-treated patients (29.2%), 16 of 23 cenegermin-treated patients (69.6%) achieved less than 0.5 mm of lesion staining (+40.4%; 95% confidence interval [CI], 14.2%–66.6%; $P = 0.006$). Conservative assessment of corneal healing also reached statistical significance at week 8: compared to 4 of 24 vehicle-treated patients (16.7%), 15 of 23 cenegermin-treated patients (65.2%) achieved 0 mm of lesion staining and no other residual staining (+48.6%; 95% CI, 24.0%–73.1%; $P < 0.001$). Moreover, the conservative measure of corneal healing showed statistical significance at week 4 (key secondary end point). Compared to vehicle, cenegermin-treated patients showed statistically significant reductions in lesion size and disease progression rates during masked treatment. Cenegermin was well tolerated; adverse effects were mostly local, mild, and transient.

Conclusions: Cenegermin treatment showed higher rates of corneal healing than vehicle in neurotrophic keratopathy associated with nonhealing corneal defects. *Ophthalmology* 2020;127:14-26 © 2019 by the American Academy of Ophthalmology. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

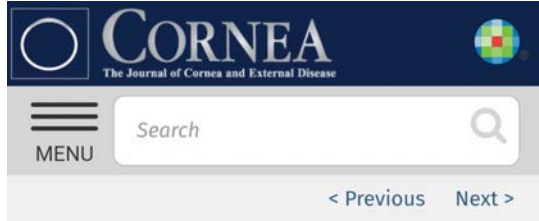


Supplemental material available at www.aaojournal.org.

Ocular surface integrity relies on the corneal nerves, which not only enable sensory-mediated reflexes (such as blinking and tearing), but also mediate production of trophic factors that critically help maintain corneal epithelium and the nerves themselves.¹ Corneal nerve damage may disrupt this homeostasis and lead to neurotrophic keratopathy (also known as neurotrophic keratitis or neurotrophic keratoconjunctivitis), a degenerative disease with an

estimated prevalence of 1.6 to 4.2 cases per 10 000 persons.^{1,2} Various conditions (such as ocular herpetic infection, ocular or neurologic surgery, trauma, diabetes, and dry eye disease) are associated with neurotrophic keratopathy³⁻⁵; however, correlations between underlying etiologies and neurotrophic keratopathy severity or clinical outcomes (such as visual acuity and corneal sensitivity) remain unclear.⁵

Neurotrophic Keratitis



CLINICAL SCIENCE

Topical Insulin—Utility and Results in Refractory Neurotrophic Keratopathy in Stages 2 and 3

 Soares, Ricardo José dos Santos Machado MD;
Arêde, Carlos MD; Sousa Neves, Filipe MD; da Silva
Fernandes, Joana MD; Cunha Ferreira, Catarina MD;
Sequeira, Joaquim MD

[Author Information](#) 

Cornea 41(8):p 990-994, August 2022. | DOI:
10.1097/ICO.0000000000002858

- Insulin eye drops
- 25 IU/ml QID
- Mechanism: Insulin-like growth factors promote epithelial cell development from limbal stem cells

Trefoil Therapeutics Announces First Patient Dosed in Phase 1 Study of TTHX1114 for Treatment of Corneal Epithelial Defects

January 18, 2023

Topical formulation of TTHX1114 has potential to accelerate the healing of epithelial defects – a leading cause of blindness worldwide

SAN DIEGO–([BUSINESS WIRE](#))–[Trefoil Therapeutics](#), a clinical-stage biotechnology company focused on restoring sight to people with corneal diseases, today announced the dosing of the first patient in its Phase 1 safety study evaluating TTHX1114 as a topical eye drop formulation designed to reduce

Corneal neuropathic pain

- Symptoms: burning, photophobia, tingling, hot.
- Corneal neuropathic pain is NOT dry eye, however these patients can have dry eye.
- DED-related neuro-sensory dysfunction accounts for the lack of association between signs and symptoms.



Corneal neuropathic pain, how do we test?

Proparacaine challenge



- If the pain is due to activity of ocular surface nerve fibers, it should improve with a topical anesthetic.
- If it involves abnormal activity at higher levels of neural pathways, pain may persist.

Other diagnostic testing:

- Confocal microscope
- Corneal sensitivity-cotton swab
 - Dental floss
 - Cochet-bonet esthesiometer
 - Brill non contact esthesiometer



Corneal Neuropathic pain: Treatment Options?

- Conventional treatments: topical steroids
 - Autologous serum/PRP
 - Scleral lenses
 - Punctal plugs
 - Immunomodulators
 - Regener Eyes- recent issues
 - Amniotic membranes
- Pain management -co manage with neurologist/pain management specialist/mental health
- Gabapentin/LDN (low dose naltrexone)/ Pregabalin(Lyrica)

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The neuropathic pain: An overview of the current treatment and future therapeutic approaches

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First-line therapy	Gabapentinoids	Gabapentin	150–600 mg/day	Lethargy, vertigo, peripheral swelling, blurred vision	Second-line therapy	Opioids	Tramadol	25–400 mg/day	Nausea/vomiting, constipation, lethargy, seizures, ataxia
		Pregabalin	300–3600 mg/day	Lethargy, vertigo, peripheral swelling, increased body weight			Tapentadol	50–600 mg/day	Nausea/vomiting, constipation, lethargy, seizures, ataxia
						Topical treatment	Lidocaine	5%	Local erythema, patches itching and rash or gel
	Tricyclic antidepressants (TCAs)	Amitriptyline	10–150 mg/day	Anticholinergic effects, QT prolongation (arrhythmia), suicide risk, urinary retention	Third-line therapy		Capsaicin	8%	Pain, erythema, patches itching; rare cases of high blood pressure
						Strong opioids	Morphine	10–120 mg/day	Nausea, vomiting, constipation, dizziness and lethargy
							Oxycodone	10–120 mg/day	Nausea/vomiting, constipation, lethargy, respiratory control
	Serotonin–norepinephrine reuptake inhibitors (SNRI)	Duloxetine	20–120 mg/day	Nausea, lethargy, constipation, ataxia, dry mouth		Neurotoxin	Botulinum toxin	25–300 U BTX-A 0.9% saline	Pain at injection site
		Venlafaxine	150–225 mg/day	Nausea, vertigo, lethargy, hyperhidrosis, hypertension					

What to look forward to?

- **First investigational drug for neuropathic corneal pain: OK-101**
- The study of 240 participants with dry eye disease, who were randomized into three cohorts and dosed twice daily with 0.05% OK-101, 0.1% OK-101 or vehicle for 12 weeks after a 2-week run-in period on placebo.

OK-101 (0.05%) ophthalmic solution

- A lipid-conjugated chemerin peptide agonist.
- Significantly reduced ocular pain and improved TBUT as early as day 15. Conj staining and blurred vision improved day 29.
- The treatment also improved multiple symptoms, including pain, burning, stinging, eye dryness and itching, within the first 2 weeks of treatment, as reported in patient daily diaries.
- Treatment-emergent adverse events were comparable between placebo and treatment groups, with no severe drug-related ocular events observed.

Any questions?

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