

Update on Dry Eye Treatments

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Financial Disclosures

- Aerie Pharmaceuticals
- Allergan
- Dompé
- Eyevance Pharmaceuticals
- Horizon
- Kala Pharmaceuticals
- Johnson and Johnson Vision Care, Inc
- Novartis
- NovaBay Pharmaceuticals
- Ocular Therapeutix
- Science Based Health
- Sight Sciences
- Sun Pharma
- Zeiss
- Tissue-Tech



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Objectives

- Ubiquity of Dry Eye Disease
- Learn about the newest treatments tools for DED
- Learn about the new drugs and new treatments coming to market
- Case management



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Introduction

- Why is Dry Eye Disease (DED) such a big deal?
 - 30M people have it
 - 15M people Dx
 - 1.5M people treated



Dry Eye Disease designation



1. Baudouin C, Irkeç M, Messmer EM, et al. Clinical impact of inflammation in dry eye disease: proceedings of the ODISSEY group meeting. Acta Ophthalmol. 2017 Apr 8.

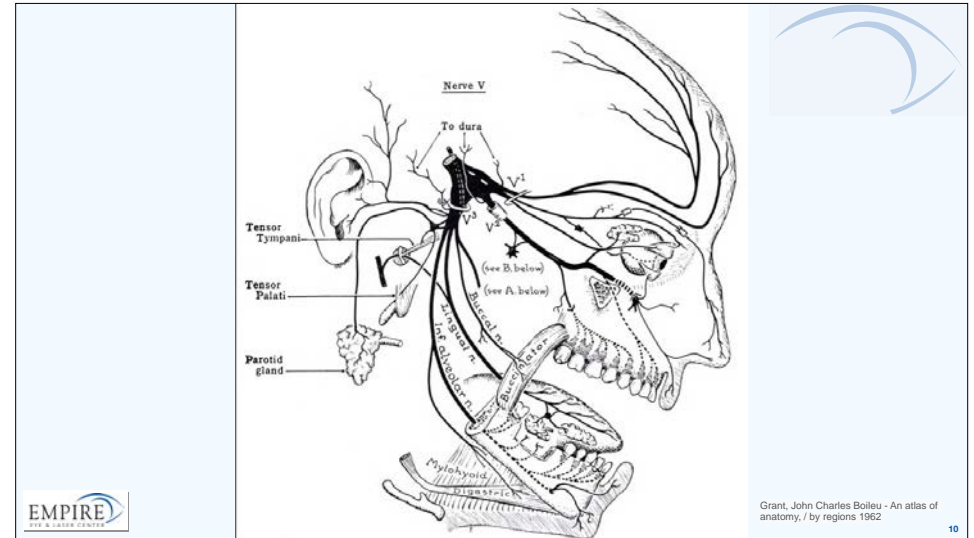
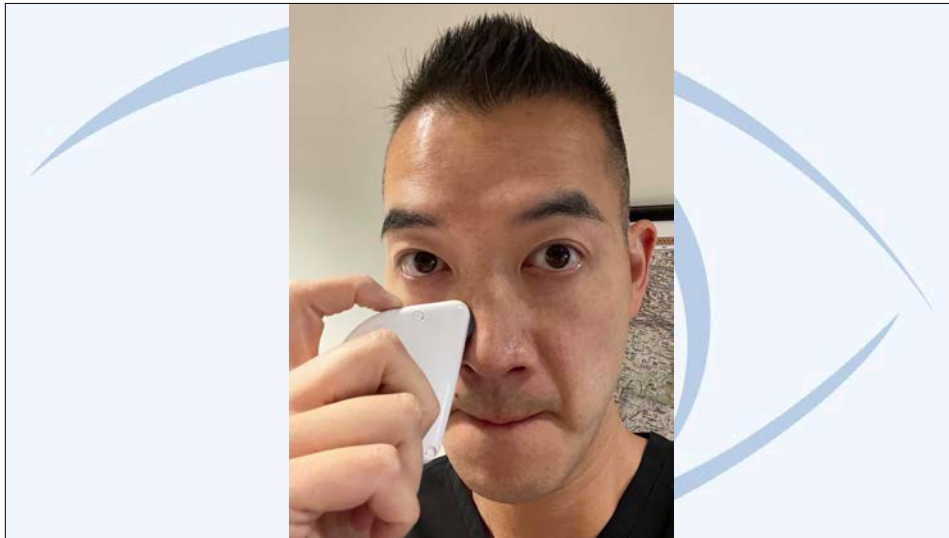
What's New in Treatment and What's Coming?

- iTear100 by Olympic Ophthalmics
- Regener-eyes forte and lite
- Radio frequency
- Low level light therapy
- Tarvaya by Oyster point
- Theravision drug eluting contact lens by Johnson & Johnson
- AR-15512 by Aerie pharmaceuticals
- Reproxalab (RASP inhibitor) by Aldeyra
- NOV-03 by Bausch & Novaliq

iTear100 by Olympic Ophthalmics

- FDA approval in US May 2020
- Soft launch
- Not electrical stimulation
- Vibration stimulation of Trigeminal nerve -> Lacrimal Functioning Unit
- LFU -> basal tears, meibomian glands, and mucin stimulation





“Tyrvaya” by Oyster Point Pharma

- Varenicline 0.03 mg
- PF free nasal spray BID
- Designed to stimulate the trigeminal parasympathetic pathway to promote natural tear film production
- Acts nicotinic acetylcholine receptor to release selected proteins, peptides, antibodies, hormones, enzymes or cytokines secreted from the lacrimal gland into the tear film and onto the ocular surface
- Rapid onset of action within 5 minutes
- FDA approval 18 October 2021
- Available Nov 2021

Regener-eyes

- Biologic eye drops
- Contains anti-inflammatory cytokines, chemokines for healing, growth factors and Hyaluronic acid (HC-HA/PTX3)
- Professional strength and “Lite”
- Think of it as amniotic membrane tissue in a drop



Low Level Light Therapy - “Red” light therapy

- First developed in dermatology
- Red light or near infrared light excites the mitochondrial chromophores which releases energy to heal and repair tissue
- In dermatology, LLLT has beneficial effects on wrinkles, acne scars, hypertrophic scars, and healing of burns.
- In the US, Marco Equinox
- 3 x 15 mins treatment



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Radiofrequency

- Uses radio waves to selectively warm tissue
- Lower frequencies delivered to the dermis and epidermis can:
 - Stimulate collagen production
 - Stimulate elastin production
- Good at melting meibum and reducing fine lines and wrinkles (crow's feet)



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AR-15512 by Aerie Pharmaceuticals

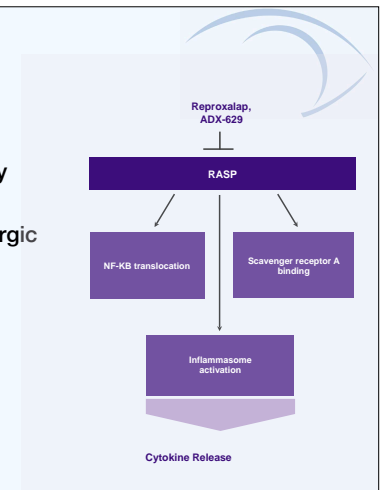
- Selective agonist for the TRPM8 cold thermoreceptor
- Provides cooling sensation to relieve ocular discomfort and increase tear production (basal tear, not reflex)
- TRPM8 receptors also help modulate blinking¹
- Currently in phase 3 trials, expected results Q3 2021

1. Quallo, T., Vastani, N., Horridge, E. et al. TRPM8 is a neuronal osmosensor that regulates eye blinking in mice. Nat Commun 6, 7150 (2015).

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ADX-629 by Aldeyra

- Reproxalap - RASP inhibitor
- RASP works in the initial phase of the inflammatory cascade that cause release of cytokine
- Currently studied in 2 phase 3 studies for both allergic conjunctivitis and dry eye disease
- Rapid onset of action (within 1 day based on early data)
- Helps reduce redness



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NOV-03 by Novaliq & Bausch

- Perfluorohexyloctane
- First drug to treat evaporative dry eye disease
- Works to stabilize the lipid layer
- Can potentially penetrate meibomian glands and dissolve thickened meibum
- Released favorable results from 1st phase 3 trial (April 2021)
- Currently in 2nd phase 3 (Mojavi) and 12 month safety trial (Kalahari)

Take home points

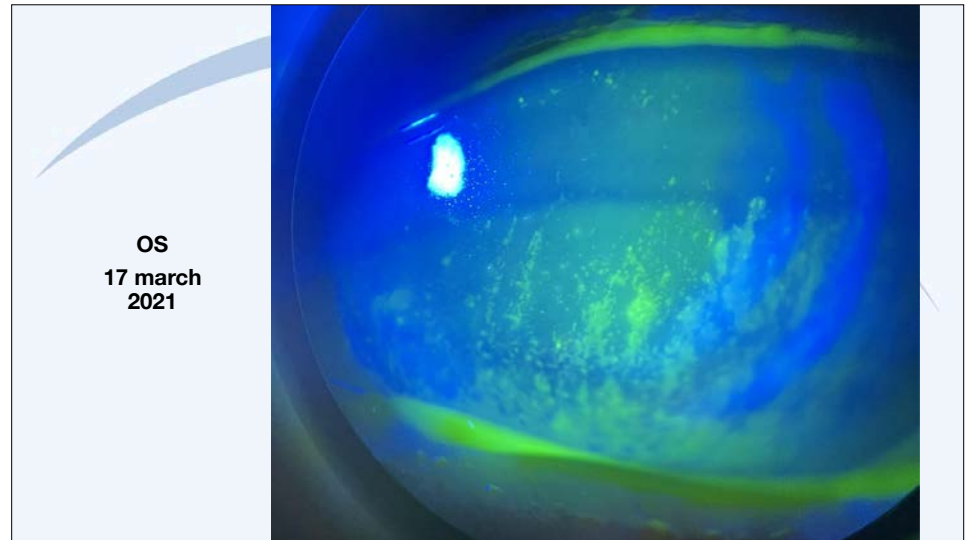
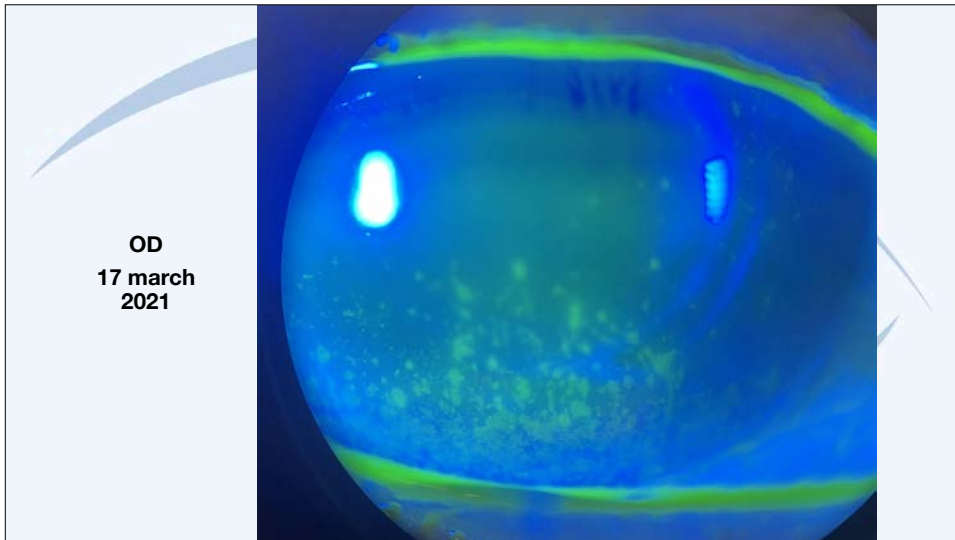
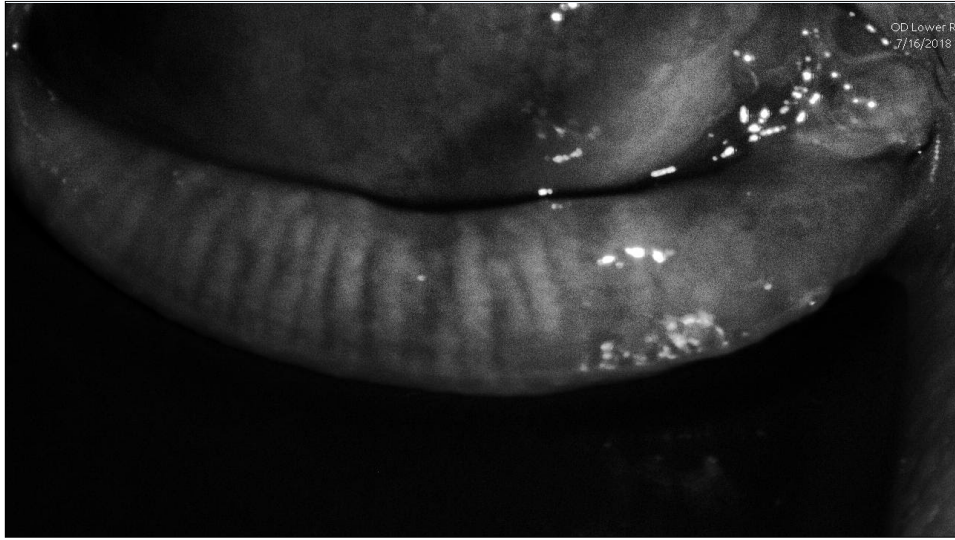
- Exciting times
- Lots of cool new treatment options

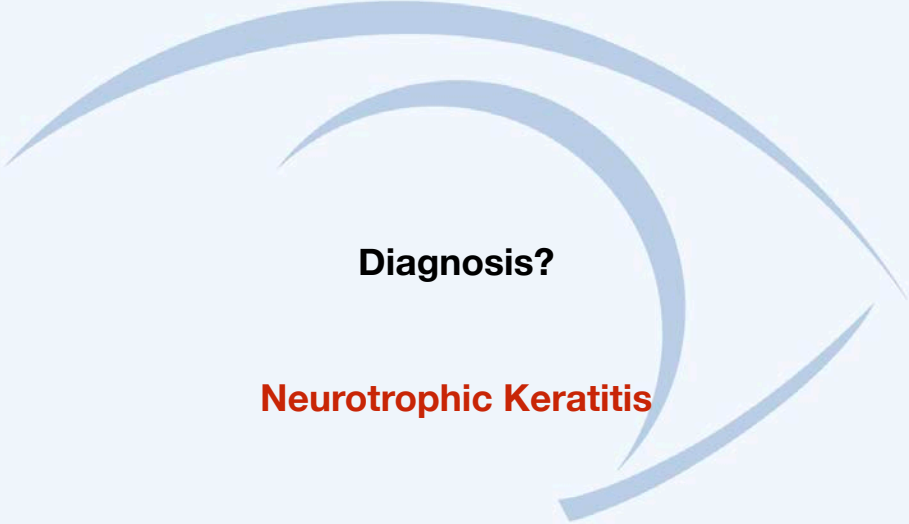
Case IS

- 1st saw her in 2016
- 64 yo hispanic
- PMHx: DM, SLE, hyperlipidemia, asthma, HTN
- POHx: CE w/ IOL 2002 OU, h/o chalazion, blepharitis, MGD, KCS
- Pertinent Meds: Januvia, Hydroxychloroquine, Flonase,

Case IS

- Ocular meds: Refresh optive TID OU
- August 2017 -started her Restasis BID OU
- September 2017 - SPK improved. Treat MGD with lipiflow
- November 2017 - Lipiflow OU
- January 2018 - KCS/MGD improved
- April 2018 - KCS worsens, inc Restasis to TID OU
- June 2018 - still dry, rec collagen plugs. Keratinization on MGs, start maxitrol ung





Diagnosis?

Neurotrophic Keratitis



Case IS

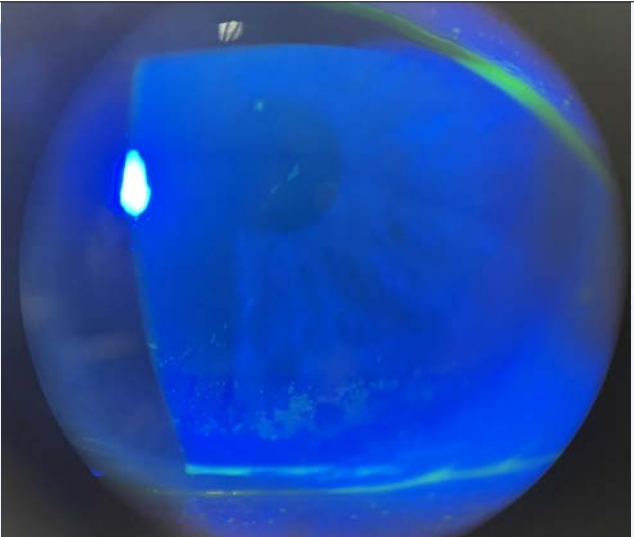
- Plan: Started Oxervate OU on 19 April 2021
- Finished Oxervate on 10 June 2021



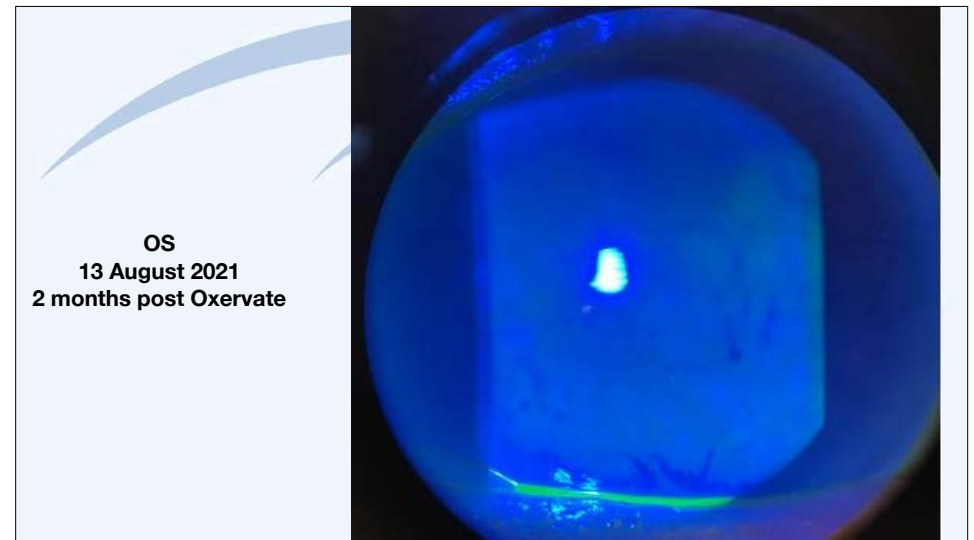
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OD
30 June 2021



OS
30 June 2021



Pathophysiology of NK

- Impaired CN V innervation
- Reduction in release of neuro-mediator
- Decreased tear production, blink reflex
- Decreased corneal epithelial renewal and healing rate
- Corneal epithelial breakdown and epithelial defects -> corneal ulceration -> stromal melting -> perforation

Questions?

Case MB

- CC/HPI: 38 HF presents dec VA OD>OS X 2 weeks, “starbursts around lights, double vision”, wears colored contacts, referred by OD at Stanton optical
- Ophthalmic meds: none
- Systemic meds: none
- Family Hx: unremarkable
- Allergies: none

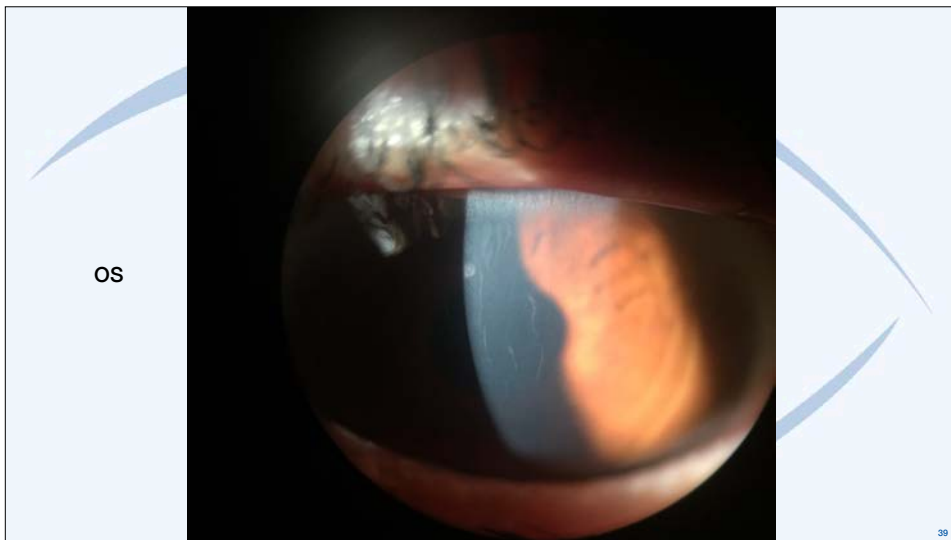
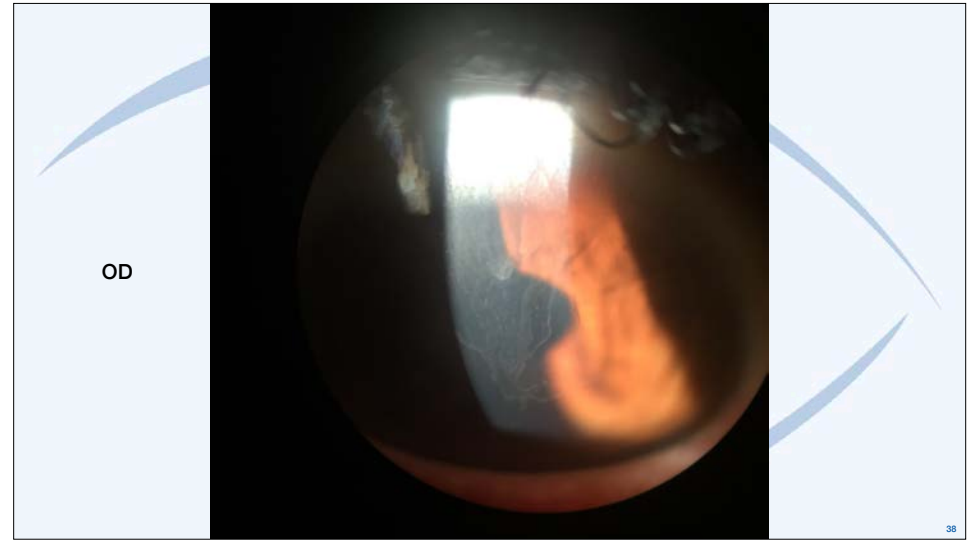
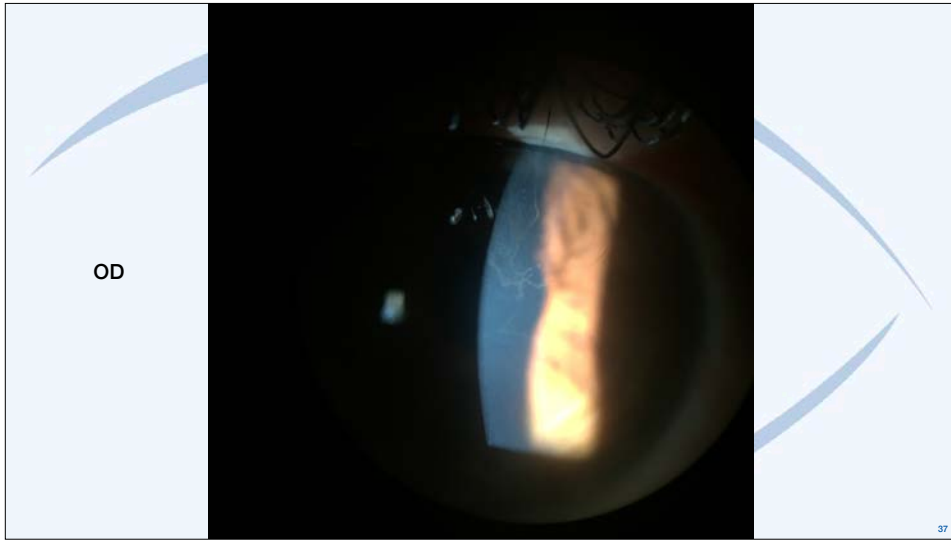
Case MB

- VA cc CTLs: **20/80-2 PHNI OD, 20/70+1 PH 20/60 OS**
- Pupils: PERRLA (-)
- EOM: FROM OU
- VF: FTFC OD/OS via CVF
- IOP: OD: 17 mmHg, OS: 17 mmHg with iCare rebound tonometry

Case MB

- Slit Lamp Exam:
- Lid margin: **1+ MGD OU**
- Conj: **1+ injection OD, tr-1+ injection OS**
- K: **1+ corneal neovascularization OU 360, limbal whorls superiorly onto cornea OU, central stromal scarring OD, 2 + PEK OD and 1+ PEK OS**
- Everything else unremarkable





Diagnosis?

Limbal Stem Cell Deficiency

Case MB

- Treatment included cAMT (prokera) which +/- helped
- Heavy lubrication
- No contacts
- Pred forte QID initially -> tapered to BID for 3 months



Limbal Stem Cell Deficiency (LSCD)

- Limbal stem cells (LSCs) help renew and regenerate corneal epithelium¹
- LSCs keep the cornea clear and prevent the invasion of the conjunctiva onto the cornea¹
- Palisades of Vogt houses the LSCs²
- Direct damage to LSCs lead to LSCD¹
- Corneal epithelium is replaced by conjunctival epithelium cells which is the “waterfall” appearance¹
- Neovascularization can also occur¹



Questions?



AR - “Mucous in my eye”

- CC/HPI: 34 yo HF presents with mod-severe dryness OU x 5 years, “white mucous discharge”. Light sensitive, itching OU on/off. Gtts helps a little.
- LEE: 7 month prior
- Ocular meds: Restasis BID OU x 1.5 years. Refresh tears QD OU and Refresh liquigel QHS OU
- Med Hx: unremarkable



AR

- VAcc: 20/20 OD/OS
- Pupils: PERRLA (-)
- EOM: FROM OU
- VF: FTFC via CVF
- IOP: OD: 15 mmHg, OS: 16 mmHg with iCare rebound tonometry

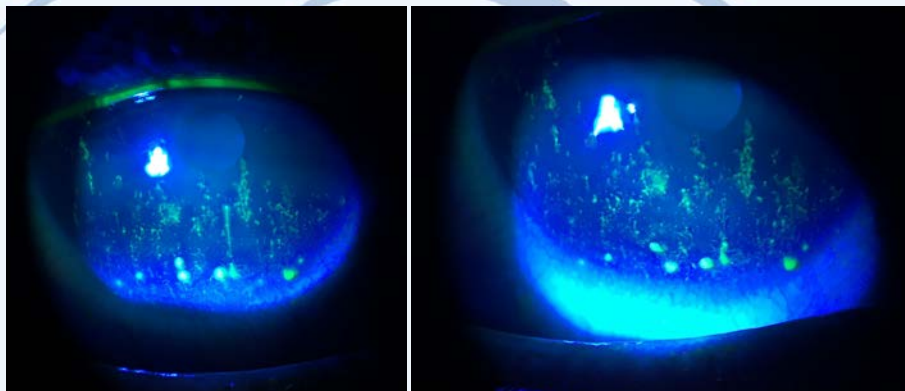


AR

- Slit lamp exam:
- LL: **1+ MGD OU**
- C: **1-2+ injection, conj staining with NaFL and LG OU**
- K: **see next slide**
- Everything else unremarkable



OD



Poll 3 - DDx?

- HSV K
- Filamentary Keratitis
- Exposure Keratitis
- Salzmann nodular degeneration



Diagnosis

- Filamentary Keratitis OU - early filament buds
- K. Sicca OU
- MGD OU



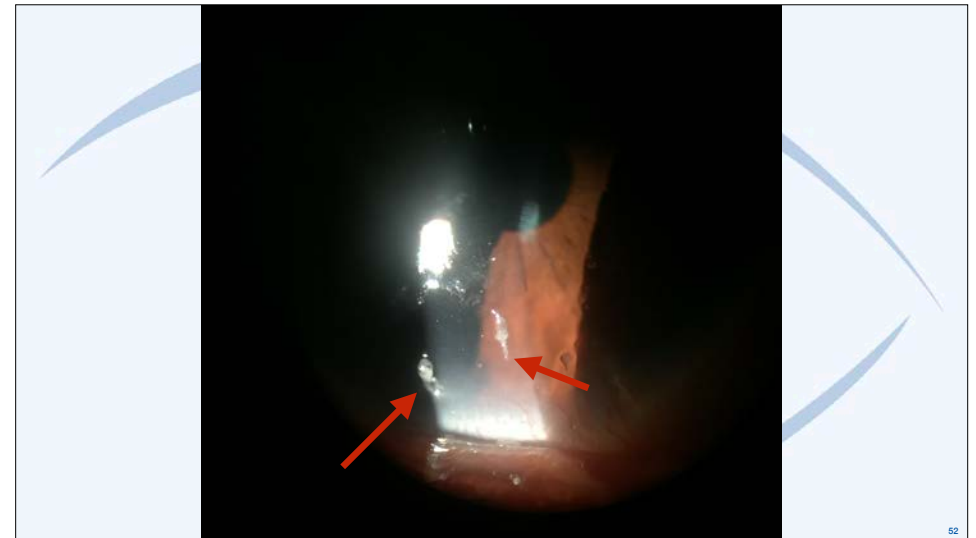
Treatment/Follow up

- Pt was cash pay. Couldn't afford corneal filaments removal
- Rec increasing restasis QID OU
- Add Flarex BID OU to control inflammation
- RTC 1 month



AR - Follow up #1

- CC/HPI: 34 yo HF presents mild imp since last visit
- Ocular meds: Restasis QID OU, Flarex 0.1% BID OU
- Med Hx: unremarkable



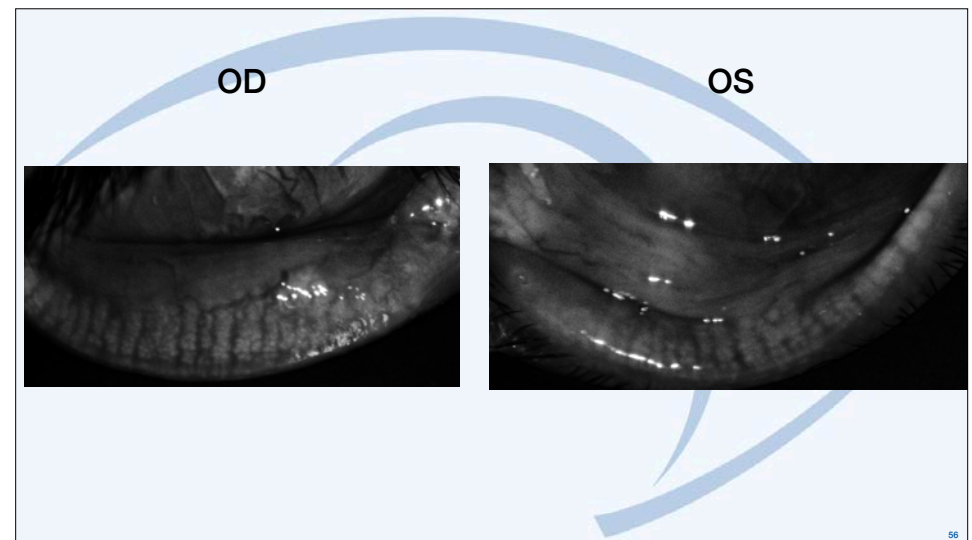
Diagnosis/Treatment

- Filamentary Keratitis OU - Worse with full filaments
- K. Sicca OU
- MGD OU

- Filaments removed OU, initiate compounded 10% acetylcysteine gtts OU
- D/c restasis and switch to Cequa BID OU, cont Flarex
- RTC 1 month

AR - Follow up #2 (1 month later)

- CC/HPI: 34 yo HF presents mild imp since last visit
- Ocular meds: cequa QID OU, 10% Acetylcysteine gtts QID OU, Flarex 0.1% BID OU



Assessment/Plan

- Filamentary Keratitis OU - worse despite 10% acetylcysteine drops
- Keratoconjunctivitis Sicca OU - underlying cause of Fil K
- MGD OU - lipiscan mild dropout OS>OD with poor expressibility of MGs
- Removed filaments with jewelers forceps, cont acetylcysteine QID OU
- +/- imp with Cequa. Cont meds for now
- Initiate home therapies with warm compresses and omega 3/6 supplements
- Due to insurance issues she transferred her care to another provider

Filamentary Keratitis

- Cornea-mucus findings are pathognomonic
- Focal "head" aka filament buds with sometimes a strand like "tail"
- Mechanism - core of filament is desquamated epithelial cells surrounded by mixture of conjunctival epithelial cells and muffsins^{1,2}
- Eyelids acting like squeegee and creating the filaments

Treatment for Filamentary Keratitis

- Corneal filament removal
- Mucolytic agent (bronchial disease to thin mucus buildup) like Mucomyst (Acetylcysteine) - Compound only
 - O'Brien pharmacy (Kansas) or Nora apothecary (Indiana)
- Soft BCL to decrease friction
- Amniotic membrane
- Long term management of underlying issue

Questions?

A stylized graphic of an eye, composed of several overlapping, curved blue lines that form the shape of an eye, set against a light blue background.

Questions?

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Thank you!

