


Managing Neurotrophic Keratitis with Contact Lenses

Planning for a Painless Problem

A Case Series
Avani Dave OD FAAO



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Financial Disclosure Statement

Avani Dave has received honorarium from Boston Sight. She is on the Speaker Bureau for Bausch and Lomb Specialty Vision Products, Bausch and Lomb Pharmaceuticals and Tarsus Pharmaceuticals.
All relevant relationships have been mitigated



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Objectives

- Identify and Review Clinical Manifestations
- Diagnostic Screening Tools
- Current Treatment and Management
- Case Discussion

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Neurotrophic Keratopathy

- Impaired corneal healing due to decreased or loss of corneal sensory innervation
 - Reduced corneal sensitivity
 - Reduced reflex tearing and blinking rates
 - Reduced lubrication and epithelial healing
 - More susceptible to corneal injury

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Corneal Anatomy

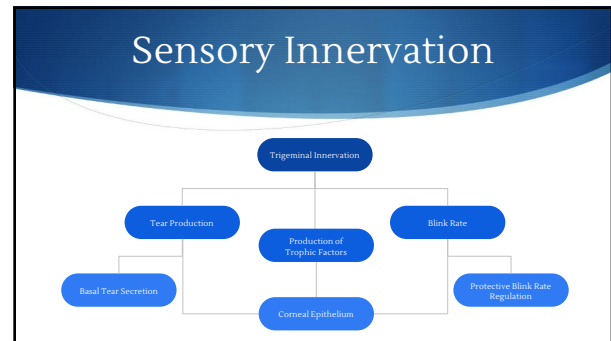
💧 Sensory Innervation through Cranial Nerve Trigeminal (V)

- 💧 Ophthalmic Branch (VI)
- 💧 Nasociliary Branch

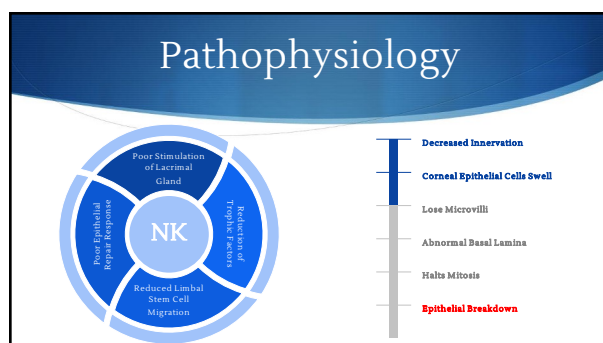
💧 7000 Nociceptors per mm²

- 💧 400 x more than skin
- 💧 100 x more than conjunctiva

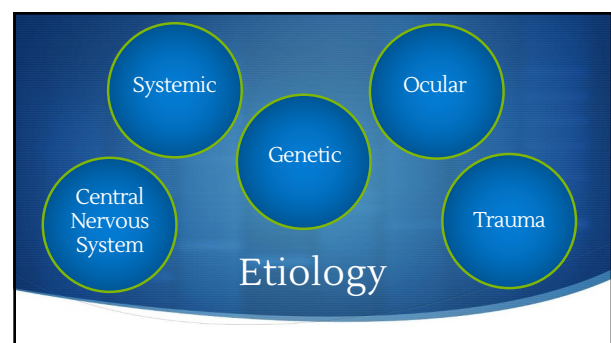
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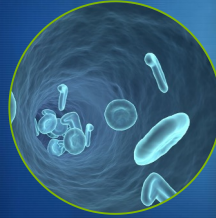
Central Nervous System



- Brainstem Lesions
- Post Neurological Procedures
 - Trigeminal Neuralgia
- Aneurysm
- Neoplasm
- Stroke
- Degenerative Disorders

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Systemic



- Diabetes
- Leprosy
- Vitamin A Deficiency
- Acoustic Neuroma Surgery
- Multiple Sclerosis
- Amyloidosis

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Genetic



- Riley-Day Syndrome
- Goldenhar-Gorlin Syndrome
- Moebius Syndrome
- Familial Corneal Hypoesthesia

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Ocular



- Herpetic Disease
- Corneal Nerve Lesion
- Topical Drug Toxicity
- Contact Lens Wear
- Chronic Ocular Surface Disease
- Corneal Dystrophy

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Trauma



- Facial Trauma
- Chemical Burn
- Radiation
- Ocular Surgery
 - Refractive/Corneal
 - Glaucoma
 - Retinal
- Orbital Surgery

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Nerve Damage



- Trigeminal
- Ocular
- Ciliary
- Brainstem
- Corneal

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Screening Tools

- 💧 Early Diagnosis is KEY!
 - 💧 Detailed Patient History
 - 💧 Slit Lamp Evaluation
 - 💧 Tear Production (Schirmer's Testing without Anesthetic)
 - 💧 Corneal Sensitivity Measurement
 - 💧 Imaging

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Slit Lamp Evaluation

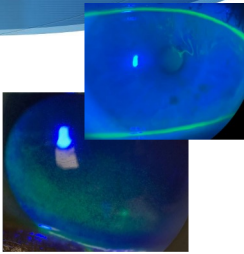


- 💧 Lids and Lashes
 - 💧 Lash Extensions, Make-Up
 - 💧 Blepharitis
 - 💧 Floppy Eyelids
- 💧 Conjunctiva
 - 💧 Chalasis, Allergies
- 💧 Cornea
 - 💧 Staining, Scarring

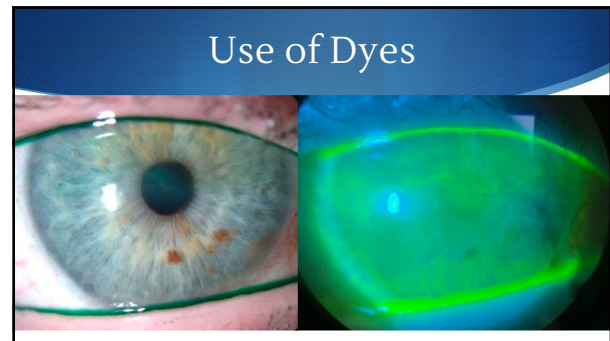
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Use of Dyes

- Fluorescein
 - Identify Tear Film and Cornea
- Rose Bengal and Lissamine Green
 - NK → Diffuse and/or Central Staining
 - DES → Inferior and/or Interpalpebral
 - Conjunctival Staining more indicative of Dry Eye vs. NK



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Corneal Sensitivity

Cotton Thread	Cochet-Bonnet Esthesiometer	Gas Esthesiometer
Qualitative	Quantitative	Quantitative
Cotton Swab Unwaxed Dental Floss Tip of Tissue	Instrument with Nylon Filament with different lengths (0-6 cm) applied to cornea to elicit response	Calibrated Air Emission stimulates cornea without contact from injector tip close to surface
<ul style="list-style-type: none"> • Normal Reaction • Hypoesthesia • Anesthesia 	<ul style="list-style-type: none"> • Each Quadrant Tested Separately • Quantitative Measurement based on filament length • Central Cornea most important for NK 	<ul style="list-style-type: none"> • Sit Lamp Mounted Instrument • Variable Composition and Temperature of Gas: <ul style="list-style-type: none"> ○ Mechanical ○ Chemical ○ Thermal

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Corneal Sensitivity

Cotton Thread
Qualitative
Cotton Swab Unwaxed Dental Floss Tip of Tissue
<ul style="list-style-type: none"> • Normal Reaction • Hypoesthesia • Anesthesia



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Corneal Sensitivity



Cochet-Bonnet Esthesiometer

Quantitative

Instrument with Nylon Filament with different lengths (0.6 cm) applied to cornea to elicit response

Longer Filament = More Stable = More Sensitive

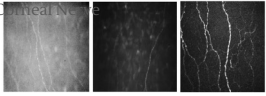

- Each Quadrant Tested Separately
- Quantitative Measurement based on filament length (shorter length = higher pressure)
- Central Cornea most important for PK

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In Vivo Confocal Microscopy

- High Resolution Assessment of Corneal Nerve
 - Epithelial Nerves
 - Subepithelial nerve Plexus
 - Subbasal Nerve Plexus
 - Stromal Nerves
- Corneal Apex = Nerve Bundles Oriented Vertical
- Surrounding Cornea = Nerve Bundles Oriented Horizontal

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Mackie Classification

STAGE 1: MILD

STAGE 2: MODERATE

STAGE 3: SEVERE



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Mackie Stage 1

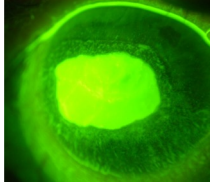
SYMPTOMS	<ul style="list-style-type: none"> Dry Eye Blurred Vision Photophobia Reduced Blink Rate
CORNEAL FINDINGS	<ul style="list-style-type: none"> Reduced Epithelial Cell Turnover Reduced Central Corneal Epithelial Thickness Punctate Epithelial Erosions +/- Neovascularization
TEAR FILM	<ul style="list-style-type: none"> Increased Viscosity of Tear Mucus Lid Wiper Epitheliopathy (BLEB Shedding) Decreased Tear Film Thickness Decreased Tear Break Up Time Decreased Tear Production



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Mackie Stage 2

SYMPTOMS	<ul style="list-style-type: none"> Blurred Vision - Worsening
CORNEAL FINDINGS	<ul style="list-style-type: none"> Non-healing epithelial defects <ul style="list-style-type: none"> Oval shaped, rolled border edges Acute Loss of Epithelial (Upper Eyelid) Damage to Bowman's Membrane Stroma susceptible to damage
TEAR FILM	<ul style="list-style-type: none"> Hypersensitivity Increase in Proinflammatory Cytokines




Source: Ahmed et al. Int J Ophthalmol 2015; 8(10): 1955-1960

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Mackie Stage 3

SYMPTOMS	<ul style="list-style-type: none"> Redness Blurred Vision - Worsening Possible Pain
CORNEAL FINDINGS	<ul style="list-style-type: none"> Stromal Involvement with Thinning/Lysis MMP Instability Corneal Melk - Corneal Perforation
TEAR FILM	<ul style="list-style-type: none"> MMPs Activation Increased Inflammatory Mediators



MMP: Matrix Metalloproteinase

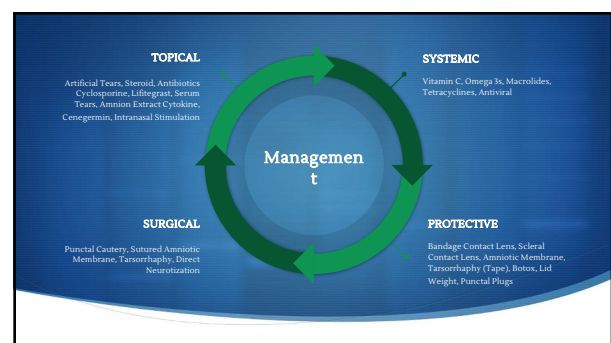
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Management

💧 Treatment based on NK Stage

- 💧 Stage 1 → Avoid Epithelial Breakdown
- 💧 Stage 2 → Promote Healing and Prevent Ulceration
- 💧 Stage 3 → Reduce Stromal Scarring and Prevent Corneal Perforation

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Biologics

- Autologous Serum Tears vs. Plasma Rich Growth Factors
- Cost
- Difficult to Acquire
- Composition Varies (serum to tear ratio)
 - Ranges from 20% to 100%
- Dosage Differences
 - 6-8x/day for 1 month for NK then taper to QID ongoing
- Risk of Infection
- Increased Risk of Pro-inflammatory Mediators
- Not suitable for all patients



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Cenegermin

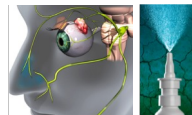
- E.Coli derived recombinant human nerve growth factor (NGF)
- Approved by United States FDA in August 2018
 - *Cenegermin ophthalmic solution 0.002%*
 - 8 week treatment, 6x/day dosage
 - Two Clinical Trials: REPARO (Europe), NGF0214 (USA)
 - Side Effect: Ocular Pain
 - Nociceptor Re-activation?



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Intranasal Stimulation

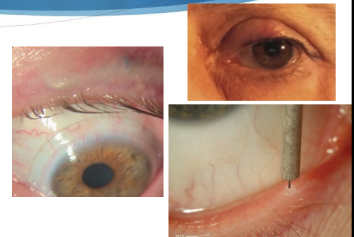
- Activate Nasolacrimal Reflex to increase Tear Production
 - Intranasal Tear Stimulator
 - Electrical vs. Sonic
 - Pharmacological
 - *Varenicline* - Nicotinic acetylcholine receptor agonist to stimulate the trigeminal parasympathetic pathway



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Non-Surgical Treatment

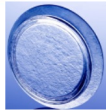
- Oral Tetracycline
- Punctal Occlusion
- Tarsorrhaphy
- Lid Weight
- Amniotic Membrane
- Bandage Contact Lens
- Scleral Contact Lens



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Amniotic Membranes

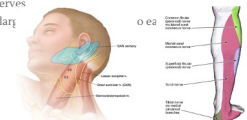
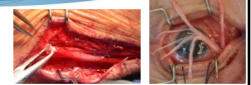
- Innermost layer of placenta (avascular)
 - Treated with antibiotics during collection
 - Barrier acts as protection for cornea to heal
 - BM Collagen similar to Cornea/Conjunctiva
 - Stroma contains anti-inflammatory markers (HA, Cytokines)
- Amniotic Membrane:
 - Cryopreserved
 - Stored at -80°C freezer - Reduce to Room Temperature for use
 - Dehydrated or Lyophilized
 - Stored at Room Temperature



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Surgical Treatment

- Corneal Neurotization Surgery
 - Ipsilateral versus Contralateral Direct Neurotization
 - Transfer of Supratrochlear and Supraorbital Nerves
 - Healthy nerve replaced from under Eyebrow (larger)
 - Indirect Neurotization
 - Sural Nerve (leg)
 - Great Auricular Nerve (ear)
 - Cadaveric Nerve Graft



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Contact Lenses

- Protect and preserve ocular surface integrity
- Non-surgical and restorative
- Effective at any stage of NK disease

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Bandage Contact Lenses

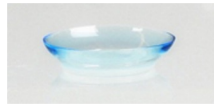
- Mechanical protection
- Moisturization with thin fluid reservoir
- Lower cost
- Maintains Cosmesis
- Ease of handling
- Easily applicable to pediatric patients
- Adjunct with topical therapeutics
 - Future role of Smart Contacts (drug delivery)



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Bandage Contact Lenses

- 💧 FDA approved Silicone Hydrogel
 - 💧 Lotrafilcon A, Balaafilcon A, Senofilcon A
 - 💧 Safe for overnight wear, higher Dk
 - 💧 Off Label
 - 💧 Hydrogel: methafilcon A
- Poor wettability; Thinner Tear to Cornea Interface
Risk of Infection
Minimal improvement in vision with scarring



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Scleral Lenses

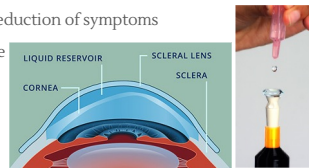
- 💧 Larger Oxygenated Fluid reservoir
 - 💧 Hydrated microenvironment (thicker fluid reservoir)
 - 💧 Prevents corneal desiccation, vascularization, keratinization
- 💧 Physical Barrier
 - 💧 Protection
- 💧 Cosmetically Friendly
- 💧 Economical Long-term choice
 - 💧 "Last Resort"
- 💧 Improvement of Visual Acuity (Rigid)



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Looking Beyond Visual Correction

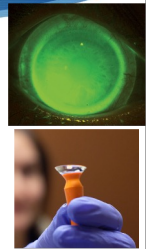
- 💧 Attenuation of pain and reduction of symptoms
- 💧 Support the ocular surface
 - 💧 **Protection**
 - 💧 **Lubrication**



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Scleral Lenses

- 💧 Lower risk of microbial keratitis
- 💧 Extended wear option for re-epithelization before transition to daily wear
 - 💧 Prevent disease progression
 - 💧 Alternative or adjunct to surgical intervention
- Cost
- Insertion and removal ability
- Targeted patient support and education
 - Unrecognized complications due to lack of corneal sensitivity



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Case 1: Healing Wounds

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Case History

- 💧 66 yo M presents for Scleral Lens consultation OS
- 💧 Ocular History:
 - 💧 s/p Retinal Detachment Repair OS x 8 (scleral buckle in place)
 - 💧 CE/Aphakia OS
 - 💧 Secondary Glaucoma OS – on Cosopt PF BID OS, Zioptan QHS OS
 - 💧 Neurotrophic Keratopathy OS
 - 💧 Neurotrophic Ulcer OS Dec 2016, recurrence Jan 2017
 - 💧 **Resultant Non-healing Central Corneal Epithelium Defect**
 - 💧 Outside MD consideration for *enucleation* OS

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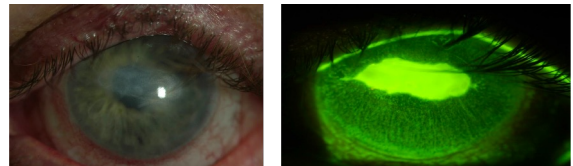
Non-Healing Epithelial Defect

- 💧 7 months duration
 - 💧 Poor response to topical treatment
 - 💧 History of multiple amniotic membranes (failed)
- 💧 Setting of Neurotrophic Keratopathy OS
- 💧 Current Treatment:
 - 💧 Ofloxacin QID OS
 - 💧 Preservative Free Artificial Tears QID
 - 💧 Bandage Contact Lens
 - 💧 Replaced every 2 weeks by local MD

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Examination Findings

- 💧 OS: Corneal Epithelial Defect 2mm x 9mm central oval shape, 10% thinning, no infiltrate, 1+ conjunctival injection



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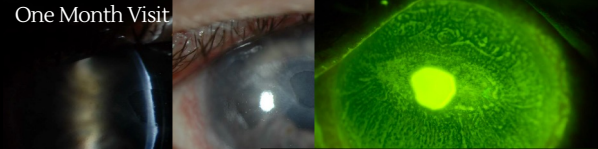
Two Week Visit

- Reduced size 2mmx4mm, no infiltrate, no AC reaction, no KP, no discharge, mild stromal thinning
- Fit with Scleral Lens daily wear, good comfort, removes nightly
- AWT: 12 hours, day-time wear only
- No difficulty with I&R

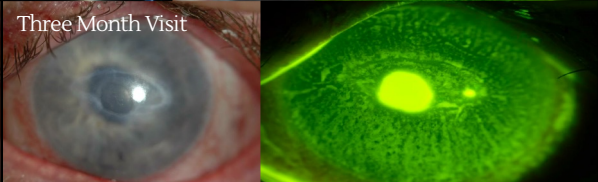


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One Month Visit



Three Month Visit



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Four Month Visit

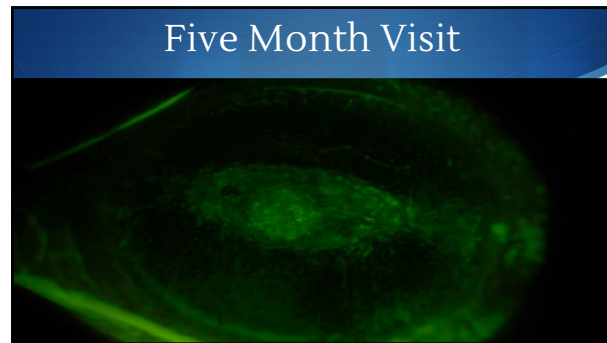


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Nocturnal Exposure

- Neurotrophic Keratoconjunctivitis OS with central non-healing epithelial defect OS x 12 months
 - Reduction in epithelial defect size however significant thinning
 - Increase risk of corneal perforation
- Limitation of Healing possibly due to Nocturnal Exposure
 - Consideration for Partial Tarsorrhaphy – may limit PROSE wear
 - Initiate Autologous Serum Tears
- Consult with outside Cornea MD with patient options, continue with Scleral wear daily for now and initiate tape tarsorrhaphy at night

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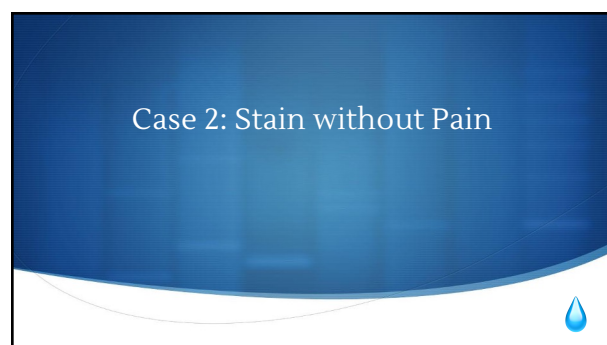


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Learning Lessons

- 💧 Scleral Lens can be both Protective and Restorative
- 💧 Importance of Multiple Treatment Combinations
- 💧 Photo Documentation
- 💧 Close Monitoring and Co-Management

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Case History

- 💧 50 Year Old Female
- 💧 *Chief Complaint:* Recent hospital stay where patient did not have access to drops. Presents with Blurred Vision and Redness OD (CF Vision)
 - 💧 History of Neurotrophic Ulcer OD (2016) likely secondary to CNV damage from Brain Tumor
 - 💧 Current Treatment: PFAT QID

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Medical and Ocular History

- 💧 History of Brain Tumor
 - 💧 Tumor Removed from brain stem in 2013
 - 💧 Initial symptoms of diplopia and exotropia OD (later found to be due to tumor likely affecting oculomotor/abducens nerve)
 - 💧 Slight compression of right carotid; suspicion for Horner's OD with slight ptosis
- 💧 Neurotrophic Keratopathy OD with large central scar due to prior corneal ulcer (2016)
 - 💧 BCVA reduced to 20/150
 - 💧 Punctal Plugs RUL and RLL placed in 2018
 - 💧 Using Preservative Free Artificial Tears 4-6x/day and ointment at night
- 💧 High Myopia (~9 D)

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Clinical Presentation

	OD	OS
Lids	Mild Ptosis, Plugs in place UL/LL	Normal position, clear
Cornea	Epithelium Defect within central area of stromal scar 4.5 mm H x 2.5 mm Vertical, Mild neovascularization inferior	Clear
Anterior Chamber	Deep and Quiet, No Cell/Flare	Deep and Quiet
Iris	Flat	Flat
Lens	Trace Nuclear Sclerosis	Trace Nuclear Sclerosis

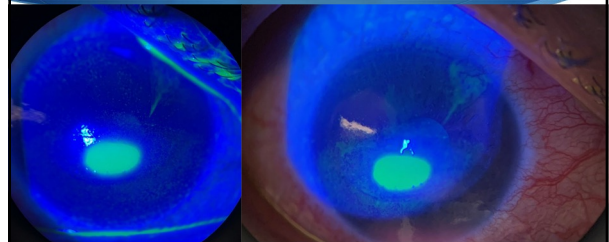
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Plan

- 💧 Neurotrophic Keratopathy OD
 - 💧 No evidence of infection/ulcer
 - 💧 Rx Moxifloxacin q2h
 - 💧 Start Preservative Free Artificial Tears q1h
 - 💧 Rx Erythromycin ointment qhs

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One Week Follow-Up



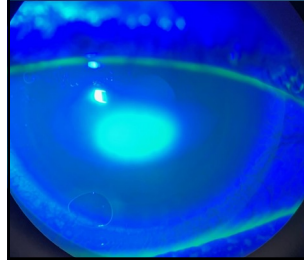
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Plan

- 💧 Neurotrophic Keratopathy OD
 - 💧 Culture for etiology
 - 💧 Start oral Valtrex 1g PO x 10 days
 - 💧 Continue Moxifloxacin QID
 - 💧 Placement of Bandage Contact Lens
 - 💧 Continue Preservative Free Artificial Tears q1h
 - 💧 Hold off Erythromycin ointment qhs given BCL

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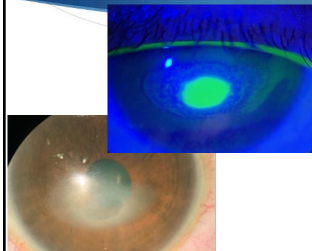
Two Week Follow-Up



- 💧 Epithelial Defect
 - 💧 Reduced to 2.2 mm x 3.7 mm
- 💧 Culture Results
 - 💧 Gram Positive (Micrococcus Luteus)
 - 💧 Discontinued Moxifloxacin, Start Polytrim QID OD
 - 💧 Completed Valtrex
- 💧 Bandage Contact Lens replaced every 2 weeks

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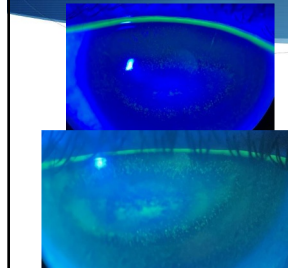
Six Week Follow-Up



- 💧 Epithelial Defect
 - 💧 Reduced to 1.0 mm x 1.4 mm
- 💧 PFAT QID
- 💧 Polytrim QID
- 💧 Bandage Contact Lens replaced every 2 weeks

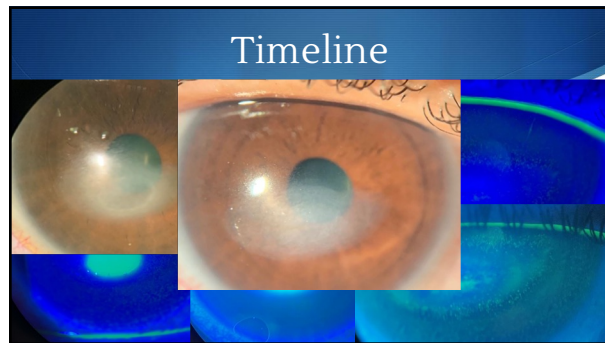
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Eight Week Follow-Up



- 💧 Epithelial Defect Healed!
 - 💧 Residual PEE
- 💧 PFAT QID
- 💧 Discontinue Polytrim QID
- 💧 Start Scleral Lens Fitting Process
 - 💧 Ocular Surface Protection
 - 💧 Ocular Surface Preservation

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Learning Lessons

- 💧 Maintenance Treatment Crucial for Ocular Surface Preservation
- 💧 Importance of Culturing
- 💧 Simplicity with Bandage Contact Lens Therapy

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Case 3: Time Heals All Wounds

UBI/HID Ophthalmology
ROSS
EYE INSTITUTE
See better, live happier

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Case History

- 💧 62 Year Old Female referred for NK OS and history of Recurrent Epithelial Defects
 - 💧 History of Amniotic Membrane x 2 (Prokera) - 1/2021
 - 💧 On Oral Valtrex previously - d/c after HSV PCR Negative
 - 💧 Currently wearing BCL (replaced monthly)
 - 💧 Punctal Plugs in place BLL OU
 - 💧 PFAT QID OU and Moxifloxacin BID OS

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Ocular History

- Former Myope (>6 D) s/p LASIK OU 2004
- RD x 2 OS s/p PPV with Gas
 - 12/2019 SB/20g/PPV/PFO/EL/AFx/C3F8
 - 1/2020 S/P 20g PPV/EL/SF6
- ERM OS
- s/p CE/IOL OS 6/25/2020
- IOL dislocation repair 7/8/2020
 - Persistent Bullous Keratopathy treated
- PCO OS (dense)

NK

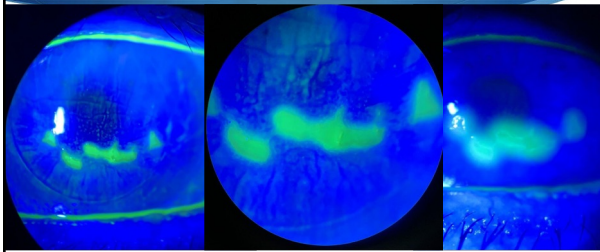
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Testing

- Schirmers Testing 3 mm OU
- Corneal Sensitivity
 - Cotton Thread
 - OD Normal Response 12, 6, 3, 9, Centrally
 - OS Absent Response in All Quadrants
- Staining with NaFl

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Epithelial Defect Staining



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Management

SHORT-TERM

- Initiate Cenegermin 6x/day x 8 weeks OS
- Start Genteal Ointment at night
- Remove Bandage Contact Lens
- Continue PFAT q1-2h

LONG-TERM

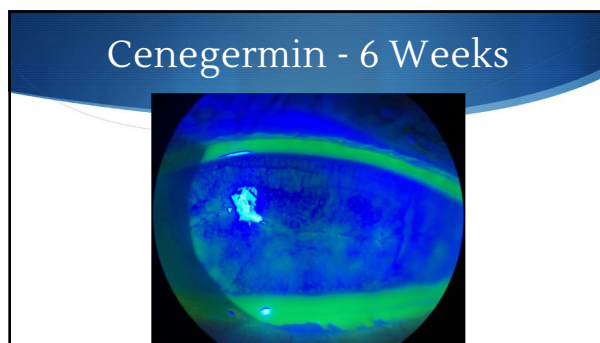
- Scleral Lens Fitting



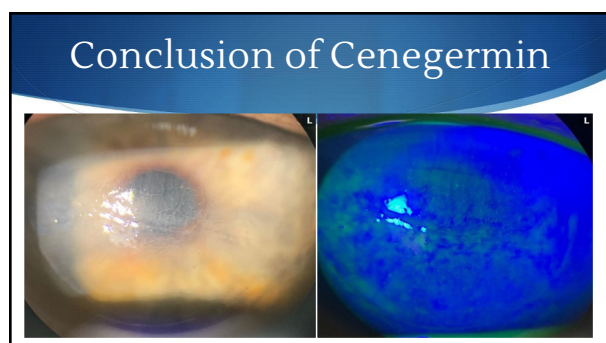
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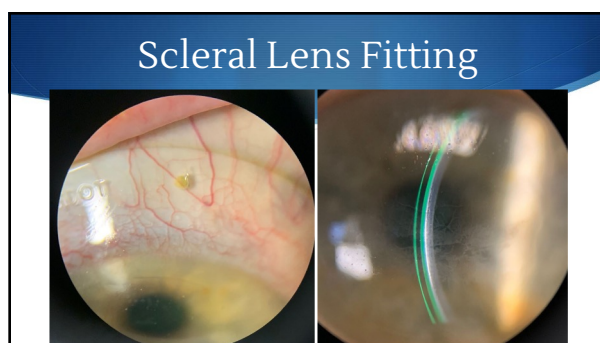
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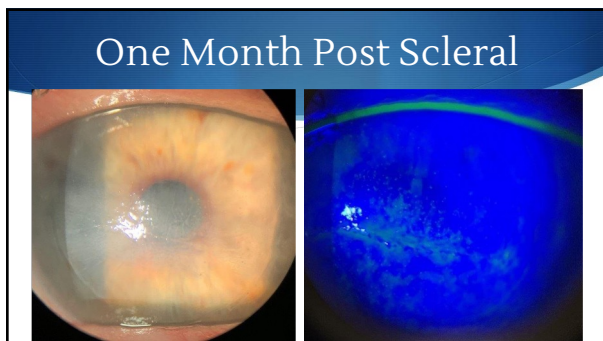
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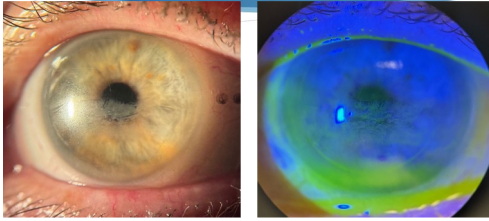


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3 Years Post Scleral



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Learning Lessons

- 💧 Importance of Staining
- 💧 Value of NGF Topical Treatment in Therapeutic Healing
- 💧 Adjunct Role of Scleral Lenses with short term + long term healing
- 💧 Patience is a Virtue

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Case 4: One Size Fits All



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Case History

- 💧 62 Year Old Female presents for emergency visit with redness, blurred vision, light sensitivity
- 💧 Ocular History: s/p LASIK OU, s/p CE/MF PC IOL OU, recent history of HZV OS
- 💧 Seen at Urgent Care and given "corneal bandaid" for abrasion
- 💧 Medications: Valtrex 500 mg PO, Pred QD and PFAT

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Clinical Presentation

↓

Day 1	Day 3	Day 7	Day 14	Week 4	Week 5
VA CF at 5 Ft	VA 20/200	VA 20/300	VA 20/100	VA 20/100	VA 20/100
Epithelial Defect 3 mm x 3 mm	Ovoid Defect 2.5 mm x 2 mm	Worsening Defect 2.5 x 4 mm, no infiltrate, mild stromal edema	Hazy corneal view through AMT/BCCL	Healed Epithelial Defect	Fine Central Punctate Staining
Bandage Contact Lens Placed (Left lower paracel plug placed, taping of lid)	Bandage Contact Lens replaced	Amniotic Membrane Placed + BCCL with Temporary Partial Suture Tarsorrhaphy	Continue PF QID, FML QD, Valproe 500 mg	High Risk of Epithelial Breakdown - Bandage Contact Lens Replaced	Tarsorrhaphy Removed
Polytrim-QD, FML, QD, Valproe TID, PFAT qd 2h	Continue drops	Continue eyelid taping		Order Kontur Conventional Lens	Kontur BCCL placed
					Continue drops

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Clinical Presentation

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Week 8	Week 17	Week 23
VA 20/200	VA 20/50	VA 20/70
Central PEE, recurrence of paracentral crescent shaped defect	Epithelial Defect Healed, Central PEE	Central PEE, new front of Vascularization
Remove Kontur	First Round of Overdrive Complete - approved for second 8 week course	Stop Overdrive
Initiate Oregovirin (Overdrive)		Start Scleral Lens Fitting

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Scleral Lens Fitting

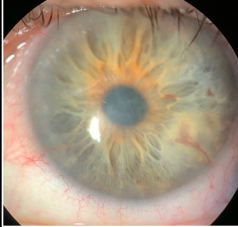
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Bandage Contact Lens

- 💧 Acuvue Oasys Dk 103, H2O Content 38%
- 💧 Kontur Dk 18.8, H2O Content 55%
- 💧 Definite Dk 60, H2O Content 74%

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Current Treatment



- 💧 Patient nervous about CL use
 - 💧 Wears Dailies Total One Brand (Dk 140) PRN
- 💧 PFAT 6x/day
- 💧 Plugs UL and LL
- 💧 AT ointment at night
- 💧 Tape Tarsorrhaphy at night
- 💧 Closely monitoring vision
- 💧 Monitored every 3-4 months

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Learning Lessons

- 💧 Consider NK on Differential Diagnoses
- 💧 Monitor for Vascularization
- 💧 Contact Lens Therapy not suitable for all patients
- 💧 Keep it simple!

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Conclusion

- Etiology** - Multiple causes of trigeminal denervation
- Screening** - Early diagnosis prevents disease progression
- Treatment** - Restore, Regenerate and Preserve Ocular Surface
- Management** - Combination Treatment Driven by Disease Severity




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On behalf of Vision Expo, we sincerely thank you for being with us this year.

Vision Expo Has Gone Green!

We have eliminated all paper session evaluation forms. Please be sure to complete your electronic session evaluations online when you login to request your CE Letter for each course you attended! Your feedback is important to us as our Education Planning Committee considers content and speakers for future meetings to provide you with the best education possible.



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