

Rule These Out Before You Diagnose it as Dry Eye

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Disclosures

- I have received honoraria in the past 2 years for speaking, writing, participating in an advisory capacity, research or meeting support from: Apellis, ABB Optical, Alcon Laboratories, Allergan, Art Optical, Bausch + Lomb Health, Contamac, CooperVision, CSEye, Horizon Therapeutics, Johnson & Johnson Vision Care, Kala, Lenstech, Notal Vision, Novartis, Optovue, Oyster Point, RVL, Sun Pharma, Tarsus, Tangible Science, Santen, Visus, Walman Optical and Zea Vision.
- All relevant relationships have been mitigated

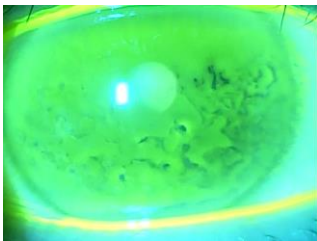
Epithelial Basement Membrane Dystrophy

- Also referred to as map-dot-fingerprint, Cogan's microcystic dystrophy, or anterior basement membrane dystrophy
- Questions of true dystrophy versus degeneration
- Risk factors: family history (although difficult to track from patient history), ocular injuries (abrasions), ocular surgeries
- Basement membrane extend, abnormally, into the corneal epithelium
- This irregularity increases risk of recurrent corneal erosion (RCE), reduced vision, fluctuating vision

Epithelial Basement Membrane Dystrophy



Epithelial Basement Membrane Dystrophy



- Negative staining
- Needs to be differentiated from TBUT
- vision can be different on a day to day basis because of variation in corneal irregularities

Epithelial Basement Membrane Dystrophy



- Increased risk of RCE
- Symptoms of eye discomfort can complicate diagnosis

Floppy Eyelid Syndrome

- Ointment in the evening
- Sleep rite
- Eye mask in the evening
- Blepharoplasty
- Lacriserts
- Punctal occlusion



Kearns-Sayre Syndrome

- Affects many parts of the body
- Usually appears before 20 years old
- Caused by mitochondrial DNA abnormalities
- Causes progressive external ophthalmoplegia
 - i. Paralysis of extraocular muscles
 - ii. Ptosis
- Pigmentary retinopathy

Kearns-Sayre Syndrome

- Other systemic findings
- i. Cardiac conduction defects
 - ii. Ataxia
 - iii. Other muscle weakness
 - iv. Deafness
 - v. Kidney problems
- Occurs because of mitochondrial deficiencies
Prevalence: 1-3/100,000

Kearns-Sayre Syndrome

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- Sleep rite
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Mucous fishing syndrome

- Cyclical worsening of symptoms
- Patients will "fish" mucous out of their eye usually from some irritant
- Mucous usually in the lower fornix
- Continual attempted removal causes more mucous to be formed
- Treatment often times requires educating patients to stop touching their eyes

Monitoring Ocular Adverse Events

Ophthalmic Exam Findings Requiring Dose Modifications

Ophthalmic exam finding	Severity of finding	Action
Keratitis/keratopathy	Noninfectious superficial keratitis	Monitor
	Confluent superficial keratitis, a cornea epithelial defect, or 3-line or more loss in best corrected visual acuity	Notify treating oncologist*
	Corneal ulcer or stromal opacity or best corrected distance visual acuity of 20/200 or worse	
	Corneal perforation	
Uveitis	Grade 1/rare cell in anterior chamber	Monitor
	Grade 2/1-2+ cell or flare in anterior chamber	Notify treating oncologist*
	Grade 3/+ cell or flare in anterior chamber	
	Grade 4/hypopyon	

Ocular adverse events should be treated by the eye care provider per standard clinical guidelines

*The treating oncologist will withhold dose, reduce dose, or permanently discontinue ELAHERE™ depending on the severity and persistence of ocular adverse events.
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Please see indication on slide 2 and Important Safety Information on slides 17-22, and accompanying full Prescribing Information, including **BOXED WARNING**.

Coordinating With the Treating Oncologist

ELAHERE™ Ocular Assessment Form to Guide Ophthalmic Exams and Communicate With Treating Oncologists

- Reporting exam findings to the treating oncologist can guide the need for dose modification due to ocular events
- Dose reductions or modifications may help resolve ocular events
- Ocular adverse events led to permanent discontinuation of ELAHERE in 0.6% of patients

For questions or information about billing and coding, reference the ELAHERE Ocular Billing & Coding Guide

Scan this code to download a copy of the ELAHERE Ocular Assessment Form

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Types of Allergic Eye Disease

- Acute allergic conditions
 - Seasonal Allergic Conjunctivitis (Hay Fever) - SAC
 - Perennial Allergic Conjunctivitis – PAC
- Chronic allergic conditions
 - Vernal Conjunctivitis - VKC
 - Atopic Conjunctivitis - AKC
 - Giant Papillary Conjunctivitis - GPC

Allergic Conjunctivitis: Seasonal / Perennial

Causes:	Signs/Symptoms:
Environmental	Itching
Genetic predisposition	Redness
Findings:	Chemosis
Family history	Lid swelling
No eosinophils found in scrapings	Tearing
Spike in tear histamine	
Normal histaminase function	

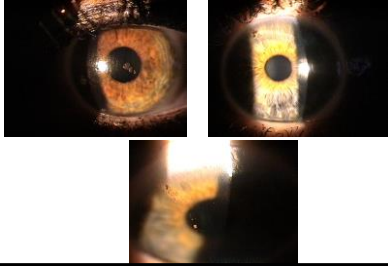
Atopic Keratoconjunctivitis (AKC)

Causes:	Signs/Symptoms:
Associated with atopic dermatitis	Itching
May be perennial	Redness
Genetic predisposition	Photophobia
Environmental antigens	Keratopathy
Clinical Findings:	SPK/Ulcers
Initiates between 20 and 50 years of age	Keratoconus
Elevated levels of eosinophils, TH ₂ , lymphocytes, and mast cells	Anterior polar cataracts
	Mucous discharge
	Atopic blepharitis

Vernal Keratoconjunctivitis (VKC)

Causes:	Signs/Symptoms:
Genetic predisposition, atopy	Ptosis
Seasonal/perennial allergens (IgE)	Ropy mucous discharge
Nonspecific hypersensitivity	Photophobia
Clinical Findings:	Large, nonuniform cobblestone papillae
Most predominant in males from 3 to 20 years old	Trantas dots
Increased levels of superficial mast cells, eosinophils, and lymphocytes	Limbal nodules
Decreased levels of histaminase	Neovascularization
	Shield ulcers
	Itching

Contact Lenses



Giant Papillary Conjunctivitis (GPC)

Causes:

Repeated mechanical irritation caused by:

- Contact lens edge
- Exposed sutures
- Extruded scleral buckle
- Ocular foreign bodies

Aggravated by concomitant allergy

Can also aggravate ocular allergy

Clinical Findings:

Increased chronic inflammatory cells

Signs/Symptoms:

- **Decreased CL tolerance**
- **Blurred vision**
- **Foreign body sensation**
- **Small, uniform papillae on upper tarsal plate**
- **Thick mucous build-up**

Treatment Options

- **Topical Medications**
 - **Antihistamine/ Mast Cell Stabilizer Combinations**
 - Blocks Histamine receptors on blood vessels, nerve endings, etc
 - Inhibits histamine degranulation from sensitized mast cells so that when these cells are challenged with antigen, they do not degranulate
 - Patanol, Pataday, Elestat, Zaditor, Lastacraft, Bepreve

RASP Inhibitors

- www.aldeyra.com
- Aldehyde is a product of metabolism
- Normally rapidly broken down
- With inflammation, is produced in quantities that are difficult to breakdown efficiently
- RASP – Reactive aldehyde species
- Reproxalap – Is a RASP inhibitor

Tear-Based POC Quantitative Testing

- 1 Rapid
- 2 Repeatable
- 3 Reproducible
- 4 Reimbursable

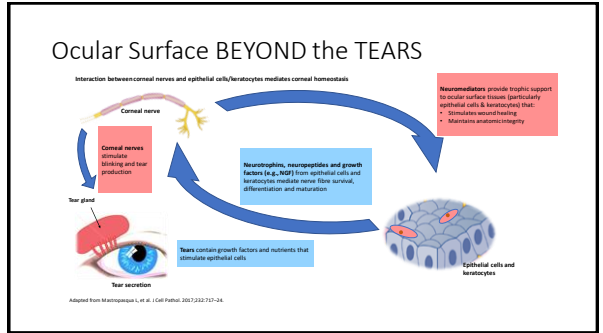
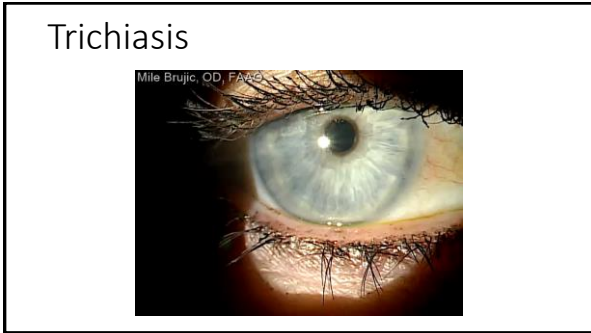


T-POC IgE Testing: Is There An Allergic Component?

- **Benefits of testing IgE levels in the tear film:**
 - Presence of IgE indicates the diagnosis of allergic conjunctivitis
 - Levels of IgE increase with the severity of the allergic response
 - IgE testing can help differentiate allergic conjunctivitis from DED
 - Changes in IgE levels may show the efficacy of prescribed treatment
- IgE value is < 80 ng/mL (33 kIU), there is a 95.7% probability that the patient does not have an ocular allergy
- IgE value is > 80 ng/mL, there is a 92.9% probability that this elevated IgE is indicative of an ocular allergy



Sensitivity: 93%
Specificity: 96%
High IgE: > 80 ng/ml
Test Time: < 80 ng/ml
Normal IgE: < 80 ng/ml
Shelf Life: 12 months



The Cornea is the Most Densely Innervated Tissue in Our Body

- Innervated by the ophthalmic branch of the trigeminal nerve¹
- Corneal nerves provide trophic support to the ocular surface and stimulate protective reflexes^{1,2}
- Corneal sensitivity is a key indicator of corneal nerve function³

1. Montemponi L, Nishida K, Saito M, et al. Understanding the pathogenesis of neurotrophic keratitis: The role of corneal nerves. J Cell Physiol. 2013;212(6):717-24. 2. Dai H, Dai Y, Nishida K, et al. Neurotrophic keratitis. Eye (Lond). 2015;29(12):1313-21. 3. Dai H, Nishida K, Dai Y, et al. Insights into the pathogenesis and treatment strategies for the corneal nerves in ocular surface diseases. Curr Opin Ophthalmol. 2020;31:2-7.

INTERNAL TRAINING (CONFIDENTIAL AND PROPRIETARY) (DO NOT DISTRIBUTE)

Endogenous NGF is Believed to Support Corneal Integrity Via Three Mechanisms

SHOWN IN PRECLINICAL MODELS¹

CORNEAL INNERVATION

Nerve Growth Factor (NGF) plays a role in nerve function and stimulates the regeneration and survival of the sensory nerves^{1,2}

TEAR SECRETION

NGF binds receptors on lacrimal glands and promotes sensory-mediated reflex tearing secretion^{1,4}

CELL PROLIFERATION AND DIFFERENTIATION

NGF stimulates proliferation, differentiation, and survival of corneal epithelial cells³

1. Montemponi L, Nishida K, Saito M, et al. Understanding the pathogenesis of neurotrophic keratitis: The role of corneal nerves. J Cell Physiol. 2013;212(6):717-24. 2. Dai H, Dai Y, Nishida K, et al. Neurotrophic keratitis. Eye (Lond). 2015;29(12):1313-21. 3. Dai H, Nishida K, Dai Y, et al. Insights into the pathogenesis and treatment strategies for the corneal nerves in ocular surface diseases. Curr Opin Ophthalmol. 2020;31:2-7. 4. Dai H, Nishida K, Dai Y, et al. Insights into the pathogenesis and treatment strategies for the corneal nerves in ocular surface diseases. Curr Opin Ophthalmol. 2020;31:2-7.

NK is Progressive and May Lead to Irreversible Ocular Surface Damage and Potential Vision Loss

STAGE 1 "Mild"

Patient of Barry Lee, MD

Punctate epithelial keratopathy (PEK)^{1,2}

STAGE 2 "Moderate"

Patient of Matthew Fang, MD

Persistent epithelial defect (PED)²

STAGE 3 "Severe"

Data on file. NGF020 (REPAIR) CSR

Corneal ulcer²

MEDICAL HISTORY

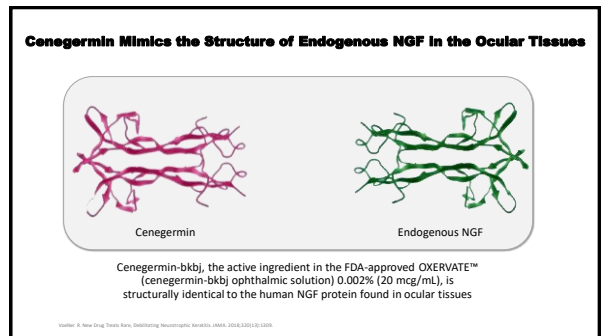
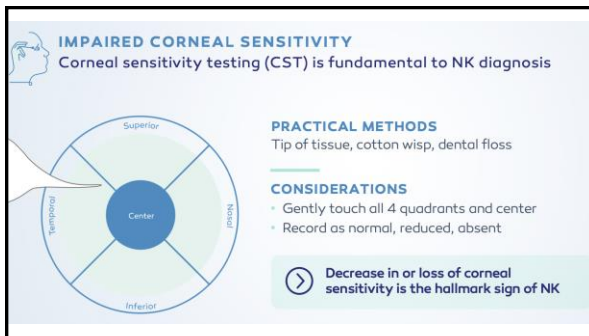
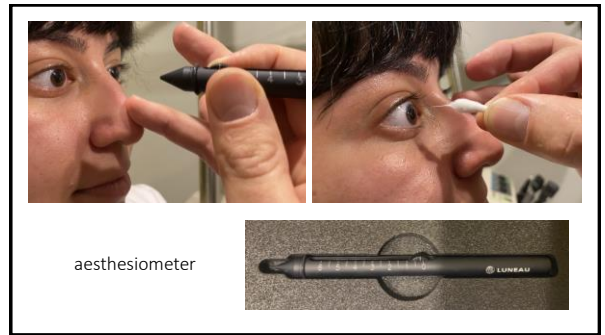
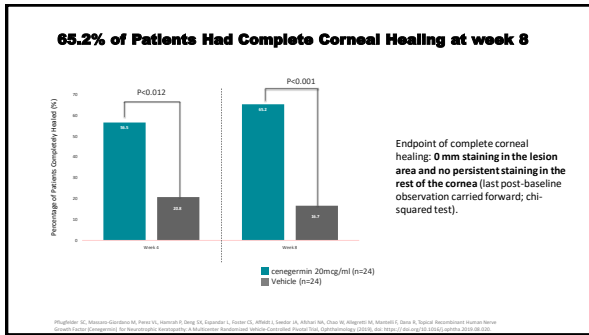
An assessment of risk factors is critical to identifying NK, especially in early stages of the disease

Common NK Etiologies¹⁻⁴

- Post-herpetic infection (VZV, HSV)
- Chronic dry eye disease
- Contact lens wear
- Ocular surgery (eg, cataract, refractive, PKP)
- Topical ophthalmic drug toxicity (eg, glaucoma drops)
- Diabetes
- Stroke
- Multiple sclerosis

A patient with one or more of these risk factors should prompt your suspicion of NK¹⁻⁴

1. Montemponi L, Nishida K, Saito M, et al. Understanding the pathogenesis of neurotrophic keratitis: The role of corneal nerves. J Cell Physiol. 2013;212(6):717-24. 2. Dai H, Dai Y, Nishida K, et al. Neurotrophic keratitis. Eye (Lond). 2015;29(12):1313-21. 3. Dai H, Nishida K, Dai Y, et al. Insights into the pathogenesis and treatment strategies for the corneal nerves in ocular surface diseases. Curr Opin Ophthalmol. 2020;31:2-7. 4. Dai H, Nishida K, Dai Y, et al. Insights into the pathogenesis and treatment strategies for the corneal nerves in ocular surface diseases. Curr Opin Ophthalmol. 2020;31:2-7.



Dry eye due to MGD is an inflammatory disease

MGD is often a skin gland disease

abnormal blood vessels release pro-inflammatory agents


These inflammatory agents propagate to the eyelids via the orbital vasculature

Source: Gerbar et al. J Invest Dermatol. 2011

- ## Intense Pulsed Light
1. Warms Meibum
 2. Emits Energy that absorbed by chromophores in hemoglobin and closes abnormal vessels in the eyelid margin and adjacent conjunctiva. Prevents release of inflammatory factors by the vessels
 3. Reduces inflammatory factors in tears (interleukin 17A, Interleukin-6, prostaglandin E2) (up-regulates expression of anti-inflammatory agents while downregulating pro-inflammatory agents)
 4. Activates fibroblasts and enhance collagen production
 5. Reduce inflammatory or neurogenic pain
 6. Reduction in bacterial load and demodex to reduce inflammation

Plasma Pen CCh-plasty

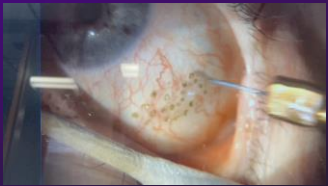
- Used extensively in aesthetics, dermatology for non-invasive treatment of mild to moderate rhytids, skin tags, AK, xanthelasma, angioma, telangiectasias, acne scars, skin tightening ("non surgical blepharoplasty")
- Controlled plasma arc that induces tissue contraction and triggers fibroblast collagen remodeling
- Highly controlled contraction of the conjunctiva with minimal thermal damage



Jablonski et al. Side effects by oral application of atmospheric pressure plasma on the mucosa in mice. PLOS ONE: 14 e 0210099 10, 1371

Plasma Pen CCH-plasty Technique

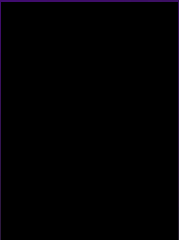
- Pre-Procedure: Lid scrub, proparacaine soaked pledget, brimonidine, moxifloxacin or tobra-dex drops
- Post-Procedure: combination antibiotic-steroid, perfluorohexyloctane
- Tylenol for pain control
- Patients report relief in CCh symptoms starting day 3



Video: Laura M Periman MD

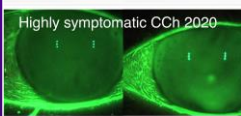
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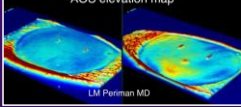


Video: Laura M Periman MD

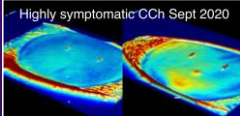
Plasma Pen CCh-Plasty Cases



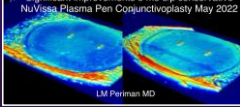
Highly symptomatic CCh 2020



AOS elevation map
LM Periman MD




Highly symptomatic CCh Sept 2020




Significant improvements 5 mo s/p conservative NuVista Plasma Pen Conjunctivoplasty May 2022
LM Periman MD


Inferior CCH-plasty Improved SLK




CCh entrapment under scleral lenses



6 weeks after plasma pen CCh-plasty
LM Periman MD



Severe SLK



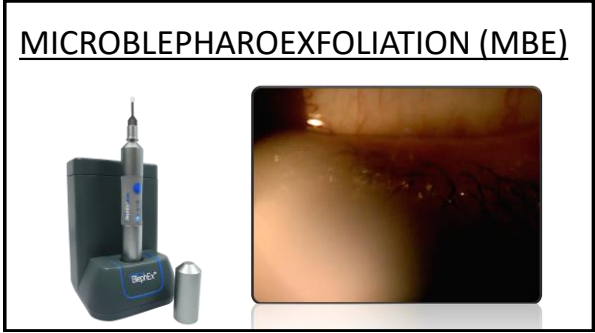
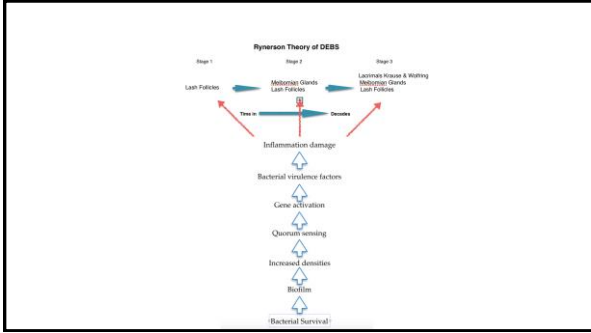
Scleral lenses plus Plasma Pen CCh-plasty to inferior fornix to treat Conj entrapment
LM Periman MD

Clinical Ophthalmology

DEBS – a unification theory for dry eye and blepharitis

James M. Periman MD
 Fellow, American Academy of Ophthalmology
 Fellow, American Society of Refractive Surgeons
 Fellow, American Society of Contact Lens Specialists
 Fellow, American Society of Contact Lens Practitioners
 Fellow, American Society of Contact Lens Designers
 Fellow, American Society of Contact Lens Fitters
 Fellow, American Society of Contact Lens Manufacturers
 Fellow, American Society of Contact Lens Retailers
 Fellow, American Society of Contact Lens Wholesalers
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 Fellow, American Society of Contact Lens Sterilizers
 Fellow, American Society of Contact Lens Inspectors
 Fellow, American Society of Contact Lens Testers
 Fellow, American Society of Contact Lens Evaluators
 Fellow, American Society of Contact Lens Researchers
 Fellow, American Society of Contact Lens Educators
 Fellow, American Society of Contact Lens Trainers
 Fellow, American Society of Contact Lens Mentors
 Fellow, American Society of Contact Lens Advisors
 Fellow, American Society of Contact Lens Consultants
 Fellow, American Society of Contact Lens Specialists
 Fellow, American Society of Contact Lens Experts
 Fellow, American Society of Contact Lens Authorities
 Fellow, American Society of Contact Lens Leaders
 Fellow, American Society of Contact Lens Innovators
 Fellow, American Society of Contact Lens Visionaries
 Fellow, American Society of Contact Lens Dreamers
 Fellow, American Society of Contact Lens Believers
 Fellow, American Society of Contact Lens Followers
 Fellow, American Society of Contact Lens Admirers
 Fellow, American Society of Contact Lens Supporters
 Fellow, American Society of Contact Lens Cheerleaders
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Introduction
 The purpose of this paper is to provide a unification theory for dry eye and blepharitis. The theory is based on the concept of a "dry eye syndrome" which is a multifactorial condition that can affect the eyes. The theory is based on the concept of a "dry eye syndrome" which is a multifactorial condition that can affect the eyes. The theory is based on the concept of a "dry eye syndrome" which is a multifactorial condition that can affect the eyes.



Thank you

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