

# Optimizing the Ocular Surface: The Pursuit of Homeostasis

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# Disclosures

- ▶ Alcon
- ▶ Barti
- ▶ Bausch + Lomb
- ▶ Bruder Healthcare and M&S Technologies (Hilco Vision)
- ▶ Dompé
- ▶ Lumenis
- ▶ Myze
- ▶ NuLids
- ▶ PRN Vision Group
- ▶ Rinsada
- ▶ Tarsus Pharmaceuticals
- ▶ Vital Tears

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# **“Optimizing the Ocular Surface”**

**What does this actually mean?**

# Homeostasis

## Central Unifying Concept of Physiology



Walter Cannon, 1930

**From Greek:**

- **Hómoios** - “similar”
- **Stásis** - “standing still”

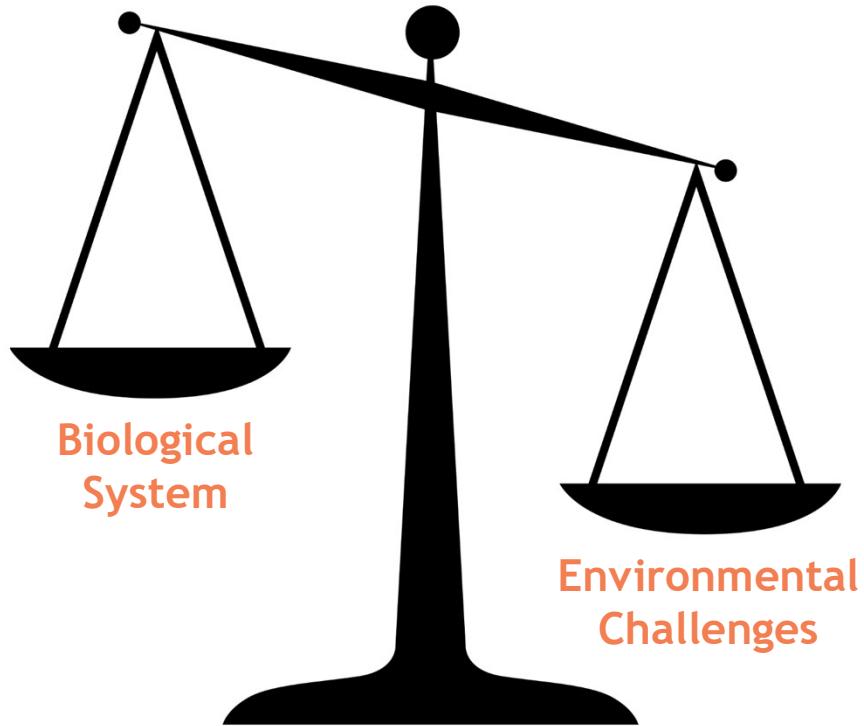
# Homeostasis

**Definition:** a self-regulating process by which biological systems maintain stability while adjusting to changing external conditions

# Homeostasis

**Simplified:** the body will try to keep physiological variables within/at a predefined range or set point, regardless of changes to the outside environment

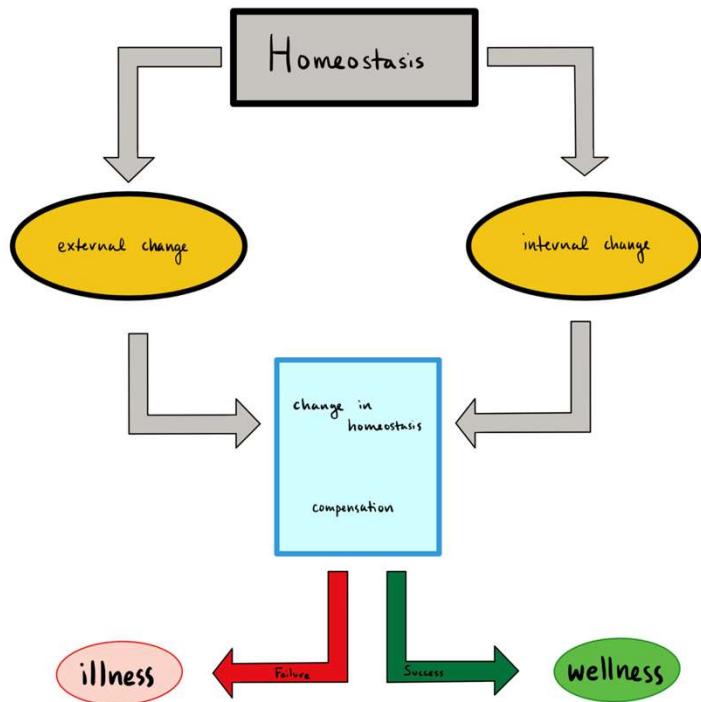
# Homeostasis



## Dynamic Equilibrium

- State of balance
  - Resists change
  - Continuously adjusted
  - Adapts to external challenges

# Homeostasis



## Feedback-Dependent Control

- Self-regulated
- Complex and integrated
  - Inputs from multiple systems
  - Can be modified by higher level control

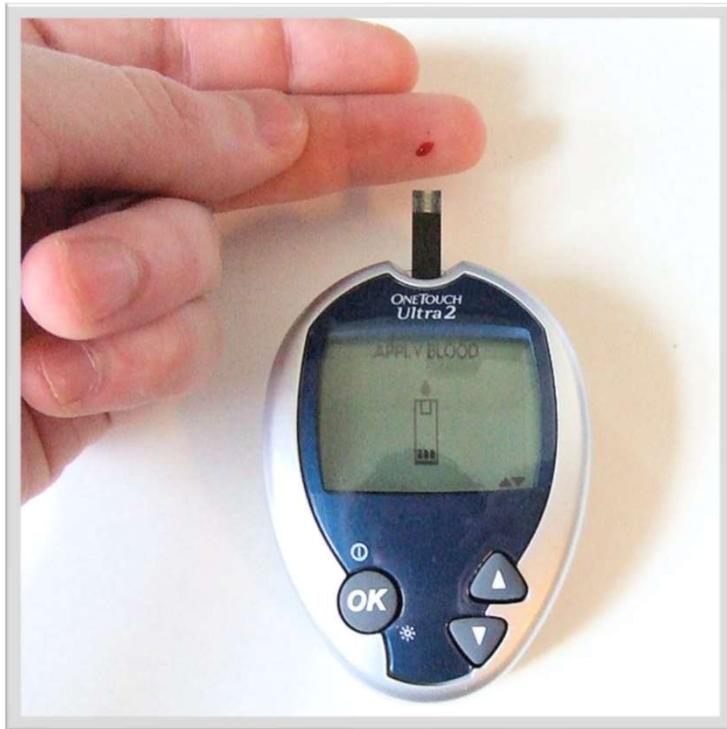
# Homeostasis



## Physiology Example: **Body Temperature**

- Set point is ~98.6 °F
  - **Too hot - sweat**
    - Evaporative cooling
    - Heat stroke
  - **Too cold - shiver**
    - Generate heat
    - Hypothermia

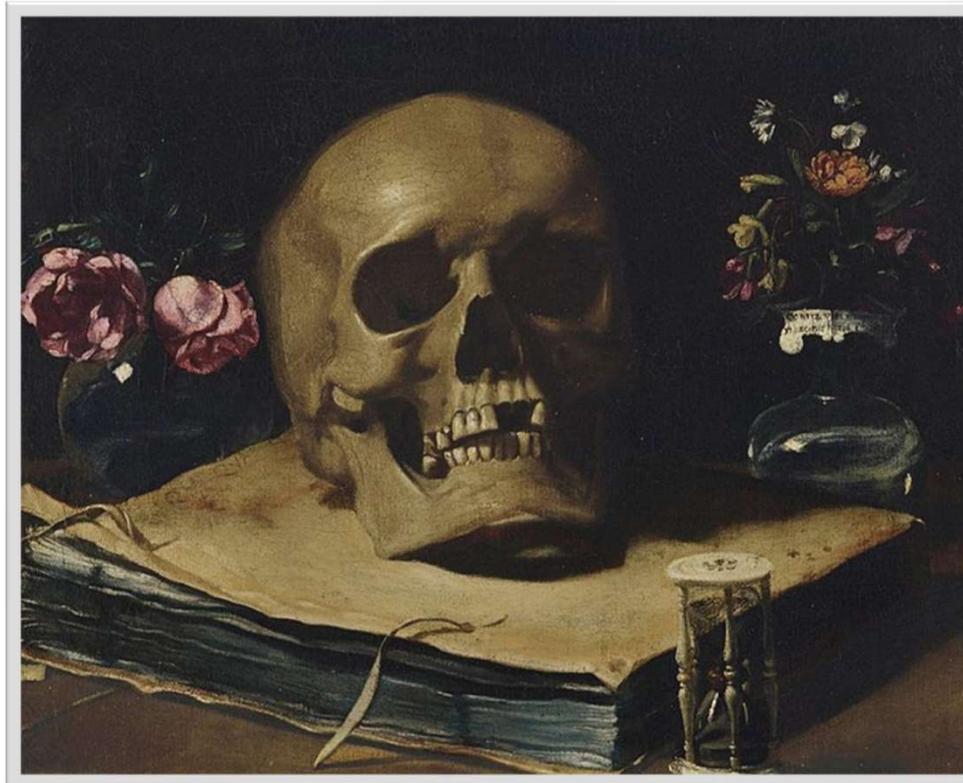
# Homeostasis



## Pathology Example: Diabetes

- Loss of homeostasis
  - Unable to maintain blood glucose levels within set range
- Treatment
  - Use of exogenous insulin to restore balance

# Homeostasis



**Inability to maintain homeostasis  
Disease and Death**

# Homeostasis

Dry eye is a multifactorial disease of the ocular surface characterized by a **loss of homeostasis** of the tear film, and accompanied by ocular symptoms, in which tear film instability and hyperosmolarity, ocular surface inflammation and damage, and neurosensory abnormalities play etiological roles.

- TFOS DEWS II Definition & Classification Subcommittee Report

# Homeostasis

**“If one does not understand this self-regulating process, then it is not possible to comprehend fully the function of the body in health and in disease.”**

**- George Billman**

# Using Homeostasis to Provide a Stepwise Approach to Optimizing the Ocular Surface

1. How is the system meant to function?
2. What causes the system to lose balance?
3. What is the result if balance is lost?
4. How do we attempt to restore balance?

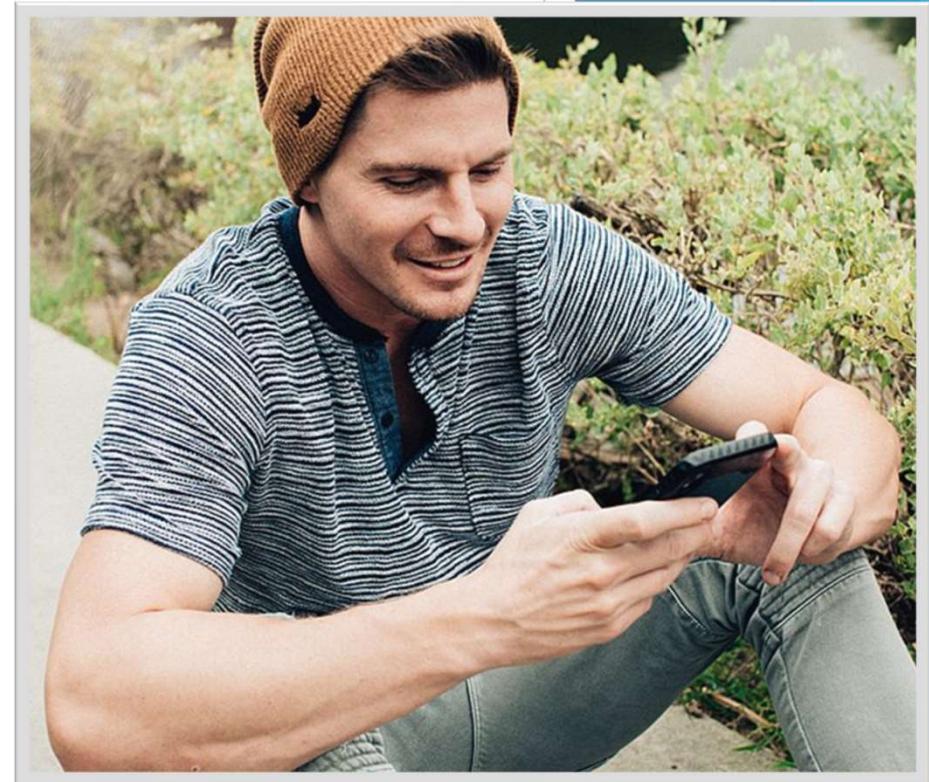
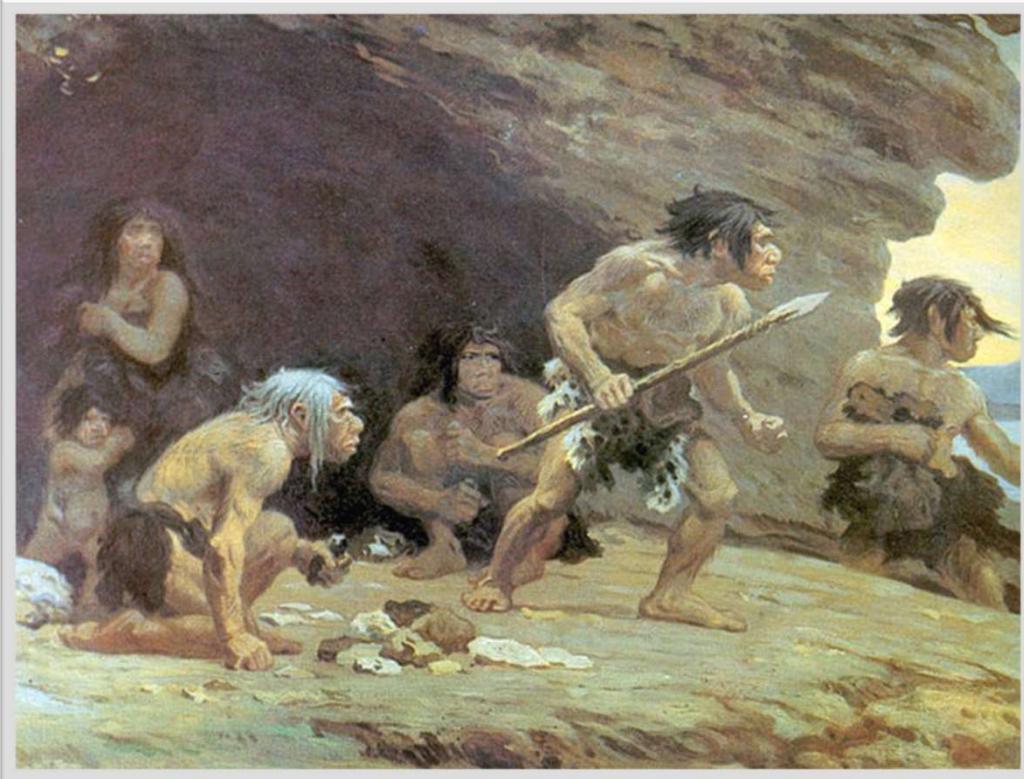
# **Using Homeostasis to Provide a Stepwise Approach to Optimizing the Ocular Surface**

**Goal of Treatment:**  
**Attempt to Restore Homeostasis**

=

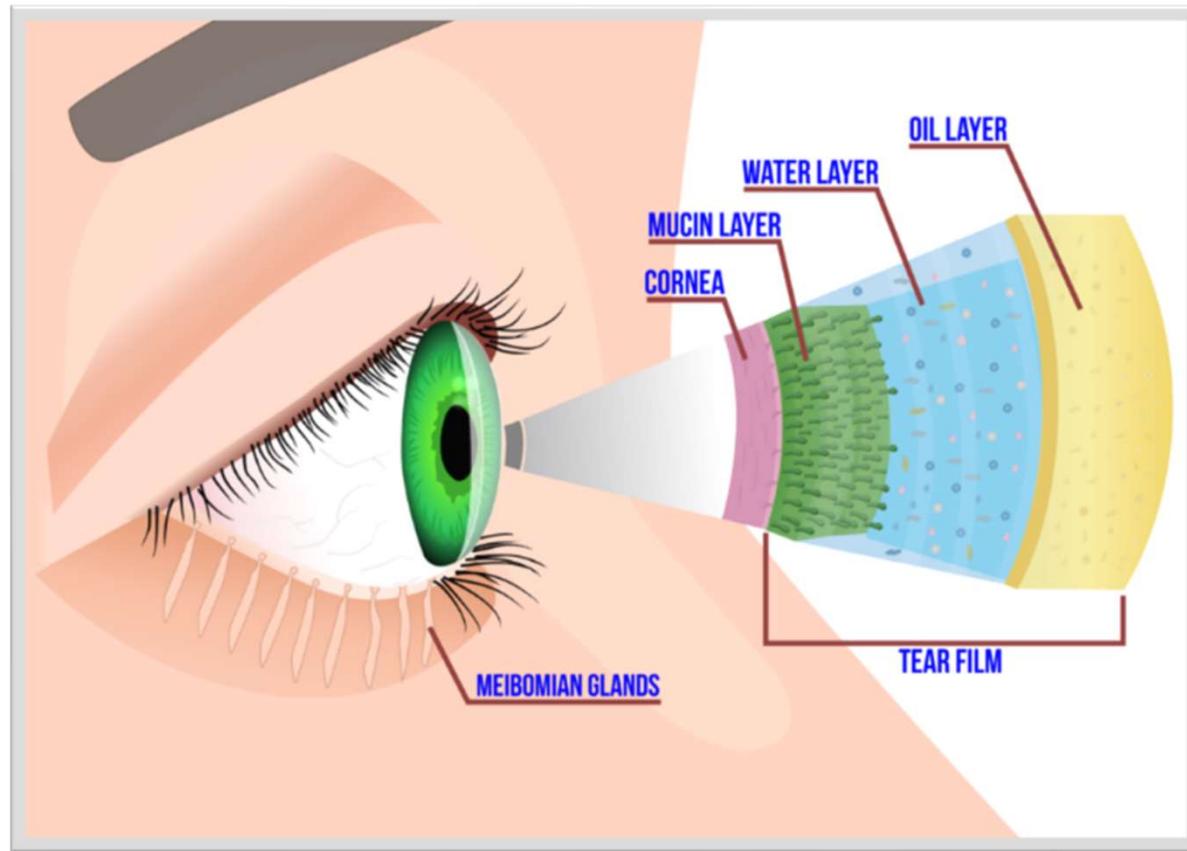
**Address Root Cause of Dysfunction**

# Dry Eye: A Modern Disease?

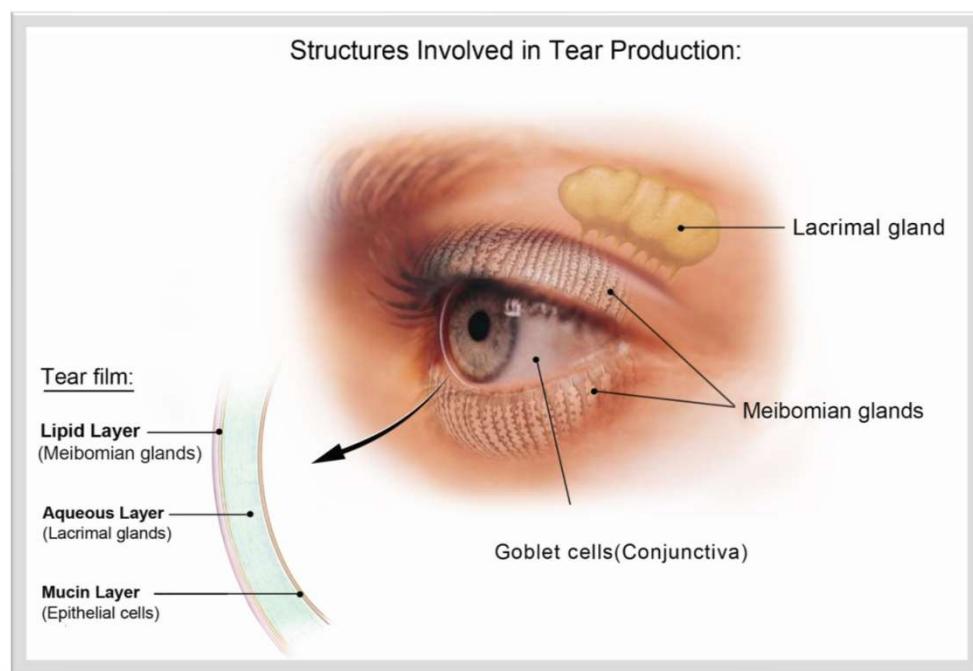


Mismatch between modern environment and evolutionary history

# Tear Film & Ocular Surface



# Mucin Layer



## Origin

- Goblet cells (primary)
- Lacrimal gland and corneal epithelium (secondary)

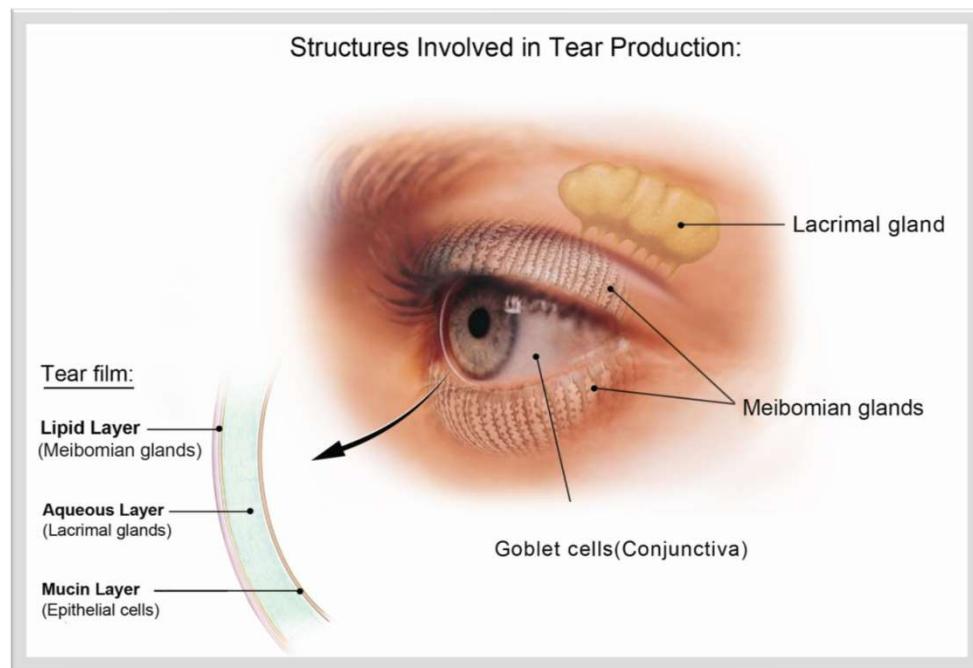
## Structure

- Mucins
- Glycoproteins
- Intermixes with aqueous layer

## Function

- Anchors tear film to cornea
- Lowers surface tension
- Protection

# Aqueous Layer



## Origin

- Lacrimal gland
- Accessory lacrimal glands
  - Glands of Wolfring
  - Glands of Krause

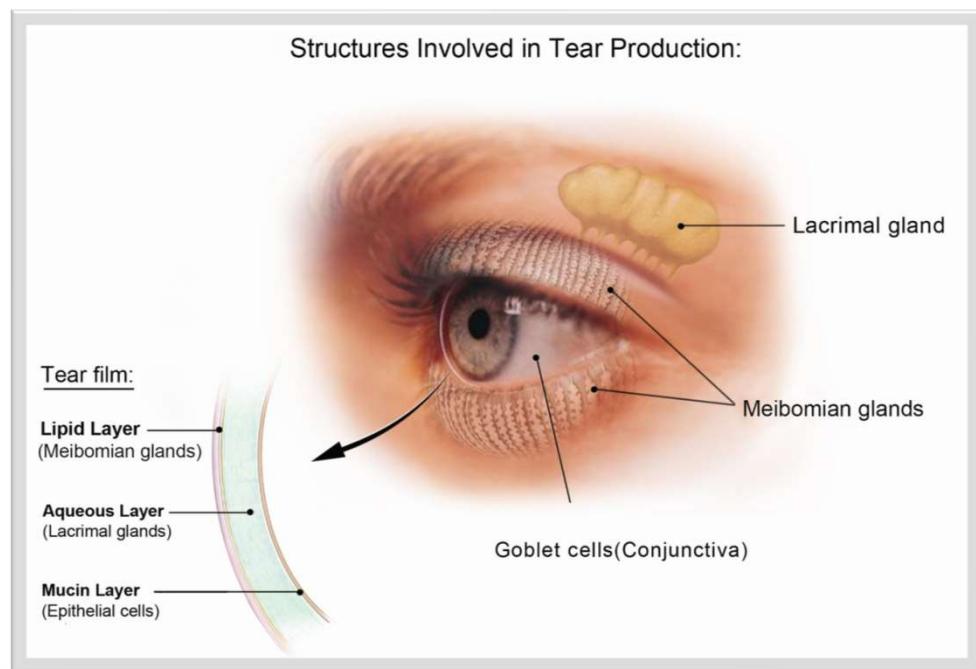
## Structure

- 98% water
- 2% gases, proteins

## Function

- Lubrication and hydration
- Nourishment
- Protection

# Lipid Layer



## Origin

- Meibomian glands

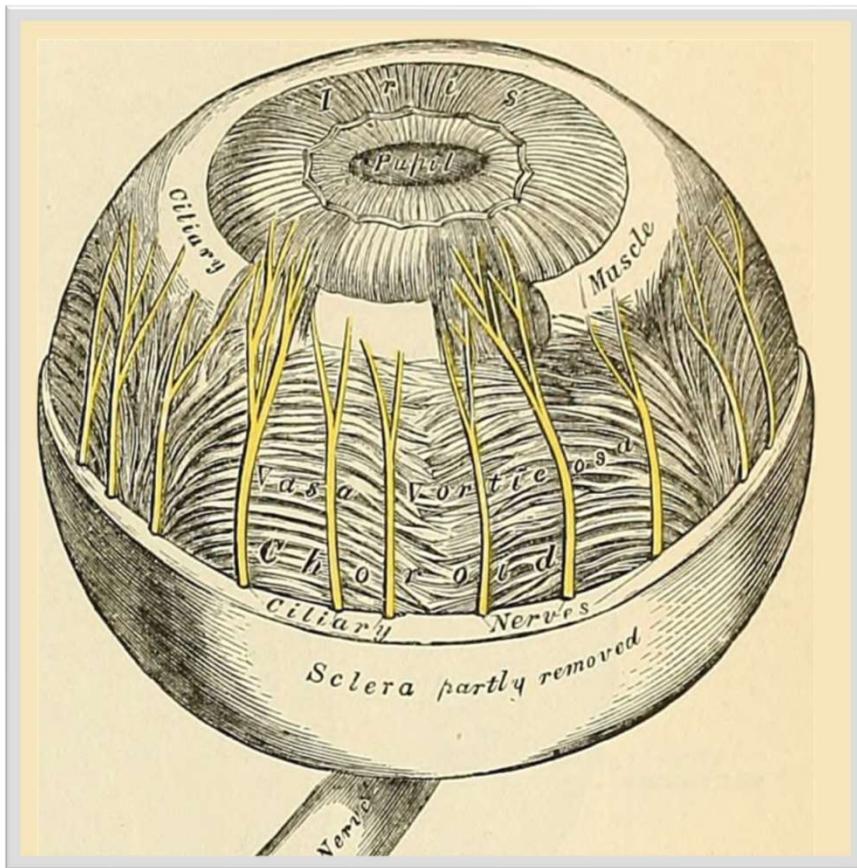
## Structure

- 50-100 nm in thickness
- 600+ unique lipids
  - Cholesterol esters
  - Wax esters
  - Phospholipids
  - Fatty acids
  - Triglycerides

## Function

- Prevent evaporation
- Provide smooth optical surface
- Lowers surface tension

# Neurogenic Control: Nerves of Sensation



## Sensory (Afferent) Nerves

- Corneal Nerves
  - Ophthalmic Branch (V1) of Trigeminal Nerve

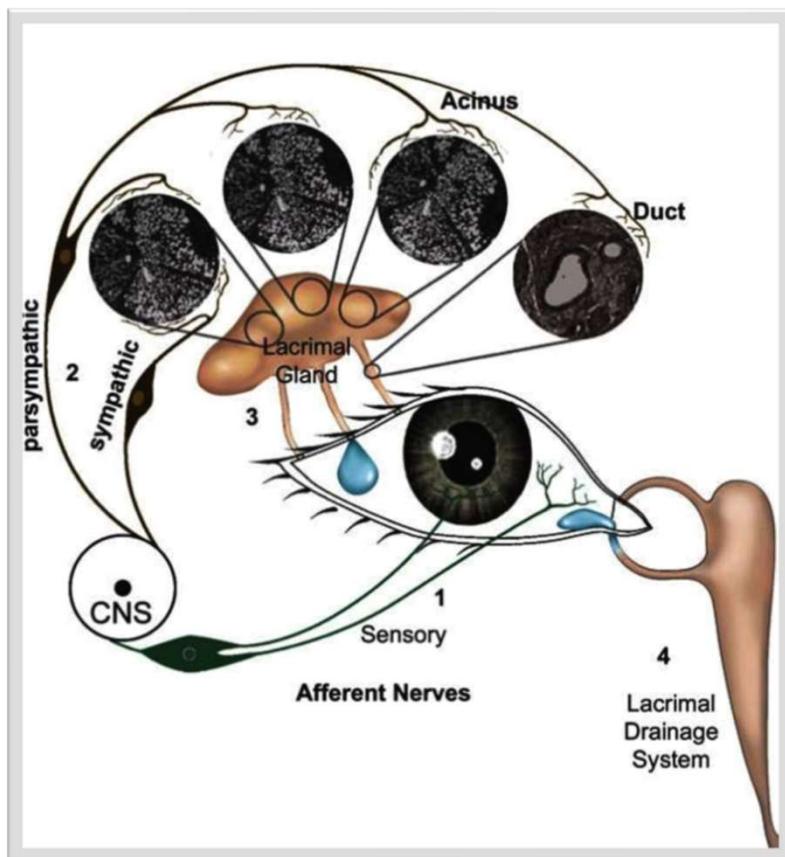
## Structure

- 7,000 nerve endings per mm<sup>2</sup>

## Function

- Sensation
- Epithelial cell turnover
- Wound healing
- Blinking and lacrimation

# Neurogenic Control: Nerves of Secretion



From Dartt DA. Neural regulation of lacrimal gland secretory processes: relevance in dry eye diseases. *Prog Retin Eye Res.* 2009;28(3):155-177.

## Parasympathetic Innervation: Motor (Efferent) Nerves

- Lacrimal Nerve

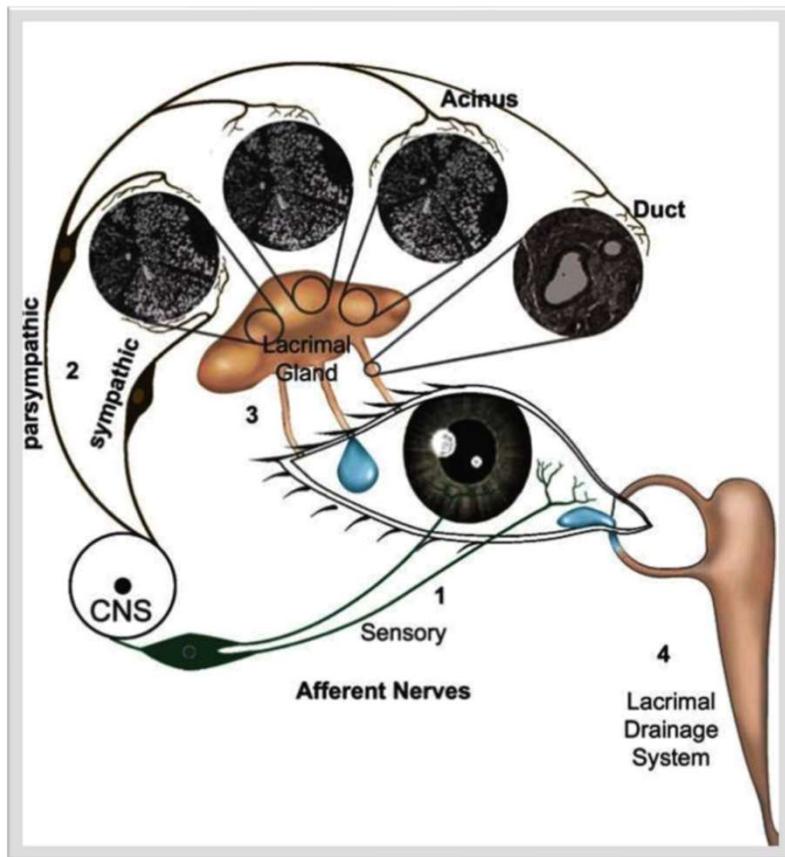
### Structure

- Branch of Ophthalmic Division (V1) of Trigeminal Nerve
- Parasympathetic innervation from Zygomatic Nerve
  - Branch of Maxillary Division (V2)

### Function

- Innervate lacrimal gland
  - Basal tear secretion
  - Reflex tearing

# Neurogenic Control: Nerves of Secretion

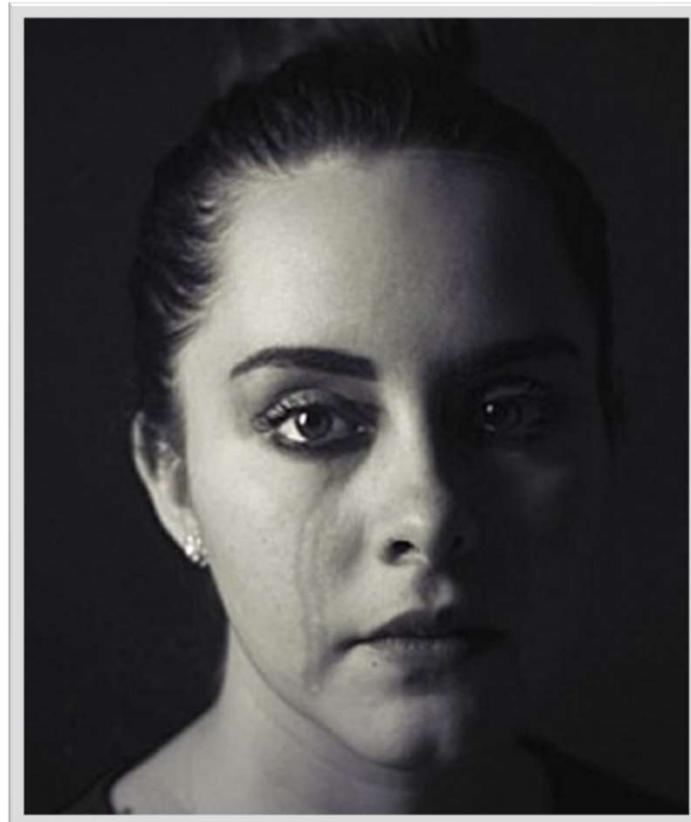


From Dartt DA. Neural regulation of lacrimal gland secretory processes: relevance in dry eye diseases. *Prog Retin Eye Res.* 2009;28(3):155-177.

## Parasympathetic Innervation: Motor (Efferent) Nerves

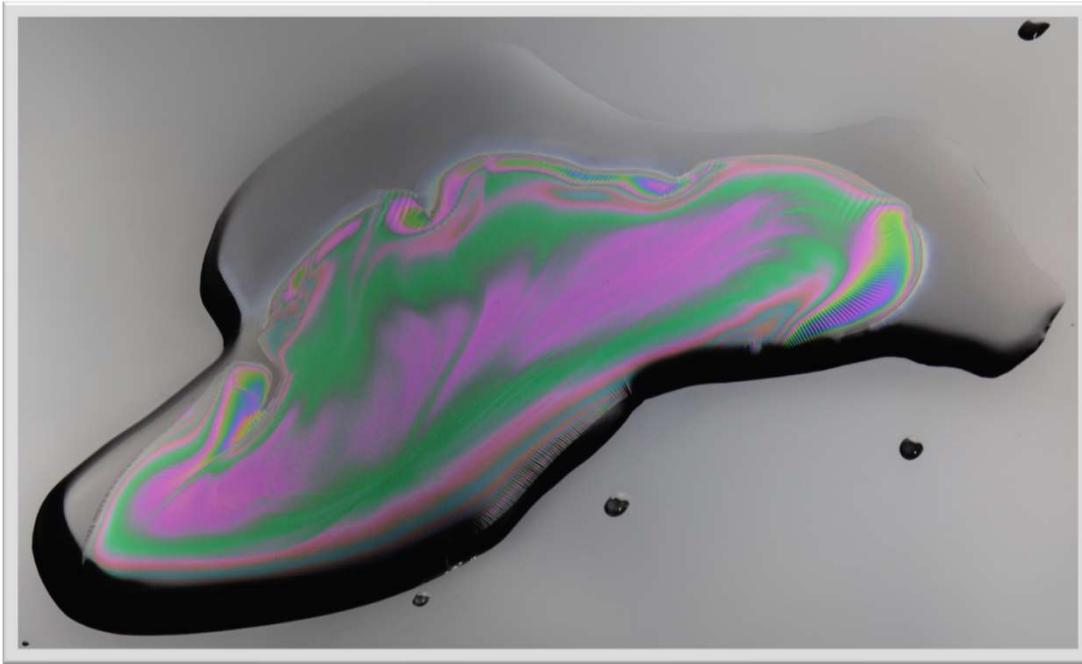
- Goblet cells
- Meibomian glands

## Compensatory Mechanism: Epiphora



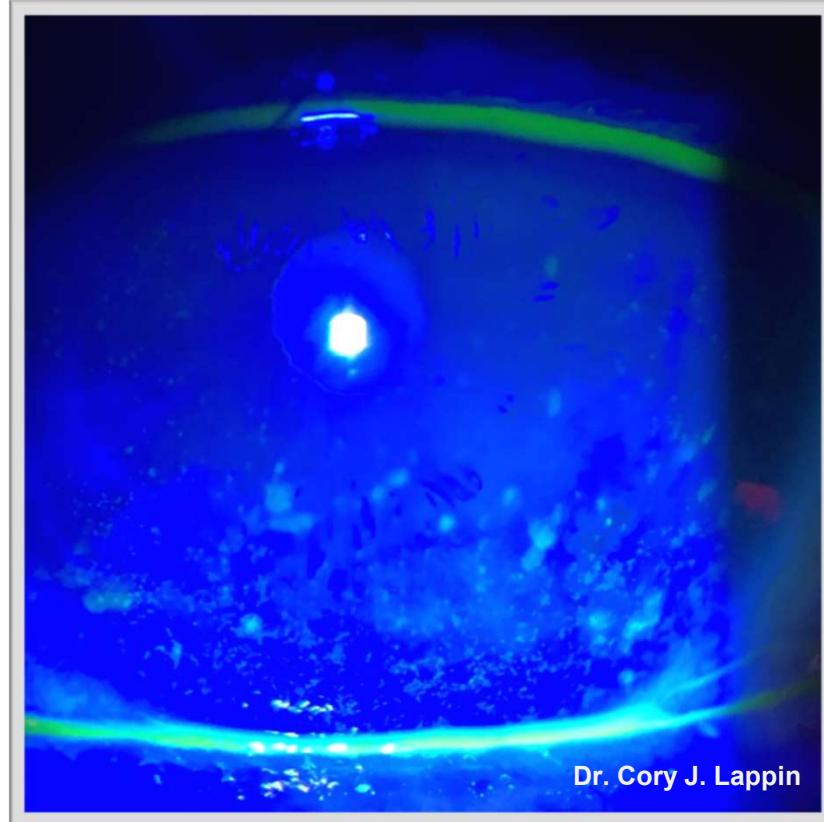
Stimulation of Reflex Tearing

## Compensatory Mechanism: Oily Tears



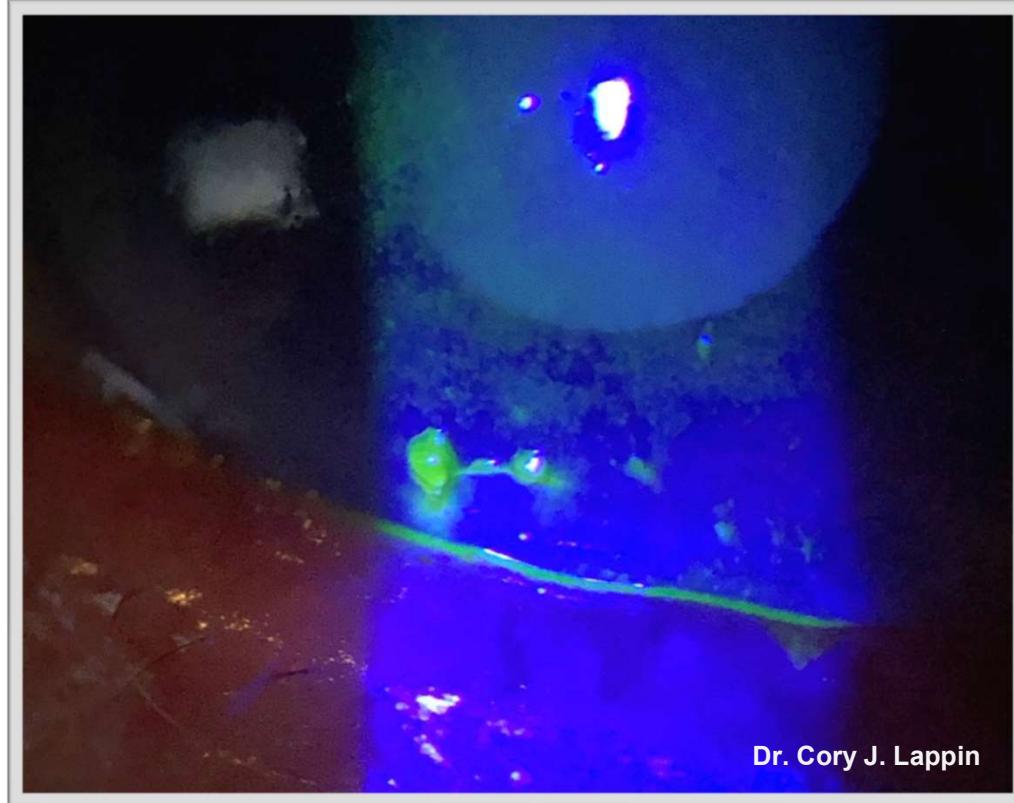
Increased Lipid Production

## Compensatory Mechanism: Mucoid Tears



Increased Mucin Production

# Compensatory Pathology: Filamentary Keratitis



# Inflammation



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## Body's Last Resort

- Homeostatic systems fail
  - “Meltdown” of system
  - Vicious cycle

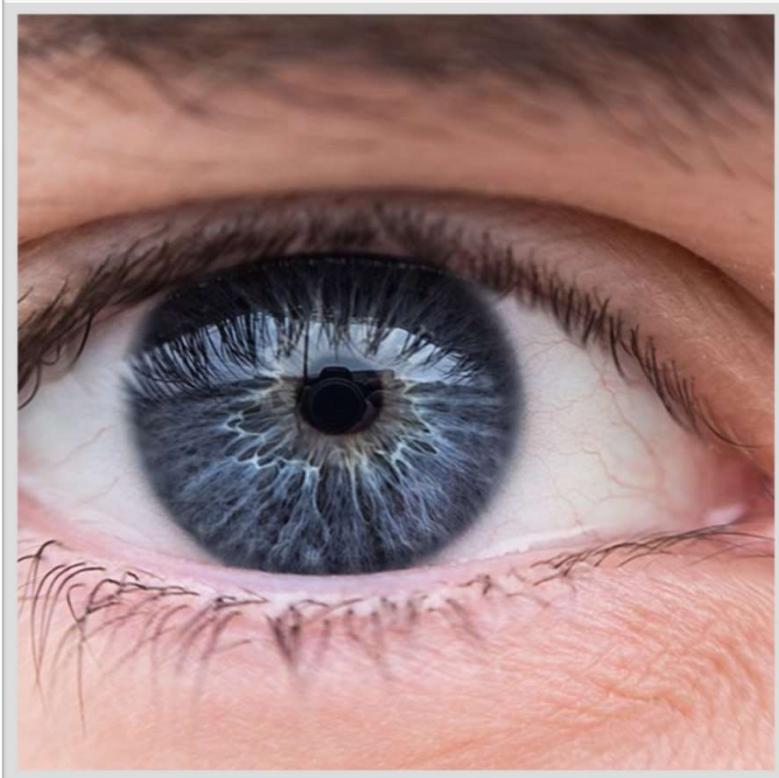
## “Primary” vs “Secondary” Inflammation

- **Primary**
  - Inflammation is cause of disruption
    - Sjogren’s Syndrome
    - Autoimmune conditions
- **Secondary**
  - Inflammation is result of disruption
    - MGD

# Loss of Homeostasis



# Meibomian Glands and the Lipid Layer



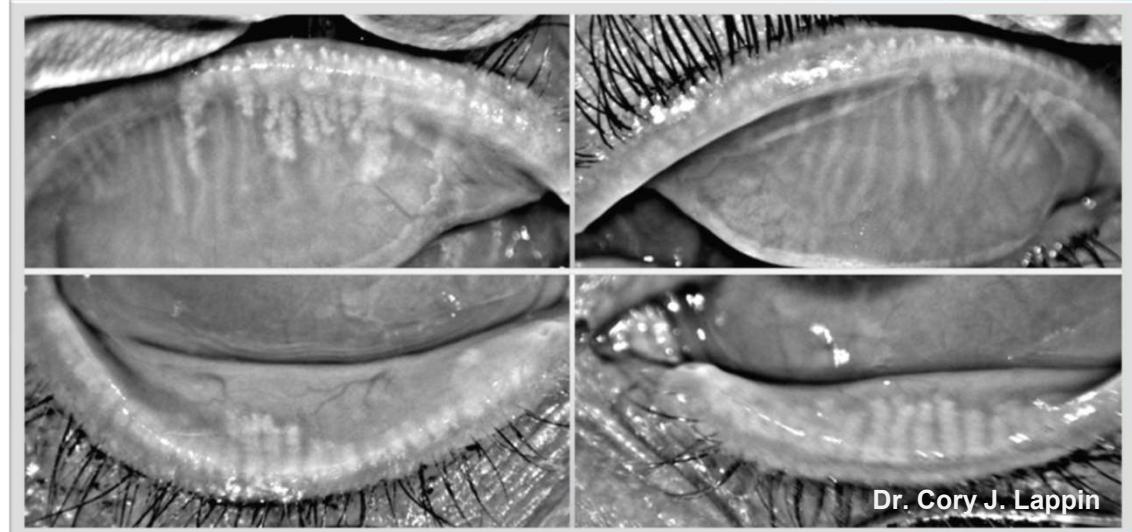
## Maintenance of Homeostasis

- Diet Rich in Omega 3 Fatty Acids
  - Olive oil-like consistency of meibum
  - Easy secretion
- Full Blinks
  - Lids completely touch
  - Meibomian glands emptied upon completion of blink
- Stable Tear Film
  - Delayed evaporation
  - Stable vision
- Eyes Comfortable

# Meibomian Glands and the Lipid Layer

## Loss of Homeostasis

- Diet Poor in Omega 3 Fatty Acids
  - Toothpaste-like consistency to meibum
    - Increased melting point
    - Impaired secretion
- Reduced and Partial Blinks
  - Impaired secretion
  - Obstructed meibomian glands
- Tear Film Instability
  - Accelerated evaporation/reduced TBUT
  - Poor/fluctuating vision
- Symptomatic
  - Burning, stinging, irritation, FB sensation, redness, fluctuating vision



# Meibomian Glands and the Lipid Layer

## Treatment

- **Dietary Treatment**
  - Omega 3 fatty acid supplementation
    - Re-esterified, triglyceride-based formulation
    - 3:1 EPA to DHA ratio
    - 2 g of combined EPA and DHA
- **Blink Training**
  - Blink exercises
  - 20-20-20 Rule
- **Palliative Treatment**
  - Warm compresses + massage
  - Lipid-based artificial tear
    - Refresh Optive Mega 3



# Meibomian Glands and the Lipid Layer

## Treatment

- Procedures
  - Thermal Pulsation
    - LipiFlow
    - iLux
    - TearCare
  - IPL Treatment
    - OptiLight
  - RF Treatment
    - OptiPlus
- Tear Film Stabilizers
  - Perfluorohexyloctane (Miebo)
- Artificial Barrier Environments
  - Scleral lenses



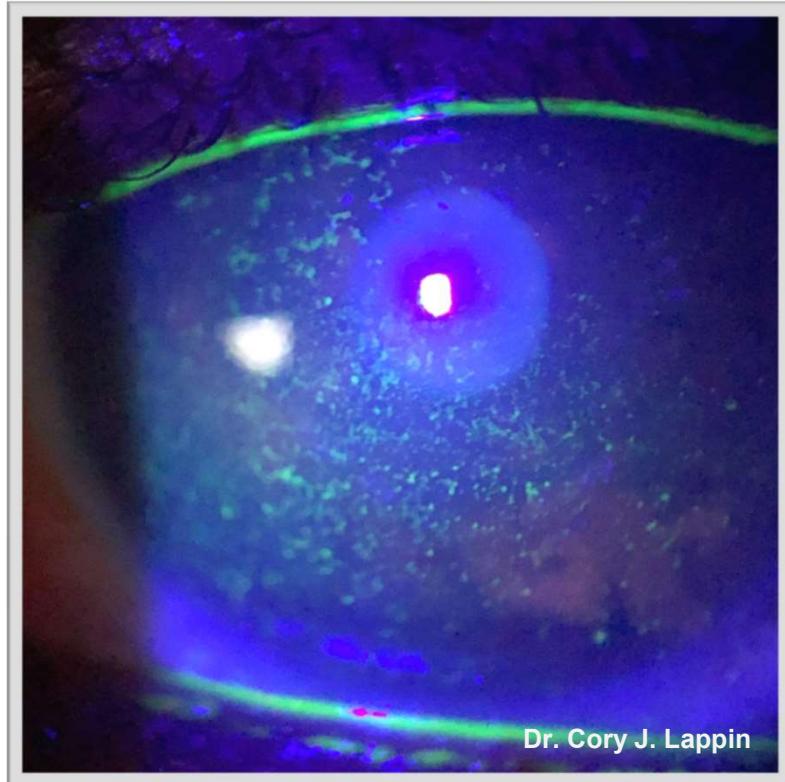
# Lacrimal Gland and the Aqueous Layer



## Maintenance of Homeostasis

- **Normal Tear Volume**
  - Cornea properly lubricated and hydrated
- **Ocular Surface Protected**
  - Debris, microbes, and foreign bodies removed
- **Eyes Comfortable**

# Lacrimal Gland and the Aqueous Layer



## Loss of Homeostasis

- Reduced Tear Volume
  - Poor lubrication
- Loss of Protection
  - Debris, microbes, and foreign bodies not adequately removed
- Symptomatic
  - Burning, stinging, irritation, FB sensation, redness
- Inflammation
  - Break down of ocular surface
- Causes
  - Often due to disorder of lacrimal gland
  - Sjogren's Syndrome

# Lacrimal Gland and the Aqueous Layer

## Treatment

- Anti-inflammatories
  - Immunomodulators
    - Lifitegrast (Xiidra)
    - Cyclosporine (Cequa, Vevye Restasis)
  - Steroids
    - “Soft” steroids (Eysuvitis)
- Neurostimulators
  - Varenicline nasal spray (Tyrvaya)
  - iTear100
- Lubricants
  - Preservative-free artificial tears
    - Systane Hydration
  - Gels
    - Carbomer-based



# Lacrimal Gland and the Aqueous Layer

## Treatment

- **Regenerative Treatments**
  - Platelet-rich plasma (PRP)
  - Autologous serum
  - Amniotic membranes
    - Cryopreserved (Prokera)
    - Lyophilized
    - Dehydrated
- **Procedures**
  - IPL Treatment
  - OptiLight
- **Artificial Barrier Environments**
  - Scleral lenses



## The Nerves and Feedback

### Maintenance of Homeostasis

- Normal corneal sensation
- Maintenance of corneal epithelial cell turnover
- Successful corneal wound healing
- Normal blinking and lacrimation



# The Nerves and Feedback

## Loss of Homeostasis

- Reduced or absent corneal sensation
  - Disrupted corneal epithelial cell turnover
  - Impaired corneal wound healing
  - Abnormal blinking and lacrimation
  - Break down of ocular surface
- Causes
- Herpetic infection
  - Surgery
    - Refractive surgery (LASIK)
    - Retinal surgery
  - Injury/Trauma
  - Medication use
    - Chronic preservative exposure (glaucoma)
  - Chronic ocular surface disease
  - Systemic disease (diabetes, stroke, etc.)



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# The Nerves and Feedback

## Treatment

- Regenerative Treatments
  - Cenegermin-bkbj (Oxervate)
    - Recombinant human NGF
  - Platelet-rich plasma (PRP)
  - Autologous serum
  - Amniotic membranes
    - Cryopreserved (Prokera)
    - Lyophilized
    - Dehydrated
- Neurostimulators
  - Varenicline nasal spray (Tyrvaya)
  - iTear100
- Surgical
  - Corneal neurotization
  - Tarsorrhaphy
  - Conjunctival flap



# Mechanical Eyelid Issues: Exposure

## Maintenance of Homeostasis

- Lids Close Completely

- Tears properly spread over surface
- Ocular surface protected
- Ocular surface recovery during sleep



# Mechanical Eyelid Issues: Exposure

## Loss of Homeostasis

- Incomplete Lid Closure
  - Poor spreading of tears over ocular surface
  - Increased friction
  - Ocular surface exposed
  - Poor ocular surface recovery and repair during sleep
- Causes
  - Lagophthalmos
    - S/P Blepharoplasty
    - Bell's Palsy
  - Floppy eyelid syndrome
  - Ectropion
  - Age-related loss of lid elasticity



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# Mechanical Eyelid Issues: Exposure

## Treatment

- Nocturnal Lubrication
  - Ointments
    - Hylo Night
  - Gels
    - Carbomer-based
- Protective Barriers
  - Sleep goggles
    - EyeSeals 4.0
  - Lid Patches
    - SleepTite/SleepRite
- Artificial Barrier Environments
  - Scleral lenses (day)
  - Soft BCLs (night)
- Surgery
  - Approach with caution



# Microbiome and Microflora

## Maintenance of Homeostasis

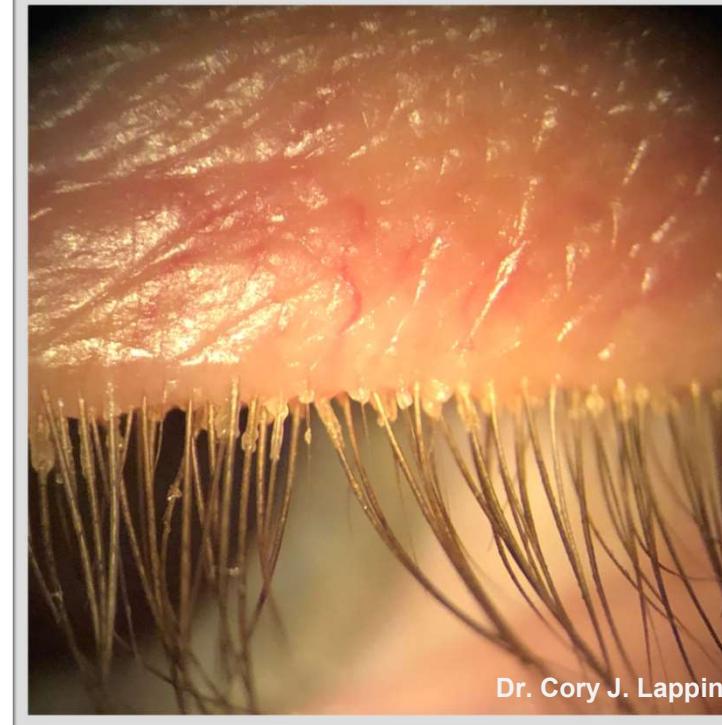
- Bacterial (Staph) and Demodex populations on lids and lashes controlled
- Normal meibum production and tear film function



# Microbiome and Microflora

## Maintenance of Homeostasis

- Bacteria (Staph) and Demodex overpopulate on lids and lashes
- Altered meibum production and tear film function
  - Increased melting point
  - Saponification of tears
- Lid margin and ocular surface inflammation
  - MGD
  - Lid notching
  - Lash disruption



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# Microbiome and Microflora

## Loss of Homeostasis

- **Bacteria (Staph) and Demodex overpopulate on lids and lashes**
- **Altered meibum production and tear film function**
  - Increased melting point
  - Saponification of tears
- **Lid margin and ocular surface inflammation**
  - MGD
  - Lid notching
  - Lash disruption



# Microbiome and Microflora

## Treatment

- Reestablish Control of Microbial Populations
  - **Bacteria (Staph)**
    - Hypochlorous acid
  - **Demodex**
    - Lotilaner ophthalmic solution (Xdemvy)
    - Tea tree oil
    - Okra-based cleansers (Zocular)
  - **Manual Debridement**
    - NuLids PRO (in-office treatment)
    - BlephEx (in-office treatment)
    - NuLids (at-home treatment)
  - **IPL Treatment**
    - OptiLight

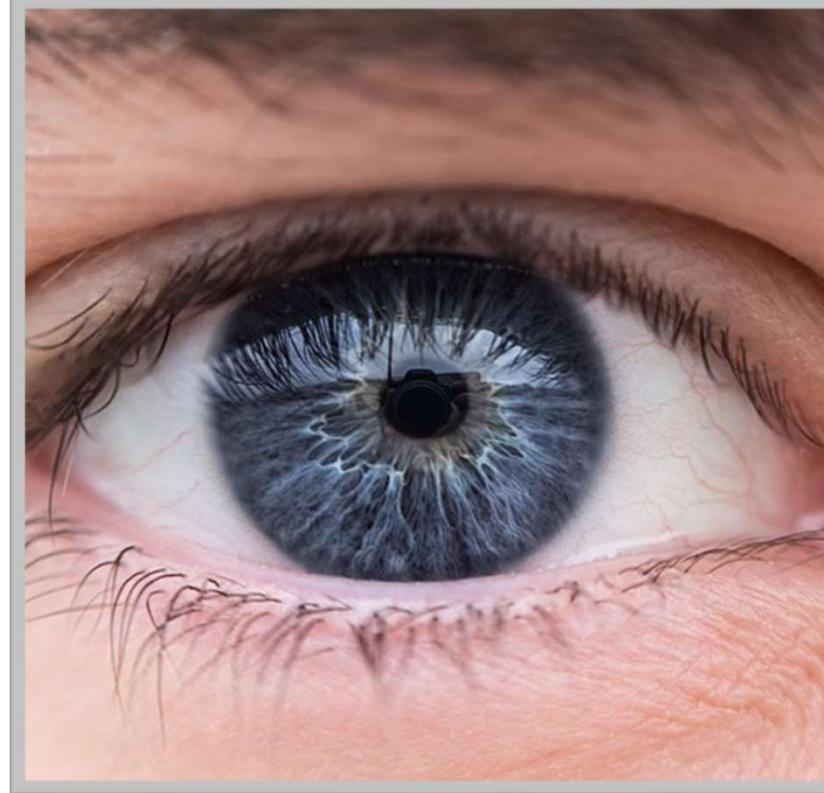


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# Ocular Rosacea

## Maintenance of Homeostasis

- Cathelicidin (antimicrobial peptide)
  - Produced in response to potential pathogens
  - Part of our innate immune system response



# Ocular Rosacea

## Loss of Homeostasis

- Cathelicidin (antimicrobial peptide)
  - Produced in response to normal environmental stimuli
    - Cold weather, alcohol, spicy food, stress, etc.
- Increases VEGF production
  - Development of telangiectatic vessels on ocular surface
    - Inflammation
    - Cosmetic redness



# Ocular Rosacea

## Treatment

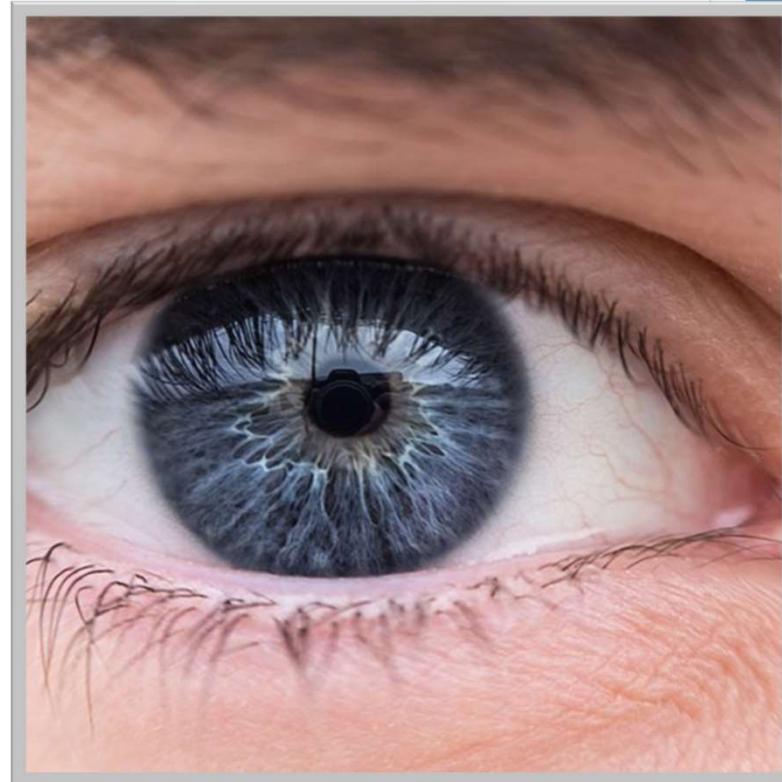
- **Lifestyle Modifications**
  - Trigger avoidance
- **Anti-inflammatories**
  - Doxycycline
  - Steroids
  - Immunomodulators
- **Vasoconstrictors**
  - Brimonidine tartrate (Lumify)
- **Supportive Treatment**
  - Standard MGD Treatment
- **IPL Treatment**
  - OptiLight



# Allergies and Hypersensitivities

## Maintenance of Homeostasis

- Ocular surface remains stable despite presence of environmental allergens
- Inflammatory response controlled



# Allergies and Hypersensitivities

## Loss of Homeostasis

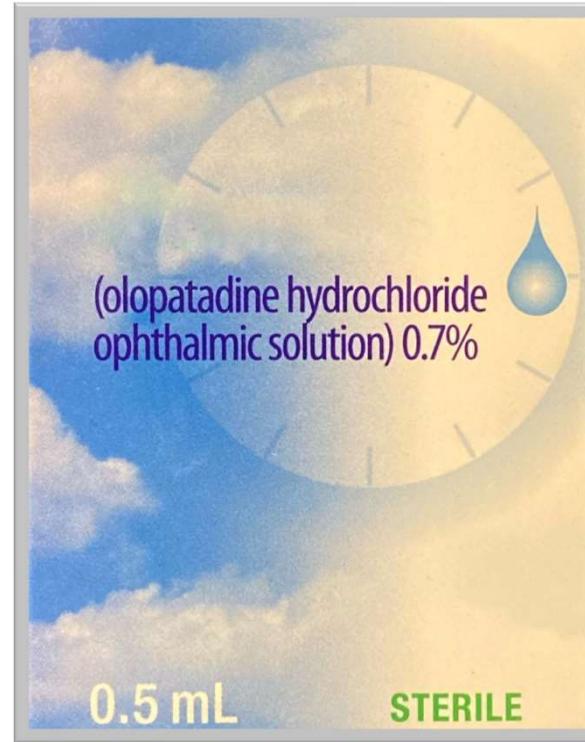
- Symptomatic
  - Itching, redness, swelling, stringy or ropey mucus production
- Inflammation
  - Break down of ocular surface
- Causes
  - Seasonal Allergies
  - Contact Dermatitis
  - Atopic Keratoconjunctivitis (AKC)
  - Vernal Keratoconjunctivitis (VKC)



# Allergies and Hypersensitivities

## Treatment

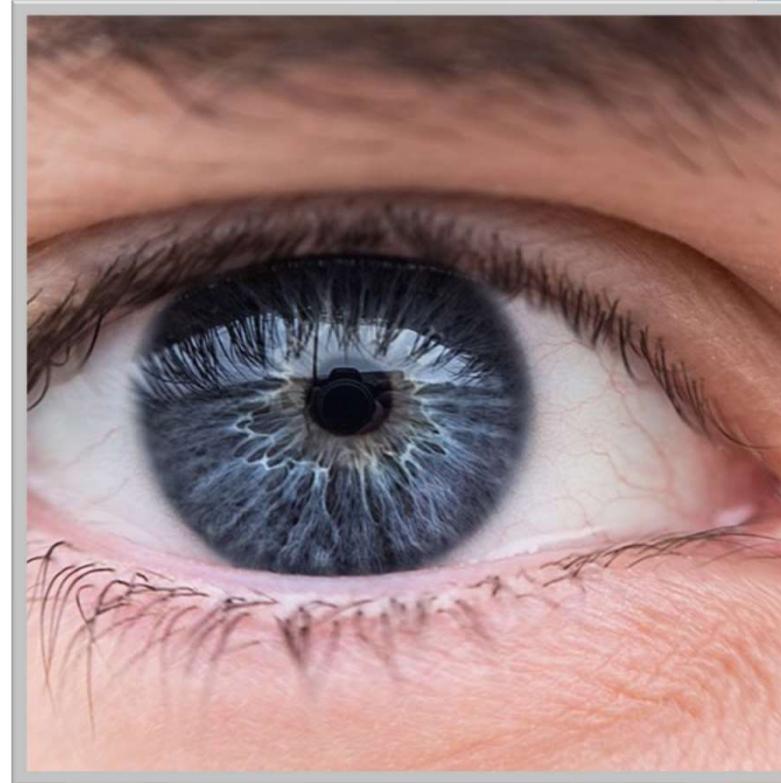
- Antihistamine-Mast Cell Stabilizer Combos
  - Olopatadine (Pataday)
  - Alcaftadine (Lastacraft)
- Preferential Exclusion
  - Ectoin (Allegro)
- Anti-inflammatories
  - Steroids (topical and oral)
- Immunomodulators
  - Cyclosporine (Verkazia)



# Environmental Challenges

## Maintenance of Homeostasis

- Ocular surface remains stable despite challenges posed by external environment and climate



# Environmental Challenges

## Loss of Homeostasis

- External Environment and Climate Challenges
  - Too great for ocular surface to maintain stability
- Common stressors
  - Outdoor Climate
    - High temperatures
    - Low humidity
    - Poor air quality
  - Indoor Environment
    - AC
    - Ceiling fans
    - Furnace



# Environmental Challenges

## Treatment

- Modify Environment
  - Humidifier
- Create Barrier to Environment
  - Ziena moisture chamber specs
  - Scleral lenses
  - BCLs
- Increase Ocular Surface Resiliency
  - Standard DED Treatment



# General Contact Lens Wear

## Intrinsically Disrupts Homeostasis

- Introduces foreign body to ocular surface
- Proinflammatory?

## Successful Contact Lens Wear

- Minimize disruption to homeostasis
- Daily disposable modality
- Polymers that mimic or are compatible with ocular surface



# Microblepharoexfoliation

## Benefits

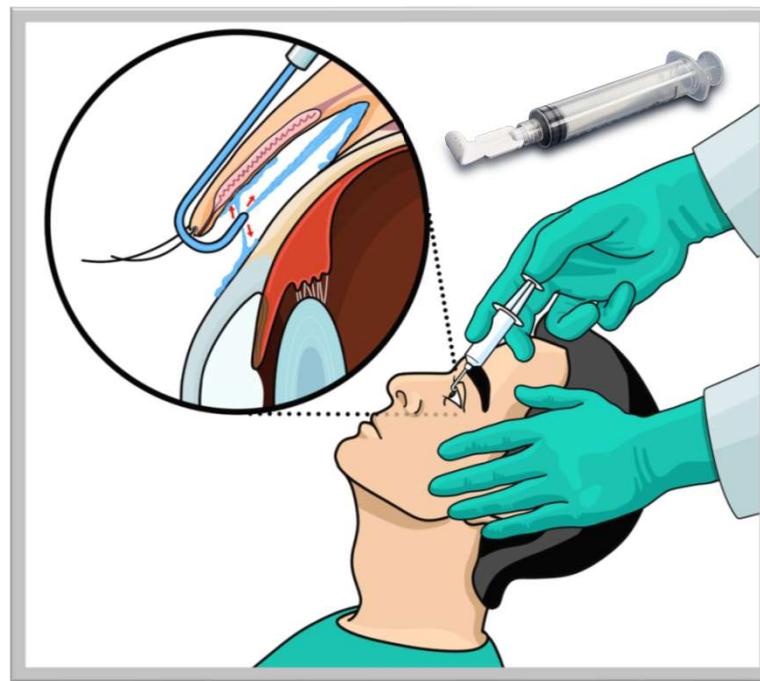
- Blepharitis
  - Reduces bacterial and Demodex populations
  - Removes lid debris, biofilm, and collarettes
- MGD
  - Clears duct openings
  - Removes pro-inflammatory pathogens and factors
- Devices
  - In-office: BlephEx, NuLids PRO
  - At-home: NuLids



# Ocular Surface Lavage

## Benefits

- High pressure saline irrigation
- “Resets” ocular surface
- Devices
  - Rinsada



<https://www.rinsada.com/>

# Thermal Pulsation

## Benefits

- MGD
  - Improves meibomian gland structure, function, quality of meibum, and tear breakup time
  - “Resets” meibomian glands
- Devices
  - LipiFlow
  - iLux
  - TearCare



# Intense Pulsed Light (IPL)

## Benefits

- **MGD**
  - Improves meibomian gland structure, function, quality of meibum, and tear breakup time
- **Inflammation**
  - Reduces inflammatory factors found in tear film and ocular surface
- **Ocular Rosacea**
  - Destroys proinflammatory telangiectatic blood vessels
- **Blepharitis**
  - Decreases Demodex and bacterial populations on lids and lashes
- **Devices**
  - OptiLight



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# Radiofrequency (RF)

## Benefits

- Targeted heat delivery
  - Frequency specific
  - Liquefies meibum
- Improves skin quality
  - Stimulates collagen synthesis
  - Potentially improves blink mechanics
- Devices
  - OptiPlus



# Punctal Plugs

## Benefits vs Cost

- Controversial
  - Based on antiquated understanding of DED
- “Cesspool” Effect
  - Potential to exacerbate inflammation
- Counter to Homeostasis
  - Fundamentally alters ocular surface environment
  - Do not address underlying issue
  - Sometimes just as beneficial to remove punctal plugs as to place them
  - Effects often diminish with time
    - Recalibration of homeostasis

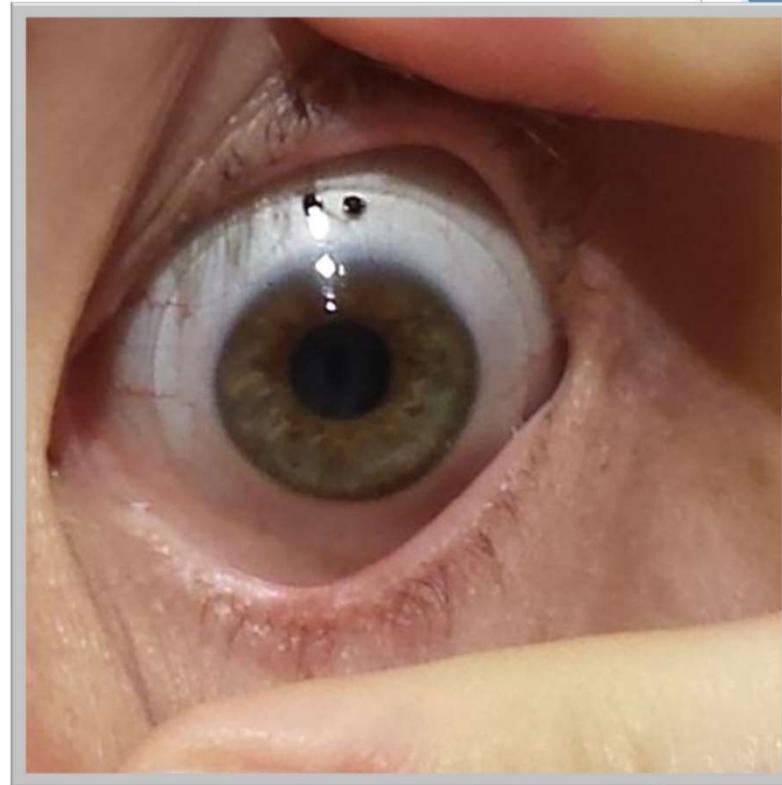


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# Artificial Barrier Environments

## Benefits

- Creates “new” homeostatic environment
- “Last resort”
- Methods
  - Soft bandage contact lenses
  - Scleral lenses



# Artificial Tears

**“Band-Aid in a Bottle”**

- Quick relief
  - But short-lived
- More palliative than therapeutic
  - Do not address underlying issues
- Preservative-free gels and drops



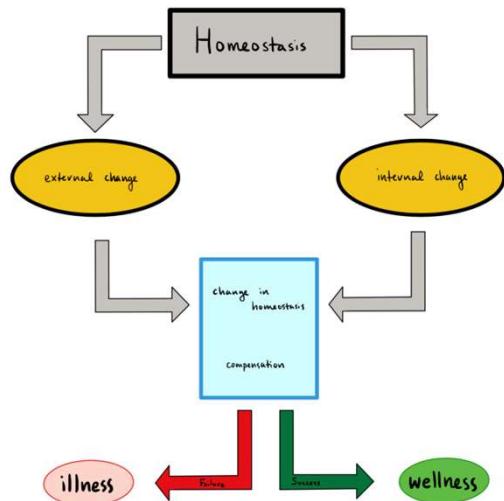
# Regenerative Treatments

## Restorative

- Fundamental goal is restoration of function at a base level
- Examples
  - Recombinant human NGF
    - [Cenegermin-bk bj \(Oxervate\)](#)
  - Amniotic membranes
    - [Cryopreserved \(Prokera\)](#)
    - [Lyophilized](#)
    - [Dehydrated](#)
  - Blood-derived products
    - [Platelet-rich plasma \(PRP\)](#)
    - [Autologous serum](#)



# Summary



To optimize the ocular surface you must understand homeostasis

To understand homeostasis you must know how the ocular surface functions in health

Once you understand how the system is meant to function you can determine:

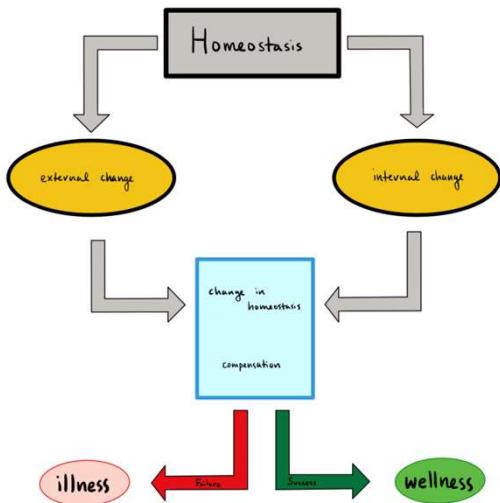
What causes the ocular surface to lose balance?  
What is the result when balance is lost?  
How do we attempt to restore balance?

# Summary

By evaluating dry eye and ocular surface disease through this homeostatic perspective, you can:

Determine the best treatment options for your patients

Optimize the ocular surface by attempting to restore homeostasis



# References

1. Cannon WB. Organization for physiological homeostasis. *Physiological Reviews*. 1929;9:399-431.
2. Billman GE. Homeostasis: The Underappreciated and Far Too Often Ignored Central Organizing Principle of Physiology. *Front Physiol*. 2020;11:200. Published 2020 Mar 10. doi:10.3389/fphys.2020.00200
3. Britannica, T. Editors of Encyclopedia (2022, August 23). *Homeostasis*. *Encyclopedia Britannica*. <https://www.britannica.com/science/homeostasis>. Published: Aug 23, 2022.
4. Rodolfo K. What is Homeostasis? Scientific American. <https://www.scientificamerican.com/article/what-is-homeostasis/#:-:text=Homeostasis%20from%20the%20Greek%20words,by%20the%20physician%20Walter%20Cannon>. Published January 3, 2000. Accessed September 11, 2022.
5. Kotas ME, Medzhitor R. Homeostasis, inflammation, and disease susceptibility. *Cell*. 2015;160(5):816-827. doi:10.1016/j.cell.2015.02.01
6. Craig JP, Nicholls KK, Akpek EK, et al. TFOS DEWS II Definition and Classification Report. *Ocul Surf*. 2017;15(3):276-283. doi:10.1016/j.jtos.2017.05.008
7. Starr CE. TFOS DEWS II: What's new? *MillennialeYE*. <https://millennialeye.com/articles/2017-sept-oct/tfoss-dews-ii-whats-new/>. Published 2017. Accessed September 11, 2022.
8. Abusharha AA. Changes in blink rate and ocular symptoms during different reading tasks. *Clin Optom (Auckl)*. 2017;9:133-138. Published 2017 Nov 20. doi:10.2147/OPTO.S142718
9. Bausch + Lomb. Impact of digital devices on eyes. Bausch + Lomb UK. <https://bausch.co.uk/news/blink-rate#:~:text=Their%20concerns%20are%20well%2Dfounded,functional1%2D2%2D3>. Published June 20, 2017. Accessed September 11, 2022.
10. Torre M. Avoiding eye strain among increased screen time for school, work and play. <https://cbaustinx.com/news/local/avoiding-eye-strain-among-increased-screen-time-for-school-work-and-play#:~:text=He%20explains%20the%20average%20person,Dr>. Published April 16, 2020. Accessed September 11, 2022.
11. Macsai MS. The role of omega-3 dietary supplementation in blepharitis and meibomian gland dysfunction (an AOS thesis). *Trans Am Ophthalmol Soc*. 2008;106:336-356.
12. Biber JM. Chapter 6 - Classification of Ocular Surface Disease. In: Holland EJ, Mannis MJ, Lee WB, eds. *Ocular Surface Disease: Cornea, Conjunctiva and Tear Film*. London: Elsevier Saunders; 2013:35-44.
13. Gipson IK. The ocular surface: the challenge to enable and protect vision: the Friedenwald lecture. *Invest Ophthalmol Vis Sci*. 2007;48(10):4390-4398. doi:10.1167/iovs.07-0770
14. Dartt DA, Willcox MD. Complexity of the tear film: importance in homeostasis and dysfunction during disease. *Exp Eye Res*. 2013;117:1-3. doi:10.1016/j.exer.2013.10.008
15. Chang AY, Purt B. Biochemistry, Tear Film. [Updated 2022 Jun 11]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK572136/>
16. Kayal, A. The Physiology of Tear Film. In: Ferreri FM, ed. *Dry Eye Syndrome - Modern Diagnostic Techniques and Advanced Treatments*. IntechOpen. 2021. <https://doi.org/10.5772/intechopen.98945>
17. Gipson IK, Argüeso P. Role of mucins in the function of the corneal and conjunctival epithelia. *Int Rev Cytol*. 2003;231:1-49. doi:10.1016/s0074-7696(03)31001-0
18. Uchino Y. The Ocular Surface Glycocalyx and its Alteration in Dry Eye Disease: A Review. *Invest Ophthalmol Vis Sci*. 2018;59(14):DE5157-DE5162. doi:10.1167/iovs.17-23756
19. Conradry CD, Joos ZP, Patel BC. Review: The Lacrimal Gland and Its Role in Dry Eye. *J Ophthalmol*. 2016;2016:7542929. doi:10.1155/2016/7542929
20. Murube J. Basal, reflex, and psycho-emotional tears. *Ocul Surf*. 2009;7(2):60-66. doi:10.1016/s1542-0124(12)70296-3
21. Bylsma LM, Gračanin A, Vingerhoets AJJM. The neurobiology of human crying. *Clin Auton Res*. 2019;29(1):63-73. doi:10.1007/s10286-018-0526-y
22. Dartt DA. Neural regulation of lacrimal gland secretory processes: relevance in dry eye diseases. *Prog Retin Eye Res*. 2009;28(3):155-177. doi:10.1016/j.preteyes.2009.04.003
23. Kulovesi P, Rantamäki AH, Holopainen JM. Surface properties of artificial tear film lipid layers: effects of wax esters. *Invest Ophthalmol Vis Sci*. 2014;55(7):4448-4454. Published 2014 May 29. doi:10.1167/iovs.14-14122
24. Patel J, Levin A, Patel BC. Epiphora. [Updated 2022 May 24]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK557449/>
25. Sowka JW, Kabat AG. Epiphora Epiphany. Review of Optometry. <https://www.reviewofoptometry.com/article/epiphora-epiphany>. Published January 16, 2009. Accessed September 11, 2022.
26. Karpecki PM. Too many tears: Is it Dry Eye? Review of Optometry. <https://www.reviewofoptometry.com/article/too-many-tears-is-it-dry-eye>. Published November 15, 2015. Accessed September 11, 2022.
27. Marlon J, Demeritt MJ, Lewandowska BI. Checking under the hood: How to evaluate the lid and ocular surface. Review of Optometry. <https://www.reviewofoptometry.com/article/checking-under-the-hood-how-to-evaluate-the-lid-and-ocular-surface>. Published November 20, 2018. Accessed September 11, 2022.
28. Kabat AG, Sowka JW. Fighting Filamentary Keratitis. Review of Optometry. <https://www.reviewofoptometry.com/article/fighting-filamentary-keratitis>. Published February 15, 2015. Accessed September 11, 2022.
29. Carson SE, Patel BC. Sjögren Syndrome. [Updated 2022 May 24]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK431049/>
30. Epstein AB. Diagnosing Dry Eye: What We're Actually Looking to Identify. *Optometricmanagement.com*. <https://www.optometricmanagement.com/supplements/2019/june-2019/the-effective-and-practical-dry-eye-practice/diagnosing-dry-eye-what-we-8217-re-actually-look>. Published June 1, 2019. Accessed June 26, 2022.
31. Linton RG, Curnow DH, Riley WJ. THE MEIBOMIAN GLANDS: AN INVESTIGATION INTO THE SECRETION AND SOME ASPECTS OF THE PHYSIOLOGY. *Br J Ophthalmol*. 1961;45(11):718-723. doi:10.1136/bjo.45.11.718
32. Pult H, Korb DR, Murphy PJ, Riede-Pult BH, Blackie C. A new model of central lid margin apposition and tear film mixing in spontaneous blinking. *Cont Lens Anterior Eye*. 2015;38(3):173-180. doi:10.1016/j.clae.2015.01.012
33. Showalter JK. Think about the blink: Part 1. Optometry Times. <https://www.optometrystimes.com/view/think-about-the-blink-part-1>. Published November 11, 2020. Accessed June 26, 2022.
34. Knop E, Knop N, Millar T, Obata H, Sullivan DA. The international workshop on meibomian gland dysfunction: report of the subcommittee on anatomy, physiology, and pathophysiology of the meibomian gland. *Invest Ophthalmol Vis Sci*. 2011;52(4):1938-1978. Published 2011 Mar 30. doi:10.1167/iovs.10-6997c
35. Kawashima M, Tsubota K. Tear lipid layer deficiency associated with incomplete blinking: a case report. *BMC Ophthalmol*. 2013;13:34. Published 2013 Jul 16. doi:10.1186/1471-2415-13-34
36. Oleñik A, Jiménez-Alfaro I, Alejandre-Alba N, Mahillo-Fernández I. A randomized, double-masked study to evaluate the effect of omega-3 fatty acids supplementation in meibomian gland dysfunction. *Clin Interv Aging*. 2013;8:1133-1138.
37. Epitropoulos AT, Donnenfeld ED, Shah ZA, et al. Effect of oral re-esterified omega-3 nutritional supplementation on dry eyes. *Cornea*. 2016;35(9):1185-1191.
38. Lim A, Wenk MR, Tong L. Lipid-based therapy for ocular surface inflammation and disease. *Trends Mol Med*. 2015;21(12):736-748.
39. Murphy CJ, Bentley E, Miller PE, et al. The pharmacologic assessment of a novel lymphocyte function-associated antigen-1 antagonist (SAR 1118) for the treatment of keratoconjunctivitis sicca in dogs. *Invest Ophthalmol Vis Sci*. 2011;52(6):3174-3180.
40. Sun Y, Zhang R, Gadek TR, O'Neill CA, Pearlman E. Corneal inflammation is inhibited by the LFA-1 antagonist, lifitegrast (SAR 1118). *J Ocul Pharmacol Ther*. 2013;29(4):395-402.

# References

41. Zhong M, Gadek TR, Bui M, et al. Discovery and development of potent Ifa-1/icam-1 antagonist sar 1118 as an ophthalmic solution for treating dry eye. *ACS Med Chem Lett.* 2012;3(3):203-206.
42. Schechter BA, Katz RS, Friedman LS. Efficacy of topical cyclosporine for the treatment of ocular rosacea. *Adv Ther.* 2009;26(6):651-659.
43. Liu J, Sheha H, Fu Y, Liang L, Tseng SC. Update on amniotic membrane transplantation. *Expert Rev Ophthalmol.* 2010;5(5):645-661.
44. Sacchetti M, Lambiasi A. Diagnosis and management of neurotrophic keratitis. *Clin Ophthalmol.* 2014;8:571-579.
45. Walker HK. Cranial nerve v: the trigeminal nerve. In: Walker HK, Hall WD, Hurst JW, eds. *Clinical Methods: The History, Physical, and Laboratory Examinations.* 3rd ed. Butterworths; 1990.
46. Mastropasqua L, Massaro-Giordano G, Nubile M, Sacchetti M. Understanding the pathogenesis of neurotrophic keratitis: the role of corneal nerves. *J Cell Physiol.* 2017;232(4):717-724.
47. Heigle TJ, Pflugfelder SC. Aqueous tear production in patients with neurotrophic keratitis. *Cornea.* 1996;15(2):135-138.
48. Jabbarvand M, Hashemian H, Khodaparast M, Rafatnejad A, Beheshtnejad A, Salami A. Do unilateral herpetic stromal keratitis and neurotrophic ulcers cause bilateral dry eye? *Cornea.* 2015;34(7):768-772.
49. Semeraro F, Forbice E, Romano V, et al. Neurotrophic keratitis. *Ophthalmologica.* 2014;231(4):191-197.
50. OXERVATE® (cenergermin-bkbj) ophthalmic solution 0.002% (20mcg/mL)[US package insert]. Boston, MA; Dompé U.S. Inc.; 2019.
51. Liu J, Sheha H, Tseng SC. Pathogenic role of Demodex mites in blepharitis. *Curr Opin Allergy Clin Immunol.* 2010;10(5):505-510.
52. Gutierrez Y. Diagnostic pathology of parasitic infections with clinical correlations, 2nd ed. New York, NY: Oxford University Press. 2000.
53. Luo X, Li J, Chen C, Tseng S, Liang L. Ocular Demodicosis as a Potential Cause of Ocular Surface Inflammation. *Cornea.* 2017;36 Suppl 1:S9-S14.
54. Fromstein SR, Harthan JS, Patel J, Opitz DL. Demodex blepharitis: clinical perspectives. *Clin Optom (Auckl).* 2018;10:57-63.
55. Kheirkhah A, Casas V, Li W, Raju VK, Tseng SC. Corneal manifestations of ocular demodex infestation. *Am J Ophthalmol.* 2007;143(5):743-749.
56. Bhandari V, Reddy JK. Blepharitis: always remember demodex. *Middle East Afr J Ophthalmol.* 2014;21(4):317-320.
57. Nicholls SG, Oakley CL, Tan A, Vote BJ. Demodex species in human ocular disease: new clinicopathological aspects. *Int Ophthalmol.* 2017;37(1):303-312.
58. Cheng AM, Sheha H, Tseng SC. Recent advances on ocular Demodex infestation. *Curr Opin Ophthalmol.* 2015;26(4):295-300.
59. English FP, Nutting WB. Demodicosis of ophthalmic concern. *Am J Ophthalmol.* 1981;91(3):362-372.
60. Epstein AB. Beyond the Meibomian Glands. *Ophthalmology Management.* 2015;19.
61. Epitropoulos AT. Lid hygiene product helps reduce blepharitis, MGD symptoms. *Ophthalmology Times.* November 15, 2015. Accessed September 30, 2021.
62. Sanford K. Comprehending, Catching and Correcting MGD. *Review of Optometry.* March 2021.
63. Green-Church KB, Butovich I, Wilcox M, et al. The international workshop on meibomian gland dysfunction: report of the subcommittee on tear film lipids and lipid-protein interactions in health and disease. *Invest Ophthalmol Vis Sci.* 2011;52(4):1799-1993. Published 2011 Mar 30. doi:10.1167/iovs.10-6997
64. Vieira ACC, Höftling-Lima AL, Mannis MJ. Ocular rosacea--a review. *Arq Bras Oftalmol.* 2012;75(5):363-369.
65. Yamasaki K, Kanada K, Macleod DT, et al. TLR2 expression is increased in rosacea and stimulates enhanced serine protease production by keratinocytes. *J Invest Dermatol.* 2011;131(3):688-697.
66. Yamasaki K, Gallo RL. The molecular pathology of rosacea. *J Dermatol Sci.* 2009;55(2):77-81.
67. Del Rosso JQ. Advances in understanding and managing rosacea: part 1: connecting the dots between pathophysiological mechanisms and common clinical features of rosacea with emphasis on vascular changes and facial erythema. *J Clin Aesthet Dermatol.* 2012;5(3):16-25.
68. Zanetti M. Cathelicidins, multifunctional peptides of the innate immunity. *J Leukoc Biol.* 2004;75(1):39-48.
69. Vieira ACC, Höftling-Lima AL, Mannis MJ. Ocular rosacea--a review. *Arq Bras Oftalmol.* 2012;75(5):363-369.
70. Connor CG, Narayanan S, Miller W. Reduction in inflammatory marker matrix metalloproteinase-9 following lid debridement with BlephEx. *Invest Ophthalmol Vis Sci.* 2017;58(8):498-498.
71. Pfeffer I, Borelli C, Zierhut M, Schaller M. Treatment of ocular rosacea with 40 mg doxycycline in a slow release form. *J Dtsch Dermatol Ges.* 2011;9(11):904-907.
72. Frucht-Pery J, Sagi E, Hemo I, Ever-Hadani P. Efficacy of doxycycline and tetracycline in ocular rosacea. *Am J Ophthalmol.* 1993;116(1):88-92.
73. Dougherty JM, McCulley JP, Silvany RE, Meyer DR. The role of tetracycline in chronic blepharitis. Inhibition of lipase production in staphylococci. *Invest Ophthalmol Vis Sci.* 1991;32(11):2970-2975.
74. Sobrin L, Liu Z, Monroy DC, et al. Regulation of MMP-9 activity in human tear fluid and corneal epithelial culture supernatant. *Invest Ophthalmol Vis Sci.* 2000;41(7):1703-1709.
75. Määttä M, Kari O, Tervahartiala T, et al. Tear fluid levels of MMP-8 are elevated in ocular rosacea--treatment effect of oral doxycycline. *Graefes Arch Clin Exp Ophthalmol.* 2006;244(8):957-962.
76. Barton K, Monroy DC, Nava A, Pflugfelder SC. Inflammatory cytokines in the tears of patients with ocular rosacea. *Ophthalmology.* 1997;104(11):1868-1874.
77. Efron N. Is contact lens-induced corneal oedema inflammatory? *Aust. J. Optom.* 1985;68(5):167-172.
78. Dell SJ. Intense pulsed light for evaporative dry eye disease. *Clin Ophthalmol.* 2017;11:1167-1173.
79. Suwal A, Hao JL, Zhou DD, Liu XF, Suwal R, Lu CW. Use of Intense Pulsed Light to Mitigate Meibomian Gland Dysfunction for Dry Eye Disease. *Int J Med Sci.* 2020;17(10):1385-1392. Published 2020 Jun 1. doi:10.7150/ijms.44288
80. Vegunta S, Patel D, Shen JF. Combination Therapy of Intense Pulsed Light Therapy and Meibomian Gland Expression (IPL/MGX) Can Improve Dry Eye Symptoms and Meibomian Gland Function in Patients With Refractory Dry Eye: A Retrospective Analysis. *Cornea.* 2016;35(3):318-322. doi:10.1097/ICO.0000000000000735.
81. Vora GK, Gupta PK. Intense pulsed light therapy for the treatment of evaporative dry eye disease. *Curr Opin Ophthalmol.* 2015;26:314-318.
82. Yin Y, Liu N, Gong L, Song N. Changes in the Meibomian Gland After Exposure to Intense Pulsed Light in Meibomian Gland Dysfunction (MGD) Patients. *Curr Eye Res.* 2018;43(3):308-313. doi:10.1080/02713683.2017.1406525
83. Albietz JM, Schmid KL. Intense pulsed light treatment and meibomian gland expression for moderate to advanced meibomian gland dysfunction. *Clin Exp Optom.* 2018;101(1):23-33. doi:10.1111/cxo.12541

# References

84. Lumenis receives FDA approval for its IPL device to manage dry eye disease and launches OptiLight™. Lumenis. <https://lumenis.com/medical/specialties/eye-care/resource-hub/lumenis-receives-fda-approval-for-its-ipl-device-to-manage-dry-eye-disease-and-launches-optilight/>. Published April 29, 2021. Accessed June 26, 2022.
85. Yan X, Hong J, Jin X, et al. The Efficacy of Intense Pulsed Light Combined With Meibomian Gland Expression for the Treatment of Dry Eye Disease Due to Meibomian Gland Dysfunction: A Multicenter, Randomized Controlled Trial. *Eye Contact Lens.* 2021;47(1):45-53. doi:10.1097/ICL.0000000000000711
86. Arita R, Fukuoka S, Morishige N. Therapeutic efficacy of intense pulsed light in patients with refractory meibomian gland dysfunction. *Ocul Surf.* 2019;17(1):104-110. doi:10.1016/j.jtos.2018.11.004
87. Liu R, Rong B, Tu P, Tang Y, Song W, Toyos R, Toyos M, Yan X. Analysis of Cytokine Levels in Tears and Clinical Correlations After Intense Pulsed Light Treating Meibomian Gland Dysfunction. *Am J Ophthalmol.* 2017 Nov;183:81-90.
88. Gao YF, Liu RJ, Li YX, et al. Comparison of anti-inflammatory effects of intense pulsed light with tobramycin/dexamethasone plus warm compress on dry eye associated meibomian gland dysfunction. *Int J Ophthalmol.* 2019;12(11):1708-1713. Published 2019 Nov 18. doi:10.18240/ijo.2019.11.07
89. Byun JY, Choi HY, Myung KB, Choi YW. Expression of IL-10, TGF-beta(1) and TNF-alpha in Cultured Keratinocytes (HaCaT Cells) after IPL Treatment or ALA-IPL Photodynamic Treatment. *Ann Dermatol.* 2009;21(1):12-17. doi:10.5021/ad.2009.21.1.12
90. Huang J, Luo X, Lu J, et al. IPL irradiation rejuvenates skin collagen via the bidirectional regulation of MMP-1 and TGF-B1 mediated by MAPKs in fibroblasts. *Lasers Med Sci.* 2011;26(3):381-387. doi:10.1007/s10103-010-0870-1
91. Lee SY, Park KH, Choi JW, et al. A prospective, randomized, placebo-controlled, double-blinded, and split-face clinical study on LED phototherapy for skin rejuvenation: clinical, profilometric, histologic, ultrastructural, and biochemical evaluations and comparison of three different treatment settings. *J Photochem Photobiol B.* 2007;88(1):51-67. doi:10.1016/j.jphotobiol.2007.04.008
92. Taylor M, Porter R, Gonzalez M. Intense pulsed light may improve inflammatory acne through TNF- $\alpha$  down-regulation. *J Cosmet Laser Ther.* 2014;16(2):96-103. doi:10.3109/14764172.2013.864198
93. Wong WR, Shyu WL, Tsai JW, Hsu KH, Lee HY, Pang JH. Intense pulsed light modulates the expressions of MMP-2, MMP-14 and TIMP-2 in skin dermal fibroblasts cultured within contracted collagen lattices. *J Dermatol Sci.* 2008;51(1):70-73. doi:10.1016/j.jdermsci.2008.02.011
94. Toyos R, Toyos M, Willcox J, Multiniks H, Hoover J. Evaluation of the Safety and Efficacy of Intense Pulsed Light Treatment with Meibomian Gland Expression of the Upper Eyelids for Dry Eye Disease. *Photobiomodul Photomed Laser Surg.* 2019;37(9):527-531. doi:10.1089/photob.2018.4599
95. Papageorgiou P, Clayton W, Norwood S, Chopra S, Rustin M. Treatment of rosacea with intense pulsed light: significant improvement and long-lasting results. *Br J Dermatol.* 2008;159(3):628-632.
96. Kassir R, Kolluru A, Kassir M. Intense pulsed light for the treatment of rosacea and telangiectasias. *J Cosmet Laser Ther.* 2011 Oct;13(5):216-22.
97. Fishman HA, Periman LM, Shah AA. Real-Time Video Microscopy of In Vitro Demodex Death by Intense Pulsed Light. *Photobiomodul Photomed Laser Surg.* 2020 Aug;38(8):472-476.
98. Prieto VG, Sadick NS, Lloreta J, Nicholson J, Shea CR. Effects of intense pulsed light on sun-damaged human skin, routine, and ultrastructural analysis. *Lasers Surg Med.* 2002;30(2):82-5.
99. Takezaki S, Omi T, Sato S, Kawana S. Ultrastructural observations of human skin following irradiation with visible red light-emitting diodes (LEDs): a preliminary *in vivo* report. *Laser Ther.* 2005;14(4):153-160.
100. Cuenda-Galindo E, Díaz-Gil G, Palomar-Gallego MA, Linares-GarcíaValdecasas R. Increased fibroblast proliferation and activity after applying intense pulsed light 800-1200 nm. *Ann Anat.* 2015;198:66-72. doi:10.1016/j.ananat.2014.11.005
102. Goldberg DJ. Current trends in intense pulsed light. *J Clin Aesthet Dermatol.* 2012;5(6):45-53.
103. Dick MK, Miao JH, Limaiem F. Histology, fibroblast. In: StatPearls. StatPearls Publishing; 2022.
104. Erol OO, Gurlek A, Agaoglu G, Topcuoglu E, Oz H. Treatment of hypertrophic scars and keloids using intense pulsed light (IPL). *Aesthetic Plast Surg.* 2008;32(6):902-909. doi:10.1007/s00266-008-9161-7
105. Greiner JV. Long-term (12-month) improvement in meibomian gland function and reduced dry eye symptoms with a single thermal pulsation treatment. *Clin Exp Ophthalmol.* 2013;41(6):524-530.
106. Blackie CA, Coleman CA, Holland EJ. The sustained effect (12 months) of a single-dose vectored thermal pulsation procedure for meibomian gland dysfunction and evaporative dry eye. *Clin Ophthalmol.* 2016;10:1385-1396.
107. Borchman D. The optimum temperature for the heat therapy for meibomian gland dysfunction. *Ocul Surf.* 2019;17(2):360-364.
108. Tavassoli S, Wong N, Chan E. Ocular manifestations of rosacea: A clinical review. *Clin Exp Ophthalmol.* 2021;49(2):104-117.
109. Connor CG, Narayanan S, Miller W. Reduction in inflammatory marker matrix metalloproteinase-9 following lid debidement with BlephEx. *Invest Ophthalmol Vis Sci.* 2017;58(8):498-498.
110. Connor CG, Narayanan S, Miller W. Reduction in inflammatory marker matrix metalloproteinase-9 following lid debidement with BlephEx. *Invest Ophthalmol Vis Sci.* 2017;58(8):498-498.
111. Mastrotta KM. Demodex: Recognize it and Treat it. Optometry Times. <https://www.optometrytimes.com/view/demodex-recognize-it-and-treat-it>. Published October 11, 2021. Accessed February 21, 2022.
112. McDonald M. ASCRS EyeWorld White Paper: Therapeutic potential of Regener-Eyes® Ophthalmic Solution in the treatment of dry eye disease. July 2021. [https://www.regenereyes.com/wp-content/uploads/2021/06/Regener-Eyes-white-paper\\_rev-5-11.pdf](https://www.regenereyes.com/wp-content/uploads/2021/06/Regener-Eyes-white-paper_rev-5-11.pdf). Accessed September 14, 2022.
113. Bachrach. Walter Bradford Cannon 1934. Wikimedia Commons. CC BY 4.0, <https://commons.wikimedia.org/w/index.php?curid=33258971>. Published June 8, 2012. Accessed September 3, 2021.
114. Nascardi D, Sved A. Homeostasis success or failure. Wikimedia Commons. CC BY-SA 4.0. [https://commons.wikimedia.org/wiki/File:Homeostasis\\_success\\_or\\_failure.png](https://commons.wikimedia.org/wiki/File:Homeostasis_success_or_failure.png). Published August 26, 2019. Accessed September 3, 2021.
115. Bossuyt F. Doha 2019 men's marathon (01). Flickr. CC BY 2.0. <https://commons.wikimedia.org/w/index.php?curid=83308235>. Published October 5, 2019. Accessed September 3, 2021.
116. Wellington J. Woman in White Hat Shivering in Snow. Freerange Stock. CCO. <https://freerangestock.com/photos/134858/woman-in-white-hat-shivering-in-snow.html>. Published June 8, 2012. Accessed September 3, 2021.
117. David-198. Blood Glucose Testing. Wikimedia Commons. CC BY-SA 3.0. <https://commons.wikimedia.org/w/index.php?curid=71825848>. Published June 2, 2007. Accessed September 3, 2021.
118. Giovanni Francesco Barbieri called Guercino. Vanitas Still Life. Wikimedia Commons. Public Domain. <https://commons.wikimedia.org/w/index.php?curid=75702616>. Accessed September 3, 2021.
119. Knight CR. Le Moustier. Wikimedia Commons. Public Domain. <https://commons.wikimedia.org/w/index.php?curid=18725346>. Accessed September 3, 2021.
120. Kene88. True-north-social-photography-person-on-phone. Wikimedia Commons. CC BY-SA 4.0. <https://commons.wikimedia.org/w/index.php?curid=71825848>. Published June 12, 2019. Accessed September 3, 2021.
121. Tear-film-diagram-original-art-1024x724. <https://www.insighteyecaretexas.com/2017/09/what-is-a-dry-eye-workup/>. Accessed September 3, 2021.
122. Structures Involved in Tear Production. <https://medialibrary.nei.nih.gov/sites/default/files/media-images/NEI-medialibrary-3842733.jpg>. Accessed September 3, 2021.

# References

- 123. Pexels. Woman Face with Tears. Freerange Stock. <https://freerangestock.com/photos/130577/woman-face-with-tears-.html>. Accessed September 3, 2021.
- 124. KellarW. Oil Slick Hummingbird. Flickr. CC BY 2.0. [https://commons.wikimedia.org/w/index.php?curid=78106967](https://www.flickr.com/photos/kellarwilson/45904939845/in/photolist-2cWsPj6-dsh3ca-6i43n9-7CbQsH-3f6UQj-B1yNE-3f6UU1-3f6UXL-rffheZ-DMrtX-5bbHKz-kjEq6-AUuPL-QemfM-dS5Vo-6tZxeV-7GdGjv-51yXY-9zXzqv-JsMTnt-GTVqk-cpX9Mq-5ZuTrE-rtJFBM-bV9Cy-thCJ9-4LxG6D-8eTfRC-JTKrv-JLPsTg-aR6k9-2eySkMk-kVZSN-8vGUCY-3PoKtz-8vGUJG-SbMtCU-kVZTn-3SXNUS-AUuNK-3PsYLW-GQjQLz-JTkx1V-2jvisJb-3STynV-84XWue-WkjBwk-qp5RBQ-kVZT6-7y9JTD/. Published January 20, 2019. Accessed September 3, 2021.</li><li>125. Saitov K. Human eye iris 5. Wikimedia Commons. CC BY 4.0. <a href=). Published October 17, 2017. Accessed September 3, 2021.
- 126. Sem J. Fish oil capsules. CC BY 2.0, www.semtrio.com. Published September 12, 2018. Accessed December 18, 2021.
- 127. L8rgator. Dry eyes scleral lens on removal plunger. Wikimedia Commons. CC BY-SA 3.0. <https://commons.wikimedia.org/w/index.php?curid=58836488>. Published May 18, 2014. Accessed September 3, 2021.
- 128. Doctor 4U. Doxycycline Antimalarial Tablets Image 4. CC BY 20, www.doctor-4-u.co.uk. Published September 3, 2019. Accessed December 18, 2021.
- 129. Clarke P. Contact Lens. Wikimedia Commons. CC BY-SA 4.0. <https://commons.wikimedia.org/w/index.php?curid=3668502>. Published August 28, 2019. Accessed September 3, 2021.
- 130. L8rgator. Scleral lens worn on an eye. Wikimedia Commons. CC BY-SA 3.0. <https://commons.wikimedia.org/w/index.php?curid=39863803>. Published May 18, 2014. Accessed September 3, 2021.
- 131. Andrea L. Man taking eyedrops. Wikimedia Commons. CC BY 2.0. <https://commons.wikimedia.org/w/index.php?curid=7301953>. Published July 13, 2009. Accessed September 3, 2021.
- 132. johnnyAutomatic. Johnny-automatic-scales-of-justice. <https://openclipart.org/detail/26849/scales-of-justice>. Wikimedia Commons. CC0, <https://commons.wikimedia.org/w/index.php?curid=46844394>. Published February 7, 2016. Accessed September 3, 2021.

**Thank you!**

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# CONTACT LENSES AND DRY EYE: THE IMPACT OF SOFT LENS WEAR ON OCULAR SURFACE HOMEOSTASIS

Cory J. Lappin, OD, MS, FAAO



- Alcon
- Barti
- Bausch + Lomb
- Bruder Healthcare and M&S Technologies (Hilco Vision)
- Dompé
- Lumenis
- Myze
- NuLids
- PRN Vision Group
- Rinsada
- Tarsus Pharmaceuticals
- Vital Tears

# DISCLOSURES

The content of this COPE accredited course was prepared independently. I have received no financial or commercial support for this presentation. All relevant relationships have been mitigated.

# HOMEOSTASIS

# Homeostasis

DRY EYE IS A MULTIFACTORIAL DISEASE OF THE OCULAR SURFACE CHARACTERIZED BY A **LOSS OF HOMEOSTASIS** OF THE TEAR FILM, AND ACCCOMPANIED BY OCULAR SYMPTOMS, IN WHICH TEAR FILM INSTABILITY AND HYPEROSMOLARITY, OCULAR SURFACE INFLAMMATION AND DAMAGE, AND NEUROSENSORY ABNORMALITIES PLAY ETIOLOGICAL ROLES

- TFOS DEWS II Definition & Classification Subcommittee Report

# **SOFT CONTACT LENS WEAR & OCULAR SURFACE HOMEOSTASIS**

# SOFT CONTACT LENSES: A HOMEOSTATIC CHALLENGE

## Benefits

- Refractive
  - Vision correction
- Therapeutic
  - BCL
- Interventional
  - Myopia management

## Challenges

- Innately disrupts homeostasis
  - Foreign body on the ocular surface
  - Disrupts tear film
  - Intrinsically inflammatory
- Complications
  - Infection
  - Inflammation

**UP TO 51% OF CONTACT LENS  
WEARERS ULTIMATELY END UP  
DISCONTINUING USE**

**20% dropout within the first year of wear**

WHY DOES THIS HAPPEN?  
WHAT CAN WE DO TO AVOID IT?



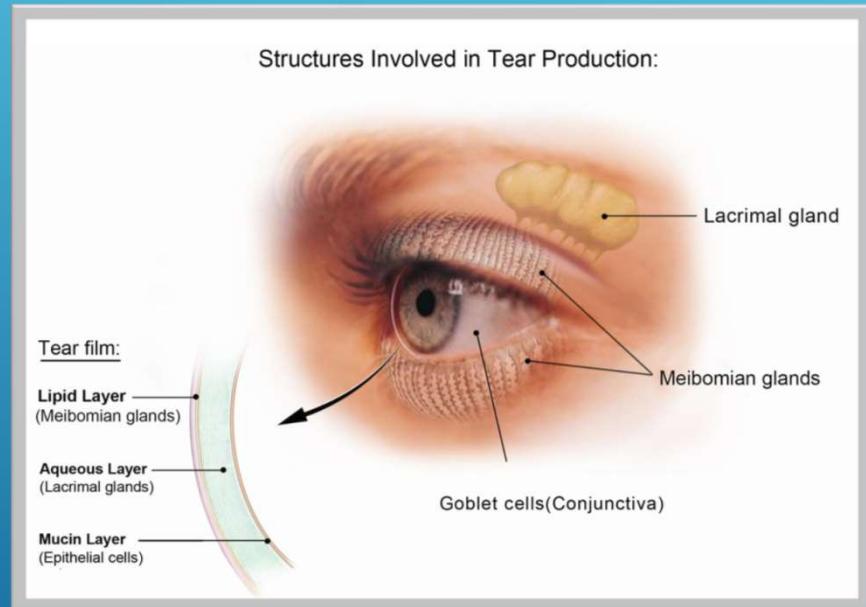
## THINGS TO KEEP IN MIND

- Conflicting findings
- No consensus on many points
- Some effects more historical

**BUT**

- General trends have emerged

# **SOFT CONTACT LENS WEAR & THE OCULAR SURFACE**



## OCULAR SURFACE

- Cornea
- Conjunctiva
- Eyelids & Lashes
- Meibomian Glands
- Main & Accessory Lacrimal Glands
- Goblet Cells
- Tear Film

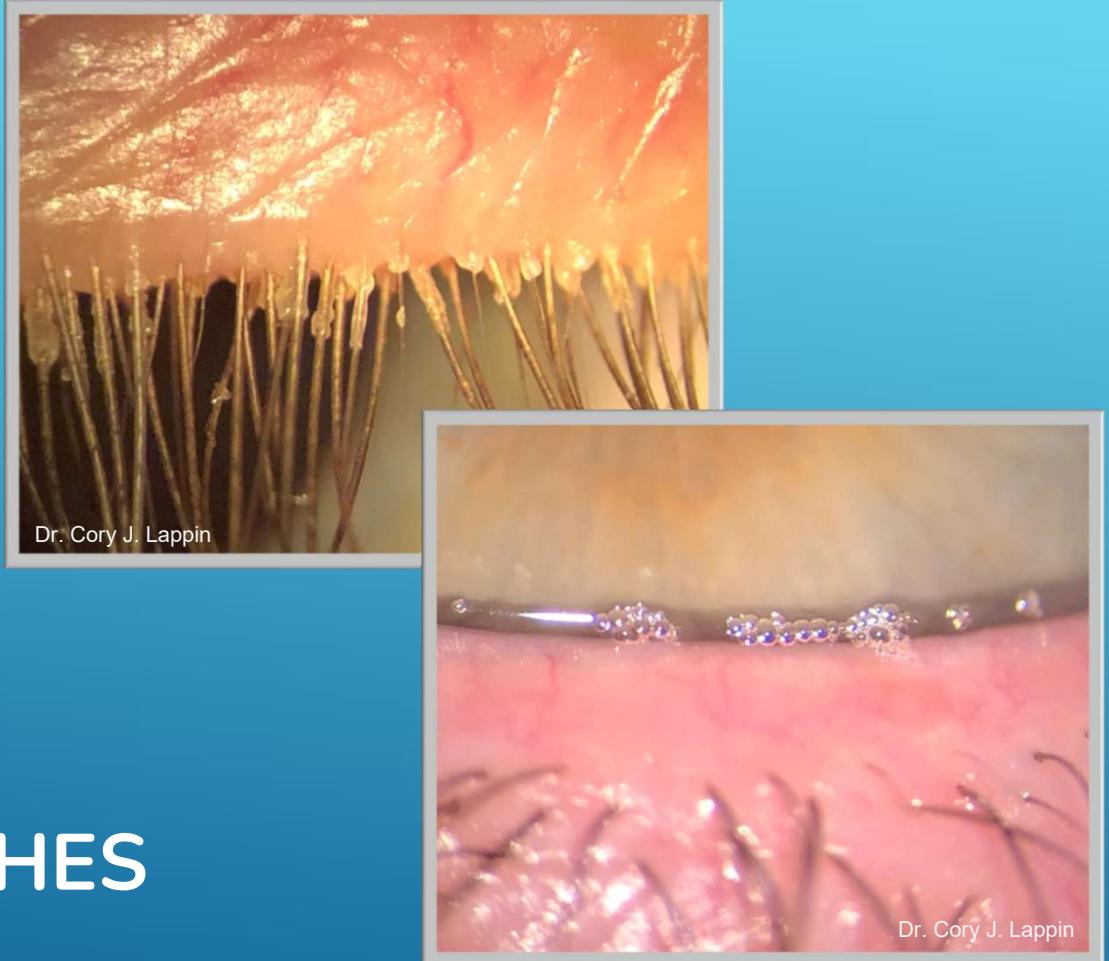
## Function

- Protection
- Tear spread



## LIDS & LASHES

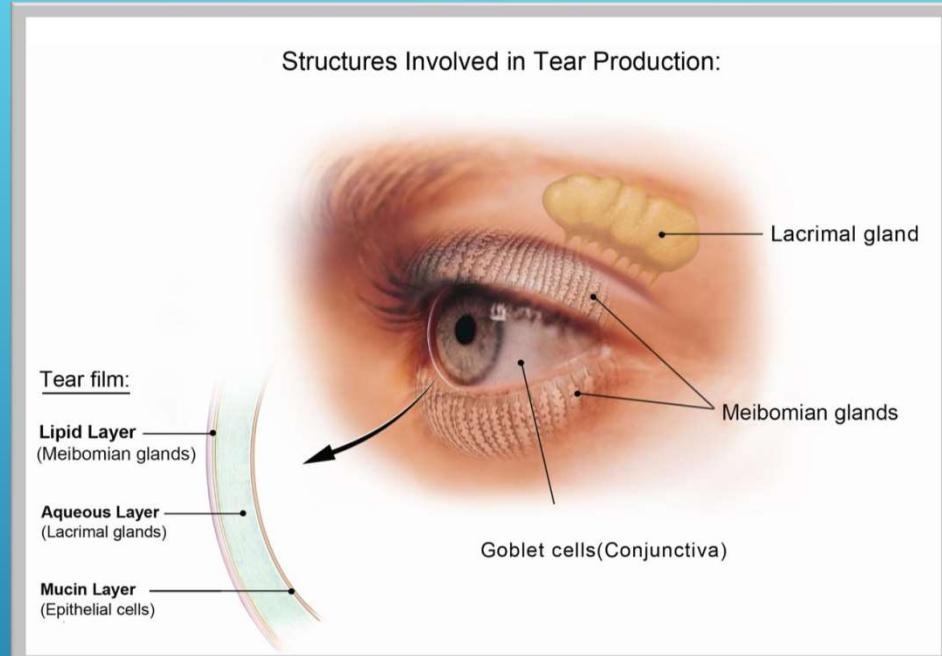
- Lens Impact on Surface
  - Increased blink rate
  - Increased incidence of ptosis
- Surface Impact on Lens
  - Demodex blepharitis
    - Collarettes
  - Bacterial blepharitis
    - Saponification



## SOFT CONTACTS LENSES: LIDS & LASHES

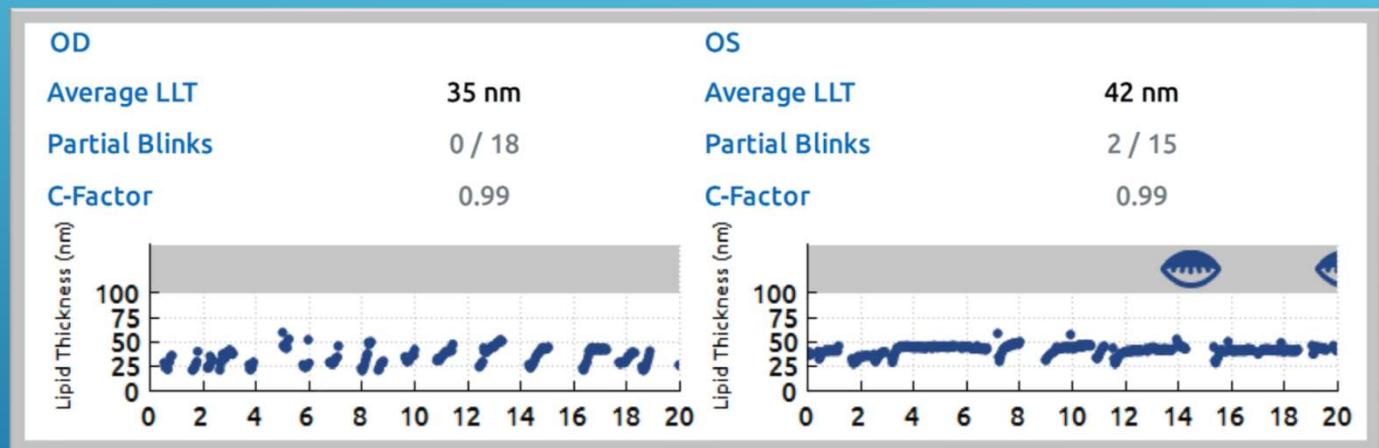
## Function

- Protection
- Nourishment
- Smooth optical surface
- Refract light



## TEAR FILM

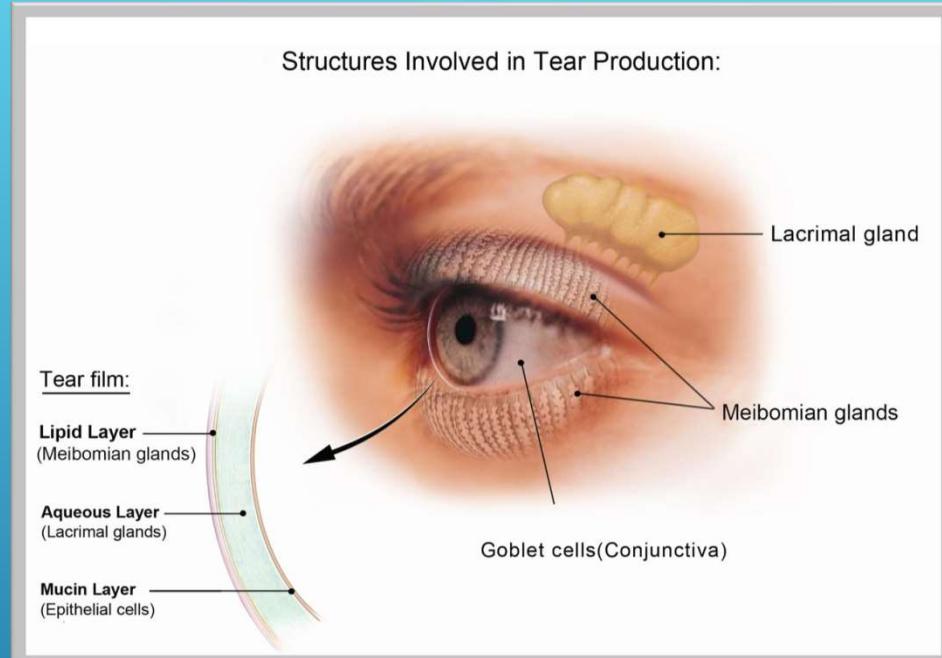
- Lens Impact on Surface
  - Splits tear film into two
    - Pre-lens tear film
    - Post-lens tear film
  - Reduced
    - Lipid layer thickness
    - Tear volume
    - Tear film turnover
    - TBUT
  - Increased
    - Evaporation
    - Osmolarity



## SOFT CONTACTS LENSSES: TEAR FILM

## ○ Surface Impact on Lens

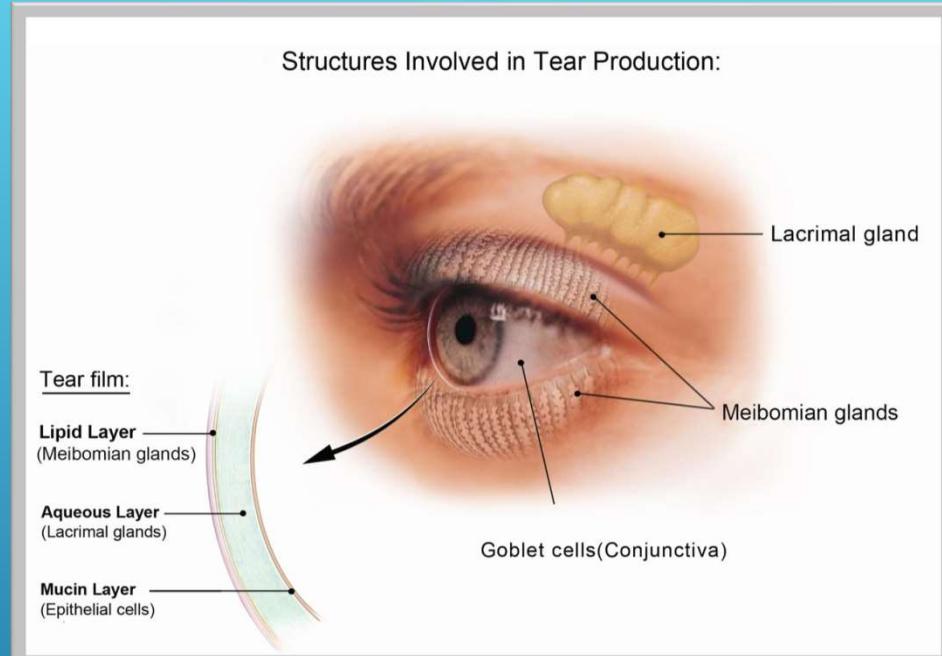
- Poor tear quality reduces
  - Comfort
  - Wear time
  - Visual quality
- Lens dehydration
  - Tightening



# SOFT CONTACTS LENSES: TEAR FILM

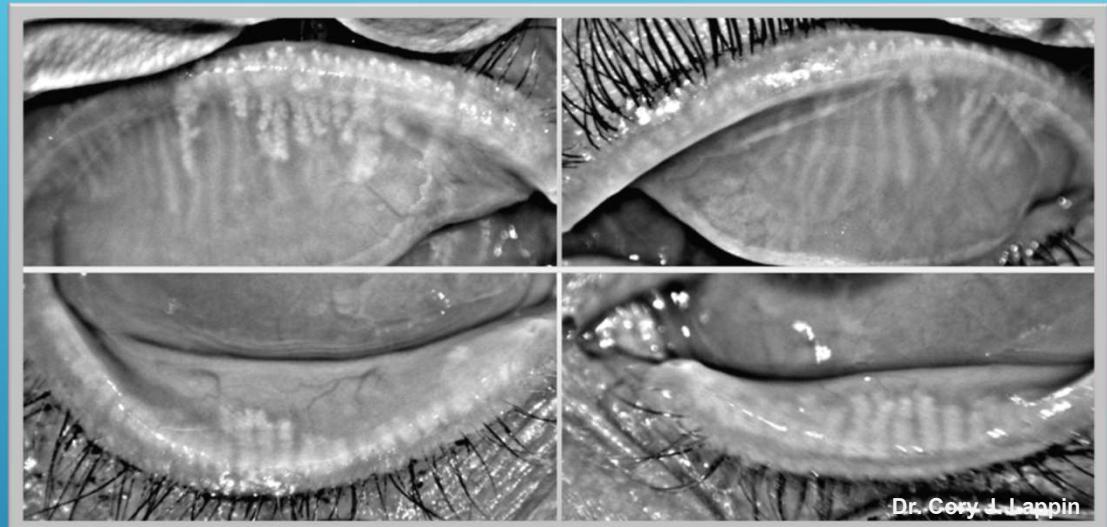
## Function

- Produce meibum component of tear film
  - Prevents evaporation
  - Provides smooth optical surface
  - Lowers surface tension



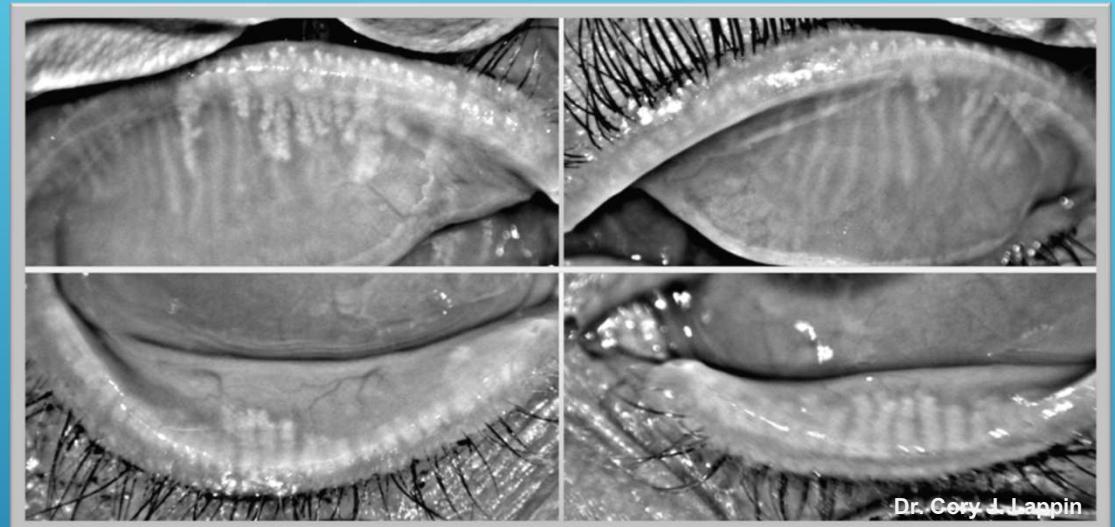
# MEIBOMIAN GLANDS

- Lens Impact on Surface
  - Altered meibum quality
    - Higher melting point
    - Independent of structural changes
  - Altered meibomian gland structure
    - Controversial
    - May worsen with wear
      - Starts after 1 year of wear
      - Stops after 2-3 years of wear
    - Upper lid glands more affected



## SOFT CONTACTS LENSES: MEIBOMIAN GLANDS

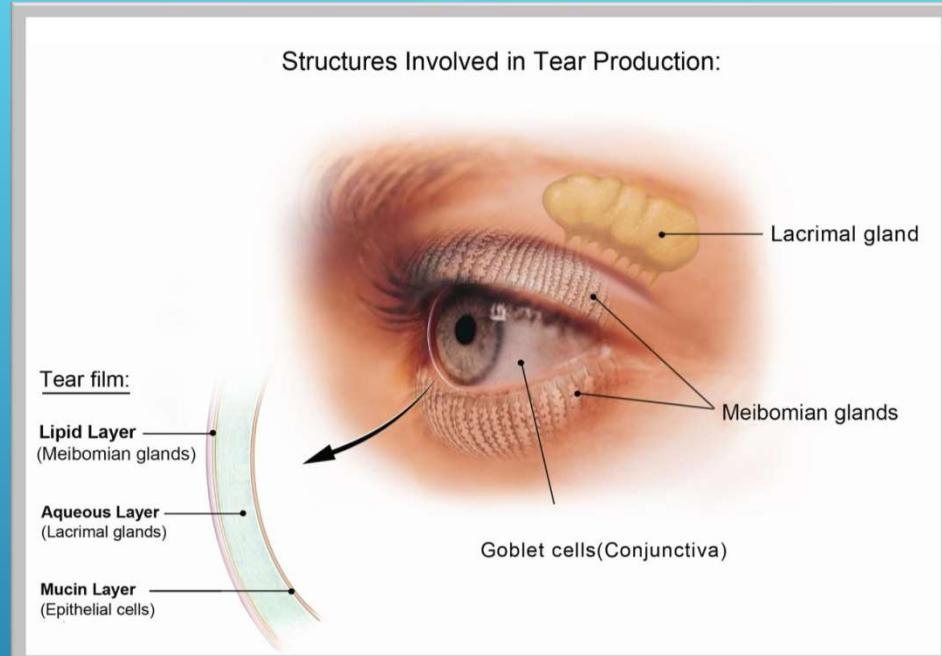
- Surface Impact on Lens
  - Reduced tear film stability
    - Reduced
    - Comfort
    - Wear time
    - Visual quality



## SOFT CONTACTS LENSES: MEIBOMIAN GLANDS

## Function

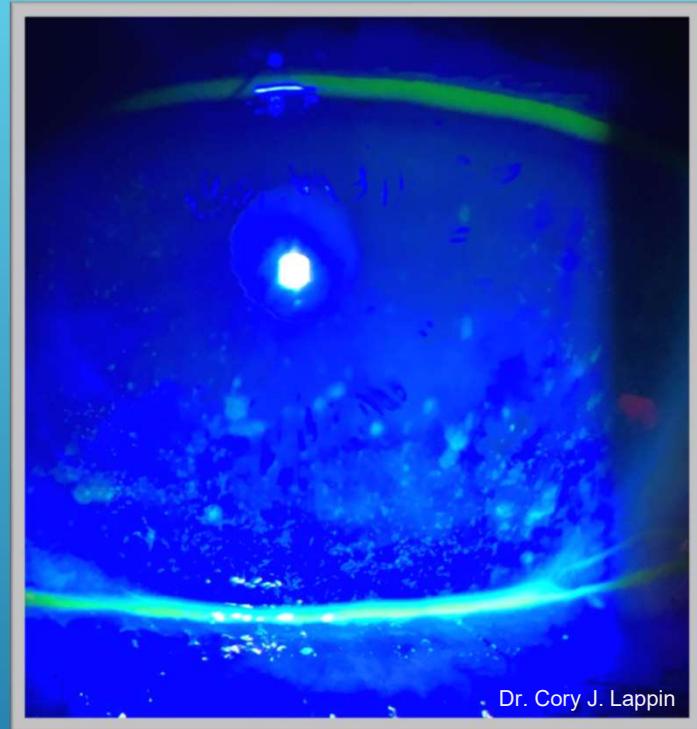
- Produces aqueous component of tears
  - Lubrication and hydration
  - Nourishment
  - Protection



# MAIN & ACCESSORY LACRIMAL GLANDS

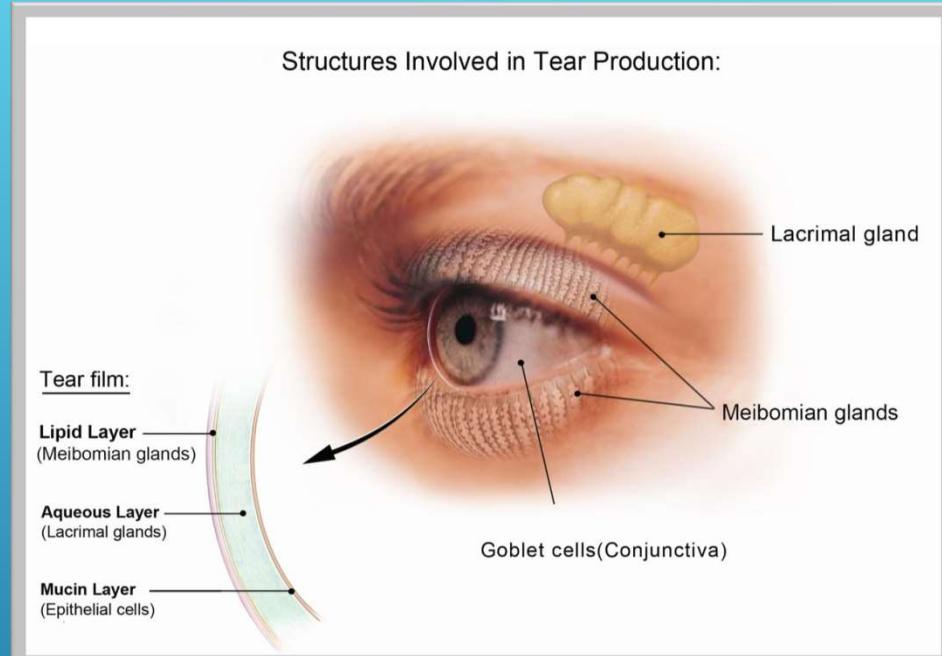
- Lens Impact on Surface
  - Splits tear film
- Surface Impact on Lens
  - Can stabilize cornea and ocular surface
    - Sjogren's Syndrome

## SOFT CONTACTS LENSES: LACRIMAL GLANDS & AQUEOUS TEARS



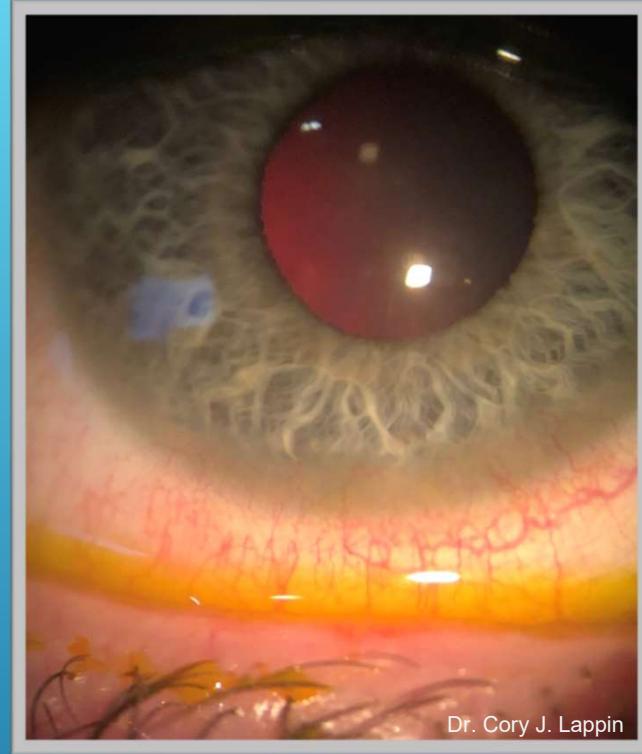
## Function

- Protection
  - Immune
- Contribute mucin component of tear film
  - Anchors tear film to cornea
  - Lowers surface tension
  - Protection



# CONJUNCTIVA & GOBLET CELLS

- Lens Impact on Surface
  - Hyperemia & Staining
    - Circumlimbal
    - Lens fit, edge interaction
  - Reduced
    - Goblet cell density
    - Mucin production
  - Increased
    - Lid-parallel Conjunctival Folds (LIPCOF)
      - Friction



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## SOFT CONTACTS LENSES: CONJUNCTIVA & GOBLET CELLS

- Lens Impact on Surface

- Giant Papillary Conjunctivitis (GPC)
  - Giant papillae ( $\geq 1\text{mm}$ )
  - Due to mechanical friction
    - Lens surface dryness, deposits
  - **6-12% of Hydrogel wearers will develop GPC**
  - **Reduced likelihood with daily disposable CLs**



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## SOFT CONTACTS LENSES: CONJUNCTIVA & GOBLET CELLS

- Lens Impact on Surface
  - Lid Wiper Epitheliopathy (LWE)
    - Region is adjacent and posterior to the line of Marx
      - In contact with globe
    - Spreads tears across ocular surface
    - Staining of lid wiper due to friction
      - Microtrauma with blinking
      - More common with SCL wear
        - Poorly wettable surface
      - **Less severe with SiHy wear**



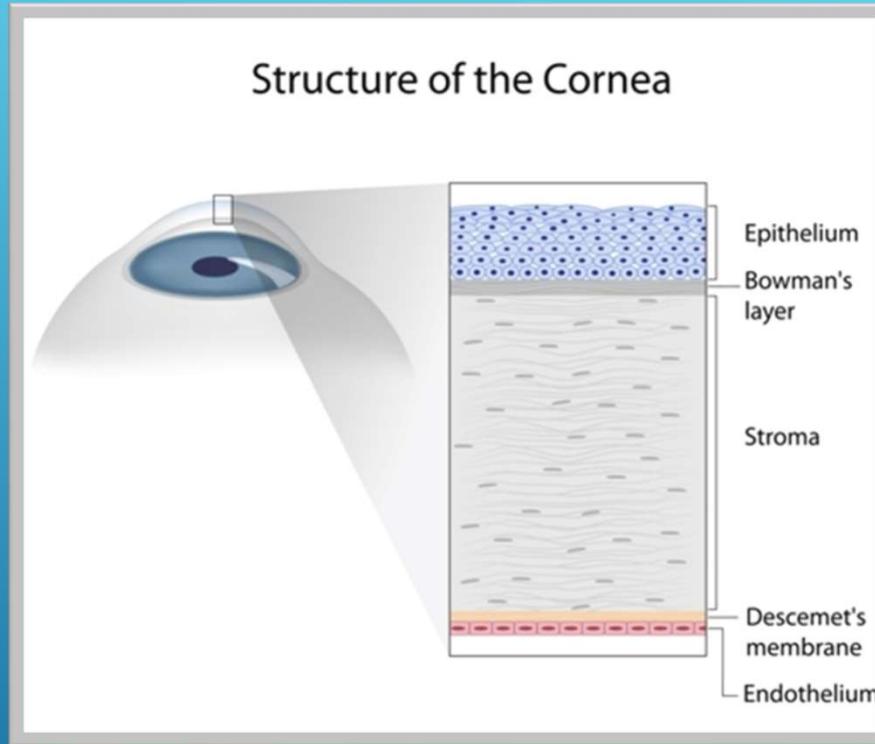
Dr. Cory J. Lappin

## SOFT CONTACTS LENSES: CONJUNCTIVA & GOBLET CELLS

## Function

- Protection
- Optical clarity
- Refract light

# CORNEA



- Lens Impact on Surface
  - Staining
    - Present in 54% of SCL wears
      - Less with SiHy wear
    - “Smile” pattern
      - Lens desiccation
    - Limbal staining
      - Excess movement



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## SOFT CONTACTS LENSES: CORNEA

- **Lens Impact on Surface**

- **Hypoxia**

- Reduced epithelial cell metabolism and mitosis
- Epithelial thinning
- Premature endothelial cell loss
- Increased bacterial binding to surface

- **Epithelial microcysts**

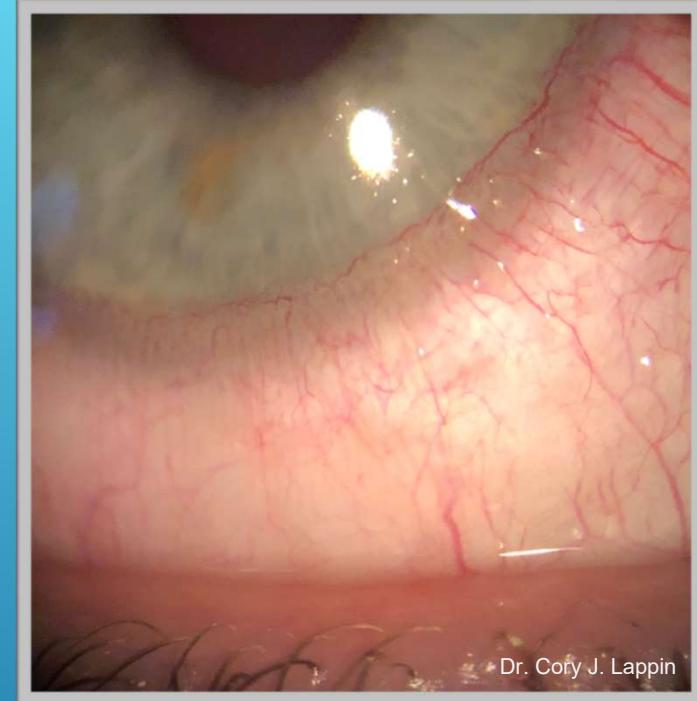
- Reverse illumination (appear dark)
- Degenerated basal epithelial cells
- **Associated with Hydrogels**
- **Rare with SiHy wear**

- **Vacuoles**

- Fluid between epithelia cells
- Unreversed illumination

- Neovascularization

- Edema



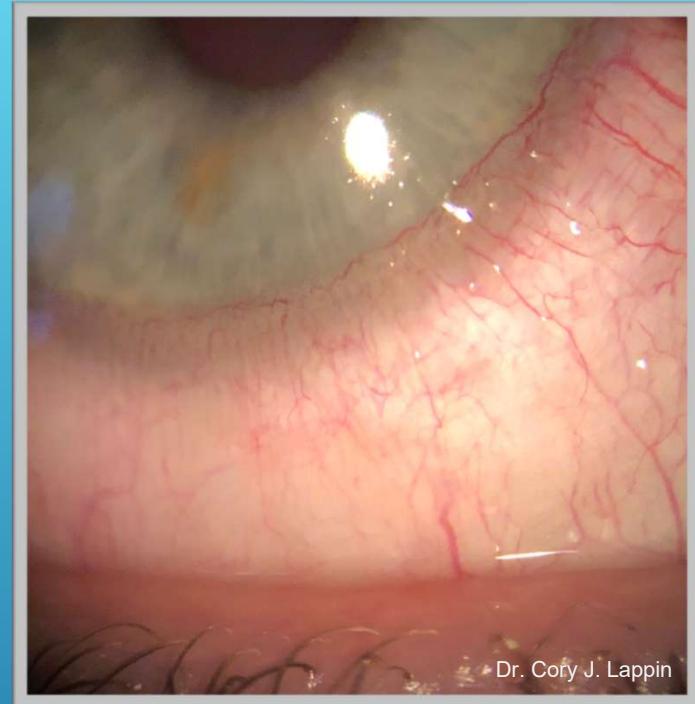
Dr. Cory J. Lappin

# SOFT CONTACTS LENSES: CORNEA

- Lens Impact on Surface

- **Neovascularization**

- Due to hypoxia
- Limbal injection
  - Precursor
- Lipid exudation
- Scarring
- Greater risk with overnight lens wear



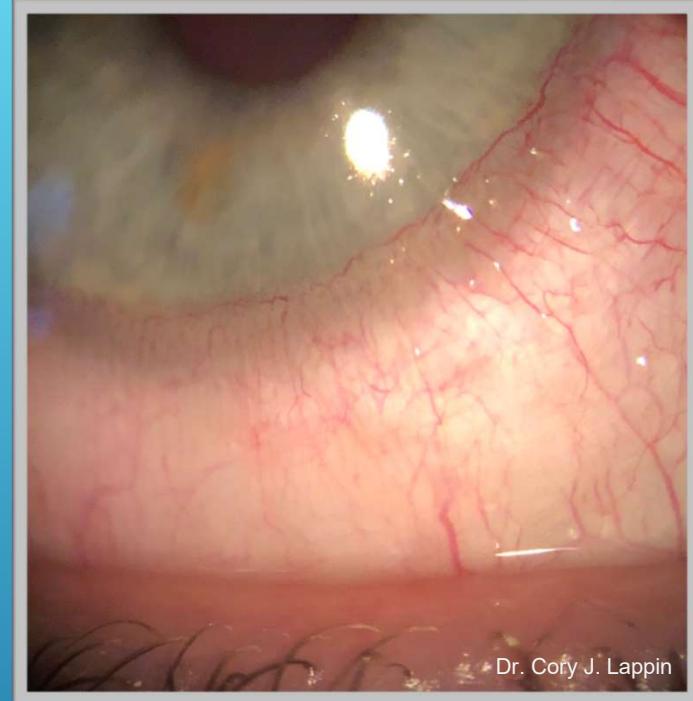
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## SOFT CONTACTS LENSES: CORNEA

- **Lens Impact on Surface**

- **Edema**

- CL wear can reduce oxygen availability
  - Increased anaerobic metabolism by epithelial cells
  - Lactic acid byproduct diffuses into stroma and alters osmotic gradient
    - Stromal edema
    - Striae and/or folds
- Visual disturbances
  - Glare, halos, rainbows
- Increased risk with overnight lens wear
- **Less common with SiHy wear**



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# SOFT CONTACTS LENSES: CORNEA

- Lens Impact on Surface
  - Stromal thinning
    - Reduced keratocyte density
    - Due mechanically induced inflammation
  - **Present in both SiHy and Hydrogel wear**

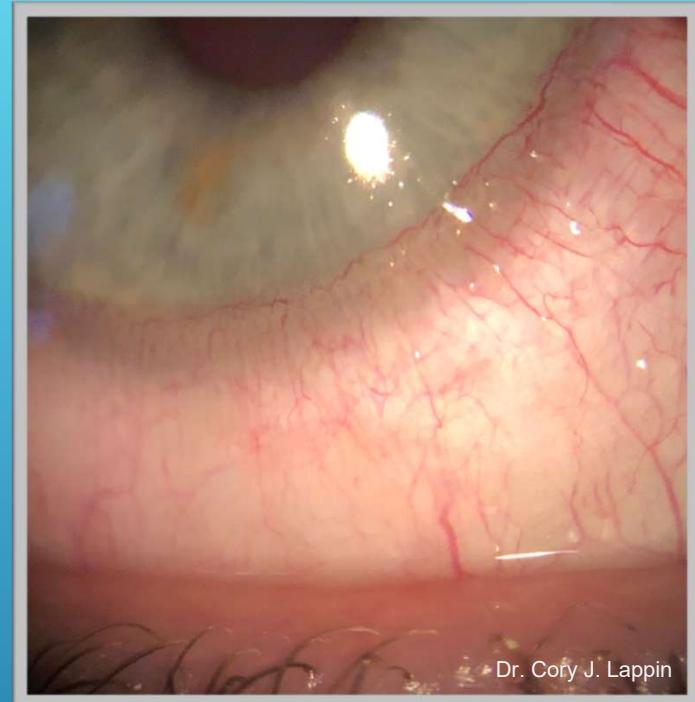


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## SOFT CONTACTS LENSES: CORNEA

- Lens Impact on Surface

- Corneal warpage
  - Increased regular astigmatism
  - Irregular astigmatism
  - **More common in older, low Dk/t Hydrogels**



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## SOFT CONTACTS LENSES: CORNEA

- Lens Impact on Surface
  - Limbal Stem Cell Deficiency (LSCD)
    - Chronic contact lens-induced:
      - Limbal hypoxia
      - Mechanical trauma to limbus
    - Results in loss of limbal stem cells
      - Impaired wound healing
      - Reduced epithelial cell turnover
      - Corneal conjunctivalization
        - Neovascularization
        - Loss of transparency

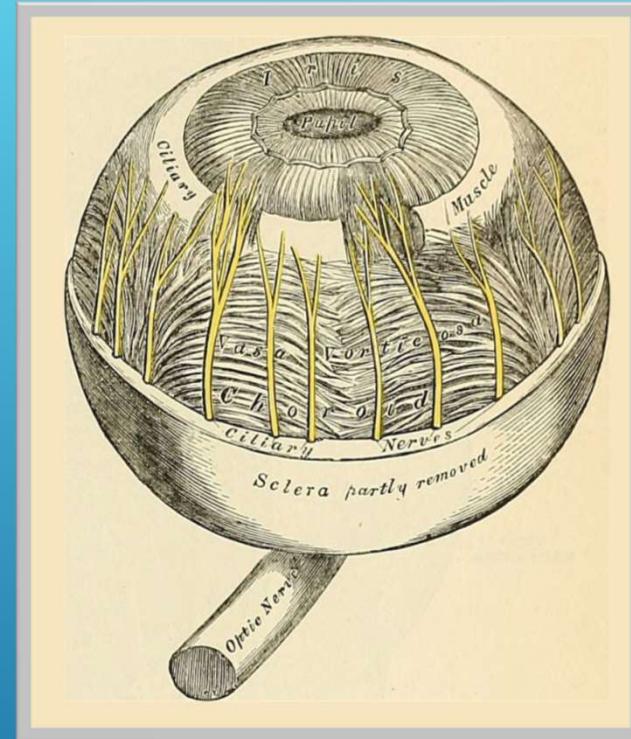


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## SOFT CONTACTS LENSES: CORNEA

## Function

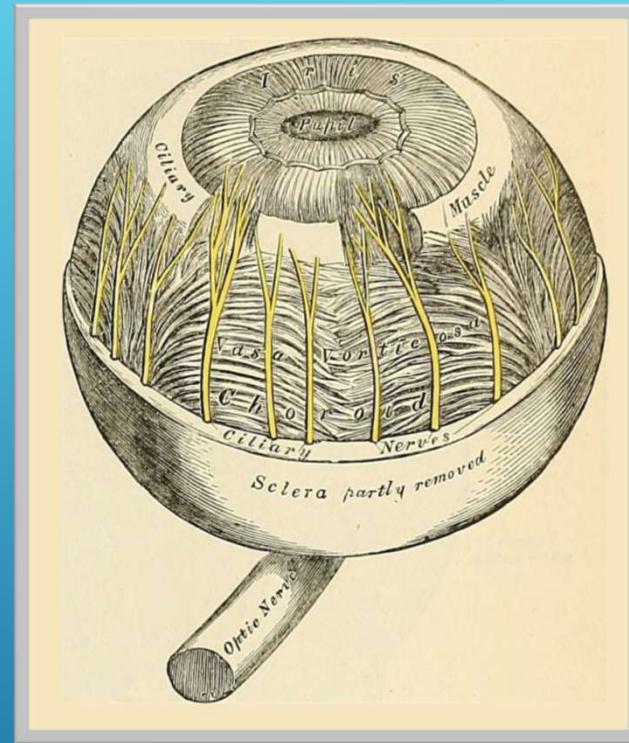
- Cornea densely innervated
  - 7,000 nerve enders per mm<sup>2</sup>
- Control
  - Sensation
  - Blinking & Lacrimation
  - Protection
- Corneal surface maintenance
  - Routine epithelial cell turnover
  - Wound healing
  - Nourishment and metabolism



# NERVES

- **Lens Impact on Surface**

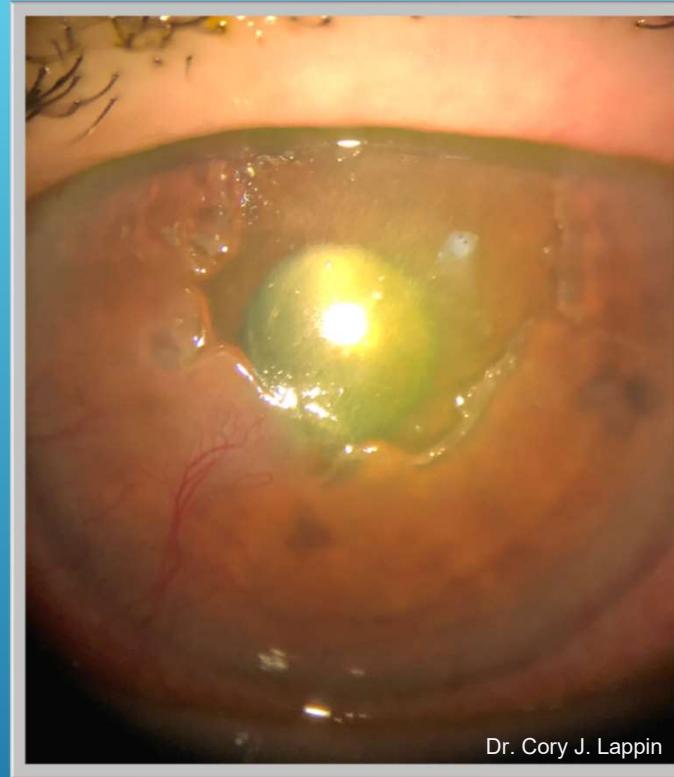
- Reduced corneal sensitivity
  - Adaptation
- Increased sensitivity at limbus
  - Interaction with lens edge
  - Specialized pressure sensors
- Reduced palpebral conjunctival sensitivity
- Reduced lid margin sensitivity
  - Second most sensitive ocular surface structure
- NGF upregulated in contact lens discomfort
  - Sign of nerve damage



# SOFT CONTACTS LENSSES: NERVES

- Lens Impact on Surface
  - Neurotrophic Keratitis (NK)
  - Can be induced by chronic CL-related inflammation
    - Damages corneal nerves resulting in loss of sensation
      - Impaired blinking and lacrimation
      - Reduced epithelial cell turnover
      - Disrupted wound healing

## SOFT CONTACTS LENSSES: NERVES



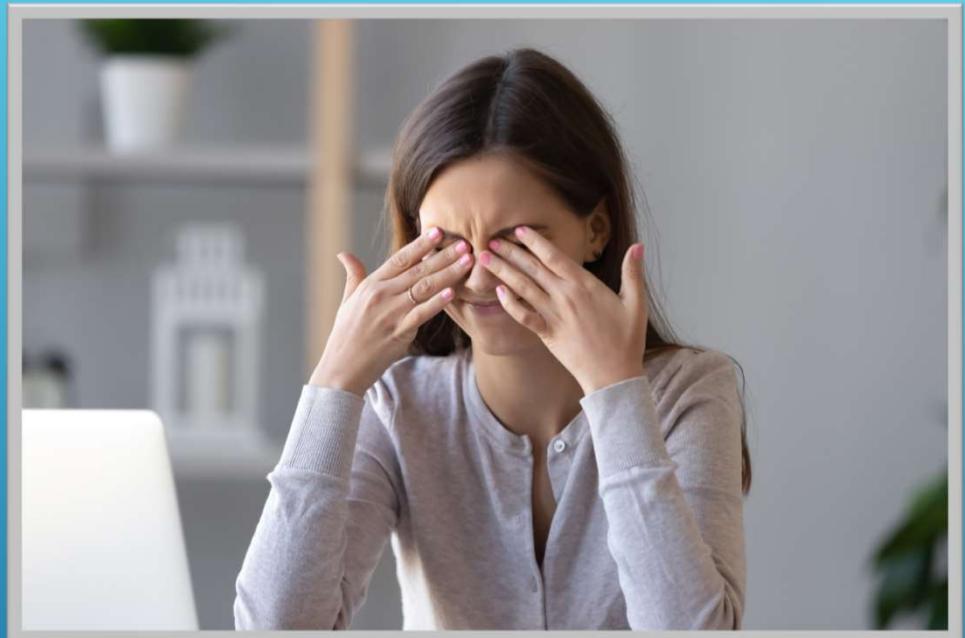
- **Surface Impact on Lens**
  - Neuropathic Ocular Pain
  - Pain derived from nerves rather than external stimulus
    - Peripheral or Central
    - Leads to hypersensitivity of cornea
      - Allodynia
      - Photoallodynia
      - Hyperalgesia
    - Lens wear can improve or exacerbate condition



## SOFT CONTACTS LENSSES: NERVES

- **Lens Impact on Surface**

- CLs may be intrinsically inflammatory
  - Subclinical
  - Dendritic cells (DC)
    - pathognomonic for immune response
- Bulbar Conjunctiva and Lid Margin
  - Transient increase in DC
    - Due to deposits, microbes on case
- Cornea
  - Transient increase in DC
  - Possible microtrauma
  - **Less pronounced with daily disposables**



## SOFT CONTACTS LENSES: INFLAMMATION

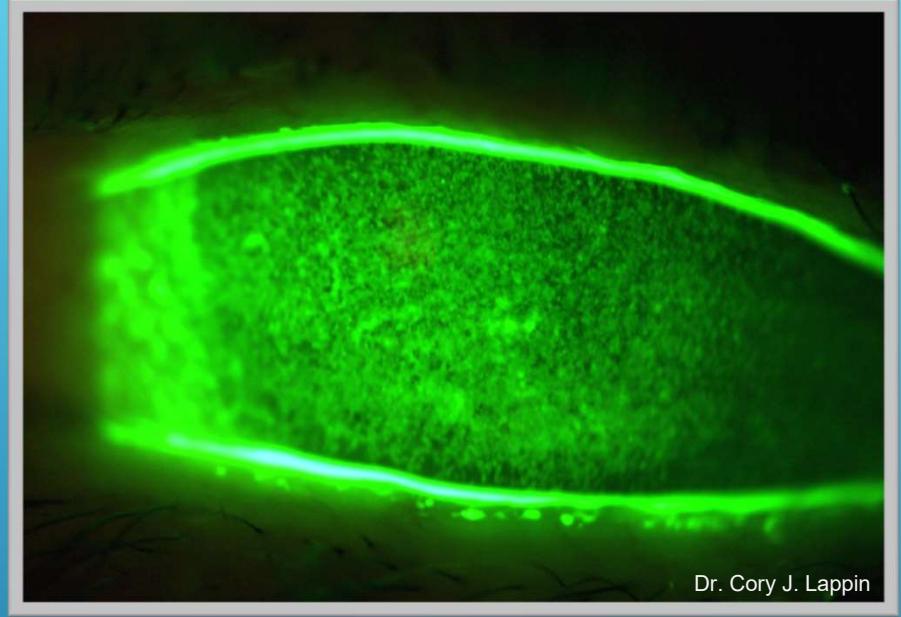
- Surface Impact on Lens
  - Ocular Allergies
  - 40% of contact lens wears experience allergies
  - Lens discomfort
    - Itching
    - Mucus discharge

## SOFT CONTACTS LENSSES: ALLERGIES



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- **Impact on Surface**
  - Packing solutions
    - Borate
    - Phosphate
    - Both potentially cytotoxic to corneal epithelium
  - Care solutions
    - Multipurpose
      - Preservatives as Antimicrobials
        - PBHB
        - Polyquad (BAK-derived)
      - Potential preservative toxicity



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# SOFT CONTACTS LENSES: PACKING SOLUTIONS AND CARE SYSTEMS

- Lens Impact on Surface
  - Contact Lens Discomfort (CLD)
  - Due to lens itself, **NOT** external condition
    - Only occurs when lens is worn, discomfort improves upon removal
  - Mechanism unknown
    - Likely nervous component
  - Can be influenced by
    - Lens material
    - Lens design
    - Wear schedule
    - Care solution



## SOFT CONTACTS LENSES: CONTACT LENS DISCOMFORT (CLD)

# MANAGEMENT

# Soft Contact Lens and Ocular Surface Management

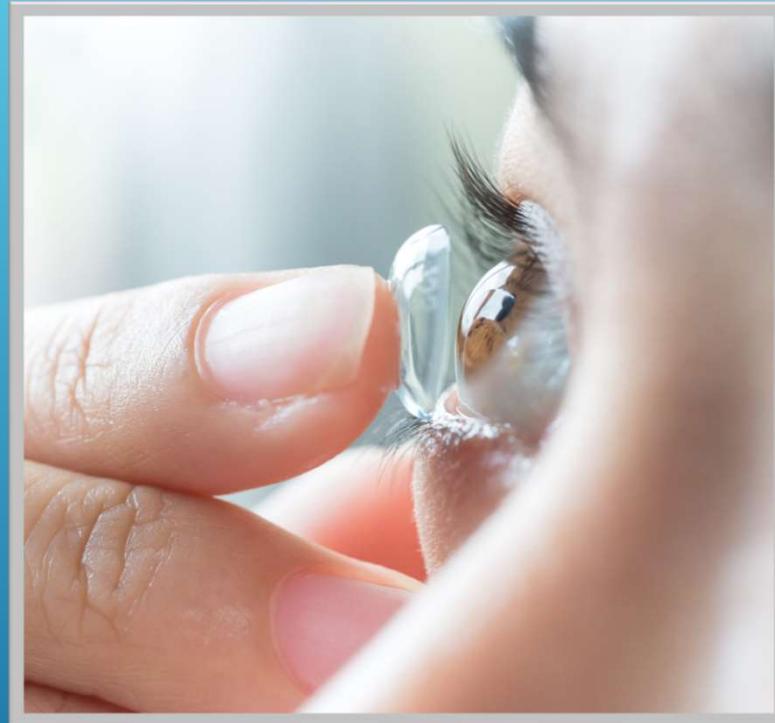
Lens Selection

Ocular Surface Optimization

# LENS SELECTION

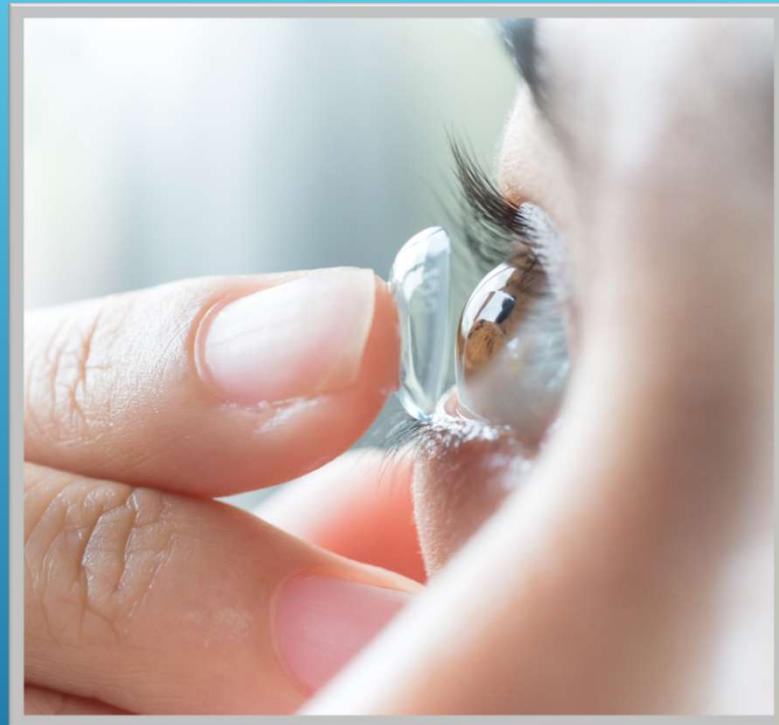
# LENS SELECTION: SOFT CONTACT LENS MATERIAL PROPERTIES

- **Dk/t**
  - Oxygen permeability
- **Modulus**
  - Rigidity
- **Lubricity**
  - Friction
- **Wettability**
  - Tear spread & adherence
- **Surface treatments**
  - Surfactants
  - Plasma
  - Wetting Agents
    - Polyvinyl alcohol
    - Hyaluronic acid



# LENS SELECTION: SOFT CONTACT LENS DESIGN

- **Base curve**
  - Flatter
  - Steeper
- **Diameter**
  - Larger
  - Smaller
- **Lens edge design**
  - Rounded
  - Knife
  - Chisel
- **Thickness**



# LENS SELECTION: SOFT CONTACT LENS POLYMER TYPES

## Silicone Hydrogels

- High oxygen permeability
- Better comfort
- Silicone intrinsically hydrophobic
  - Requires surface treatments
- Lower water content
- Lipid deposition
- “Stiffer” modulus

## Hydrogels

- Relatively lower oxygen permeability
- More potential issues with comfort
- More hydrophilic
- Higher water content
- Protein deposition
- “Softer” modulus

# LENS SELECTION: WEAR SCHEDULES

## Daily Disposables

- Deposits negligible
- Increased comfort
- Care solutions not required
- Parameter limitations (relative)
- Convenience
- Higher cost
- Environmental concerns

## Monthly & Biweekly Replacement

- More prone to deposit buildup, lens degradation
- Variable comfort with wear duration
- Require care solutions
- Wider parameters (relative)
- Cost effective
- Compliance issues

# CARE SOLUTION SELECTION

## Hydrogen Peroxide

- Convenience
  - One step
- Preservative-free
- Better comfort
- Better protection
  - Coverage against Acanthamoeba

## Multipurpose Solutions

- Compliance issues
  - Two-step (Rubbing or Rinsing)
- Preservative-containing (Antimicrobial agents)
  - Polyquaternium-1 (PQ-1)
  - Polyhexamethylene biguanide (PHMB)

# Lens Selection: Takeaways

DAILY DISPOSABLES WHENEVER POSSIBLE

SILICONE HYDROGELS TEND TO PROVIDE BETTER COMFORT

HYDROGEN PEROXIDE SOLUTIONS ARE THE CARE SYSTEMS  
OF CHOICE

# OCULAR SURFACE MANAGEMENT

- Omega-3 fatty acid supplementation
  - High quality, re-esterified, triglyceride-based supplement with 3:1 EPA to DHA ratio and at least 2 grams of combined EPA and DHA
- Warm compresses
  - May not be ideal for all patients, use with caution in patients with ocular rosacea
- Artificial tears
  - Primarily palliative
  - Recommend preservative-free, lipid-based formulations or gels
- Blink exercises
- Lid hygiene
  - Hypochlorous acid
  - Tea tree oil
  - Okra-based cleansers (Zocular)
- Immunomodulators
  - Lifitegrast (Xiidra)
  - Cyclosporine (Cequa, Vevye, Restasis)
- Neurostimulators
  - Varenicline nasal spray (Tyrvaya)
  - iTear100
- Tear film stabilizers
  - Perfluorohexyloctane (Miebo)
- Nocturnal exposure
  - Gels or Ointments
  - Moisture goggles
- Allergies
  - Antihistamine-Mast Cell Stabilizer Combos
    - Olopatadine (Pataday)
    - Alcaftadine (Lastacraft)
  - Preferential Exclusion
    - Ectoin (Allegro)
  - Immunomodulators
    - Cyclosporine (Verkazia)
    - Tacrolimus
  - Ketotifen-eluting Contact Lenses
- Biologics
  - Platelet-rich plasma (PRP)
  - Autologous serum
  - Amniotic membranes
  - Cenegermin-bkbj (Oxervate)
- Other treatments
  - Lotilaner (Xdemvy)
- Advanced procedures
  - Microblepharoexfoliation
    - NuLids
    - BlephEx
  - Ocular surface lavage
    - Rinsada
  - Intense Pulsed Light (IPL)
    - Improves symptoms in contact-lens related DE
    - OptiLight
  - Radiofrequency (RF)
    - OptiPlus

# DRY EYE AND OCULAR SURFACE DISEASE TREATMENTS

# CLINICAL PEARLS

## CLINICAL PEARLS

- A sign of things to come
- Do not overestimate adaptation
- Discuss expectations
- Save wearing time for when most needed
- “If it ain't broke, don't fix it”
- Do not fear spherical equivalent
- The right artificial tear for the job
- Red means stop
- Rinse lenses out of blister pack
- Part-time wearers are excellent candidates for dailies
- When in doubt, go with dailies
- Complications: Strike one...you're still out (and into a new lens)
- Lens selection **AND** ocular surface optimization, **NOT OR**
- Personally try lenses

# SUMMARY

# Summary

SOFT CONTACT LENS WEAR PRESENTS A HOMEOSTATIC CHALLENGE

PROPER LENS SELECTION MINIMIZES DISRUPTION TO THE OCULAR SURFACE

OPTIMIZING THE OCULAR SURFACE WILL MAXIMIZE CONTACT LENS COMFORT AND SUCCESS

# REFERENCES

1. Abusharha AA. Changes in blink rate and ocular symptoms during different reading tasks. *Clin Optom (Auckl)*. 2017;9:133-138. Published 2017 Nov 20. doi:10.2147/OPTO.S142718
2. Allergy-fighting contact lens approved. Review of Optometry. March 2, 2022. Accessed August 6, 2023. <https://www.reviewofoptometry.com/article/allergyfighting-contact-lens-approved>.
3. Ammer R. Effect of Contact Lens Wear on Tear Film Break up Time (TBUT) among Contact Lens Users. *Pakistan Journal of Ophthalmology*. 2017; 33:182-186.
4. Arita R, Fukuoka S, Morishige N. Meibomian Gland Dysfunction and Contact Lens Discomfort. *Eye Contact Lens*. 2017;43(1):17-22. doi:10.1097/ICL.0000000000000351
5. Barnett M. Are you making the most of the newest soft lenses? Review of Optometry. August 15, 2020. Accessed August 6, 2023. <https://www.reviewofoptometry.com/article/are-you-making-the-most-of-the-newest-soft-lenses>
6. Bhargava R, Kumar P. Oral omega-3 fatty acid treatment for dry eye in contact lens wearers. *Cornea*. 2015;34(4):413-420. doi:10.1097/ICO.000000000000038
7. Billman GE. Homeostasis: The Underappreciated and Far Too Often Ignored Central Organizing Principle of Physiology. *Front Physiol*. 2020;11:200. Published 2020 Mar 10. doi:10.3389/fphys.2020.00200
8. Bradley CS, Sicks LA, Pucker AD. Common Ophthalmic Preservatives in Soft Contact Lens Care Products: Benefits, Complications, and a Comparison to Non-Preserved Solutions. *Clin Optom (Auckl)*. 2021;13:271-285. Published 2021 Sep 7. doi:10.2147/OPTO.S235679
9. Britannica, T. Editors of Encyclopedia (2022, August 23). Homeostasis. Encyclopedia Britannica. <https://www.britannica.com/science/homeostasis>. Published: Aug 23, 2022.
10. Cannon WB. Organization for physiological homeostasis. *Physiological Reviews*. 1929;9:399-431.
11. Chaudhary S, Ghimire D, Basu S, Agrawal V, Jacobs DS, Shanbhag SS. Contact lenses in dry eye disease and associated ocular surface disorders. *Indian J Ophthalmol*. 2023;71(4):1142-1153. doi:10.4103/IJO.IJO\_2778\_22
12. Cole J. Choosing the right contact lens modality. Review of Optometry. August 15, 2017. Accessed August 26, 2023. <https://www.reviewofoptometry.com/article/ro0817-choosing-the-right-contact-lens-modality>.
13. Cope JR, Collier SA, Rao MM, et al. Contact Lens Wearer Demographics and Risk Behaviors for Contact Lens-Related Eye Infections--United States, 2014. *MMWR Morb Mortal Wkly Rep*. 2015;64(32):865-870. doi:10.15585/mmwr.mm6432a2
14. Coroi MC, Bungau S, Tit M. PRESERVATIVES FROM THE EYE DROPS AND THE OCULAR SURFACE. *Rom J Ophthalmol*. 2015;59(1):2-5.
15. Craig JP, Nichols KK, Akpek EK, et al. TFOS DEWS II Definition and Classification Report. *Ocul Surf*. 2017;15(3):276-283. doi:10.1016/j.jtos.2017.05.008
16. Davis R, Eiden B. Contact Lens Spectrum. February 1, 2013. Accessed August 6, 2023. <https://www.clspectrum.com/issues/2013/february-2013/problem-solving-soft-toric-contact-lenses>.
17. Downie LE, Bandlitz S, Bergmanson JPG, et al. CLEAR - Anatomy and physiology of the anterior eye. *Cont Lens Anterior Eye*. 2021;44(2):132-156. doi:10.1016/j.clae.2021.02.009
18. Downie LE, Craig JP. Tear film evaluation and management in soft contact lens wear: a systematic approach. *Clin Exp Optom*. 2017;100(5):438-458. doi:10.1111/cxo.12597
19. Dumbleton K, Caffery B, Dogru M, et al. The TFOS International Workshop on Contact Lens Discomfort: report of the subcommittee on epidemiology. *Invest Ophthalmol Vis Sci*. 2013;54(11):TFOS20-TFOS36. Published 2013 Oct 18. doi:10.1167/iovs.13-13125
20. Efron N, Morgan PB, Nichols JJ, et al. All soft contact lenses are not created equal. *Cont Lens Anterior Eye*. 2022;45(2):101515. doi:10.1016/j.clae.2021.101515
21. Fernández-Jiménez E, Díz-Arias E, Peral A. Improving ocular surface comfort in contact lens wearers. *Cont Lens Anterior Eye*. 2022;45(3):101544. doi:10.1016/j.clae.2021.101544
22. Fjærøvoll K, Fjærøvoll H, Magno M, et al. Review on the possible pathophysiological mechanisms underlying visual display terminal-associated dry eye disease. *Acta Ophthalmol*. 2022;100(8):861-877. doi:10.1111/aos.15150
23. Frogozo M. How contact lenses contribute to Dry Eye. Review of Optometry. May 15, 2023. Accessed August 6, 2023. <https://www.reviewofoptometry.com/article/how-contact-lenses-contribute-to-dry-eye>.
24. Guillou M, Maissa C. Dry eye symptomatology of soft contact lens wearers and nonwearers. *Optom Vis Sci*. 2005;82(9):829-834. doi:10.1097/01.opt.0000178060.45925.5d
25. Hamedani AG, Gold DR. Eyelid Dysfunction in Neurodegenerative, Neurogenetic, and Neurometabolic Disease. *Front Neurol*. 2017;8:329. Published 2017 Jul 18. doi:10.3389/fneur.2017.00329
26. Harthan JS. Which factors matter in contact lens selection? Review of Optometry. August 15, 2022. Accessed August 6, 2023. <https://www.reviewofoptometry.com/article/which-factors-matter-in-contact-lens-selection>.
27. Haworth K, Travis D, Abariga SA, Fuller D, Pucker AD. Silicone hydrogel versus hydrogel soft contact lenses for differences in patient-reported eye comfort and safety. *Cochrane Database Syst Rev*. 2021;2021(5):CD014791. Published 2021 May 10. doi:10.1002/14651858.CD014791
28. Hirota M, Uozato H, Kawamorita T, Shibata Y, Yamamoto S. Effect of incomplete blinking on tear film stability. *Optom Vis Sci*. 2013;90(7):650-657. doi:10.1097/OPX.0b013e31829962ec
29. Hydrogen peroxide gets the edge on comfort. Review of Optometry. December 28, 2020. Accessed August 6, 2023. <https://www.reviewofoptometry.com/article/hydrogen-peroxide-gets-the-edge-on-comfort>.
30. Iskeleli G, Karakoç Y, Aydin O, Yetik H, Uslu H, Kızılıkaya M. Comparison of tear-film osmolarity in different types of contact lenses. *CLAO J*. 2002;28(4):174-176. doi:10.1097/01.ICL.0000024117.46518.A4
31. Inomata T, Nakamura M, Iwagami M, et al. Stratification of Individual Symptoms of Contact Lens-Associated Dry Eye Using the iPhone App DryEyeRhythm: Crowdsourced Cross-Sectional Study. *J Med Internet Res*. 2020;22(6):e18996. Published 2020 Jun 26. doi:10.2196/18996
32. Jalbert I, Rejab S. Increased numbers of Demodex in contact lens wearers. *Optom Vis Sci*. 2015;92(6):671-678. doi:10.1097/OPX.0000000000000605

# REFERENCES

33. Jansen ME, Begley CG, Himebaugh NH, Port NL. Effect of contact lens wear and a near task on tear film break-up. *Optom Vis Sci.* 2010;87(5):350-357. doi:10.1097/OPX.0b013e3181d951df
34. Jie Y, Sella R, Feng J, Gomez ML, Afshari NA. Evaluation of incomplete blinking as a measurement of dry eye disease. *Ocul Surf.* 2019;17(3):440-446. doi:10.1016/j.jtos.2019.05.00
35. Jones L, Efron N, Bandamwar K, et al. TFOS Lifestyle: Impact of contact lenses on the ocular surface [published online ahead of print, 2023 May 4]. *Ocul Surf.* 2023;29:175-219. doi:10.1016/j.jtos.2023.04.010
36. Kaido M, Kawashima M, Ishida R, Tsubota K. Tear Film Dynamics of Soft Contact Lens-Induced Dry Eye. *Curr Eye Res.* 2020;45(7):782-788. doi:10.1080/02713683.2019.1700530
37. Kojima T. Contact Lens-Associated Dry Eye Disease: Recent Advances Worldwide and in Japan. *Invest Ophthalmol Vis Sci.* 2018;59(14):DES102-DES108. doi:10.1167/ios.17-23685
38. Lee J. Proactive contact lens problem-solving. Review of Optometry. March 9, 2004. Accessed August 6, 2023. <https://www.reviewofoptometry.com/article/proactive-contact-lens-problem-solving>.
39. Lum E, Perera I, Ho A. Osmolality and buffering agents in soft contact lens packaging solutions. *Cont Lens Anterior Eye.* 2004;27(1):21-26. doi:10.1016/j.clae.2003.11.002
40. Machałńska A, Ząkrzewska A, Adamek B, et al. Comparison of Morphological and Functional Meibomian Gland Characteristics Between Daily Contact Lens Wearers and Nonwearers. *Cornea.* 2015;34(9):1098-1104. doi:10.1097/ICO.0000000000000511
41. Markoulli M, Kolani S. Contact lens wear and dry eyes: challenges and solutions. *Clin Optom (Auckl).* 2017;9:41-48. Published 2017 Feb 15. doi:10.2147/OPTO.S111130
42. McDermott GK. A fix-it guide for Toric Lens Fits. Review of Optometry. July 19, 2001. Accessed August 6, 2023. <https://www.reviewofoptometry.com/article/a-fix-it-guide-for-toric-lens-fits>.
43. McLaughlin R. Contact Lens Spectrum. September 1, 2001. Accessed August 6, 2023. <https://www.clspectrum.com/issues/2001/september-2001/rub-vs-no-rub>.
44. Molina K, Graham AD, Yeh T, et al. Not All Dry Eye in Contact Lens Wear Is Contact Lens-Induced. *Eye Contact Lens.* 2020;46(4):214-222. doi:10.1097/ICL.00000000000000661
45. Morgan PB, Murphy PJ, Gifford KL, et al. CLEAR - Effect of contact lens materials and designs on the anatomy and physiology of the eye. *Cont Lens Anterior Eye.* 2021;44(2):192-219. doi:10.1016/j.clae.2021.02.006
46. Muntz A, Subbaraman LN, Sorbara L, Jones L. Tear exchange and contact lenses: a review. *J Optom.* 2015;8(1):2-11. doi:10.1016/j.optom.2014.12.001
47. Musgrave CSA, Fang F. Contact Lens Materials: A Materials Science Perspective. *Materials (Basel).* 2019;12(2):261. Published 2019 Jan 14. doi:10.3390/ma12020261
48. Laxmi Narayana B, Rao P, Bhat S, Vidyalakshmi K. Comparison of the Antimicrobial Efficacy of Various Contact Lens Solutions to Inhibit the Growth of *Pseudomonas aeruginosa* and *Staphylococcus aureus*. *Int J Microbiol.* 2018;2018:5916712. Published 2018 May 31. doi:10.1155/2018/5916712
49. Navascues-Cornago M, Sun T, Read ML, Morgan PB. The short-term effect of contact lens wear on blink characteristics. *Cont Lens Anterior Eye.* 2022;45(5):101596. doi:10.1016/j.clae.2022.101596
50. Nichols JJ, Chalmers RL, Dumbleton K, et al. The Case for Using Hydrogen Peroxide Contact Lens Care Solutions: A Review. *Eye Contact Lens.* 2019;45(2):69-82. doi:10.1097/ICL.0000000000000542
51. Nichols JJ, Willcox MD, Bron AJ, et al. The TFOS International Workshop on Contact Lens Discomfort: executive summary. *Invest Ophthalmol Vis Sci.* 2013;54(11):TFOS7-TFOS13. Published 2013 Oct 18. doi:10.1167/ios.13-13212
52. Nichols JJ, Willcox MD, Bron AJ, et al. The TFOS International Workshop on Contact Lens Discomfort: executive summary. *Invest Ophthalmol Vis Sci.* 2013;54(11):TFOS7-TFOS13. Published 2013 Oct 18. doi:10.1167/ios.13-13212
53. Pisella PJ, Malet F, Lejeune S, et al. Ocular surface changes induced by contact lens wear. *Cornea.* 2001;20(8):820-825. doi:10.1097/00003226-200111000-00009
54. Rodolfo K. What is Homeostasis? Scientific American. <https://www.scientificamerican.com/article/what-is-homeostasis>. Published January 3, 2000. Accessed September 11, 2022. Saliman NH, Maldonado-Codina C, Morgan PB. Effect of material and care system combination on subclinical inflammation of the ocular surface in soft contact lens wear. *Cont Lens Anterior Eye.* 2022;45(4):101489. doi:10.1016/j.clae.2021.101489
55. Saliman NH, Morgan PB, MacDonald AS, Maldonado-Codina C. Subclinical Inflammation of the Ocular Surface in Soft Contact Lens Wear. *Cornea.* 2020;39(2):146-154. doi:10.1097/ICO.00000000000002192
56. Schorner S. Some facts about SiHy lenses. Review of Optometry. July 15, 2010. Accessed August 6, 2023. <https://www.reviewofoptometry.com/article/some-facts-about-sihy-lenses>.
57. Sindt CW. What's In your blister pack? Review of Cornea and Contact Lenses. June 18, 2010. Accessed August 6, 2023. <https://www.reviewofcontactlenses.com/article/whats-in-your-blister-pack>.
58. Sindt CW, Longmuir RA. Contact lens strategies for the patient with dry eye. *Ocul Surf.* 2007;5(4):294-307. doi:10.1016/s1542-0124(12)70095-2
59. Sridhar MS. Anatomy of cornea and ocular surface. *Indian J Ophthalmol.* 2018;66(2):190-194. doi:10.4103/ijo.IJO\_646\_17
60. Srinivasan S. Today's contact lens materials and designs. Review of Optometry. August 15, 2017. Accessed August 6, 2023. <https://www.reviewofoptometry.com/article/ro0817-todays-contact-lens-materials-and-designs>.
61. Stapleton F, Stretton S, Papas E, Skotnitsky C, Sweeney DF. Silicone hydrogel contact lenses and the ocular surface. *Ocul Surf.* 2006;4(1):24-43. doi:10.1016/s1542-0124(12)70262-8
62. Surfactant. Contact Lens Update. 2023. Accessed August 6, 2023. <https://contactlensupdate.com/2012/03/20/surfactant>.
63. Tahhan N, Naduvilath TJ, Woods C, Papas E. Review of 20 years of soft contact lens wearer ocular physiology data. *Cont Lens Anterior Eye.* 2022;45(1):101525. doi:10.1016/j.clae.2021.101525
64. Tarkowski W, Moneta-Wielgoś J, Młocicki D. Demodex sp. as a Potential Cause of the Abandonment of Soft Contact Lenses by Their Existing Users. *Biomed Res Int.* 2015;2015:259109. doi:10.1155/2015/259109
65. Urgacz A, Mrukwa E, Gawlik R. Adverse events in allergy sufferers wearing contact lenses. *Postepy Dermatol Alergol.* 2015;32(3):204-209. doi:10.5114/pdia.2015.48071
66. Vidal-Rohr M, Wolffsohn JS, Davies LN, Cerviño A. Effect of contact lens surface properties on comfort, tear stability and ocular physiology. *Cont Lens Anterior Eye.* 2018;41(1):117-121. doi:10.1016/j.clae.2017.09.009

# REFERENCES

67. Wagner H. Lifelong contact lens success: Keep allergy and dry eye at bay. *Review of Optometry*. June 15, 2017. Accessed August 6, 2023. <https://www.reviewofoptometry.com/article/lifelong-contact-lens-success-keep-allergy-and-dry-eye-at-bay>.
68. Willcox M, Keir N, Maseedupally V, et al. CLEAR - Contact lens wettability, cleaning, disinfection and interactions with tears. *Cont Lens Anterior Eye*. 2021;44(2):157-191. doi:10.1016/j.clae.2021.02.004
69. Yang L, Pazo EE, Zhang Q, et al. Treatment of contact lens related dry eye with intense pulsed light. *Cont Lens Anterior Eye*. 2022;45(2):101449. doi:10.1016/j.clae.2021.101449
70. Yeung KK. Dissecting the soft contact lens. *Review of Optometry*. August 15, 2018. Accessed August 6, 2023. <https://www.reviewofoptometry.com/article/dissecting-the-soft-contact-lens>.
71. York M, Ong J, Robbins JC. Variation in blink rate associated with contact lens wear and task difficulty. *Am J Optom Arch Am Acad Optom*. 1971;48(6):461-467. doi:10.1097/00006324-197106000-00001
72. Zhu H, Bandara MB, Vijay AK, Masoudi S, Wu D, Willcox MD. Importance of rub and rinse in use of multipurpose contact lens solution. *Optom Vis Sci*. 2011;88(8):967-972. doi:10.1097/OPX.0b013e31821bf976
73. 3 mistakes you're making with your contact lenses. SELF. November 2, 2011. Accessed August 26, 2023. <https://www.self.com/story/3-mistakes-youre-making-with-y>.
74. Nascari D, Sved A. Homeostasis success or failure. Wikimedia Commons. CC BY-SA 4.0. [https://commons.wikimedia.org/wiki/File:Homeostasis\\_success\\_or\\_failure.png](https://commons.wikimedia.org/wiki/File:Homeostasis_success_or_failure.png). Published August 26, 2019. Accessed September 3, 2021.
75. Sem J. Fish oil capsules. CC BY 2.0. www.semtrio.com. Published September 12, 2018. Accessed December 18, 2021.
76. johnnyAutomatic. Johnny-automatic-scales-of-justice. <https://openclipart.org/detail/26849/scales-of-justice>. Wikimedia Commons. CC0. <https://commons.wikimedia.org/w/index.php?curid=46844394>. Published February 7, 2016. Accessed September 3, 2021.

# THANK YOU!

INSTAGRAM: @CORY.LAPPIN

# Seeing Red: How to Manage Ocular Rosacea

Cory J. Lappin, OD, MS, FAAO



# Disclosures

- ▶ Alcon
- ▶ Barti
- ▶ Bausch + Lomb
- ▶ Bruder Healthcare and M&S Technologies (Hilco Vision)
- ▶ Dompé
- ▶ Lumenis
- ▶ Myze
- ▶ NuLids
- ▶ PRN Vision Group
- ▶ Rinsada
- ▶ Tarsus Pharmaceuticals
- ▶ Vital Tears

The content of this COPE accredited course was prepared independently. I have received no financial or commercial support for this presentation. All relevant relationships have been mitigated.

# What is Rosacea?

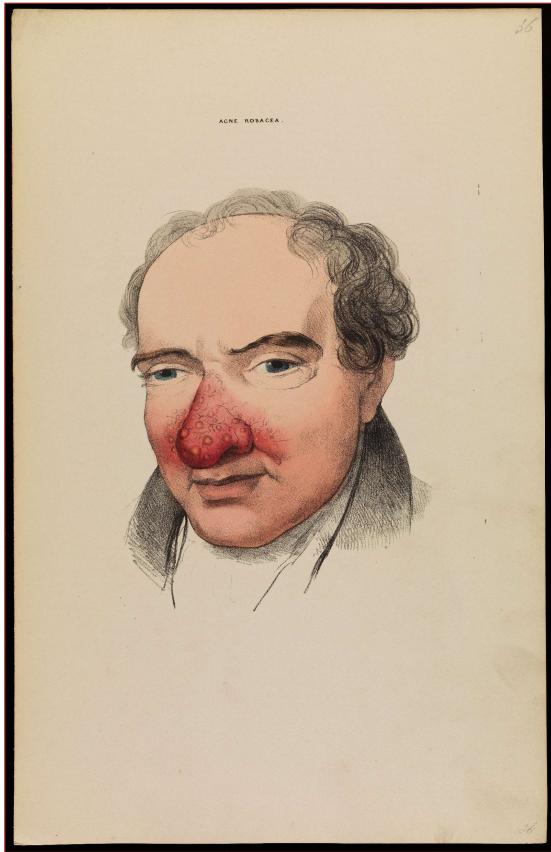


- ▶ **Chronic inflammatory disease of skin due to hypersensitivity to normal environmental stimuli**
  - ▶ Affects skin of face, sebaceous glands
  - ▶ Development of telangiectatic vessels
  - ▶ Relapsing and remitting
    - ▶ Signs and symptoms exacerbated by triggers
  - ▶ Negative impact on cosmetic appearance, tissue function

# Epidemiology - Rosacea

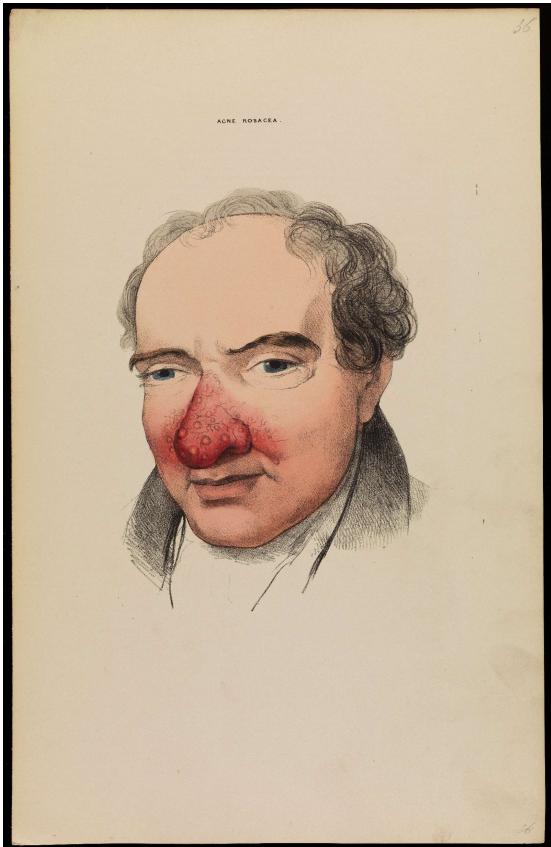
- ▶ Affects estimated 5% of population
- ▶ 16 million people in US with rosacea
- ▶ Most common in middle-age
  - ▶ 80% 30+ years old
  - ▶ Peak incidence 40-59 years of age
  - ▶ Relatively uncommon in children
- ▶ Females > Males?
  - ▶ Differences in care seeking behaviors
- ▶ Can affect any race
  - ▶ More common in Caucasians

# Diagnosing Rosacea



- ▶ **Clinical diagnosis**
  - ▶ No histologic or serologic markers
- ▶ **Varying signs**
  - ▶ Many combinations of signs and symptoms
- ▶ **National Rosacea Society Guidelines**
  - ▶ Help standardize diagnosis

# Diagnosing Rosacea



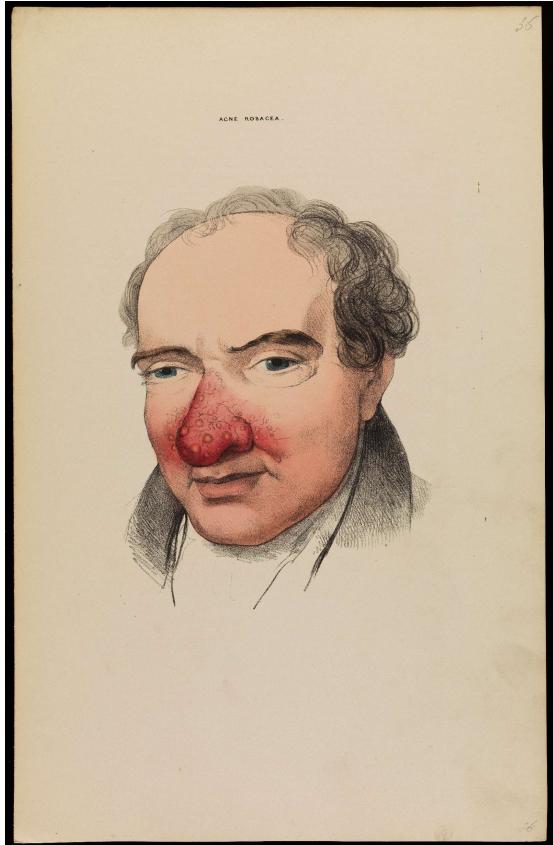
## National Rosacea Society Guidelines

- ▶ Primary Features\*

  - ▶ Flushing (transient)
  - ▶ Erythema (non-transient)
  - ▶ Papules and/or pustules
  - ▶ Telangiectasia

\*Will exhibit one or more

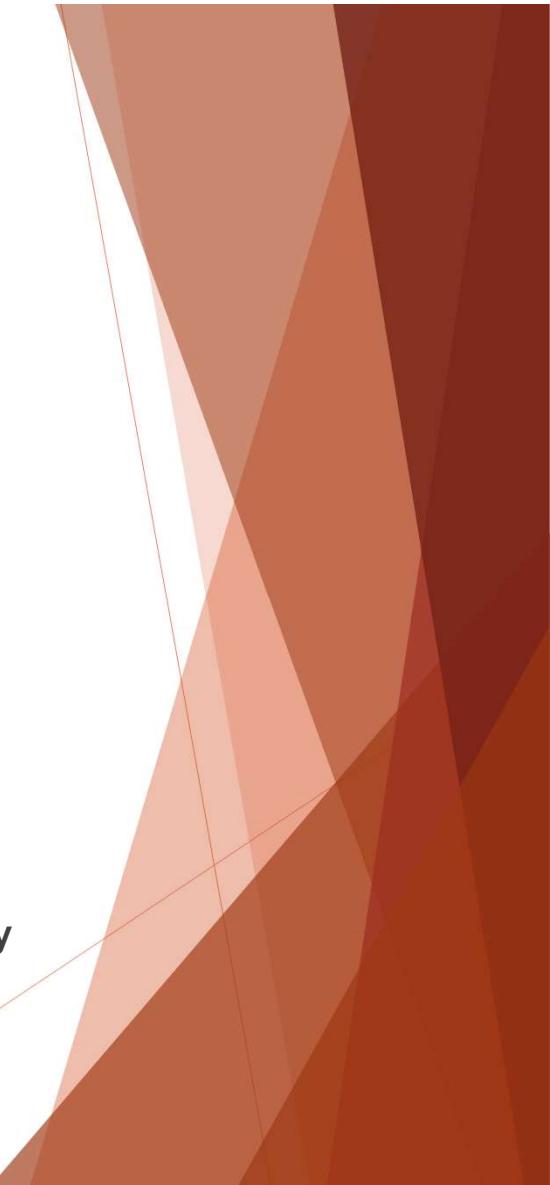
# Diagnosing Rosacea



## National Rosacea Society Guidelines

- ▶ **Secondary Features\***
  - ▶ Burning and/or stinging
  - ▶ Plaques
  - ▶ Dry appearance to skin
  - ▶ Phymatous changes
  - ▶ Ocular Manifestations
  - ▶ Peripheral locations

\*Typically appear along with Primary Features but can be independent



# Types of Rosacea

The National Rosacea Society Expert Committee Rosacea Subtypes

1. Erythematotelangiectatic
2. Papulopustular
3. Phymatous
4. Ocular Rosacea
  - o Granulomatous variant

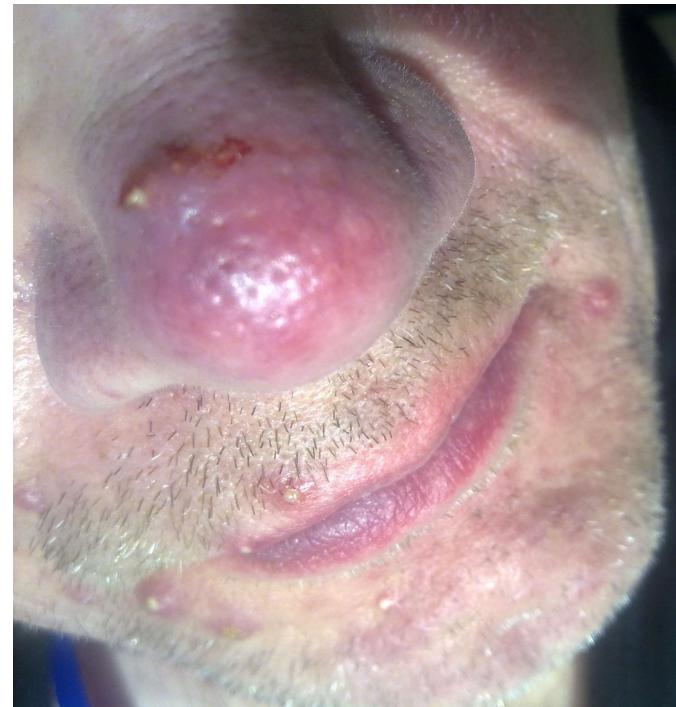
## Types of Rosacea - Erythematotelangiectatic

- ▶ Characterized by
  - ▶ Facial flushing
  - ▶ Persistent facial erythema (classic appearance)
  - ▶ +/- visible telangiectatic vessels



## Types of Rosacea - Papulopustular

- ▶ Characterized by
  - ▶ Facial erythema
  - ▶ Transient papules and pustules
  - ▶ Can vary in size



## Types of Rosacea - Phymatous

- ▶ Characterized by
  - ▶ Thickening and enlargement of affected tissues
  - ▶ Rhinophyma most commonly
    - ▶ Can also affect chin, forehead, cheeks, and ears



## Types of Rosacea - Granulomatous variant

- ▶ Characterized by
  - ▶ Non-inflammatory, indurated papules or nodules
    - ▶ Nodules are uniform in size
    - ▶ Can lead to scarring



# Types of Rosacea - Ocular Rosacea

- ▶ Characterized by
  - ▶ Telangiectasia
    - ▶ Affects lid, lid margin, and ocular surface
  - ▶ Meibomian gland dysfunction
  - ▶ Chronic inflammation
- ▶ Can occur independently of facial rosacea



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# Types of Rosacea - Ocular Rosacea

- ▶ 58-72% of rosacea patients have OR
- ▶ Incidence of 6-72%
- ▶ OR occurs first in 20% of rosacea cases
- ▶ Facial rosacea subtle in 90% of cases involving both cutaneous and OR
- ▶ Females = Males



# Pathophysiology

- ▶ **Inflammatory condition**
  - ▶ Exact cause unknown
- ▶ **Mechanism widely agreed upon**
  - ▶ Hypersensitivity to normal environmental stimuli

# Pathophysiology

## Hypersensitization of innate immune system

- ▶ Abnormally high expression of TLR2 receptors in keratinocytes
  1. Environmental stimuli triggers TLR2 receptors
  2. Enhanced KLK5 (serine protease) activity
  3. Increased cathelicidin production
    - ▶ Antimicrobial peptide of innate immune system
  4. Increased VEGF expression
  5. Development of telangiectatic blood vessels

# Pathophysiology

## Other implicated factors

- ▶ **MMP-8 and 9**
- ▶ **Interleukin-1 $\alpha$  and  $\beta$**
- ▶ **ICAM-1**
- ▶ **TNF- $\alpha$**
- ▶ **Phospholipase A2 Group IIA**
  - ▶ Antimicrobial proteins, kill Gram-positive bacteria

# Pathophysiology

- ▶ Proposed etiologies
  - ▶ Bacterial
    - ▶ *Helicobacter pylori* and *Staphylococcus epidermidis*
  - ▶ Parasitic
    - ▶ *Demodex folliculorum* and *Demodex brevis*
  - ▶ “Hybrid”
    - ▶ Demodex as vector for other infectious microorganisms (*Bacillus olenorium*)
  - ▶ Genetic
    - ▶ More common in certain races and ethnicities

# Ocular Rosacea - Clinical Presentation

## Signs

- ▶ Telangiectatic vessels
- ▶ Lid margin scalloping/notching
- ▶ Inspissated meibomian glands
- ▶ Recurrent hordeola and chalazia
- ▶ Papillary reaction
- ▶ Lash debris/collarettes
- ▶ Saponification
- ▶ Corneal neovascularization
- ▶ Conjunctival hyperemia (most pronounced in interpalpebral region)

## Symptoms

- ▶ Chronic redness
- ▶ Foreign body sensation
- ▶ Burning/stinging
- ▶ Dryness
- ▶ Itching
- ▶ Photophobia
- ▶ Epiphora
- ▶ Blurred/fluctuating vision

# Clinical Presentation

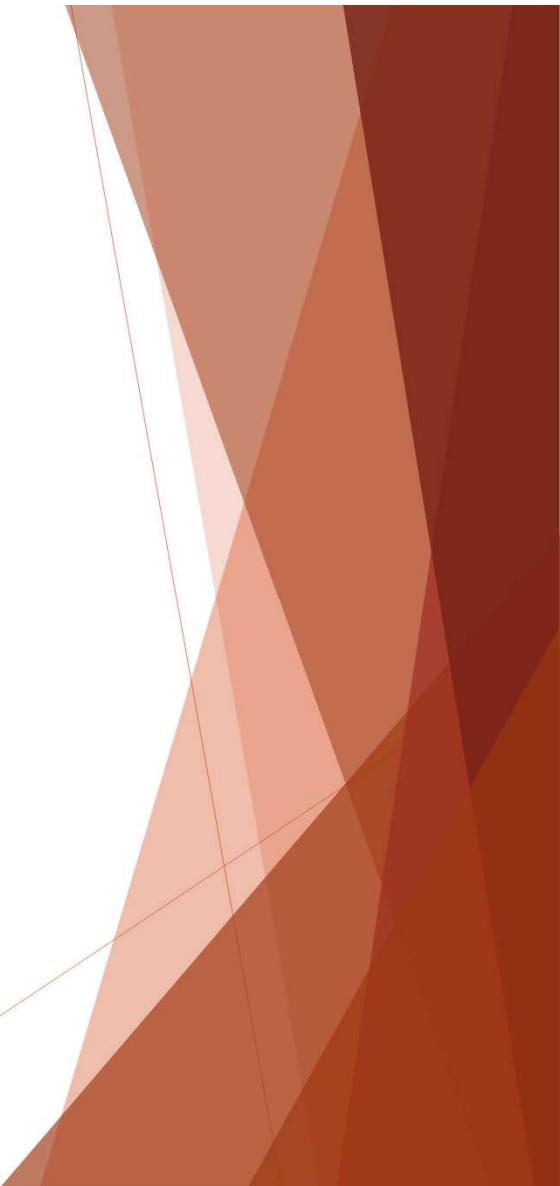


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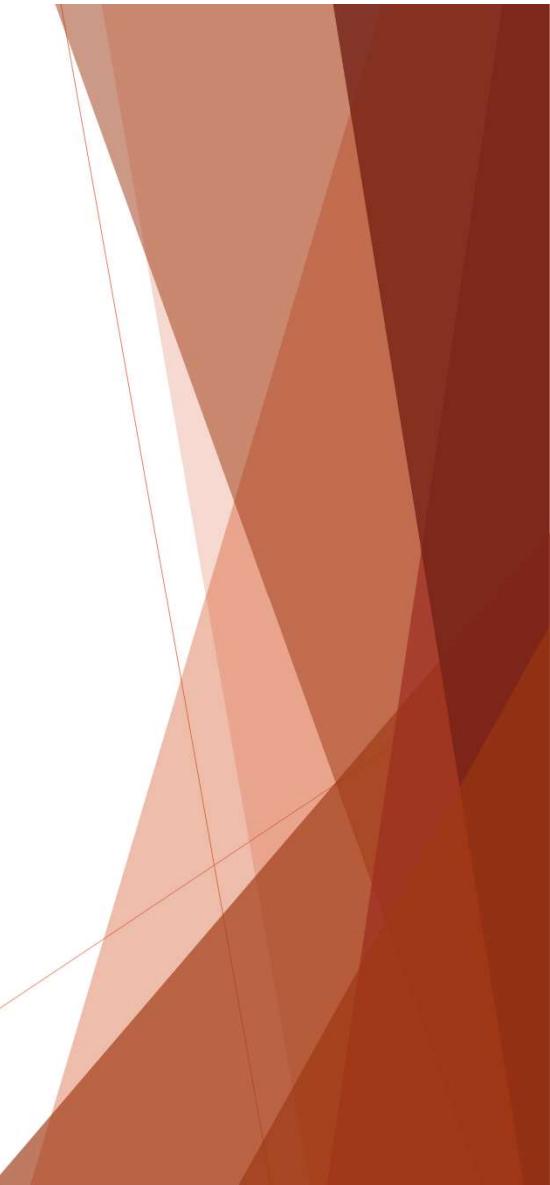
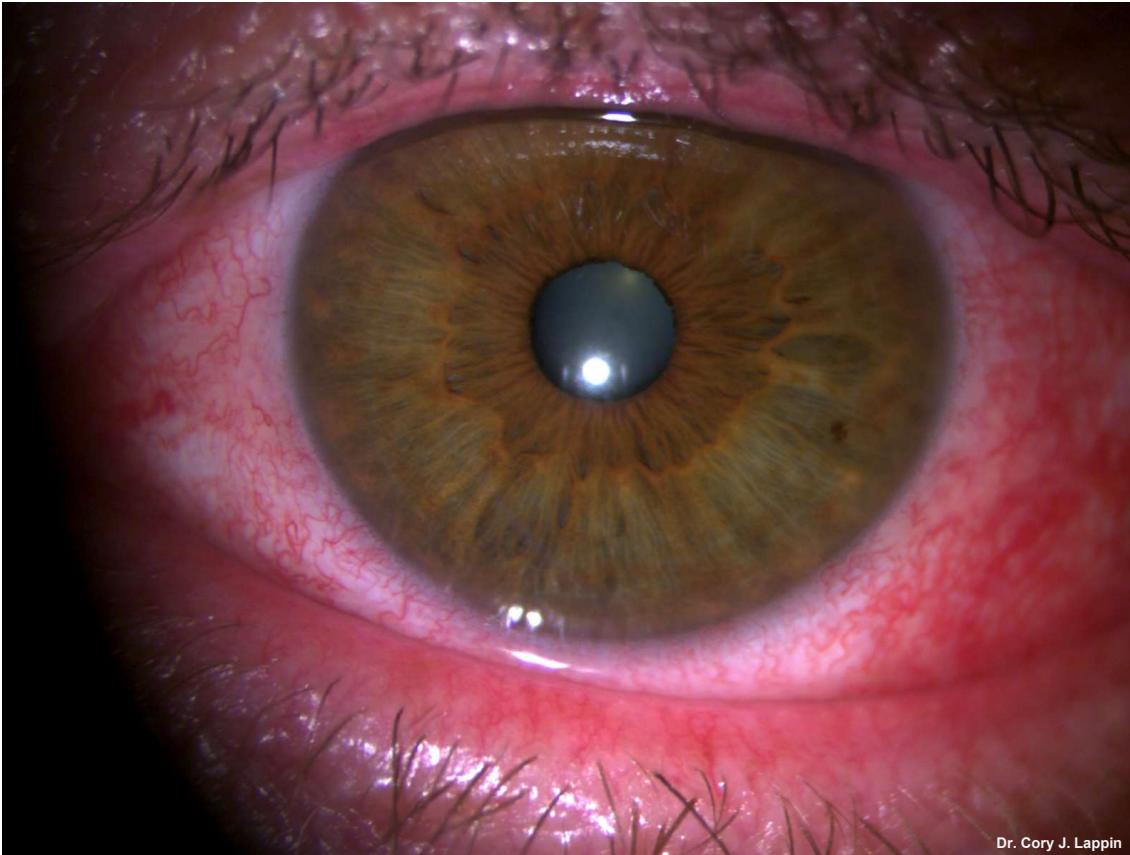


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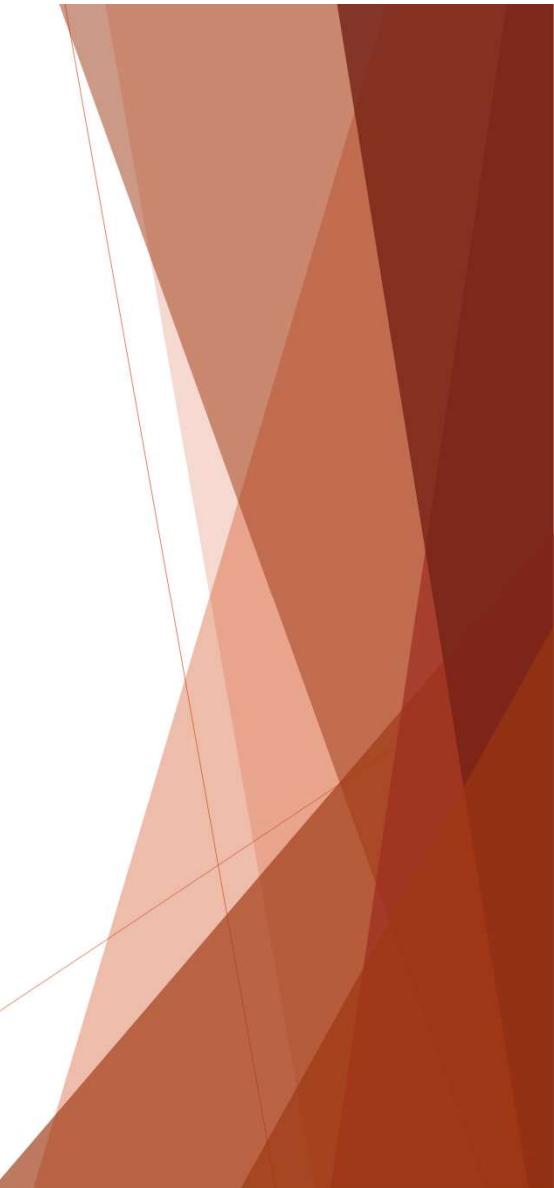
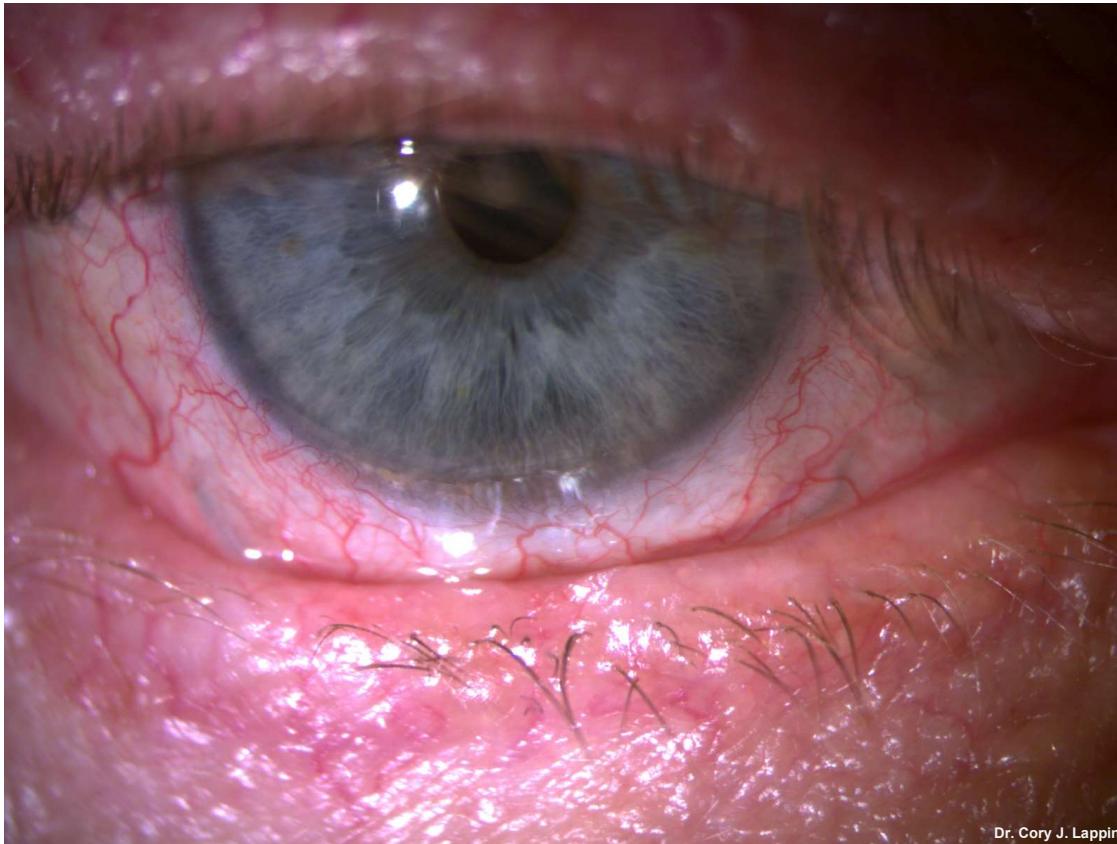
# Clinical Presentation



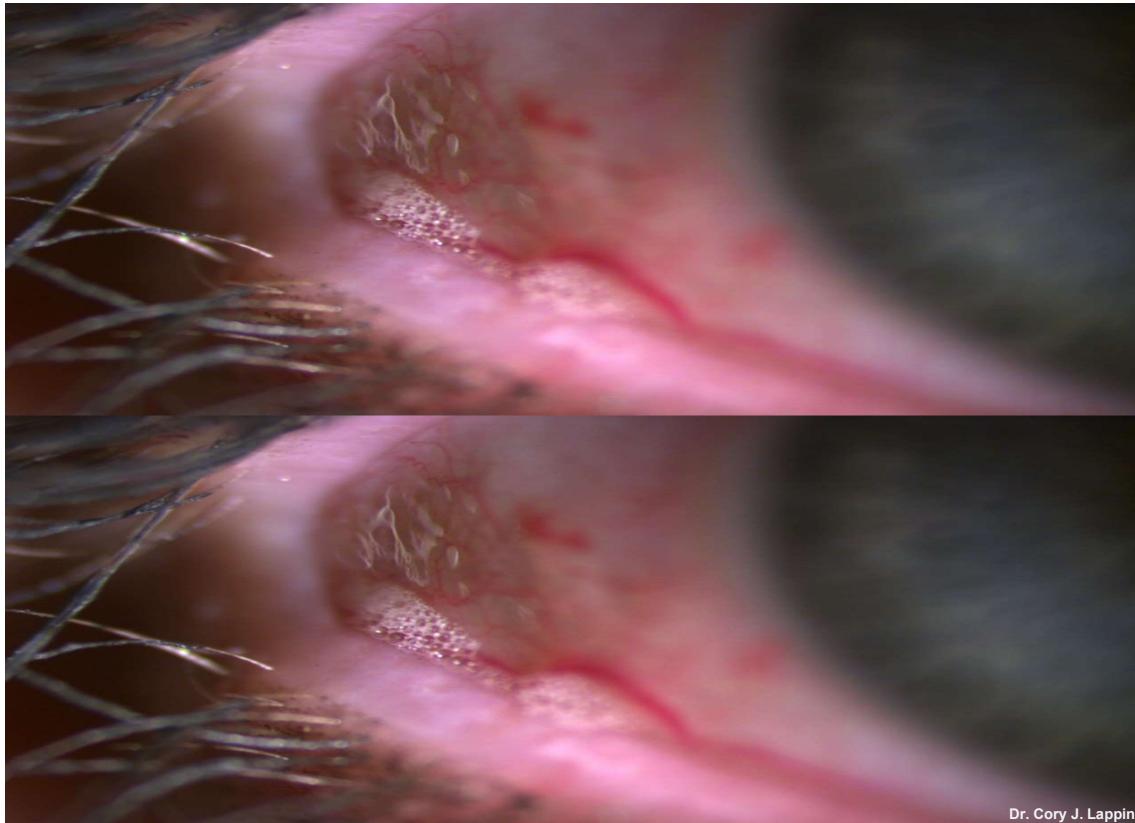
# Clinical Presentation



# Clinical Presentation



# Clinical Presentation



# Clinical Presentation



# Clinical Presentation



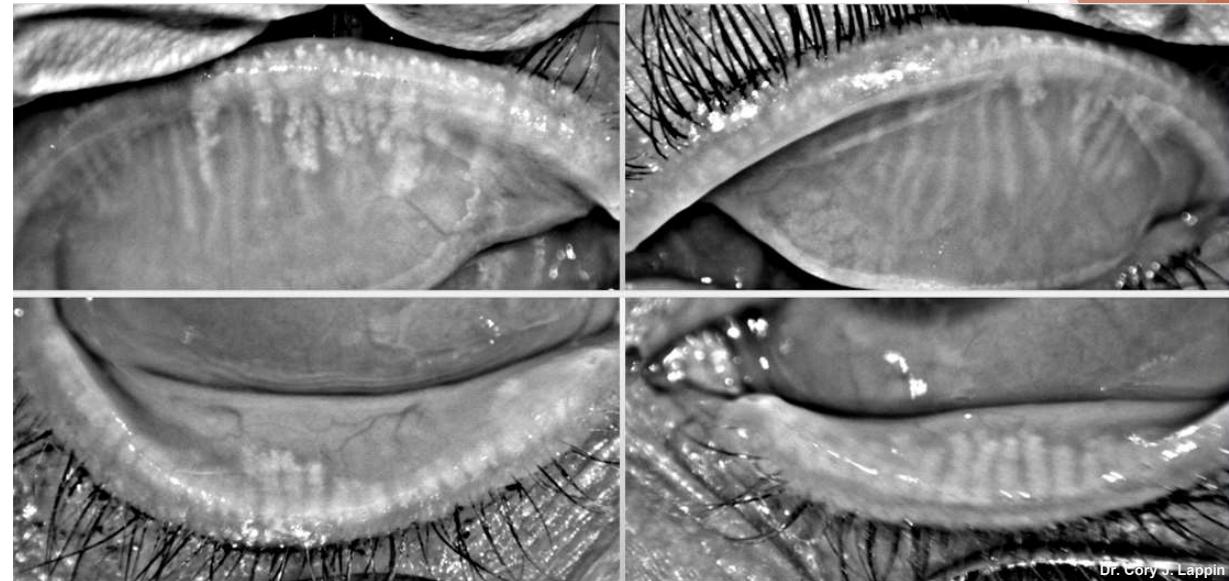
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# Clinical Presentation - Comorbidities

- ▶ **Dry Eye**
  - ▶ 52-62.5% of OR cases
- ▶ **MGD**
  - ▶ 92% of OR cases
- ▶ **Blepharitis**
  - ▶ Common



# Clinical Presentation - Diagnosis

- ▶ Signs and symptoms are nonspecific
  - ▶ Overlap with manifestations of other ocular surface diseases
    - ▶ Often comorbid
  - ▶ Easily overlooked or misattributed to other condition

## Clinical Presentation - Diagnosis

The National Rosacea Society Expert Committee recommends considering a diagnosis of ocular rosacea if ANY of these signs or symptoms are present

# Clinical Presentation - Diagnosis

- ▶ Can result in significant disruption to the eyelids and ocular surface
  - ▶ Negative impacts on
    - ▶ Vision
    - ▶ Comfort
    - ▶ Cosmetic appearance

# Clinical Presentation - Diagnosis

- ▶ Diagnosis of all forms of rosacea made clinically
- ▶ Appears similar and often concomitantly with other OSD conditions
  - ▶ National Rosacea Society Expert Committee recommends considering OR if any of previously signs or symptoms noted
- ▶ Differentiating characteristics
  - ▶ Lid and lid margin telangiectasia
  - ▶ Exacerbations with environmental triggers

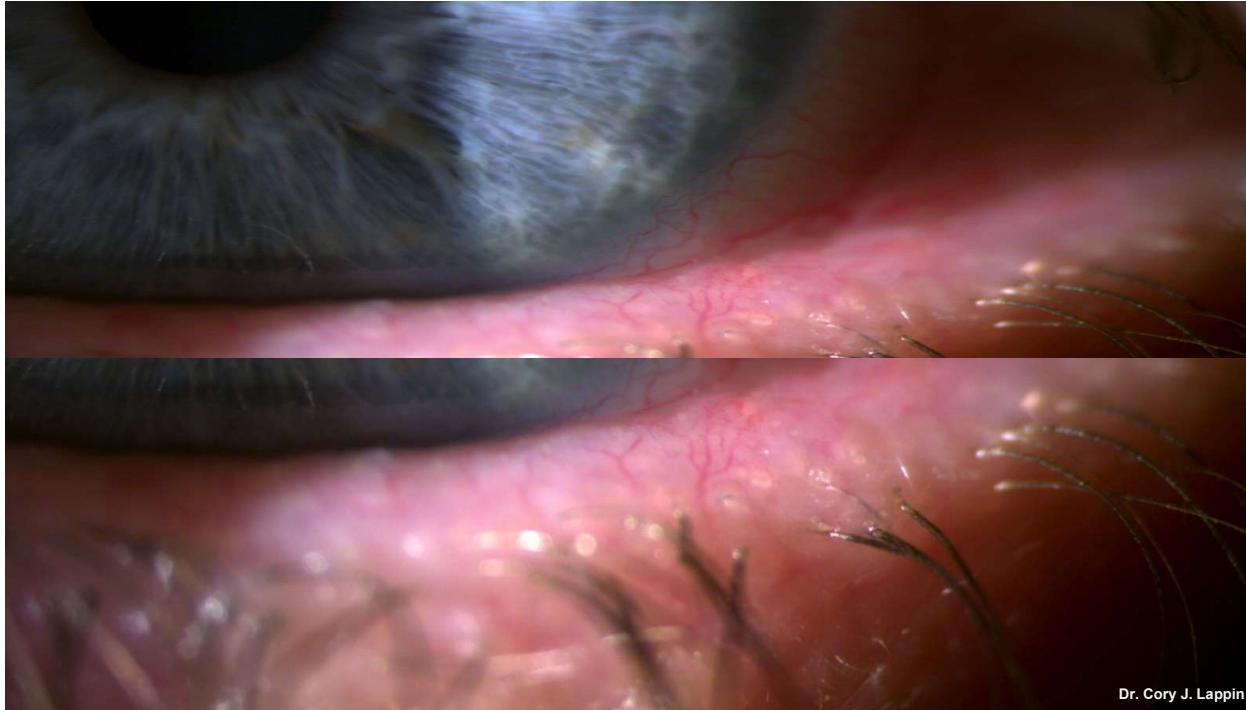
# Grading Severity

## The Global ROSacea COnsensus (ROSCO) Expert Panel Grading System

- ▶ Based on extent of tissue involvement
  - 1. Mild OR: blepharitis with lid margin telangiectasia
  - 2. Mild-to-Moderate OR: blepharoconjunctivitis
    - ▶ Chronic inflammation can lead cicatrization
  - 3. Moderate-to-Severe OR: blepharokeratoconjunctivitis
    - ▶ Corneal involvement in 1/3 of cases
  - 4. Severe OR: sclerokeratitis and/or uveitis

# Mild Ocular Rosacea

- ▶ Blepharitis with lid margin telangiectasia



# Mild-to-Moderate Ocular Rosacea

- ▶ Blepharoconjunctivitis



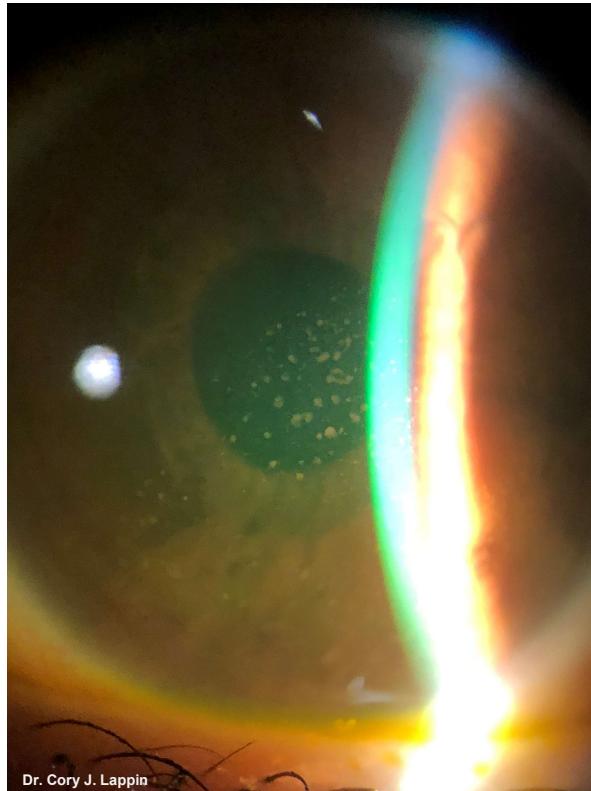
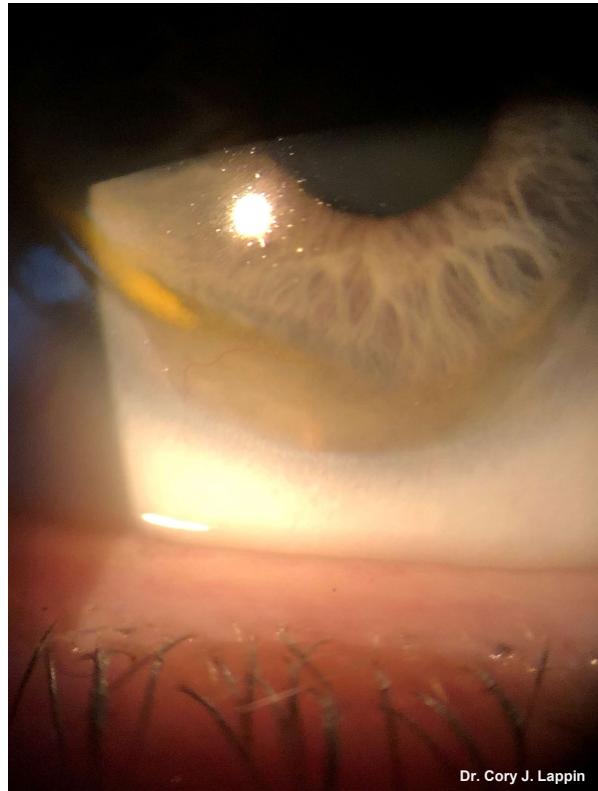
# Moderate-to-Severe Ocular Rosacea

- ▶ Blepharokeratoconjunctivitis



# Severe Ocular Rosacea

- ▶ Sclerokeratitis and/or uveitis

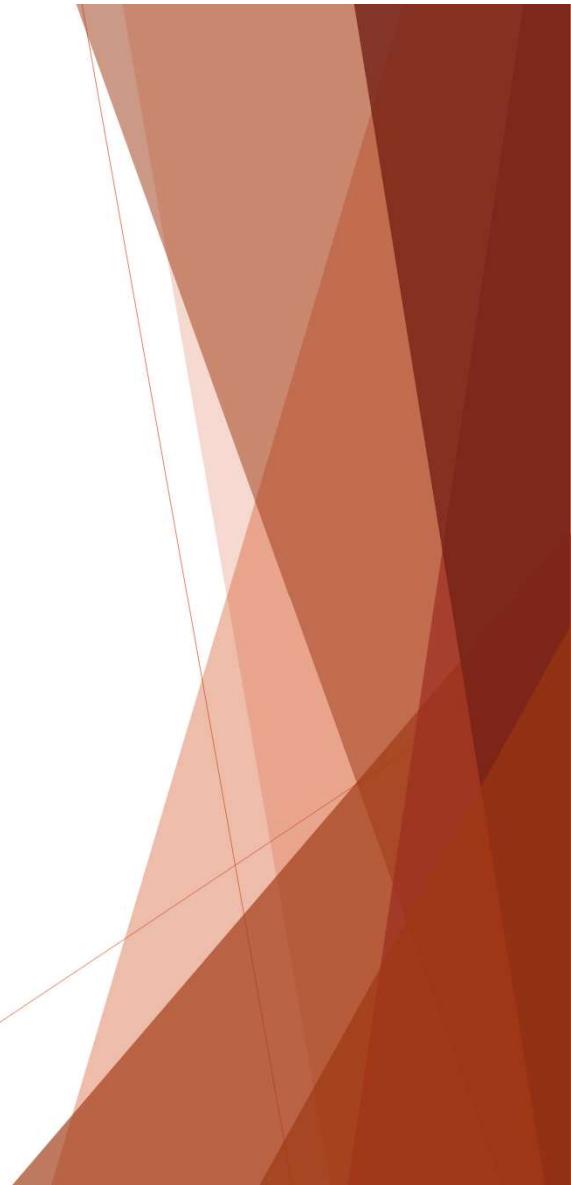


# Treatment - Overview

- ▶ **No cure for OR**
  - ▶ Goal is management
- ▶ **Chronic condition**
  - ▶ Manage acute and chronic signs and symptoms
- ▶ **Dry Eye, MGD, Blepharitis are common comorbidities**
  - ▶ Significant treatment overlap
- ▶ **Need to address all elements of condition for successful treatment**
  - ▶ Lifestyle modification
  - ▶ Prescription treatments
  - ▶ Diet and supplements

# Trigger Avoidance

- ▶ **Environmental stimuli**
  - ▶ Extreme heat, Extreme cold, Wind and sun exposure
- ▶ **Emotional triggers**
  - ▶ Stress, Anger, Embarrassment
- ▶ **Physiological stimuli**
  - ▶ Strenuous exercise
- ▶ **Dietary triggers**
  - ▶ Caffeine, Chocolate, Alcohol, Dairy products, Hot beverages, Spicy food
- ▶ **Pharmaceuticals and supplements**
  - ▶ Nasal and topical (cutaneous) steroids, Beta blockers, Amiodarone, Niacin, Vitamins B6 and B12
- ▶ **Cosmetics**



# Topical Cutaneous Treatments

- ▶ **Metronidazole**
  - ▶ Topical antibiotic
  - ▶ 0.75% and 1% gel and cream
  - ▶ Dosed BID
- ▶ **Azelaic acid**
  - ▶ Topical antiseptic
  - ▶ 15% gel and 20% gel and cream
  - ▶ Dosed BID
- ▶ **Primarily for facial rosacea**
  - ▶ May be beneficial for eyelid-related inflammation
- ▶ **Consult comanaging dermatologist**
- ▶ **Avoid topical cutaneous corticosteroids**
  - ▶ Can trigger rosacea flares

# Artificial Tears

- ▶ **Primarily palliative**

- ▶ Offer quick relief
- ▶ Avoid irritation with prophylactic use
- ▶ Dosed QID-PRN
  - ▶ If using >QID, recommend preservative free AT

- ▶ **Lipid-based ATs**

- ▶ Drops of choice
- ▶ Stabilize lipid component of tear film
- ▶ May reduce inflammatory factors in tear film

# Lid Hygiene

- ▶ **Lotilaner ophthalmic solution (Xdemvy)**
  - ▶ Addresses associated Demodex overgrowth
- ▶ **Tea Tree Oil (*Melaleuca alternifolia*)**
  - ▶ 50% formulation (foams, scrubs)
  - ▶ Anti-inflammatory
  - ▶ Antimicrobial
- ▶ **Okra-based cleansers (Zocular)**
  - ▶ Anti-inflammatory
  - ▶ Antimicrobial



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# Lid Hygiene

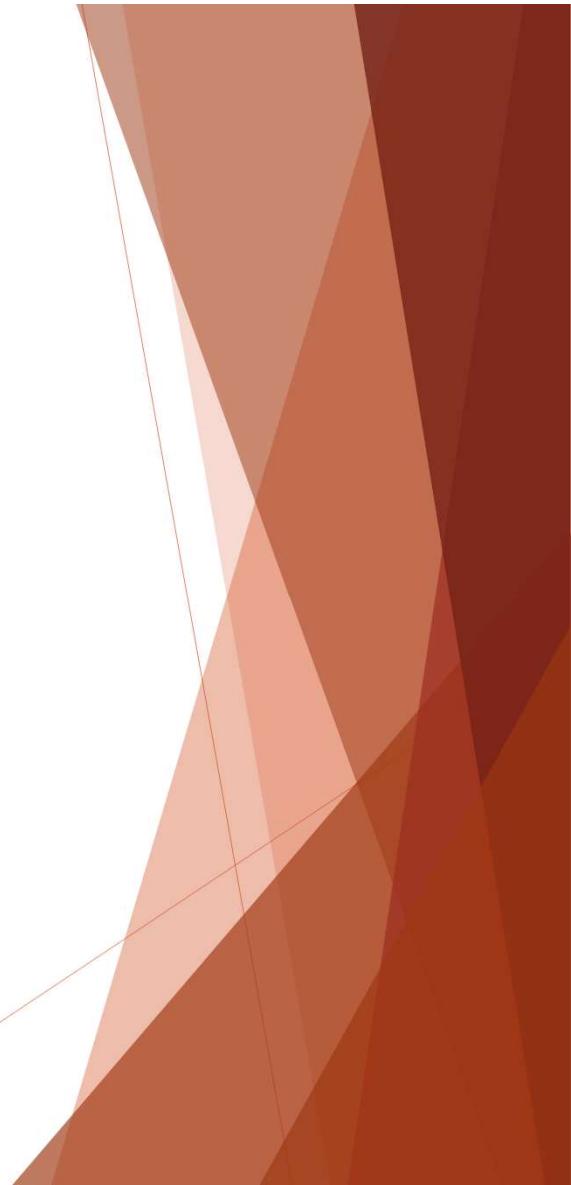
- ▶ Hypochlorous Acid (HOCl)
  - ▶ 0.01%
  - ▶ Anti-inflammatory
  - ▶ Antiseptic/Broad Antibacterial
  - ▶ Naturally produced by leukocytes
  - ▶ Dosed BID
  - ▶ Reducing overgrowth of *Staphylococcus epidermidis*



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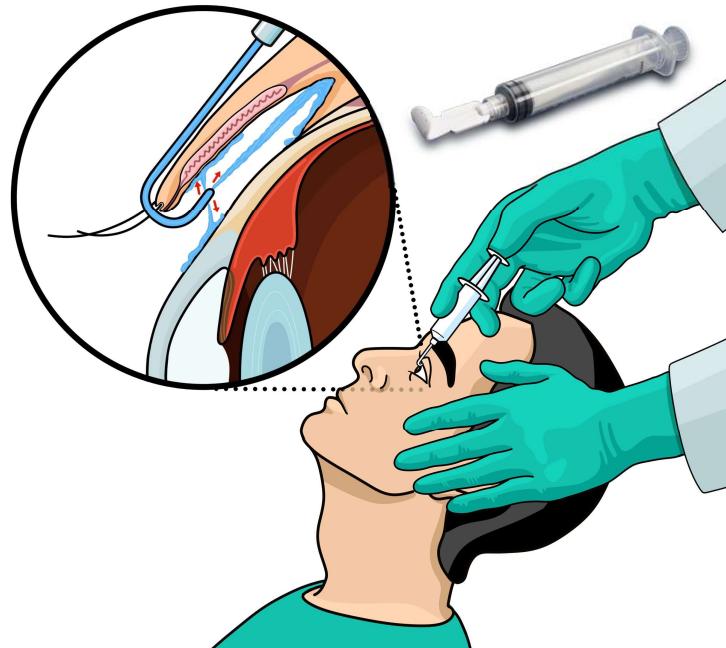
# Lid Therapies

- ▶ Warm compresses
  - ▶ Use with caution
    - ▶ Cold better option?
- ▶ Thermal Pulsation
  - ▶ LipiFlow
  - ▶ iLux
  - ▶ TearCare
- ▶ Microblepharoexfoliation
  - ▶ NuLids PRO (in-office)
  - ▶ BlephEx (in-office)
  - ▶ NuLids (at home)



# Ocular Surface Lavage

- ▶ **High pressure saline irrigation**
  - ▶ Flushes proinflammatory factors from ocular surface
  - ▶ “Resets” ocular surface
- ▶ **Devices**
  - ▶ Rinsada



<https://www.rinsada.com/>

# Oral Antibiotics

- ▶ Considered standard of care by many
- ▶ Oral tetracyclines
- ▶ Doxycycline is drug of choice
  - ▶ Used for anti-inflammatory properties rather than antibacterial
  - ▶ Dosed below minimum effective dose for antibacterial activity



# Oral Antibiotics

## ► Doxycycline

- ▶ Higher loading dose, followed by lower maintenance dose
- ▶ Typical Dosing: 40-100 mg BID for 1-2 weeks, followed by 20-40 mg QD for 1-4 months

## ► Oracea

- ▶ 40 mg tablet (30 mg of immediate-release and 10 mg of extended-release)
- ▶ Dosed QD



# Oral Antibiotics

## ► Contraindications

- Pregnant and nursing women
- Children 7 years old and younger

## ► Side Effects

- GI disturbances
- Photosensitivity



# Oral Antibiotics

## Doxycycline Alternatives

- ▶ Azithromycin
  - ▶ 500 mg BID x 2 weeks
- ▶ Tetracycline
  - ▶ Dosed QID
- ▶ Minocycline
  - ▶ Less supporting evidence
- ▶ Isotretinoin
  - ▶ Significant side effects
    - ▶ Blepharitis, conjunctivitis, and meibomian gland destruction



# Topical Antibiotics

## ► Erythromycin ung

- Dosed QHS
- Can reduce bacterial burden
- Provide lubrication

## ► Azithromycin

- Dosed QHS x 2-4 weeks once every other night for maintenance
- Anti-inflammatory
- Improves MGD

# Topical Anti-Inflammatories

## Short-Term Inflammation Management

- ▶ **Soft Steroids**
  - ▶ 0.5% loteprednol etabonate BID-QID
  - ▶ Mild inflammation, periodic flares
- ▶ **Traditional Steroids**
  - ▶ 1% prednisolone acetate
  - ▶ Longer taper (4-3-2-1 dosing)
  - ▶ Significant inflammation
- ▶ **Side Effects**
  - ▶ IOP spikes/glaucoma
  - ▶ Cataracts



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# Topical Anti-Inflammatories

## Long-Term Inflammation Management

### ► Immunomodulators

- **Xiidra** (5% lifitegrast ophthalmic solution)
  - Blocks LFA-1 from binding ICAM-1
- **Cequa** (0.09% cyclosporine ophthalmic solution)
  - Inhibits calcineurin
- **Vevye** (0.1% cyclosporine ophthalmic solution)
  - Inhibits calcineurin
- **Restasis** (0.05% cyclosporine ophthalmic emulsion)
  - Inhibits calcineurin
- **Tacrolimus 0.03%**
  - Inhibits calcineurin

- All dosed BID
- All inhibit T cell activity
  - Differing mechanisms by which this is accomplished

# Diet and Supplements

- ▶ **Omega-3 supplementation**
  - ▶ High quality, re-esterified, triglyceride-based omega-3
  - ▶ 3:1 EPA to DHA ratio
  - ▶ At least 2 grams of combined EPA and DHA
- ▶ **Dietary Considerations**
  - ▶ Avoid triggering foods
  - ▶ Probiotics
  - ▶ High Fiber diet



# Intense Pulsed Light (IPL)

- ▶ **Basics**
  - ▶ High intensity polychromatic light (400-1200 nm)
  - ▶ 4 treatments spaced 2-4 weeks apart
- ▶ **FDA-approved for treatment of MGD and dry eye**
  - ▶ OptiLight IPL Device



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# Intense Pulsed Light (IPL)

- ▶ **Mechanisms of action**
  - ▶ Photobiomodulation
    - ▶ Decreases inflammatory factors
    - ▶ Increases anti-inflammatory cytokines
  - ▶ Improves MGD
    - ▶ Liquifies clogged oil
  - ▶ Antimicrobial
    - ▶ Eradicates Demodex
    - ▶ Decreases bacterial burden
  - ▶ Improves cosmetic appearance
    - ▶ Destroys telangiectatic vessels



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# Other Treatments

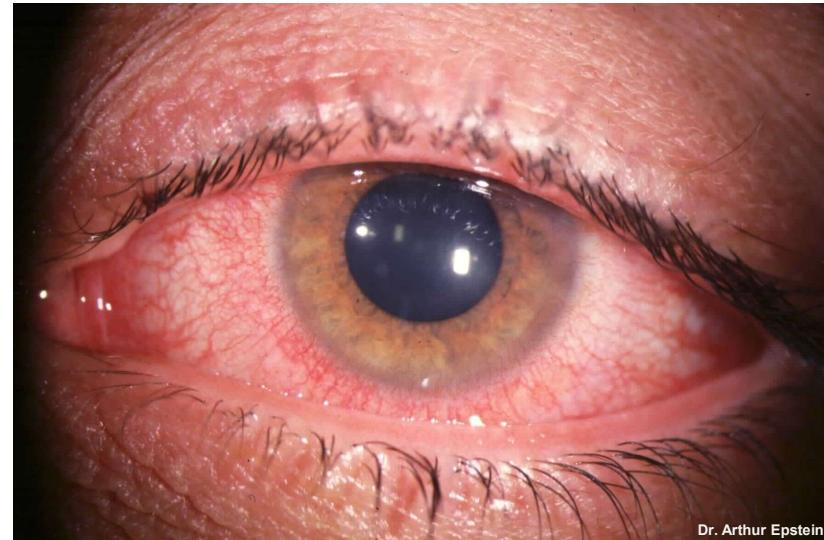
- ▶ **Vasoconstrictive agents**
  - ▶ Lumify (0.025% brimonidine tartrate ophthalmic solution)
    - ▶ highly selective  $\alpha_2$ -adrenergic agonist
- ▶ **Punctal Plugs**
  - ▶ Controversial
  - ▶ “Cesspool” effect
- ▶ **Amniotic Membranes**
  - ▶ Excellent for cases involving cornea/ulcers
- ▶ **Tear film stabilizers**
  - ▶ Perfluorohexyloctane (Miebo)



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# Contact Lens Wear in Ocular Rosacea

- ▶ Avoid CL wear during flares
- ▶ Ideally avoid CL wear until inflammation is controlled
  - ▶ CL wear may be intrinsically inflammatory
- ▶ Daily disposable CLs recommended
- ▶ Discontinue CL wear indefinitely if use worsens condition
  - ▶ Increased irritation, neovascularization



# Patient Education

- ▶ Emphasize condition is not curable, but can be managed
  - ▶ Set expectations
- ▶ Explain what is occurring
  - ▶ Increase understanding
- ▶ Explain each element of treatment plan
  - ▶ Improves compliance

# Summary - Address all components of OR

- ▶ Identify triggers
  - ▶ Environmental, Emotional, Physiologic, Dietary, Pharmaceutical, Cosmetics
- ▶ Provide comfort
  - ▶ Artificial Tears (preservative free lipid-based)
  - ▶ Compresses (warm vs cold)
- ▶ Manage inflammation
  - ▶ Oral Antibiotics (Doxycycline, Azithromycin)
  - ▶ Steroids (short-term)
  - ▶ Immunomodulators (long-term)
    - ▶ Xiidra, Cequa, Vevye, Restasis, Tacrolimus
  - ▶ Omega-3 supplementation
- ▶ Treat comorbidities: MGD, Dry Eye, Blepharitis, Demodex
  - ▶ Lid Hygiene (Tea Tree Oil, Hypochlorous Acid)
  - ▶ Antiparasitics
    - ▶ Xdemovy
  - ▶ Lid Therapies (Thermal pulsation, Microblepharoexfoliation)
  - ▶ Intense Pulsed Light (IPL)
  - ▶ Radiofrequency (RF)
  - ▶ Tear film stabilizers
    - ▶ Miebo
- ▶ Address cosmetic appearance
  - ▶ Vasoconstrictive agents (Lumify)
  - ▶ Cutaneous treatments (Metronidazole, Azelaic Acid)

# Summary



# References

1. Starr PA, Macdonald A. Oculocutaneous aspects of rosacea. *Proc R Soc Med.* 1969;62(1):9-11.
2. Oge' LK, Muncie HL, Phillips-Savoy AR. Rosacea: diagnosis and treatment. *Am Fam Physician.* 2015;92(3):187-196.
3. Elewski BE, Draeflos Z, Dréno B, Jansen T, Layton A, Picardo M. Rosacea - global diversity and optimized outcome: proposed international consensus from the Rosacea International Expert Group. *J Eur Acad Dermatol Venereol.* 2011;25(2):188-200.
4. Drake L, ed. *Rosacea Now Estimated to Affect at Least 16 Million Americans. Rosacea Review.* Rosacea.org website. <https://www.rosacea.org/rosacea-review/2010/winter/rosacea-now-estimated-to-affect-at-least-16-million-americans>. 2010. Accessed June 27, 2021.
5. Spoedlin J, Voegele JJ, Jick SS, Meier CR. A study on the epidemiology of rosacea in the U.K. *Br J Dermatol.* 2012;167(3):598-605.
6. Hong E, Fischer G. Childhood ocular rosacea: considerations for diagnosis and treatment. *Australas J Dermatol.* 2009;50(4):272-27.
7. Baldwin HE. Diagnosis and treatment of rosacea: state of the art. *J Drugs Dermatol.* 2012;11(6):725-730.
8. Browning DJ, Rosenwasser G, Lugo M. Ocular rosacea in blacks. *Am J Ophthalmol.* 1986;101(4):441-444.
9. Alexis AF, Callender VD, Baldwin HE, Desai SR, Rendon MI, Taylor SC. Global epidemiology and clinical spectrum of rosacea, highlighting skin of color: Review and clinical practice experience. *J Am Acad Dermatol.* 2019;80(6):1722-1729.e7.
10. Abram K, Silm H, Oona M. Prevalence of rosacea in an Estonian working population using a standard classification. *Acta Derm Venereol.* 2010;90(3):269-273.
11. Wladis EL, Adam AP. Treatment of ocular rosacea. *Surv Ophthalmol.* 2018;63(3):340-346.
12. Bakar O, Demircay Z, Toker E, Cakir S. Ocular signs, symptoms and tear function tests of papulopustular rosacea patients receiving azithromycin. *J Eur Acad Dermatol Venereol.* 2009;23(5):544-549.
13. Ghannem VC, Mehra N, Wong S, Mannis MJ. The prevalence of ocular signs in acne rosacea: comparing patients from ophthalmology and dermatology clinics. *Cornea.* 2003;22(3):230-233.
14. Wise G. Ocular rosacea. *Am J Ophthalmol.* 1943;26:591-609.
15. Vieira ACC, Höfling-Lima AL, Mannis MJ. Ocular rosacea—a review. *Arq Bras Oftalmol.* 2012;75(5):363-369.
16. Yamasaki K, Kanada K, Macleod DT, et al. TLR2 expression is increased in rosacea and stimulates enhanced serine protease production by keratinocytes. *J Invest Dermatol.* 2011;131(3):688-697.
17. Yamasaki K, Gallo RL. The molecular pathology of rosacea. *J Dermatol Sci.* 2009;55(2):77-81.
18. Del Rosso JQ. Advances in understanding and managing rosacea: part 1: connecting the dots between pathophysiological mechanisms and common clinical features of rosacea with emphasis on vascular changes and facial erythema. *J Clin Aesthet Dermatol.* 2012;5(3):16-25.
19. Zanetti M. Cathelicidins, multifunctional peptides of the innate immunity. *J Leukoc Biol.* 2004;75(1):39-48.
20. Awais M, Anwar MI, Iftikhar R, Iqbal Z, Shehzad N, Akbar B. Rosacea - the ophthalmic perspective. *Cutan Ocul Toxicol.* 2015;34(2):161-166.
21. Kari O, Aho JV, Peltonen S, et al. Group IIA phospholipase A(2) concentration of tears in patients with ocular rosacea. *Acta Ophthalmol Scand.* 2005;83(4):483-486.
22. Crawford GH, Peller MT, James WD. Rosacea: I. Etiology, pathogenesis, and subtype classification. *J Am Acad Dermatol.* 2004;51(3):327-341; quiz 342-344.
23. Lacey N, Delaney S, Kavanagh K, Powell FC. Mite-related bacterial antigens stimulate inflammatory cells in rosacea. *Br J Dermatol.* 2007;157(3):474-481.
24. Szlachcic A, Sliwowski Z, Karczewski B, Bielański W, Pytko-Poloczyk J, Konturek SJ. Helicobacter pylori and its eradication in rosacea. *J Physiol Pharmacol.* 1999;50(5):777-786.
25. Diaz C, O'Callaghan CJ, Khan A, Ilchyshyn A. Rosacea: a cutaneous marker of Helicobacter pylori infection? Results of a pilot study. *Acta Derm Venereol.* 2003;83(4):282-286.
26. Lazaridou E, Giannopoulou C, Fotiadou C, Vakiris E, Trigoni A, Ioannides D. The potential role of microorganisms in the development of rosacea. *J Dtsch Dermatol Ges.* 2019;9(1):21-25.
27. O'Reilly N, Menezes N, Kavanagh K. Positive correlation between serum immunoreactivity to Demodex-associated *Bacillus* proteins and erythematotelangiectatic rosacea. *Br J Dermatol.* 2012;167(5):1032-1036.
28. Whitfield M, Gunasingam N, Lewy LJ, Shirato K, Preda V. *Staphylococcus epidermidis*: a possible role in the pustules of rosacea. *J Am Acad Dermatol.* 2011;64(1):49-52.
29. Steinhoff M, Buddenkotte J, Aubert J, et al. Clinical, cellular, and molecular aspects in the pathophysiology of rosacea. *J Investig Dermatol Symp Proc.* 2011;15(1):2-11.
30. Steinhoff M, Schauben J, Leyden JJ. New insights into rosacea pathophysiology: a review of recent findings. *J Am Acad Dermatol.* 2013;69(6 Suppl 1):S15-26.
31. Liu J, Sheha H, Tseng SCG. Pathogenic role of Demodex mites in blepharitis. *Curr Opin Allergy Clin Immunol.* 2010;10(5):505-510.
32. Li J, O'Reilly N, Sheeha H, et al. Correlation between ocular Demodex infestation and serum immunoreactivity to *Bacillus* proteins in patients with Facial rosacea. *Ophthalmology.* 2010;117(5):870-877.e1.
33. Lazaridou E, Fotiadou C, Ziakas NG, Giannopoulou C, Apalla Z, Ioannides D. Clinical and laboratory study of ocular rosacea in northern Greece. *J Eur Acad Dermatol Venereol.* 2011;25(12):1428-1431.
34. Meyer-Hoffert U, Schröder J-M. Epidermal proteases in the pathogenesis of rosacea. *J Investig Dermatol Symp Proc.* 2011;15(1):16-23.
35. Oltz M, Check J. Rosacea and its ocular manifestations. *Optometry.* 2011;82(2):92-103.
36. Wilkin J, Dahl M, Detmar M, et al. Standard classification of rosacea: report of the national rosacea society expert committee on the classification and staging of rosacea. *J Am Acad Dermatol.* 2002;46(4):584-587.
37. Quarterman MJ, Johnson DW, Abele DC, Lesher JL, Hull DS, Davis LS. Ocular rosacea. Signs, symptoms, and tear studies before and after treatment with doxycycline. *Arch Dermatol.* 1997;133(1):49-54.
38. Odorn R, Dahl M, Dover J, et al. Standard management options for rosacea, part 2: options according to subtype. *Cutis.* 2009;84(2):97-104.
39. Keshtkar-Jafari A, Akhyani M, Ehsani AH, et al. Correlation of the severity of cutaneous rosacea with ocular rosacea. *Indian J Dermatol Venereol Leprol.* 2009;75(4):405-406.
40. Pisella PJ, Brignole F, Debbasch C, et al. Flow cytometric analysis of conjunctival epithelium in ocular rosacea and keratoconjunctivitis sicca. *Ophthalmology.* 2000;107(10):1841-1849.
41. Gudmundsen KJ, O'Donnell BF, Powell FC. Schirmer testing for dry eyes in patients with rosacea. *J Am Acad Dermatol.* 1992;26(2 Pt 1):211-214.
42. Doxanas MT, Green WR. Sebaceous gland carcinoma. Review of 40 cases. *Arch Ophthalmol.* 1984;102(2):245-249.
43. Cohen AF, Tiemstra JD. Diagnosis and treatment of rosacea. *J Am Board Fam Pract.* 2002;15(3):214-217.
44. Ravage ZB, Beck AP, Macsai MS, Ching SST. Ocular rosacea can mimic trachoma: a case of cicatrizing conjunctivitis. *Cornea.* 2004;23(6):630-631.
45. Gracner B, Pahor D, Gracner T. [Repair of an extensive corneoscleral perforation in a case of ocular rosacea with a keratoplasty]. *Klin Monbl Augenheilkd.* 2006;223(10):841-843.
46. Al Arfaj K, Al Zamli W. Spontaneous corneal perforation in ocular rosacea. *Middle East Afr J Ophthalmol.* 2010;17(2):186-188.
47. Akpe EK, Merchant A, Pinar V, Foster CS. Ocular rosacea: patient characteristics and follow-up. *Ophthalmology.* 1997;104(11):1863-1867.
48. Jenkins MS, Brown SI, Lempert SL, Weinberg RJ. Ocular rosacea. *Am J Ophthalmol.* 1979;88(3 Pt 2):618-622.
49. Ramamurthy S, Rahman MQ, Dutton GN, Ramaesh K. Pathogenesis, clinical features and management of recurrent corneal erosions. *Eye (Lond).* 2006;20(6):635-644.
50. Alvarenga LS, Mannis MJ. Ocular rosacea. *Ocul Surf.* 2005;3(1):41-58.

# References

51. Tan J, Almeida LMC, Bewley A, et al. Updating the diagnosis, classification and assessment of rosacea: recommendations from the global ROSacea COnsensus (Rosco) panel. *Br J Dermatol.* 2017;176(2):431-438.
52. Levin J, Miller R. A guide to the ingredients and potential benefits of over-the-counter cleansers and moisturizers for rosacea patients. *J Clin Aesthet Dermatol.* 2011;4(8):31-49.
53. Thiboutot DM, Fleischer AB, Del Rosso JQ, Graupe K. Azelaic acid 15% gel once daily versus twice daily in papulopustular rosacea. *J Drugs Dermatol.* 2008;7(6):541-546.
54. Barnhorst DA, Foster JA, Chern KC, Meisler DM. The efficacy of topical metronidazole in the treatment of ocular rosacea. *Ophthalmology.* 1996;103(11):1880-1883.
55. Lim A, Wenk MR, Tong L. Lipid-based therapy for ocular surface inflammation and disease. *Trends Mol Med.* 2015;21(12):736-748.
56. Cheng AM, Sheha H, Tseng SC. Recent advances on ocular Demodex infestation. *Curr Opin Ophthalmol.* 2015;26(4):295-300.
57. Tarsus Pharmaceuticals, Inc. Announces Positive Results of Saturn-1 Pivotal Trial Evaluating TP-03 for the Treatment of Demodex Blepharitis. Tarsus Pharmaceuticals website. <https://ir.tarsusrx.com/news-releases/news-release-details/tarsus-pharmaceuticals-inc-announces-positive-results-saturn-1>. June 21, 2021. Accessed July 1, 2021.
58. Epitropoulos AT. Lid hygiene product helps reduce blepharitis, MGD symptoms. *Ophthalmology Times.* November 15, 2015. Accessed June 27, 2021.
59. Schubert JR, Murakami DK, Blackie CA, Korb DR. Using warm compresses to treat meibomian gland disease. *Optometry Times.* <https://www.optometrytimes.com/view/using-warm-compresses-treat-meibomian-gland-disease>. Published August 11, 2015. Accessed June 29, 2021.
60. Collins M, Heron H, Larsen R, Lindner R. Blinking patterns in soft contact lens wearers can be altered with training. *Am J Optom Physiol Opt.* 1987;64(2):100-3.
61. Greiner JV. Long-term (12-month) improvement in meibomian gland function and reduced dry eye symptoms with a single thermal pulsation treatment. *Clin Exp Ophthalmol.* 2013;41(6):524-530.
62. Blackie CA, Coleman CA, Holland EJ. The sustained effect (12 months) of a single-dose vectored thermal pulsation procedure for meibomian gland dysfunction and evaporative dry eye. *Clin Ophthalmol.* 2016;10:1385-1396.
63. Borchman D. The optimum temperature for the heat therapy for meibomian gland dysfunction. *Ocul Surf.* 2019;17(2):360-364.
64. Tavassoli S, Wong N, Chan E. Ocular manifestations of rosacea: A clinical review. *Clin Exp Ophthalmol.* 2021;49(2):104-117.
65. Connor CG, Narayanan S, Miller W. Reduction in inflammatory marker matrix metalloproteinase-9 following lid debridement with BlephEx. *Invest Ophthalmol Vis Sci.* 2017;58(8):498-498.
66. Pfeffer I, Borelli C, Zierhut M, Schaller M. Treatment of ocular rosacea with 40 mg doxycycline in a slow release form. *J Dtsch Dermatol Ges.* 2011;9(11):904-907.
67. Frucht-Pery J, Sagiv E, Hemo I, Ever-Hadani P. Efficacy of doxycycline and tetracycline in ocular rosacea. *Am J Ophthalmol.* 1993;116(1):88-92.
68. Dougherty IM, McCulley JP, Silvany RF, Meyer DR. The role of tetracycline in chronic blepharitis. Inhibition of lipase production in staphylococci. *Invest Ophthalmol Vis Sci.* 1991;32(11):2970-2975.
69. Sobrin L, Liu Z, Monroy DC, et al. Regulation of MMP-9 activity in human tear fluid and corneal epithelial culture supernatant. *Invest Ophthalmol Vis Sci.* 2000;41(7):1703-1709.
70. Määttä M, Kari O, Tervahartiala T, et al. Tear fluid levels of MMP-8 are elevated in ocular rosacea—treatment effect of oral doxycycline. *Graefes Arch Clin Exp Ophthalmol.* 2006;244(8):957-962.
71. Stone DU, Chodosh J. Oral tetracyclines for ocular rosacea: an evidence-based review of the literature. *Cornea.* 2004;23(1):106-109.
72. Afonso AA, Sobrin L, Monroy DC, Selzer M, Lokeshwar B, Pflugfelder SC. Tear fluid gelatinase B activity correlates with IL-1 $\alpha$  concentration and fluorescein clearance in ocular rosacea. *Invest Ophthalmol Vis Sci.* 1999;40(11):2506-2512.
73. Yamasaki K, Di Nardo A, Bardan A, et al. Increased serine protease activity and cathepsin D promotes skin inflammation in rosacea. *Nat Med.* 2007;13(8):975-980.
74. Valentini S, Morales A, Sánchez JL, Rivera A. Safety and efficacy of doxycycline in the treatment of rosacea. *Clin Cosmet Invest Dermatol.* 2009;2:129-140.
75. Chamaillard M, Mortemousque B, Boralevi F, et al. Cutaneous and ocular signs of childhood rosacea. *Arch Dermatol.* 2008;144(2):167-171.
76. Kim J-H, Oh YS, Choi EH. Oral azithromycin for treatment of intractable rosacea. *J Korean Med Sci.* 2011;26(5):694-696.
77. Modi S, Hartung M, Rosen T. Azithromycin as an alternative rosacea therapy when tetracyclines prove problematic. *J Drugs Dermatol.* 2008;7(9):898-899.
78. Safran AB, Hallioua B, Roth A, Saurat J-H. Ocular side effects of oral treatment with retinoids. *Retinoids: 10 Years On.* 1991;315-326.
79. Mantelli F, Di Zazzo A, Sacchetti M, Dianzani C, Lambiasi A, Bonini S. Topical azithromycin as a novel treatment for ocular rosacea. *Ocul Immunol Inflamm.* 2013;21(5):371-377.
80. Leyden JJ, Thew M, Kligman AM. Steroid rosacea. *Arch Dermatol.* 1974;110(4):619-622.
81. Murphy CJ, Bentley E, Miller PE, et al. The pharmacologic assessment of a novel lymphocyte function-associated antigen-1 antagonist (SAR 1118) for the treatment of keratoconjunctivitis sicca in dogs. *Invest Ophthalmol Vis Sci.* 2011;52(6):3174-3180.
82. Sun Y, Zhang R, Gadek TR, O'Neill CA, Pearlman E. Corneal inflammation is inhibited by the LFA-1 antagonist, lifitegrast (SAR 1118). *J Ocul Pharmacol Ther.* 2013;29(4):395-402.
83. Zhong M, Gadek TR, Bui M, et al. Discovery and development of potent Ifa-1/cam-1 antagonist sar 1118 as an ophthalmic solution for treating dry eye. *ACS Med Chem Lett.* 2012;3(3):203-206.
84. Schechter BA, Katz RS, Friedman LS. Efficacy of topical cyclosporine for the treatment of ocular rosacea. *Adv Ther.* 2009;26(6):651-659.
85. Sakasagawa-Naves FE, Ricci HMM, Moscovici BK, et al. Tacrolimus ointment for refractory posterior blepharitis. *Curr Eye Res.* 2017;42(11):1440-1444.
86. Kapturczak MH, Meier-Kriesche HU, Kaplan B. Pharmacology of calcineurin antagonists. *Transplant Proc.* 2004;36(2 Suppl):255-325.
87. Sheppard JD, Singl R, McClellan AJ, et al. Long-term supplementation with n-6 and n-3 pufas improves moderate-to-severe keratoconjunctivitis sicca: a randomized double-blind clinical trial. *Cornea.* 2013;32(10):1297-1304.
88. Pinna A, Piccinini P, Carta F. Effect of oral linoleic and gamma-linolenic acid on meibomian gland dysfunction. *Cornea.* 2007;26(3):260-264.
89. Gumus K, Cavanagh DH. The role of inflammation and antiinflammation therapies in keratoconjunctivitis sicca. *Clin Ophthalmol.* 2009;3:57-67.
90. Macsai MS. The role of omega-3 dietary supplementation in blepharitis and meibomian gland dysfunction (An aos thesis). *Trans Am Ophthalmol Soc.* 2008;106:336-356.
91. Oleñik A, Jiménez-Alfaro I, Alejandro-Alba N, Mahillo-Fernández I. A randomized, double-masked study to evaluate the effect of omega-3 fatty acids supplementation in meibomian gland dysfunction. *Clin Interv Aging.* 2013;8:1133-1138.
92. Epitropoulos AT, Donnenfeld ED, Shah ZA, et al. Effect of oral re-esterified omega-3 nutritional supplementation on dry eyes. *Cornea.* 2016;35(9):1185-1191.
93. Ellis SR, Nguyen M, Vaughn AR, et al. The skin and gut microbiome and its role in common dermatologic conditions. *Microorganisms.* 2019;7(11):E550.
94. Weiss E, Katta R. Diet and rosacea: the role of dietary change in the management of rosacea. *Dermatol Pract Concept.* 2017;7(4):31-37.
95. Dell SJ. Intense pulsed light for evaporative dry eye disease. *Clin Ophthalmol.* 2017;11:1167-1173.
96. Toyos R, McGill W, Briscoe D. Intense pulsed light treatment for dry eye disease due to meibomian gland dysfunction; a 3-year retrospective study. *Photomed Laser Surg.* 2015;33(1):41-46.
97. Yuan M, Marmalidou A, Brissette A. Ocular Rosacea: Essentials for Providers. *Surface Matters. MillennialEYE website.* <https://millennialeye.com/articles/2020-nov-dec/ocular-rosacea-essentials-for-providers/>. November, 2020. Accessed June 27, 2021.
98. Papageorgiou P, Clayton W, Norwood S, Chopra S, Rustin M. Treatment of rosacea with intense pulsed light: significant improvement and long-lasting results. *Br J Dermatol.* 2008;159(3):628-632.
99. Smith K. The photobiological basis of low level laser radiation therapy. *Laser Ther.* 1991;3:19-24.
100. Young S, Bolton P, Dyson M, Harvey W, Diamantopoulos C. Macrophage responsiveness to light therapy. *Lasers Surg Med.* 1989;9(5):497-505.

# References

101. Yin Y, Liu N, Gong L, Song N. Changes in the meibomian gland after exposure to intense pulsed light in meibomian gland dysfunction (Mgd) patients. *Curr Eye Res.* 2018;43(3):308-313.
102. Stevenson W, Chauhan SK, Dana R. Dry eye disease: an immune-mediated ocular surface disorder. *Arch Ophthalmol.* 2012;130(1):90-100.
103. Byun JY, Choi HY, Myung KB, Choi YW. Expression of il-10, tgf-beta(1) and tnf-alpha in cultured keratinocytes (Hacat cells) after ipl treatment or ala-ipl photodynamic treatment. *Ann Dermatol.* 2009;21(1):12-17.
104. Huang J, Luo X, Lu J, et al. IPL irradiation rejuvenates skin collagen via the bidirectional regulation of MMP-1 and TGF-β1 mediated by MAPKs in fibroblasts. *Lasers Med Sci.* 2011;26(3):381-387.
105. De Paiva CS, Volpe EA, Gandhi NB, et al. Disruption of TGF-β signaling improves ocular surface epithelial disease in experimental autoimmune keratoconjunctivitis sicca. *PLoS One.* 2011;6(12):e29017.
106. Lee SY, Park K-H, Choi J-W, et al. A prospective, randomized, placebo-controlled, double-blinded, and split-face clinical study on LED phototherapy for skin rejuvenation: clinical, profilometric, histologic, ultrastructural, and biochemical evaluations and comparison of three different treatment settings. *J Photochem Photobiol B.* 2007;88(1):51-67.
107. Taylor M, Porter R, Gonzalez M. Intense pulsed light may improve inflammatory acne through TNF-α down-regulation. *J Cosmet Laser Ther.* 2014;16(2):96-103.
108. Bäumler W, Vural E, Landthaler M, Muzzi F, Shafirstein G. The effects of intense pulsed light (ipl) on blood vessels investigated by mathematical modeling. *Lasers Surg Med.* 2007;39(2):132-139.
109. Liu Y, Kami WR, Sullivan DA. Influence of omega 3 and 6 fatty acids on human meibomian gland epithelial cells. *Cornea.* 2016;35(8):1122-1126.
110. Prieto VG, Sadick NS, Lloreta J, Nicholson J, Shea CR. Effects of intense pulsed light on sun-damaged human skin, routine, and ultrastructural analysis. *Lasers Surg Med.* 2002;30(2):82-85.
111. Kirn T. Intense pulsed light eradicates Demodex mites. *Skin Allergy News.* 2002;33(1):37.
112. Lumenis Receives FDA Approval for Its IPL Device to Manage Dry Eye Disease and Launches OptiLight. *Eyewire News website.* <https://eyewire.news/articles/lumenis-receives-fda-approval-for-its-ipl-device-to-manage-dry-eye-disease-and-launches-optilight/>. Published April 29, 2021. Accessed June 29, 2021.
113. Hutton D. FDA approves IPL device to manage dry eye disease. *Ophthalmology Times website.* <https://www.opthalmologytimes.com/view/fda-approves-ipl-device-to-manage-dry-eye-disease>. Published April 29, 2021. Accessed June 29, 2021.
114. Torkildsen GL, Sanfilippo CM, DeCory HH, Gomes PJ. Evaluation of efficacy and safety of brimonidine tartrate ophthalmic solution, 0. 025% for treatment of ocular redness. *Curr Eye Res.* 2018;43(1):43-51.
115. Vaidyanathan S, Williamson P, Clearie K, Khan F, Lipworth B. Fluticasone reverses oxymetazoline-induced tachyphylaxis of response and rebound congestion. *Am J Respir Crit Care Med.* 2010;182(1):19-24.
116. Soparkar CN, Wilhelms KR, Koch DD, Wallace GW, Jones DB. Acute and chronic conjunctivitis due to over-the-counter ophthalmic decongestants. *Arch Ophthalmol.* 1997;115(1):34-38.
117. McLaurin E, Cavet ME, Gomes PJ, Ciolino JH. Brimonidine ophthalmic solution 0. 025% for reduction of ocular redness: a randomized clinical trial. *Optom Vis Sci.* 2018;95(3):264-271.
118. LUMIFY Redness Reliever Eye Drops. *Bausch + Lomb website.* <https://www.bausch.com/our-products/allergy-redness-relief/lumify-eye-drops>. Accessed July 1, 2021.
119. Barton K, Monroe DC, Nava A, Pflugfelder SC. Inflammatory cytokines in the tears of patients with ocular rosacea. *Ophthalmology.* 1997;104(11):1868-1874.
120. Liu J, Sheha H, Fu Y, Liang L, Tseng SC. Update on amniotic membrane transplantation. *Expert Rev Ophthalmol.* 2010;5(5):645-661.
121. Efron, N. Is contact lens-induced corneal oedema inflammatory? *Aust. J. Optom.* 1985;68(5): 167-172.
122. Sand M, Sand D, Thrnadorf C, Paech P, Bechara FG. Rosacea. In: Head & Face Medicine Band 6, 2010, S. 7, ISSN 1746-160X. doi:10.1186/1746-160X-6-7. PMID 20525327. (Review). Wikimedia Commons. Open Access, CC BY 2.0, <https://commons.wikimedia.org/w/index.php?curid=15606564>. Published Jun 4, 2010. Accessed December 18, 2021.
123. Henning A. Acne Roscea, man. In: Skin Diseases. Acne Rosacea, Robert Willis, 1841. Wikimedia Commons. CC BY 4.0, [https://wellcomeimages.org/indexplus/ofbf\\_images/a2/a3/72fb3acc020ec438bccb2819ae7c.jpg](https://wellcomeimages.org/indexplus/ofbf_images/a2/a3/72fb3acc020ec438bccb2819ae7c.jpg) Gallery: <https://wellcomeimages.org/indexplus/image/L0074338.html> Wellcome Collection gallery (2018-03-23): <https://wellcomecollection.org/works/v77mrtkr> CC-BY-4.0, CC BY 4.0, <https://commons.wikimedia.org/w/index.php?curid=36296645>. Published October 22, 2014. Accessed December 18, 2021.
124. Kennedy C. Steroid Rosacea. Wikimedia Commons. CC BY-SA 4.0, <https://commons.wikimedia.org/w/index.php?curid=55294750>. Published January 23, 2017. Accessed December 18, 2021.
125. RicHard-59. Acne rosacea on face. Wikimedia Commons. CC BY-SA 3.0, <https://commons.wikimedia.org/w/index.php?curid=40915844>. Published August 26, 2014. Accessed December 18, 2021.
126. Sand M, Sand D, Thrnadorf C, Paech P, Bechara FG. Rhinophyma. In: Head & Face Medicine Band 6, 2010, S. 7, ISSN 1746-160X. doi:10.1186/1746-160X-6-7. PMID 20525327. (Review). Wikimedia Commons. Open Access, CC BY 2.0, <https://commons.wikimedia.org/w/index.php?curid=15606257>. Published Jun 4, 2010. Accessed December 18, 2021.
127. Srecan. Rosacea in un soggetto maschio adulto. Wikimedia Commons. CC BY-SA 4.0, <https://commons.wikimedia.org/w/index.php?curid=49910819>. Published July 5, 2016. Accessed December 18, 2021.
128. Szkutnik W, Wine. CC BY-SA 2.0, <https://www.flickr.com/photos/wojtekszkutnik/7395684972/in/photolist-cgwpTs-33Nvp-5v8ix-5FPipH-8ou5f1-8z3CSW-e4ogE1-dVLwd-k7ETP-5T5RTK-qpjPld-7CefQi-qprVdx-pjTLd5-pjTLtW-8UFVHW-dFAKR3-95NzqG-ecmM7o-8crgYv-qprVaB-qpkzoA-6bcWWb-9i6Ygi-xUF8i1-5AW8Tr-3QFzJ2-qpkzdq-bc1Zy6-bqgBEi-9AwbHz-7ifqtU-qDBFSN-5FTf27-7ZCeGG-a8oD7T-9DJg8G-8GtS6z-7uD6G-7P7tCk-9i7fFj-q3GoHJ-xjtH4B-8uBgbX-ahue55-5CcTu-nBMpd-9g2jhL>. Published June 18, 2012. Accessed December 18, 2021.
129. Doctor 4U. Doxycycline Antimalarial Tablets Image 4. CC BY 20, [www.doctor-4-u.co.uk](http://www.doctor-4-u.co.uk). Published September 3, 2019. Accessed December 18, 2021.
130. MorgueFile. Various Pills. CC BY-SA 3.0, <https://commons.wikimedia.org/w/index.php?curid=1570359>. Published January 16, 2007. Accessed December 18, 2021.
131. Sem J. Fish oil capsules. CC BY 2.0, [www.semtrio.com](http://www.semtrio.com). Published September 12, 2018. Accessed December 18, 2021.

**Thank you!**  
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