




My Approach to Treating Moderate and Severe Dry Eye

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Disclosure: Eric Donnenfeld, M.D.

◆ I am a consultant for:

▪ Acufocus	▪ Lensgen	▪ PRN
▪ Allergan	▪ Mati Pharmaceuticals	▪ ReTear
▪ Alcon	▪ MBackline	▪ RPS
▪ AMO	▪ Merck	▪ Shire
▪ Avedro	▪ Mynosis	▪ Strathspey Crown
▪ Bausch & Lomb	▪ Novabay	▪ Surface
▪ BVI	▪ Novaliq	▪ SUN
▪ Blephex	▪ Ocuhub	▪ Tearlab
▪ CRST	▪ Ocular Therapeutics	▪ TearScience
▪ Dompe	▪ Oculis	▪ TLC Laser Centers
▪ Elenza	▪ Odyssey	▪ TrueVision
▪ EyePoint Pharma	▪ Omega Ophthalmics	▪ Versant Ventures
▪ Foresight	▪ Omeros	▪ Visionary Ventures
▪ Glaukos	▪ Orasis	▪ Zeiss
▪ Icon Biosciences	▪ Oyster Point	
▪ Kala	▪ Pogotec	
▪ Katena		
▪ Lacripen		

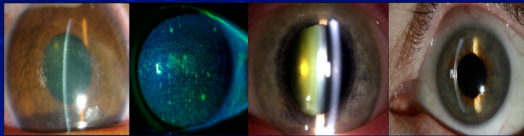
The Tear Film is the Most Important Refracting Surface of the Eye



Ocular Surface Disease

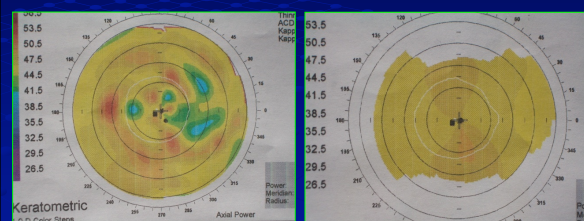
- ◆ Quality of vision starts with a healthy tear film.
- ◆ All of the recent advances in technology are lost with even minimal disruption of the ocular surface.

Ocular Surface Disease is the Rate Limiting Step for Surgical Outcomes



- ◆ Ocular surface affects:
 - IOL calculations
 - Topographic and wavefront ablations
 - Postoperative healing
 - Quality of vision and patient satisfaction

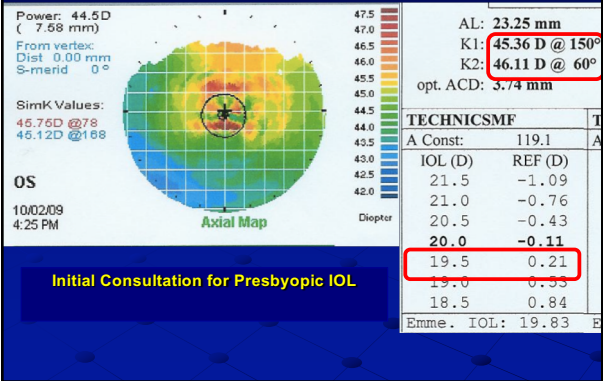
Tear Film Placido Disc Image Before and After Dry Eye Treatment



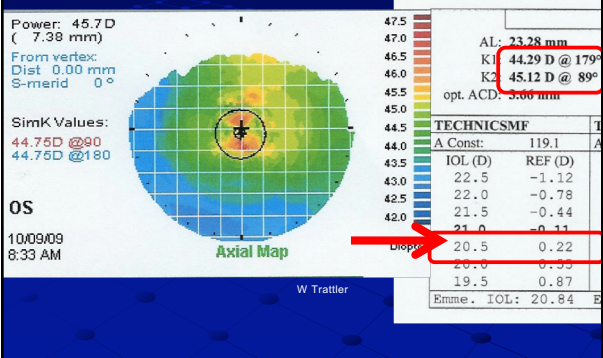
Before

After

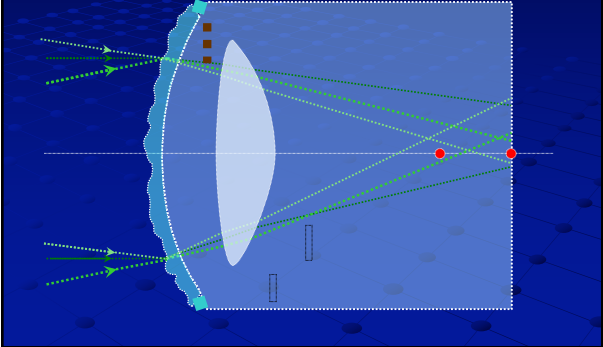
Preop Evaluation



Dry Eye Disease Identified: One week after Dry Eye Treatment



Disruption of the Ocular Surface Induces Distortion that is Magnified by a Multifocal IOL



Disruption of the Tear Film Magnifies the Glare and Halo Inherent in all Multifocal IOLs

IOLs

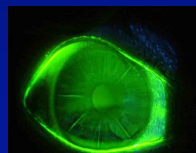
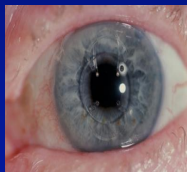
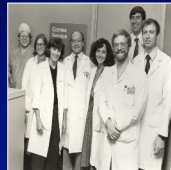
- Glare and halo in a patient with a multifocal IOL without and with ocular surface disease:



1904



1985





What is Dry Eye Disease?

- Dry Eye is extremely common and is often under-diagnosed¹
- Dry Eye can negatively impact vision quality and can cause blurred vision, fluctuating vision, reduced contrast sensitivity and increased glare²⁻⁴
- Quality of life and daily activities can be greatly impacted by Dry Eye symptoms⁵
- Significant psychological impact – patients have reported a willingness to trade years at the end of life to be free of Dry Eye disease⁵

[1] Perry HD, Donnerfeld ED. Dry eye diagnosis and management in 2004. *Curr Opin Ophthalmol*. 2004;15:299-304. [2] Pflugfelder SC, Blaumauer RW, Stern NE, eds. *Dry Eye and Ocular Surface Disorders*. New York, NY: Marcel Dekker, Inc; 2004. [3] Rolando M, Lester M, Hertz A, Calabro G. Low spatial-contrast sensitivity in dry eyes. *Cornea*. 1996;17:376-379. [4] Morigiwa B, Dana R, Sullivan DA, Schaumborg DA. Impact of dry eye symptoms on vision-related quality of life. *Am J Ophthalmol*. 2007;143:409-415. [5] Schiffman RM, Walt JG, Jacobson F, et al. Utility assessment among patients with dry eye disease. *Ophthalmology* 2003; 110:1412-1419.

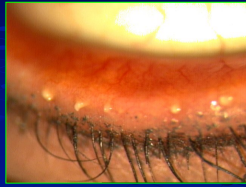
The Healthy Tear Film: A Delicate Balance

- Lipid, aqueous & mucin components
- Outer lipid layer prevents aqueous evaporation
 - Secreted by meibomian glands
- Aqueous component – a complex mixture of proteins, mucins, electrolytes
- Mucins provide viscosity and stability during the blink cycle

Lipid Secretion: Meibomian Glands



Transillumination of meibomian glands

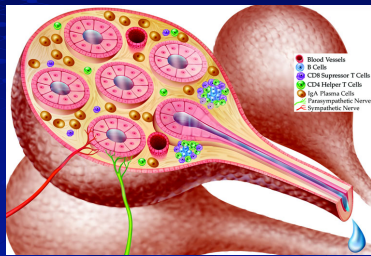


Meibomian gland dysfunction

- ◆ The lipid layer prevents evaporation to of tear flow
 - Also helps lubricate and improves quality of vision

Aqueous Secretion: Lacrimal Glands

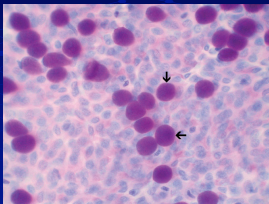
Lacrimal glands secrete
 Aqueous component
 Most tear proteins
 Similar architecture for main and accessory glands
 Androgens important for glandular homeostasis
(Sullivan et al. 1998)



- ◆ Secretions from acinar cells converge into excretory ducts, then to ocular surface

Image from Dry Eye and Ocular Surface Disorders, 2004

Mucin Secretion: Goblet Cells



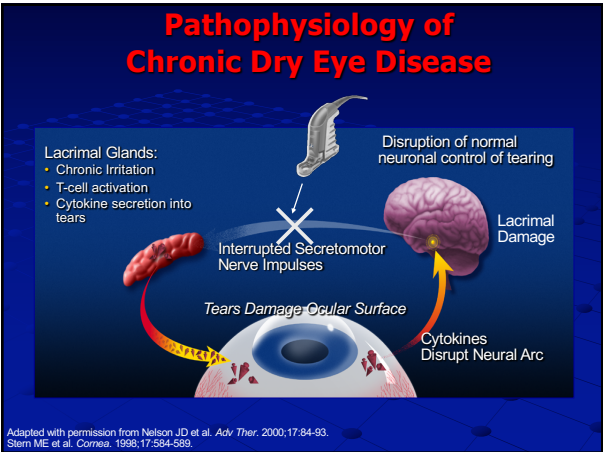
Superficial layer of bulbar conjunctiva. Goblet cells violet, epithelial cells blue.



Goblet cells secreting mucins (arrows) surrounded by epithelial cells.

- ◆ 5-20% of conjunctival epithelial cells are mucin-producing goblet cells
- ◆ Soluble mucins - essential for viscosity of the normal tear film
 - Helms resist thin spots and tear break-up

Images from Dry Eye and Ocular Surface Disorders, 2004



Tears in Chronic Dry Eye (CDE)

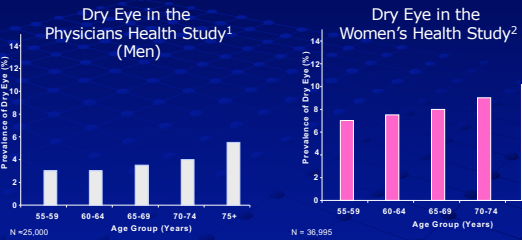
- Lesser concentrations of many proteins in CDE
 - e.g. antimicrobial proteins
- Growth factor concentrations decreased
- Soluble mucin 5AC greatly decreased
 - Due to loss of goblet cells
 - Impacts viscosity of tear film
- Cytokine balance shifted, promotes inflammation
- Activated proteases
 - Degrade extracellular matrix & tight junctions

Prevalence of Dry Eye

- Salisbury Study = 14.4%
- Melbourne Study = 5.5%
- Beaver Dam Study = 14.4%
- WHS Study = 6.7%

➤ Although percent of individuals who experience signs and symptoms of dry eye at one time or another due to environmental factors = 100%

Age, Gender and Dry Eye



Dry eye prevalence is higher in women and increases with age in both groups

1. Schaumburg DA, Dana R, Bunag JE, et al. Prevalence of dry eye disease among US men: estimates from the Physicians' Health Studies. *Arch Ophthalmol.* 2003;121(6):763-8.
 2. Schaumburg DA, Sullivan DA, Bunag JE, et al. Prevalence of dry eye syndrome among US women. *Am J Ophthalmol.* 2003;136(2):318-26.

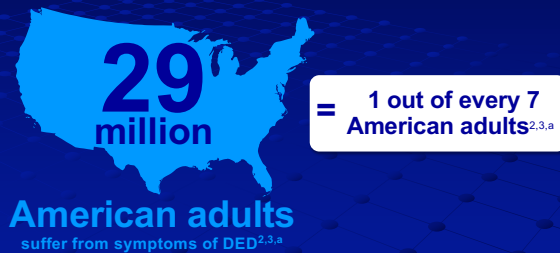
The Prevalence of Dry Eye

- ▶ Affects about **15% of the population in the US (about 5 million elderly)**^{1, 2, 3}
- ▶ Potentially affects **tens of millions more** Americans.³

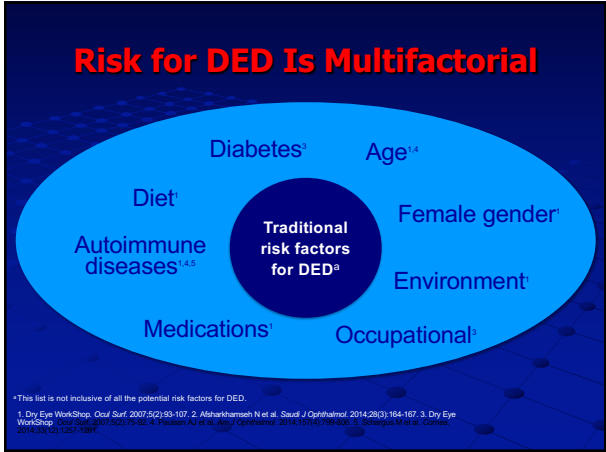
With an aging demographic, environmental changes, and increasing visual tasking demands, dry eye remains one of the greatest unmet needs for your patients!

1. Moss SE, et al. Prevalence and risk factors for dry eye syndrome. *Arch Ophthalmol.* 2000;118:1294-8.
 2. Schorn DO, Muknoz B, Tilsch JJ, et al. Prevalence of dry eye among the elderly. *Am J Ophthalmol.* 1997;124(6):723-9.
 3. Hartz JH, Sandman G, Baum J, et al. The epidemiology of dry eye disease: report of the Epidemiology Subcommittee of the International Dry Eye Workshop (2007). *Opt Vis Surf.* 2007; April;5(2):38-107.

DED Is One of the Most Common Eye Diseases in the United States¹



^aAged 25 to 84 years.
 1. Schaumburg DA et al. *Am J Ophthalmol.* 2003;136(2):318-320. 2. Paulsen AJ et al. *Am J Ophthalmol.* 2014;157(4):799-806.
 3. US Census Bureau. Annual estimates of the resident population for selected age groups by sex for the United States, states, counties, and Puerto Rico Commonwealth and municipalities: April 1, 2010 to July 1, 2012. <http://factfinder.census.gov>. Published June 2013. Accessed September 16, 2015.



DED Deserves Increased Attention

Symptoms of DED are among the most common complaints¹

- 30% of patients who seek treatment from an ophthalmologist have symptoms consistent with DED²

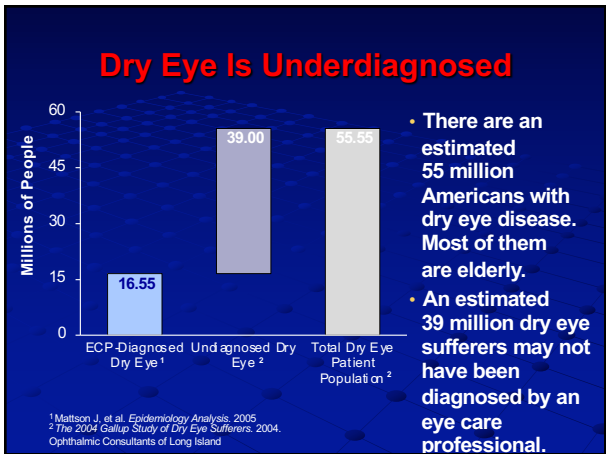
DED may impair patients' abilities to perform daily activities

- DED has been shown to:
 - Reduce work productivity^{3,4}
 - Impair the ability to drive, watch television, use technology, and function socially
 - Decrease reading speed^{6,7}

DED is chronic and may be progressive⁸

- DED may progress to corneal damage; some loss of vision is possible⁹

1. Stern ME et al. *Int Rev Immunol.* 2013;33(1):19-41. 2. Lemp MA. *Am J Ophthalmol.* 2008;146(3):355-356. 3. Farris VD et al. *Curr Med Res Pract.* 2013;3(1):1-11. 4. Farris VD et al. *Case Rep Ophthalmol.* 2013;3(1):1-11. 5. Farris VD et al. *J Ophthalmol.* 2007;143(3):409-415. 6. Riddler WH III et al. *Optom Vis Sci.* 2013;90(1):37-44. 7. Quasler GW III et al. *Cornea.* 2015;34(8):917-921. 8. Ng V et al. *Cornea.* 2013;32(9):1204-1210. 9. National Eye Institute. Facts about dry eye. <https://nei.nih.gov/health/dryeye/dryeye>. Accessed June 25, 2015.



Symptoms of DED Can Be Disruptive and Variable

1. Dry Eye Workshop. Ocul Surf. 2007;5(2):75-92. 2. Brown AJ et al. Ocul Surf. 2014;12(2 suppl):S1-S31. 3. Walter PM et al. Cornea. 2010;29(9):907-912. 4. Dry Eye Workshop. Ocul Surf. 2007;5(2):93-107.

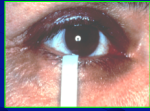
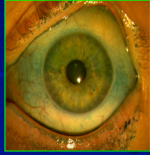
Varied ocular symptoms of dry eye disease such as tearing, dry eye, burning, irritation, and even itching make the diagnosis at times difficult.

Diagnosis: First Ask the Patient

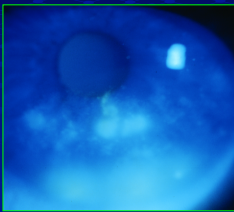
OSDI
SPEED
YOUR OWN

Conventional Diagnosis of Dry Eyes

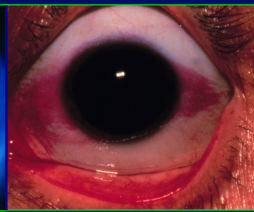
- ◆ Evaluate dry eye status conventional studies
 - Lissamine green/rose bengal conjunctival stains
 - Fluorescein corneal staining
 - Schirmer test
 - Tear meniscus and debris
 - Tear break up time
 - Corneal sensation



Diagnostic Dyes



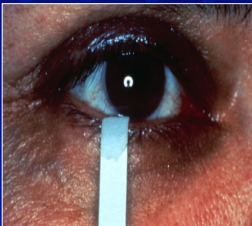
Fluorescein
Cornea



Rose Bengal/Lissamine
Conjunctiva

Schirmer Test

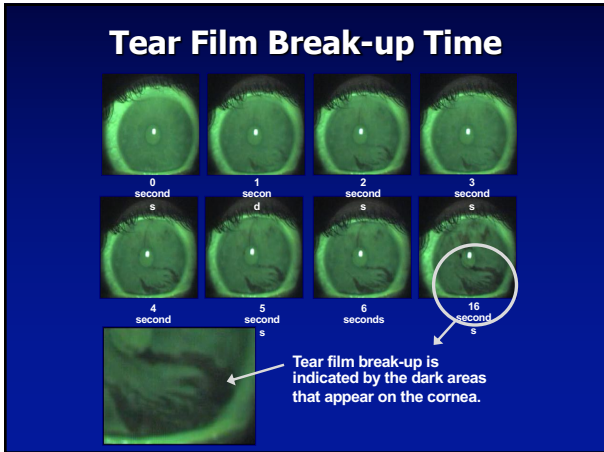
No consensus as to which method is best

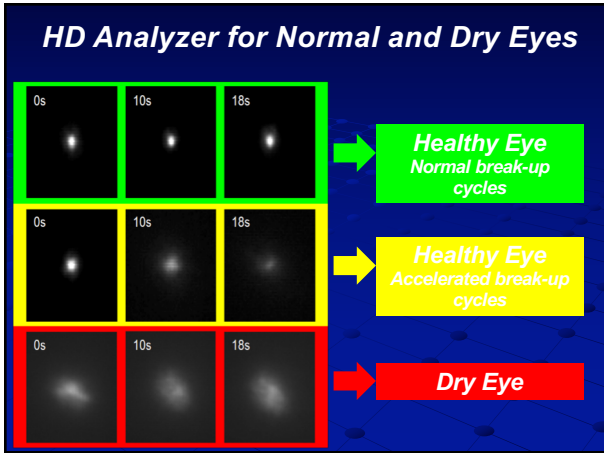


Without anesthesia
measures reflex tear
secretion

With anesthesia measures
basal tear secretion

Important for diagnosing
severity of dry eye disease





Current Challenges

- ◆ Poor correlation between subjective symptoms and objective signs!
 - Schirmer testing sensitivity 10%-30%²⁻⁴
- ◆ Difficult to diagnose in the absence of signs
- ◆ Difficult to monitor efficacy of interventions

Nichols KK et al, Cornea 2004; 2. Lamberts DW et al, Arch Ophthalmol 1979; 3. Shapiro A et al, AAO 1979; 4. Mackie IA, et al, IBO 1981.

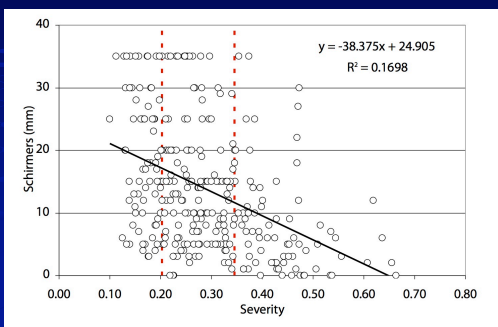
Diagnosis and Monitoring Dry Eye

- ◆ Today there is a need for more reliable, more objective and less invasive tools for ...
 - More accurately diagnosing DED and conjunctivitis
 - Better assessing treatment efficacy
 - Tighter correlation with patient symptoms

Advantages of Point-of-Care Testing

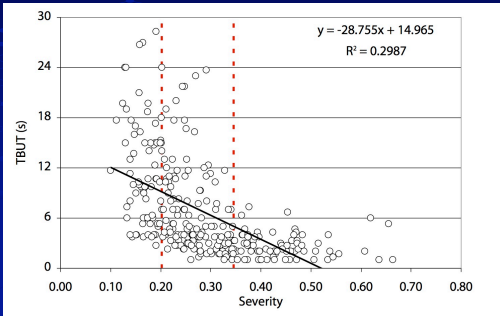
- ◆ Clinical Advantages
 - Evidence-based treatment, using point-of-care diagnostic testing, is the future of medicine
 - ↑ Objective measure and quality diagnosis =
↑ Physician confidence in diagnosis and patient care
 - Trend is to use evidence-based diagnosis that is creating a better correlation between diagnostic testing and signs and symptoms

Schirmer Strip Severity Analysis



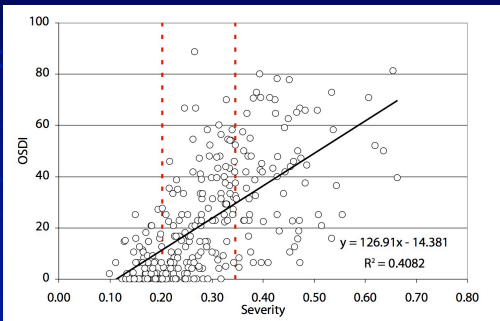
Disease severity is calculated as an unbiased, normalized composite of seven clinical signs & symptoms
IOVS Dec 2010 Vol 51, No 12

Tear Film Breakup Time (TBUT) Severity Analysis



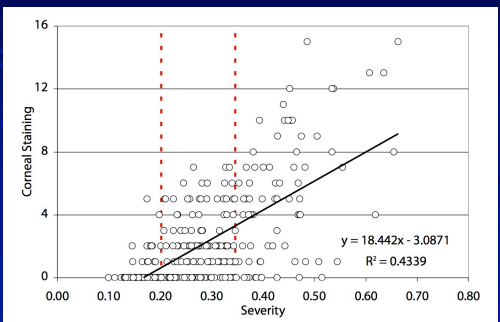
Disease severity is calculated as an unbiased, normalized composite of seven clinical signs & symptoms
IOVS Dec 2010 Vol 51, No 12

Symptoms (OSDI) Severity Analysis



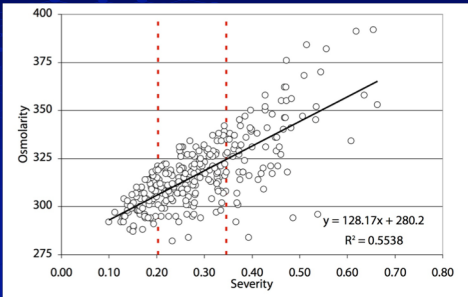
Disease severity is calculated as an unbiased, normalized composite of seven clinical signs & symptoms
IOVS Dec 2010 Vol 51, No 12

Corneal Staining Severity Analysis



Disease severity is calculated as an unbiased, normalized composite of seven clinical signs & symptoms
IOVS Dec 2010 Vol 51, No 12

Osmolarity Severity Analysis



Disease severity is calculated as an unbiased, normalized composite of seven clinical signs & symptoms
IOVS Dec 2010 Vol 51, No 12

Two Numbers Crucial to Understand Osmolarity

The MAXIMUM of the two eyes: 314.
Tears higher than 300 mOsm/L demonstrate loss of homeostasis and likely become pathogenic > 308.

The DIFFERENCE b/w two eyes: 24.
This tells you how stable the tear film is. Normal tears are stable and near 300 mOsm/L bilaterally. A difference of > 8 mOsm/L is a hallmark of tear instability.



Tear Hyperosmolarity is a Major Defect in DED

- ◆ Hyperosmolarity can lead to damage of the ocular surface and is the primary cause of discomfort associated with dry eyes^{1,2}
- ◆ Osmolarity was found to be increased with decreasing tear flow rates²
- ◆ Osmolarity is the best marker of disease severity across normal, mild/moderate & severe categories⁴

¹Tomlinson A, et al. Ocular Surface. 2005;3(2):81-95. ²Stahl U, et al. Clin Exp Optom. 2012;95(1):3-11. ³Huet, E et al. AJ of Pathology. Vol. 179 No.3. 2011. ⁴Sullivan BD, et al. Invest Ophthalmol Vis Sci. 2010;51:6125.

New Osmolarity Platforms

◆ Single-use disposable test cards

Osmolarity

Tear film quality and stability
Early diagnosis and grading severity
Therapy tracking



IL-1 Ra

Produced in proportion to active inflammation
Associated with aqueous deficient dry eye disease
Increased with disease severity

MMP-9

Epithelial stress-activated proteinase
Well-known biomarker
Indicator of severe, late stage inflammation



MMP-9 Testing

- ◆ Tells you when to initiate anti-inflammatory therapy
- ◆ Helps to identify masqueraders as well
- ◆ Positive (red line) = >40 ng/mL
- ◆ 85% sensitivity and 94% specificity



Point-of-Care Testing

- ◆ Practice flow advantages
 - Empower staff to perform testing based on physician based indications
 - When the physician sees the patients, diagnosis has already been made and physician confirms
 - Permits physician to immediately institute proper management and allowing the patient to leave the office in a timely manner
 - Less time patients spend in the office / less diagnostic time and more quality treatment time

Dry Eye Treatment Plan

- ◆ Topical
- ◆ Systemic
- ◆ Nutritional
- ◆ Medication Elimination
- ◆ Environmental Control
- ◆ Specialty Referral

Consensus Treatment Algorithm for Chronic Dry Eye

- ◆ Delphi panel of acknowledged experts
- ◆ Goals:
 - Define chronic dry eye by using evolved understanding of the disease.
 - Devise a consensus treatment algorithm for dysfunctional tear syndrome.

Classification of Dry Eye (DTS) Severity

	1	2	3	4
Discomfort	Mild and/or episodic; occurs under env stress	Moderate episodic or chronic, stress or no stress	Severe frequent or constant without stress	Severe and/or disabling and constant
Visual Symptoms	None or episodic mild fatigue	Annoying and/or activity limiting episodic	Annoying, chronic and/or constant limiting activity	Constant and/or possibly disabling
Clinical Signs	None to mild	None to mild; may or may not have staining, reduced tear meniscus; TBUT ≤ 10	Moderate to marked conj. staining and marked central corneal staining; filamentary keratitis, TBUT ≤ 5; Schirmer score ≤ 5.	Conj. injection and marked staining; severe punctate erosions; scarring, almost immediate TBUT; Schirmer ≤ 2;

Based on the 2007 International Dry Eye Workshop (DEWS) Report and Behrens, et al. Cornea 2006, International Task Force (ITF) guidelines

Treatment Recommendations by Severity Level

1 Mild, episodic, No to mild clinical signs	2 Moderate or chronic Visual symptoms Some clinical signs	3 Severe or chronic with marked staining, reduced TBUT, other signs	4 Severe, disabling with marked clinical signs and symptoms
<ul style="list-style-type: none"> • Education • Environmental/ dietary modification • Eliminate drying systemic meds • Artificial tears (preserved) • Gels/ointments • Eye lid therapy 	<p>If Level 1 treatments are inadequate, add:</p> <ul style="list-style-type: none"> • Anti-inflammatories (cyclosporine, steroids), omega-3 FA • Tetracyclines • Punctal plugs • Switch to unpreserved tears 	<p>If Level 2 treatments are inadequate, add:</p> <ul style="list-style-type: none"> • Serum • Contact lenses • Permanent punctal occlusion • Secretagogues • Moisture chamber goggles 	<p>If Level 3 treatments are inadequate, add:</p> <ul style="list-style-type: none"> • Systemic anti-inflammatory agents • Surgery (lid surgery, amniotic membrane transplant, etc.)

Based on the 2007 International Dry Eye Workshop (DEWS) Report and Behrens, et al. Cornea 2009, International Task Force (ITF) guidelines

ASCRS CC Committee: Preop Refractive Surgery Algorithm

- ◆ TFOS DEWS II provided the common algorithm for all patients ...
- ◆ ASCRS CCC mission is to re-tool the algorithm specifically for OSD as it pertains to the preoperative refractive surgical patient

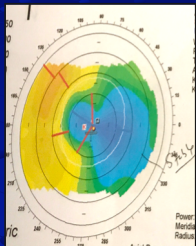


How it Differs from DEWS II: Screening

- ◆ DEWS II recommends triage Qs / questionnaires to establish symptoms
- ◆ Because DED/OSD is so common in cataract population and often asymptomatic, symptoms are LESS important
 - ◆ Most questionnaires not ideal for cataract patients
- ◆ ASCRS CCC recommends screening all preop refractive patients with POC testing (osmolarity and MMP-9)
 - ◆ If not covered, bundle into OOP refractive fees (e.g., premium package)
- ◆ Still recommend identification of subtype to tailor treatment
 - ◆ EDE >> ADDE

How it Differs from DEWS II: Screening

- ◆ Visual quality testing has a more important role preop
 - ◆ Ocular scatter index (OSI)
 - ◆ Aberrometry
 - ◆ Non-invasive TBUT
 - ◆ Topography
 - ◆ Acuity pre- and post-lubricant drops



How it Differs from DEWS II: Pace

- ◆ DEWS II:
 - ◆ Start treatment at Step 1
 - ◆ Increase if no improvement
- ◆ ASCRS CCC:
 - ◆ Preop patients don't have the luxury of time
 - ◆ Start at Step 2
 - ◆ Use a multi-pronged approach

Modify Environment and Habits: Attempt to Eliminate Exacerbating Factors

- ◆ Avoid desiccating environments
 - Use humidifier
- ◆ Minimize use of systemic anticholinergic medications
- ◆ Improve habits during computer use, reading
 - Take periodic rests with closed eyes

Drying Systemic Medications

- ◆ Antihistamines (substitute Singulaire)
- ◆ Antidepressants
- ◆ HMG Co-A Reductase Inhibitors (Statins)
- ◆ Diuretics
- ◆ Beta Blockers
- ◆ Analgesics
- ◆ Hypnotics

Drying Topical Medications

- ◆ Antihistamines (substitute Steroid or Tear)
- ◆ Beta Blockers and glaucoma medications
- ◆ Preservatives
- ◆ Vasoconstrictors

Current Treatments to Improve the Ocular Surface-Aqueous Deficiency

- ◆ Artificial tears: Preserved/Non-preserved
- ◆ Nutritional supplements
- ◆ Topical immunomodulators: cyclosporine/lifitegrast
- ◆ Topical steroids
- ◆ Punctal occlusion
- ◆ Lacriserts
- ◆ Serum tears

...AND BLOCKS THE INTERACTION OF LFA-1 WITH ICAM-1*

*As demonstrated by in vitro studies. The exact mechanism of action of lifitegrast in dry eye disease is not known.

Labels: LIFITEGRAST, T CELL, LFA-1, ICAM-1, OCULAR

Lid Scrubs With Hypochlorous Acid

Uses

- Blepharitis
- Dry Eye (MGD)
- Preoperative hygiene
- Before/After contact lens wear
- Demodex

Available Products

- Avenova - Pure Hypochlorous acid
- Hypochlor

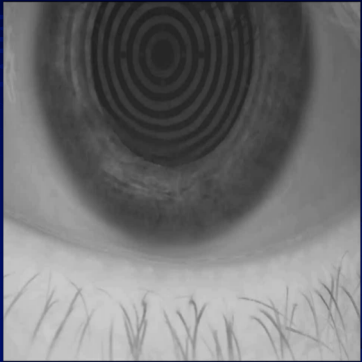
Advantages

- Effectively reduces bacterial counts and inflammation
- Lack of antimicrobial resistance

ITN : Bringing Neurostimulation to Eye Care

Labels: Disposable Tip with Hydrogel, Handheld Unit

Immediate Effect

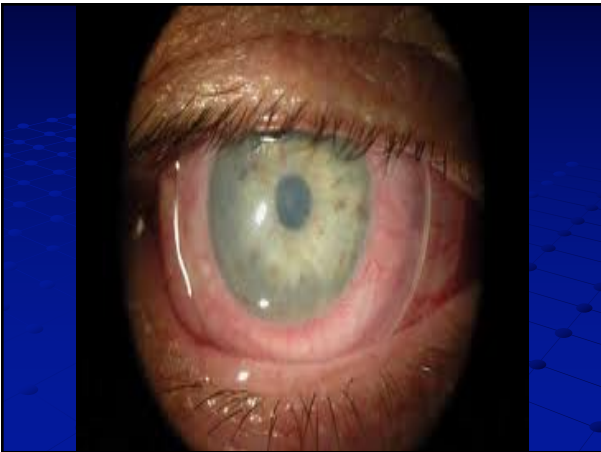


Amniotic Membrane Therapeutic Device

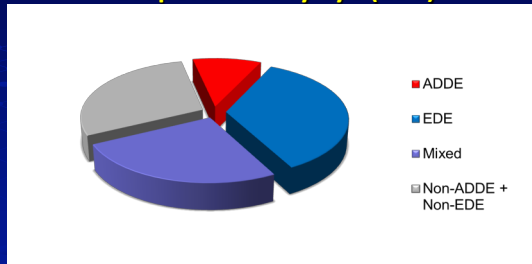
Specifics

- Reduces inflammation
- Promotes healing
- Improves comfort





Majority of DED Patients Have Evidence of Evaporative Dry Eye (EDE)



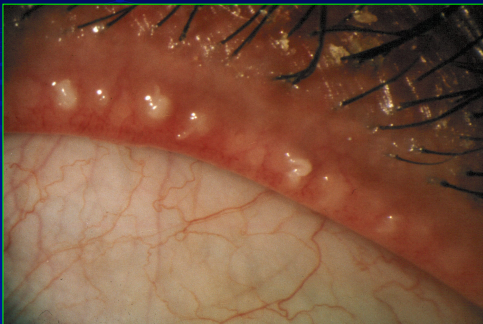
- ◆ 86% of patients with a classified DED subtype demonstrated signs of MGD
- ◆ Pure ADDE subtype represented the smallest percentage of patients (~10%)

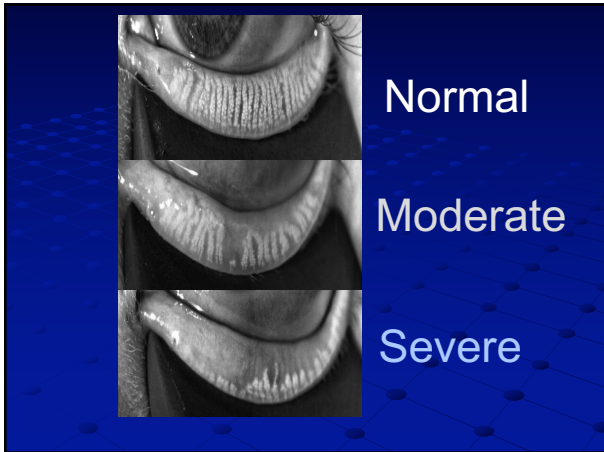
Lemp MA, et al. Cornea. 2012;31:472-478.

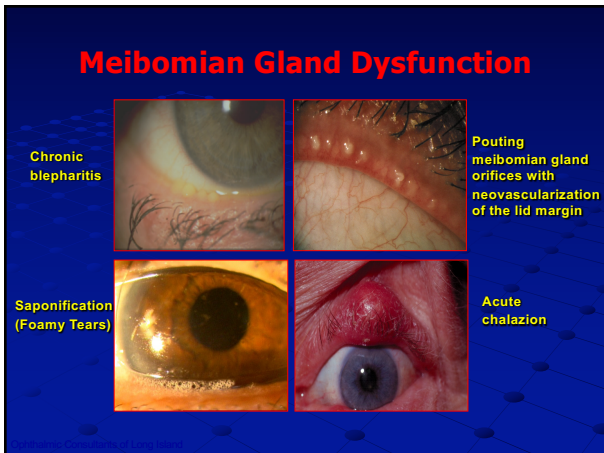
When You Think of Dry Eye



Don't Forget Meibomian Gland Disease







Prevalence of Meibomian Gland Dysfunction, A Leading Cause of Dry Eye Disease
 MGD is present in ~37% of entire ophthalmic practice patients and ~47% of optometric practice patients¹

"Meibomian gland dysfunction (MGD) may well be the leading cause of dry eye disease throughout the world."²
—The International Workshop on Meibomian Gland Dysfunction: Executive Summary

1. Lemp MA, Nichols KK. Blepharitis in the United States 2009: a survey-based perspective on prevalence and treatment. *Ocul Surf*. 2009;7(2 Suppl):S1-S14.
 2. Nichols KK, et al. The international workshop on meibomian gland dysfunction: executive summary. *Invest Ophthalmol Vis Sci*. 2011;52(4):1922-1929.

Signs and Symptoms

- ◆ Burning, foreign body sensation with dry eye symptoms (contact lens intolerance)
- ◆ Filmy vision with foam in tear film (soaps and fatty acids)
- ◆ Dilated meibomian gland orifices with plugged "toothpaste" like material
- ◆ Chalazia
- ◆ Thickened lid margin

MGD Classification

Normal

Normal – glands open, secreting clear oil

Non Obvious MGD

No inflammation or signs

Classical & Obvious MGD

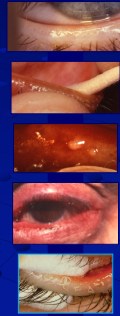
Hypersecretion (seborrheic)

Inflammatory (pouting & plugging)

Infective (glands and/or lids)

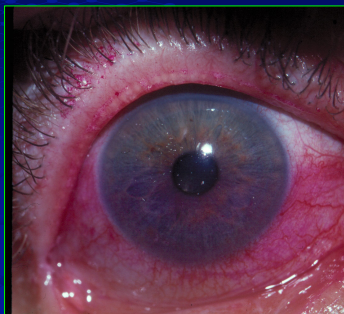
Diffuse inflammation of the lids/ blepharitis

Inspiralized material, blocked glands

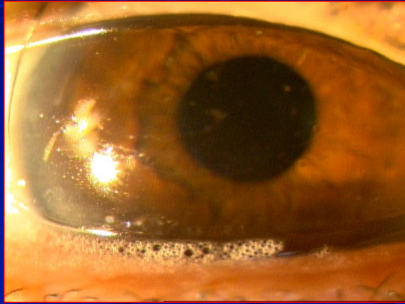


Korb and Henriquez, 1990; Mathers et al., 1991.

Inadequate Tear Film Lipids Cause Evaporative Dry Eye



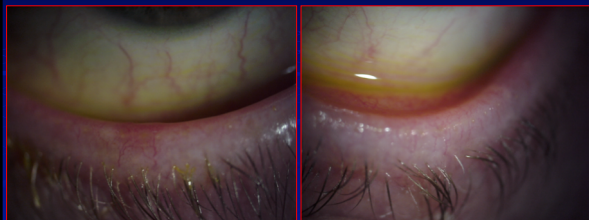
Bacterial Lipases Breakdown Lipids to Soaps
Burning=Blepharitis



Pre-Operative Care to Optimize Outcomes:
Treat Lid Disease

- ◆ Lid hyperthermia
 - Hot compresses and/or lid scrubs
- ◆ Nutritional supplements
- ◆ Topical azithromycin bid 2 days then qd 1 month
- ◆ Topical Cyclosporine A (CsA) and short term corticosteroids
- ◆ Severe cases
 - Oral doxycycline

Behrens A et al. *Cornea*. 2006;25(8):900-907.
Donnenfeld ED. *Ophthalmol Manag*. 2004. <http://www.opthmanagement.com/article.aspx?article=86170>.
Accessed Jan 11, 2008.
Ophthalmic Consultants of Long Island



Before Azithromycin

After Azithromycin

Ophthalmic Consultants of Long Island

Thermal Pulsation Systems



Thermal pulsation safely and effectively treats Meibomian gland obstruction in both upper and lower eyelids simultaneously

- In-office procedure
- 12 minutes per eye

82

Provides Heat >40°C and Pressure to Liquefy and Evacuate Obstructed Glands

Lid warmer

Composed of a heater, eye insulation, and vaulted shape

Heat applied to the palpebral surfaces of the upper and lower eyelids directly over the Meibomian glands

Activator

Composed of an inflatable air bladder and a rigid activator

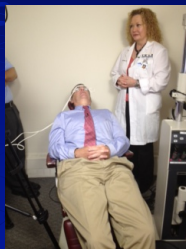
Graded pulsatile pressure delivered to the outer eyelid



83

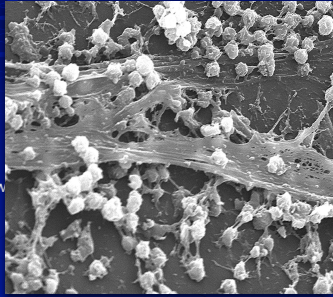
MGD - New Treatment Options

- ◆ Thermal Pulsation Systems
- ◆ Heat applied to the palpebral surfaces of the upper and lower eyelids directly over the Meibomian glands
- ◆ Graded pulsatile pressure delivered to the outer eyelid



The role of biofilm in wound healing is well accepted *over 65% of microbial infections caused by biofilms*

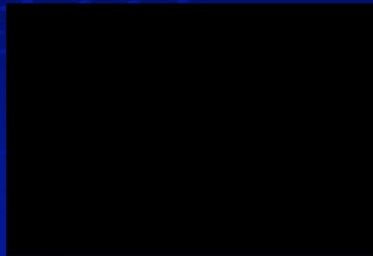
- atherosclerosis
- chronic sinusitis
- chronic wounds
- cystic fibrosis
- endocarditis
- inner ear infections
- kidney stones
- leptospirosis
- osteomyelitis
- osteonecrosis
- osteomyelitis of the jaw
- periodontal disease
- prosthetic joints
- heart valves
- urinary tract infections
- veterinary diseases



MICROBLEPHAROEXFOLIATION (MBE)

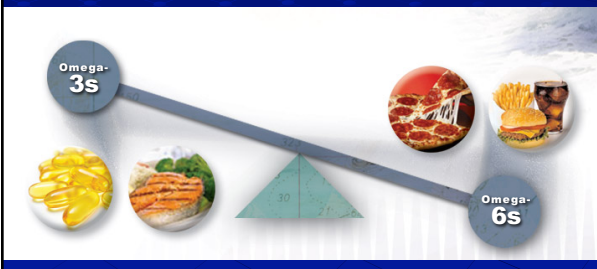
Debulking biofilms from surface of meibomian glands and eyelids

- Removal of bacterial biofilm obstructions are key to successful MGD management
- Exfoliation of the eyelid margin unroofs the meibomian glands (removes the source of the virulence factors and subsequent inflammation)
- Manual or thermal pulsation expression promotes evacuation and cleansing of the secretory passages



Epidemic of Dry Eye Disease

- ◆ A healthy diet approaches a 1:1 ratio of Omega-3s to Omega-6s
- ◆ The average North American Diet is 1:25, as high as 1:50
- ◆ This occurred when healthy unsaturated fats were replaced with trans fatty acids and diets full of processed foods (high in Omega-6)



The DEWS and International Workshop on Meibomian Gland Dysfunction Both Recommend Omega-3 Supplementation

TFOS MGD Report

Meibomian gland dysfunction
What is it, why does it occur and how may it be treated?

Report Available online

available downloads:
report overview
link to full report (IOVS)
press release

The Ocular Surface

2007 Report of the International Dry Eye Workshop (DEWS)

Sponsored by the Tear Film & Ocular Surface Society

INTRODUCTION TO THE DEWS REPORT BY THE INTERNATIONAL DRY EYE WORKSHOP (DEWS)

THE DEFINITION AND CLASSIFICATION OF DRY EYE DISEASE

THE EPIDEMIOLOGY OF DRY EYE DISEASE

METHODOLOGIES TO DIAGNOSE AND MONITOR DRY EYE DISEASE

DESIGN AND CONDUCT OF CLINICAL TRIALS

MANAGEMENT AND THERAPY OF DRY EYE DISEASE

RESEARCH IN DRY EYE

www.theocularsurface.com



Bioavailability of Omega-3 Fatty Acid Formulations

Bioavailability of n-3 Fatty Acid Formulations

Essential Fatty Acids

Bioavailability of marine n-3 fatty acid formulations*

J. Dyerberg¹

J. DYERBERG¹

1. Introduction

Omega-3 polyunsaturated fatty acids (n-3 PUFAs) are essential for human health. They are found in marine fish oils and certain plant oils. n-3 PUFAs have been shown to have beneficial effects on cardiovascular health, including reducing triglyceride levels, increasing HDL cholesterol, and reducing the risk of heart disease. n-3 PUFAs also have anti-inflammatory properties and may be beneficial for other conditions such as arthritis, asthma, and depression.

2. Methods

The study was a randomized, prospective, crossover trial. Participants were 12 healthy men aged 35-65 years. They were randomized to receive either a marine n-3 fatty acid formulation (fish oil) or a vegetable n-3 fatty acid formulation (flaxseed oil) for 12 weeks. Blood samples were collected at baseline and at 12 weeks to measure n-3 PUFA levels in the blood and in the urine. The primary endpoint was the change in n-3 PUFA levels in the blood and in the urine.

3. Results

The study found that the marine n-3 fatty acid formulation significantly increased n-3 PUFA levels in the blood and in the urine compared to the vegetable n-3 fatty acid formulation. This indicates that the marine n-3 fatty acid formulation is more bioavailable than the vegetable n-3 fatty acid formulation.

4. Conclusion

The study demonstrates that the marine n-3 fatty acid formulation is more bioavailable than the vegetable n-3 fatty acid formulation. This suggests that marine n-3 fatty acid formulations may be a more effective way to increase n-3 PUFA levels in the body.

CLINICAL SCIENCE

Effect of Oral Re-esterified Omega-3 Nutritional Supplementation on Dry Eyes

Alio F, Espinosa MD, Eric D, Donnell MD, Zhai A, Shah MPH, Eshwar J, Hillard MD, Michael Gross MD, Wilson J, Fakhree MD, Chaitin-Hastings MD, Stephen B, Linn MD, Melissa Torres MD, Frank A, Bucci, Jr, MD,FF and Henry D, Perry, MD

Purpose: To assess the effect of oral re-esterified omega-3 fatty acid on tear osmolality, lipid metabolism (DMP-11), and tear film stability (TFOS) using Meibomian Gland Dysfunction (MGD) test and omega-3 index to evaluate with the oral re-esterified omega-3.

Methods: This was a multicenter, prospective, interventional, placebo-controlled, double-masked study. Subjects were randomized to receive a capsule containing a total of 1000 mg of re-esterified omega-3 fatty acids daily for 12 weeks. Subjects were measured at baseline, week 4, and week 12 for tear osmolality (TFOS), MGD, and omega-3 index. Tear film stability was measured at baseline and at 12 weeks.

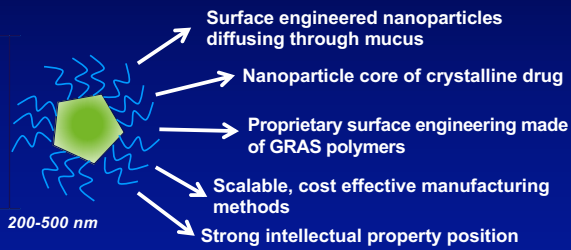
Results: One hundred five subjects completed the study. They were randomized to receive either a re-esterified omega-3 fatty acid or a placebo. The omega-3 index increased significantly in the omega-3 group from baseline to week 12 (1.1 ± 0.1 to 1.3 ± 0.1, P < 0.001). There was a significant increase in omega-3 index from baseline to week 12 (1.1 ± 0.1 to 1.3 ± 0.1, P < 0.001) in the omega-3 group.

Conclusions: Oral re-esterified omega-3 fatty acid supplementation significantly increased the omega-3 index, which is associated with improved tear film stability, reduced MGD, and improved TFOS. These findings suggest that oral re-esterified omega-3 fatty acid supplementation may be a beneficial treatment for dry eye disease.

Pipeline: Topicals

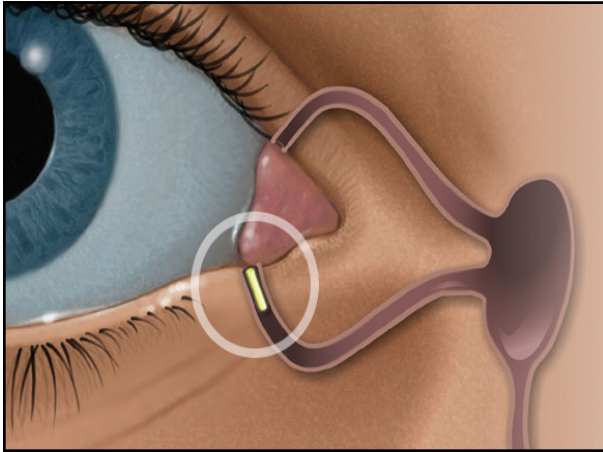
- ◆ Mucus Penetrating Particle Loteprednol
- ◆ Fonadelpar: Peroxisome receptor delta agonist
- ◆ Narrow Spectrum Kinase Inhibitor
- ◆ Neuropeptide Mucus Secretagogue
- ◆ Semifluorinated Alkane
- ◆ Thymosin Beta 4- Tβ4
- ◆ NFκB Cell Penetrating Peptide
- ◆ Epithelial Sodium Channel Inhibitor
- ◆ Narrow Spectrum Kinase Inhibitor

Mucus Penetrating Particles (MPPs)



Pipeline: Devices

- ◆ BAK Filtration Bottle
- ◆ Dexamethasone Punctal Plug



The Hydrogel Filter & How It Works



Conclusion: Management of Dry Eye

- Dry Eye Disease has been underdiagnosed and undertreated by all Eye Care Professionals
- Significantly affects cataract and refractive surgery results
- Dry Eye Disease results in significant morbidity for our patients
 - Decreased vision
 - Reduced quality of life
- Recently approved treatments as well as treatments now in clinical trials will greatly enhance our ability to manage Dry Eye Disease in the future
