

Improving Ocular Surface Disease Diagnosis

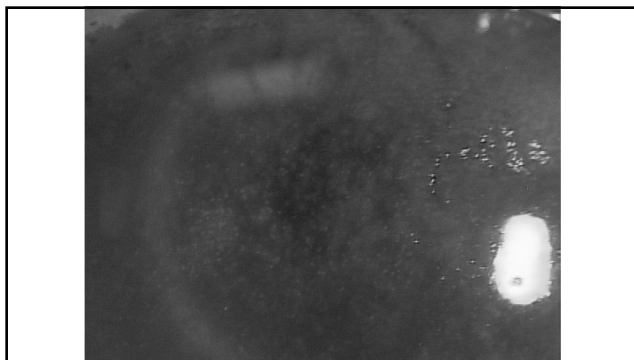
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Sparks, NV

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Douglas K Devries, OD
Disclosures
All Conflicts Have Been Mitigated

Allergan Advisor	Ocuphire Advisor
Alcon Advisor and Speaker	Oyster Point Advisor and Speaker
Asecula Advisor	Orasis Advisor
Aveilino Advisor	Ophthalmic Resource Partner
Azura Advisor	Quidel Advisor
Bio Tissue Advisor and Speaker	RVL Advisor and Speaker
Bruder Advisor	Science Based Health Advisor and Speaker
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Johnson and Johnson Advisor Speaker	Tarsus Advisor
Kala Advisor and Speaker	Thea Advisor
Lumenis Advisor and Speaker	TruKera Advisor
Novartis Advisor and Speaker	Versea Advisor
OcuSoft Advisor	Visus Advisor/Quidel Advisor

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Dry Eye Disease¹

An independent committee of Eye Care Professionals developed a contemporary definition of Dry Eye Disease

Tear Film and Ocular Surface Society (TFOS) July 2017
TFOS DEWS II

"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."

1. The Re-Definition and Classification of Dry Eye Disease. Report of the Definition and Classification Subcommittee of the International Dry Eye WorkShop (IDEWS) 2017. Ocul Surf. 2017; 15(2): 25-42.

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Prevalence of Dry Eye Disease

- Up to 33 million Americans are estimated to be suffering from Dry Eye symptoms^{1,3}
- Results from the 2015 Gallup Poll (n = 1020) project the number of adults who report experiencing Dry Eye on a regular basis²:

Projected Growth in Frequent Dry Eye Sufferers (in millions)

2015 → 9.7% GROWTH → 33.7 (2025)

Results from the 2015 Gallup poll project the number of adults who report experiencing Dry Eye on a regular basis. Projections of frequent Dry Eye sufferers are calculated by applying incidence by age to US Census population estimates in each age group in 2015 and 2025. Projections assume no change in incidence levels over the next decade.⁷

1. Fakhri, et al. Am J Ophthalmol. 2014; 2. The Gallup Organization, Inc. The 2015 Gallup Study of Dry Eye Sufferers. 2015. Online poll conducted May 26-June 23, 2015. 3. Centers for Disease Control and Prevention 2016.

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Etiology

- ADDE
- EDE
- Mixed
- Non-ADDE + Non-EDE

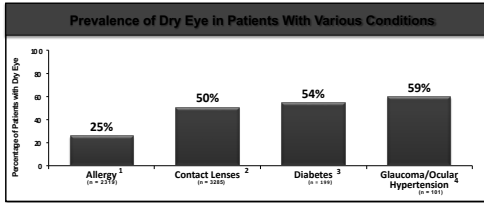
• 86% of patients with a classified subtype have evaporative dry eye/MGD as a component

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

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Dry Eye and Other Conditions

Dry Eye Disease is common among patients with other conditions



1. Wee et al. Optom Vis Sci. 2002; 79: 1000-1004. 2. Dogru et al. Optom Vis Sci. 1997; 74: 1000-1004. 3. Mawardi et al. BMC Ophthalmol. 2005; 5: 10. 4. Leung et al. J Glaucoma. 2018; 27: 1000-1004.

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Bottom Line

- Punctal Occlusion OU \$231 - 264
- Ant Seg Photos \$17.35 to 57.78
- Amniotic Membrane \$1489.02 to 2532.51
- IPL \$1000 – 1200 /4 session
- Thermal Expression OU \$500 to 750
- Manual Expression \$125 – 200
- Microblepharoexfoliation – \$150-200

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Bottom Line

- Demodex Tx \$125.00 to 200.00
- Supplements \$395.40 (\$161.00 Net)
- Scrubs, Tears, Masks, Moisture Wear (\$196.00 Net)

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Bottom Line Examples

- 4 Visits, Tears, Scrubs, Diagnostics, Net \$577
- 4 Visits, Plugs, Tears, Scrubs, Diagnostics, Net \$768.00
- 4 Visits, Plugs, Tears, Scrubs, Diagnostic, MBE Net \$948
- 6 Visits, Plugs, Tears, Scrubs, Diagnostic, MBE, Thermal Expression Net \$1248
- 6 Visits, Plugs, Tears, Scrubs, Diagnostics, MBE, IPL Thermal Expression, \$2248
- 6 Visits, Plugs, Tears, Scrubs, Diagnostics, MBE, IPL, Thermal expression, Amniotic Tissue \$3040
- 6 Visits, Plugs, Tears, Scrubs, Diagnostics, MBE, IPL, Thermal Expression 2 Amniotic Membranes \$3790

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Top Tips for Dry Eye Practice

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Top tips for dry eye practice

- Start small – you already have the equipment

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Top tips for dry eye practice

- Utilize questionnaires -scoring is helping
 - OSDI App
 - SPEED
 - Frequency of Dryness
 - SANDE DEQ-5
 - Other

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Top tips for dry eye practice

- Do Lunch and Learns

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Top tips for dry eye practice

- Do your own market evaluation

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Top tips for dry eye practice

- Run the numbers on each investment

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Top tips for dry eye practice

- Designate a "Louie"
- Dry Eye Coordinator



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Top tips for dry eye practice

- Commit to level of care within the practice
 - "Plan to Work and Work the Plan"

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Top tips for dry eye practice

- Have a conversation – Find the dialogue that you are comfortable with

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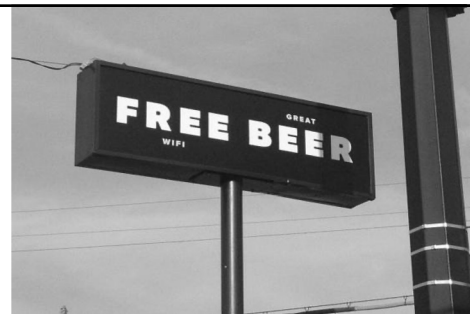
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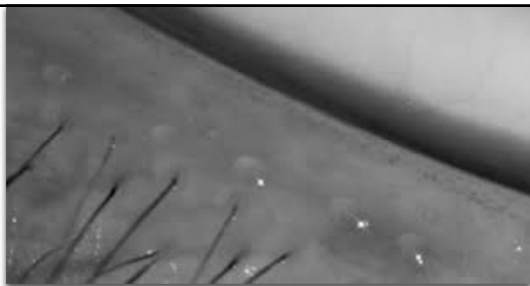
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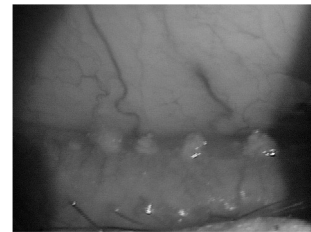
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Healthy Oils

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Standard Patient Evaluation of Eye Dryness (SPEED) Questionnaire¹

- Evaluates the frequency and severity of symptoms
- Developed as an easy to use fast screening tool for dry eye disease
- SPEED questionnaire is one of the tools used to identify candidates for LipiFlow[®]



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DRY EYE QUESTIONNAIRE (DEQ-5)

1. Questions about EYE DISCOMFORT:
 a. During a typical day in the past month, how often did your eyes feel discomfort?
 NEVER RARELY SOMETIMES FREQUENTLY CONSTANTLY
 0 1 2 3 4

2. Questions about EYE IRRITATION:
 a. During a typical day in the past month, how often did your eyes feel dry?
 NEVER RARELY SOMETIMES FREQUENTLY CONSTANTLY
 0 1 2 3 4

3. Questions about WATERY EYES:
 During a typical day in the past month, how often did your eyes look or feel excessively watery?
 NEVER RARELY SOMETIMES FREQUENTLY CONSTANTLY
 0 1 2 3 4

Score: 11 12 13 14 15 16 17 18 19 20 21 22

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CLIA Wavier

- Lab Director within your practice
- State laws vary from state to state
- Bill the tests as a lab
 - Different Deductibles and Co-Pays
- Set your practice apart
- Insurance Panels

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- SPEED Score of 6 or greater
- Roughly 15% to 20% of patients
- Varies with patient population
- Investment depends on utilization

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Osmolarity Testing



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Abnormal vs. Normal Patient Results

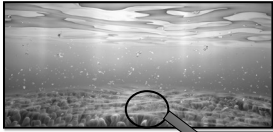


If a patient is symptomatic with normal osmolarity, additional considerations include:

- Conjunctival chelasis
- Mild allergic conjunctivitis
- Epithelial Basement Membrane Dystrophy (EBMD)
- Other

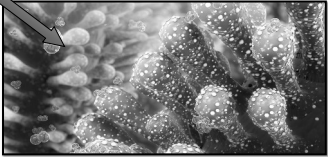
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Tear Osmolarity and Ocular Surface Health



Normal Tear Film – lipid, aqueous and mucous layer.


Decrease in aqueous production or increased evaporation results in abnormal osmolarity



The glyocalyx and microvilli help retain water on the corneal surface


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Tear Osmolarity and Ocular Surface Health

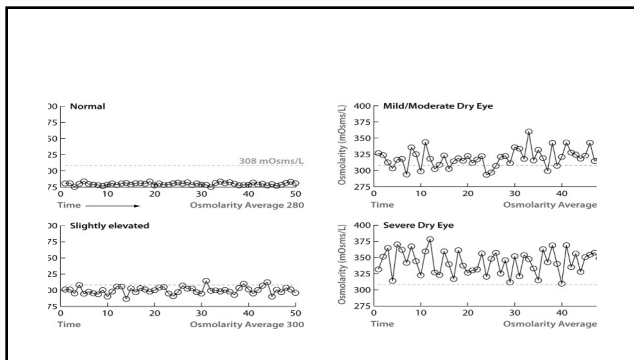


Left undiagnosed and untreated, tears with abnormal osmolarity become increasingly cytotoxic to the corneal epithelium


Death to superficial epithelial cells exposes the underlying immature cells to the cytotoxic hyperosmolar tears



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Prevalence of hyperosmolarity and symptoms of DED in the US population (ARVO Sept 2016)	US Study Average
Number of patients in the study	9947
% of patients that have 1+ dry eye symptoms	81%
% of asymptomatic patients with normal osmolarity (<308 mOsm/L) or inter-eye difference <= 8 mOsm/L	58.9%
% of patients exhibiting moderate hyperosmolarity (>316 mOsm/L)	29%
% of symptomatic patients with normal osmolarity (<308 mOsm/L) or inter-eye difference <= 8 mOsm/L	36.9%

References 1. Manoj VS. Invest Ophthalmol Vis Sci 2016; 57:ARVO E-Abstract 2850.

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Abnormal vs. Normal Patient Results

NORMAL OSMOLARITY

OD: 290 OS: 288

INTER-EYE DIFFERENCE: 2 mOsm/L

ABNORMAL OSMOLARITY

OD: 325 OS: 295

INTER-EYE DIFFERENCE: 30 mOsm/L

If a patient is symptomatic with normal osmolarity, additional considerations include:

- Conjunctival chalasis
- Mild allergic conjunctivitis
- Epithelial Basement Membrane Dystrophy (EBMD)
- Other


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Portable: Specimen collection and analysis in one

Verilyte™ Technology integrates specimen collection and analysis in a single device.

Collection


Osmolarity test cards are interchangeable for use with either ScoutPro or the TearLab Osmolarity System.



- Microfluidic lab-on-a-chip technology
- Innovative card design allows tear collection from the driest patient
- Allows nanoliter volume collection by any eye care professional

2 in 1 Analysis

The thermometer is now integrated into the tip of the ScoutPro pen to maintain test performance even when ambient temperature varies throughout the office.



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Testing Osmolarity

- Initial Investment
- \$9500
- Test Cards
 - \$11 per test card
 - 1 test card per eye
 - Billed as a lab test
 - Doesn't affect E/M Coding
 - Reimbursement \$22.48 per eye
 - Down Stream Procedures

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Osmolarity Testing

- Allowable Amounts Range From
 - \$12 to \$23 per eye
 - \$24 to \$46 per patient
 - Cost \$22 per patient

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Dry Eye Disease and *MMP-9*

Matrix metalloproteinases (MMP) are proteolytic enzymes that are produced by stressed epithelial cells on the ocular surface¹

- MMP-9 in Tears
 - Non-specific inflammatory marker
 - Normal range between 3-41 ng/ml
 - More sensitive diagnostic marker than clinical signs¹
 - Correlates with clinical exam findings¹
 - Ocular surface disease (dry eye) demonstrates elevated levels of MMP-9 in tears¹

[1] Chhabra-Rao N, de Paiva CS, Li de Ques, et al. Invest Ophthalmol Vis Sci 2006; 47(7): 2303-2309.

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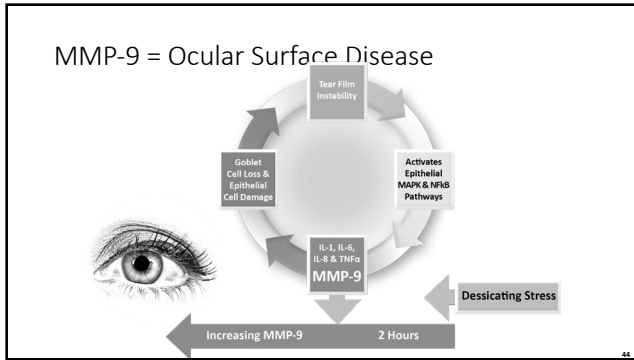
Ocular Surface Inflammatory Mediators

- Desiccating or osmotic stress to the ocular surface epithelium is sufficient to activate MAPK and nuclear factor (NF)- κ B²⁻⁷
- Activation of MAPKs stimulates production of inflammatory mediators by the ocular surface epithelium²⁻⁷:
 - IL-1 β
 - TNF- α
 - IL-6
 - IL-8
 - MMP-9



[2] Gordon MK, Stein MS, de Paiva CS, et al. Desiccating stress stimulates expression of matrix metalloproteinases by the ocular epithelium. Invest Ophthalmol Vis Sci. 2006; 47(10):2303-2310. [3] de Paiva CS, Li de Ques, et al. Osmolarity stress stimulates expression of matrix metalloproteinases by the ocular epithelium. Invest Ophthalmol Vis Sci. 2006; 47(10):2311-2318. [4] de Paiva CS, Li de Ques, et al. Osmolarity stress stimulates expression of matrix metalloproteinases by the ocular epithelium. Invest Ophthalmol Vis Sci. 2006; 47(10):2319-2326. [5] de Paiva CS, Li de Ques, et al. Osmolarity stress stimulates expression of matrix metalloproteinases by the ocular epithelium. Invest Ophthalmol Vis Sci. 2006; 47(10):2327-2334. [6] de Paiva CS, Li de Ques, et al. Osmolarity stress stimulates expression of matrix metalloproteinases by the ocular epithelium. Invest Ophthalmol Vis Sci. 2006; 47(10):2335-2342. [7] de Paiva CS, Li de Ques, et al. Osmolarity stress stimulates expression of matrix metalloproteinases by the ocular epithelium. Invest Ophthalmol Vis Sci. 2006; 47(10):2343-2350.

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MMP-9 and Ocular Surface Disease

- MMP-9 destabilizes the tear film and directly contributes to corneal barrier dysfunction by breaking down tight junctions and facilitating inflammatory cell migration¹⁻⁵
- Down modulation of MMP-9 expression is associated with improvement in ocular surface epithelia reinforcing the key role of MMP-9⁶
- MMP-9 knockout mice are resistant to developing dry eye⁷

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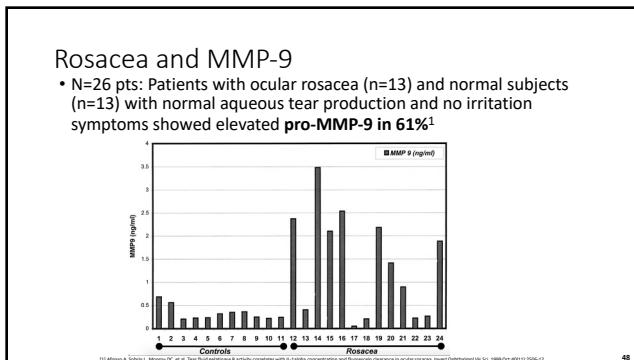
MMP-9 Point of Care Testing

MMP-9 testing is a rapid, immunoassay test for the visual, qualitative *in vitro* detection of elevated levels of the MMP-9 protein in human tears from patients suspected of having dry eye. InflammDry is to be used to aid in the diagnosis of dry eye, in conjunction with other methods of clinical evaluation. This test is intended for prescription use at point-of-care sites.

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Post LASIK Dry Eye and MMP-9

- N=16 pts: 50% of post-LASIK dry eye patients were found to have significant inflammation associated with an elevated MMP-9 by quantitative MMP-9 ELISA¹
- The OSDI was found to nonspecifically identify patients with symptomatic dry eye but does not differentiate patients with significant inflammation¹

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Artificial Tears and MMP-9

- Artificial tears provide a palliative relief of eye irritation in patients with aqueous tear deficiency, **but do not prevent the underlying inflammation** or reverse conjunctival squamous metaplasia in chronic dry eye¹
- Artificial tear eye drops alone **failed to demonstrate any reduction in MMP-9 levels**²




[1] Stern ME, Scheerberg CL, Pflegerer SC. Dry Eye as a Manifest Autoimmune Disease. International Review of Ophthalmology. 2013;33(2):104-11. [2] Agapova N, Agapova M, Sotomura M, Beckwith AJ, De Paoli M, et al. Aqueous tear metaplasia in dry eye disease. Ophthalmology. 2015;122(12):2174-81.

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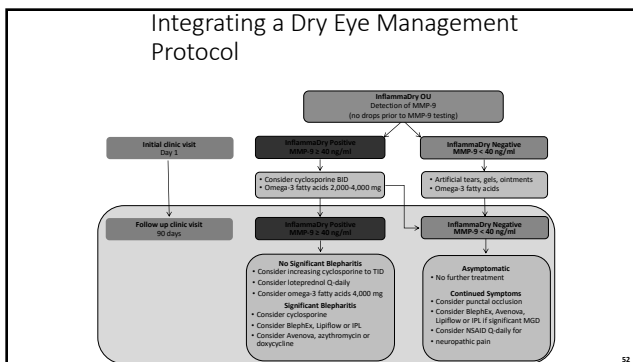
Punctal Occlusion

- Punctal occlusion has been shown to improve objective and subjective measures of dry eye to and to **exacerbate ocular surface inflammation** in subjects with overt clinical inflammation¹
- The Delphi treatment guidelines for ocular surface disorders recommends that **inflammatory conditions be treated before punctal occlusion**²



[1] Pflegerer SC. Anti-inflammatory therapy for dry eye. Acta Ophthalmologica. 2004;82(3):337-43. [2] Johnson A, Soper K, Stern L, et al. The Dry Eye Clinical Practice Guideline. Ocular Surface Disease Society. 2015;13(2):107-14.

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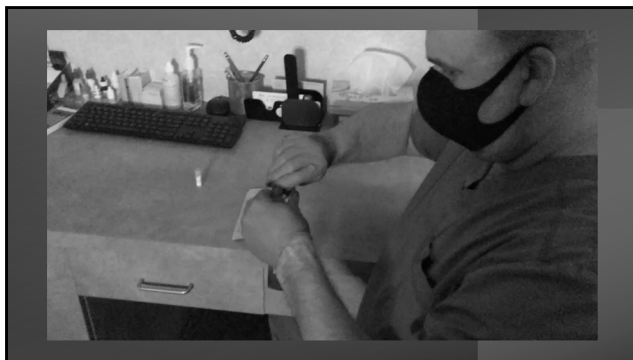
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Treatment of Dry Eye¹

- A dry eye treatment study was performed to compare the impact of steroids (lotepredinol) and saline on **MMP-9 expression after anti-inflammatory treatment**
 - 30 patients with Sjogren's Syndrome representing aqueous deficiency
 - 30 patients with evaporative dry eye due to MGD
 - 15 patients were healthy controls
- Patients were divided into 2 subgroups
 - One group was treated with saline
 - One group was treated with saline artificial tears plus topical corticosteroid eye drops (0.5% lotepredinol etabonate) 4 times daily for 15 days
- Patients with Sjogren's Syndrome showed a **66% reduction in MMP-9 expression** while MGD patients showed a **42% reduction**
- Artificial tear eye drops alone **failed to demonstrate any reduction in MMP-9 levels**

[1] Agapova N, Agapova M, Sotomura M, Beckwith AJ, De Paoli M, et al. Aqueous tear metaplasia in dry eye disease. Ophthalmology. 2015;122(12):2174-81.

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MGD is Extremely Common

Patient Condition	% with MGD
Dry Eye	86% ¹
Peri-menopause	79% ²
Polycystic Ovary Syndrome	73% ³
Glaucoma (on prostaglandins)	96% ⁴
Glaucoma (non prostaglandin)	58% ⁴
Diabetes	58% ⁵
VDT users (4+ hrs per day)	85% ⁶
Cataract Patients	59% ⁷
Contact lens wearers	60% ⁸

1. Lemp MA, Crews LA, Bron AJ, et al. Cornea 2012;31(5):472-8. 2. Jin X, et al. Medicine (Baltimore) 2014;93(14):e263. 3. Baver G, et al. Curr Eye Res 2016;28(1):5-8. 4. Mccormick, et al. J Glaucoma 2016; 25(9):770-4. 5. Yu T, et al. Int J Ophthalmol 2016;9(12):1740-1744. 6. Wu H. PLoS One 2014;9(8):e105575. 7. Algamadi et al. Cornea 2016;35(6):731-5. 8. Machalinska A, et al. Cornea 2015;34(9):1098-104.

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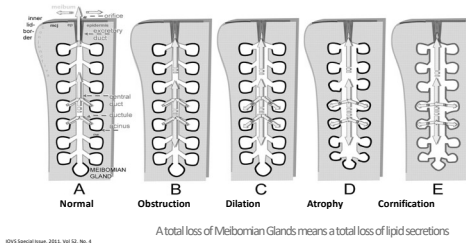
Meibomian Gland Dysfunction

Diagnosing

- Gland Evaluation
- Expression
- Meibography

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Stages of Evaporative Dry Eye Disease



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Impact of MGD on Ocular Health

• MGD Decreases

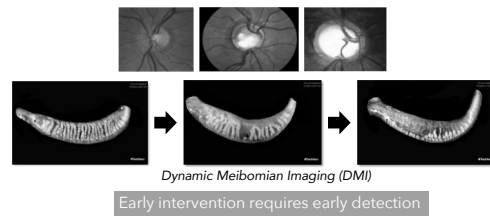
- Ocular Health & Protection¹⁻⁴
- Corneal nerve health²
- Conjunctival health³
- Tear film immunity^{1,4}
- Visual acuity^{1,5}
- Ocular comfort⁴⁻⁶
- Contact lens comfort and wear time⁴⁻⁶



1. Baudouin C, Messmer EM, Aragona P, et al. Br J Ophthalmol 2016 ;100(3):300-6. 2. Aziz S, Uçak T, Yeşar I, et al. Semin Ophthalmol 2017;32(3):377-383. 3. Liang Q, Pan Z, Zhou M, et al. Cornea 2015;34(10):1193-9. 4. Mudge P. Invest Ophthalmol Vis Sci 2014;55(11):7272-7. 5. Epitropoulos AT. J Ophthalmol 2016. 6. Machalirvika A1, Zakrzewska A, Adamek B, et al. Cornea 2015;34(9):1098-104.

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Imaging changes everything

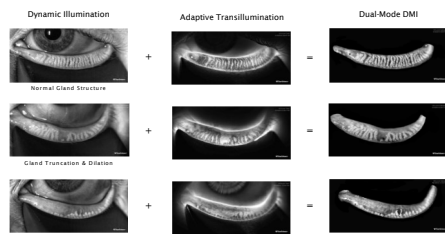


Dynamic Meibomian Imaging (DMI)
Early intervention requires early detection

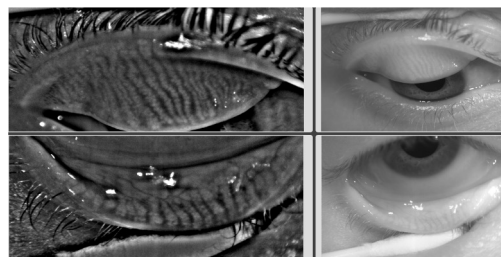
1. Baskin CA, et al. Noninvasive obstructive meibomian gland dysfunction. Cornea. 2010 Dec;29(12):1333-45. Review.
2. Nichols KK. The MGD Workshop report. Executive summary. IOVS 2011

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Dynamic Meibomian Imaging (DMI)

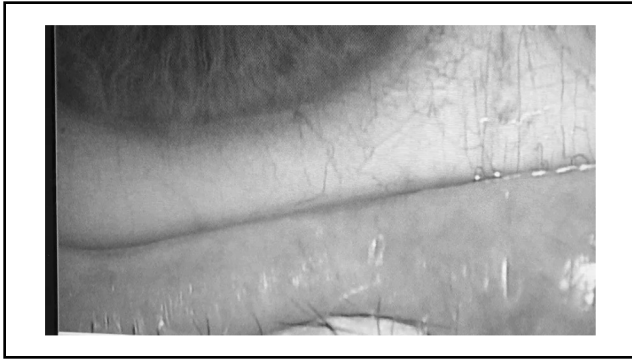


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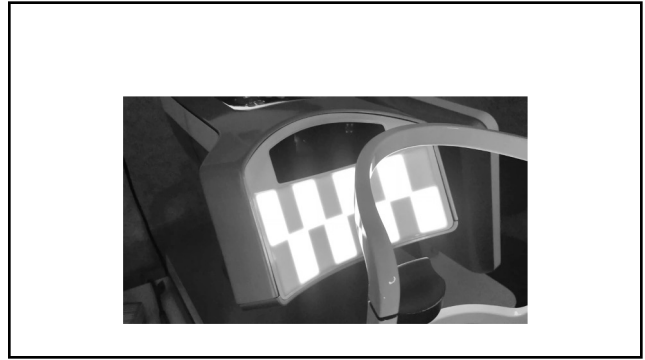


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The international Dry Eye Workshop (DEWS)

2007
2007 Report of the International Dry Eye Workshop (DEWS)

Management and Therapy of Dry Eye Disease:
Report of the Management and Therapy Subcommittee
of the International Dry Eye Workshop (2007)

Management and Therapy Subcommittee members: Stephen C. Pflugfelder, MD (Chair), Gerd Goehring, MD, Shigen Kinoshita, MD, Michael A. Lemp, MD, James McCulley, MD, Daniel Nelson, MD, Gary N. Novack, PhD, Jun Shimazaki, MD, Chive Wilson, PhD.

↓

2017
TFOS DEWS II Management and Therapy Report

Lyndon Jones, FCOptom, PhD^{1,2,3}, Laura E. Downie, BOptom, PhD⁴, Donald Korb, OD⁵, June M. Benitez-del-Castillo, MD, PhD⁶, Reza Dana, MD⁷, Sophie X. Deng, MD, PhD⁸, Pham N. Doung, MD⁹, Gerd Goehring, MD, FRBC¹⁰, Richard Vaili Hilla, MD¹¹, Song Liu, MD¹², Kyusang Yul Seo, MD, PhD¹³, Joseph Zauber, MD¹⁴, Tais H. Wakamatsu, MD, PhD¹⁵, Jianjiang Xu, MD, PhD¹⁶, James S. Wolffsohn, FCOptom, PhD¹⁷, Jennifer P. Craig, MCOptom, PhD¹⁸

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Treatment guidelines recommended by DEWS II (2017)

Step 1:

- Education regarding the condition, its management, treatment and prognosis
- Modification of local environment
- Education regarding potential dietary modifications (including oral essential fatty acid supplementation)
- Identification and potential modification/elimination of offending systemic and topical medications
- Ocular lubricants of various types (if MGD is present, then consider lipid-containing supplements)
- Lid hygiene and warm compresses of various types

Step 2:

If above options are inadequate consider:

- Non-preserved ocular lubricants to minimize preservative-induced toxicity
- Topical treatment for Demodex (if present)
- Tear conservation
 - Punctal occlusion
 - Moisture chamber spectacles/goggles
- Overnight treatments (such as ointment or moisture chamber devices)
- In-office, physical heating and expression of the meibomian glands (including device-assisted therapies, such as Lipiflow)
- Topical retinoid therapy (such as tretinoin)
- Prescription drugs to manage MGD

In-office intense pulsed light therapy for MGD:

- Topical secretagogues
- Topical non-steroidal immunomodulatory drugs (such as cyclosporine)
- Topical life-sustaining drugs (such as filgrastim)
- Oral macrolide or tetracycline antibiotics

Step 3:

If above options are inadequate consider:

- Oral secretagogues
- Autologous conditioned serum eye drops
- Therapeutic contact lens options
 - Soft bandage lenses
 - Rigid scleral lenses

Step 4:

If above options are inadequate consider:

- Topical corticosteroid for longer duration
- Autologous membrane grafts
- Surgical punctal occlusion
- Other surgical approaches (eg, laser therapy)

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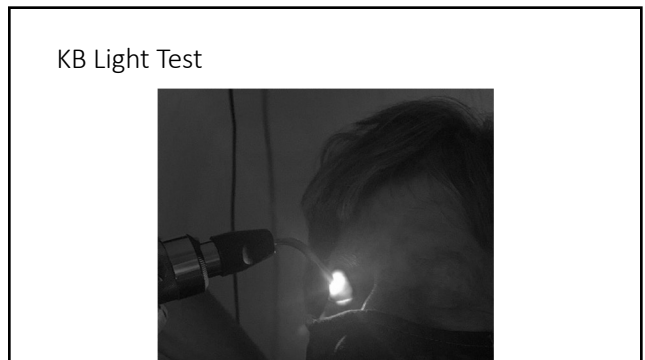
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Most Important Diagnostic Question to Ask:

Do you have morning symptoms?

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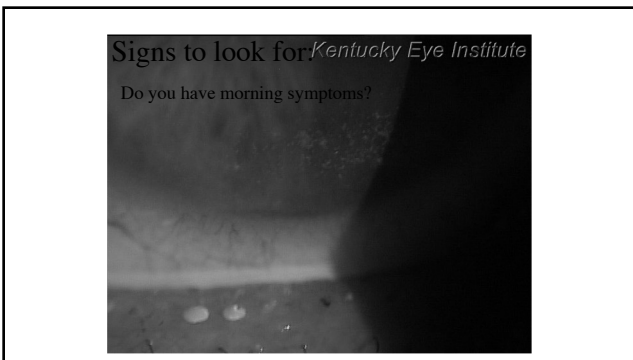
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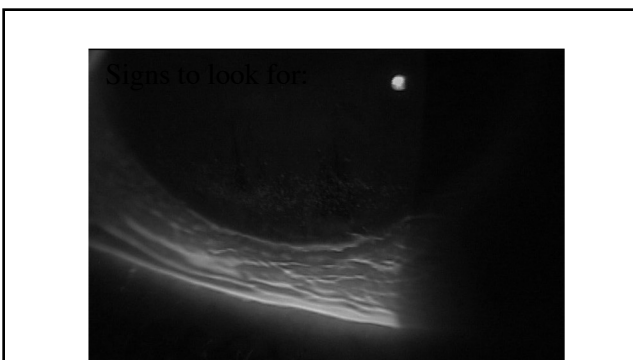
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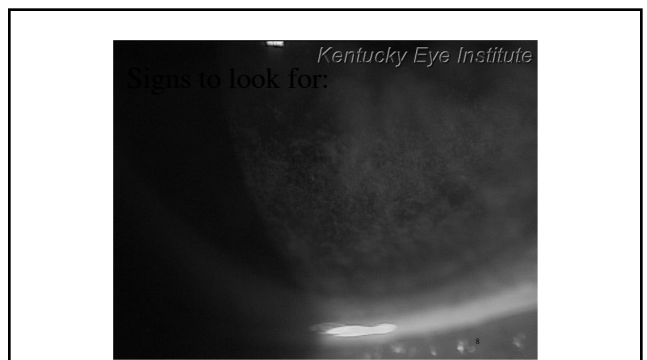
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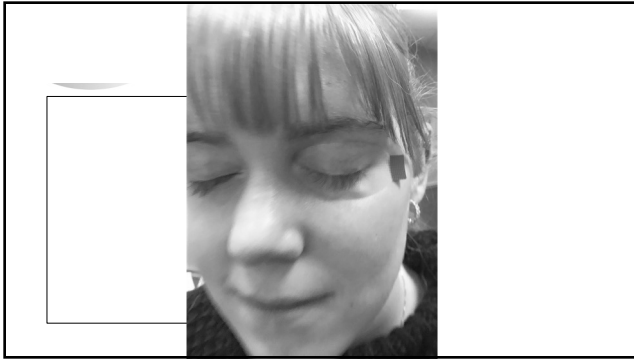
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- *Latex Free*
- *Porous and Hypoallergenic Material*
- *Contour Orbit Shape*
- *Regular (Blue tab) and Sensitive (Purple tab) available.*

Two white, curved patches with small black tabs are shown on a light-colored surface. One patch is positioned above the other, both curving to follow the shape of an eye's orbit.

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- *How To Use/Proper Placement*

A close-up black and white photograph of a person's eye with the patch applied. The patch is a white, curved strip with a fine mesh texture, secured by a small black tab on the outer edge.

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Thank You

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