In Office Lid Management Today, Tomorrow and in the Future

Douglas K Devries, OD

Eye Care Associates of Nevada, Sparks, NV

Milton Hom, OD, FAAO

Canyon Eyecare, Azusa, CA

1

Douglas K. Devries, OD Disclosures

Any conflicts have been mitigated

Allergan – Advisory Board and Speakers Bureau Avilleno Alcon– Advisory Board and Speakers Azura Advisory Aescula Tech Bio Tissue Speakers Bureau and Advisory Board Bruder Advisory Board Novartis– Advisory Board and Speakers Bureau B & L – Advisory Board and Speakers Dompe Advisory and Speakers Thea/Akorn Advisory Kala Advisory and Speakers Visus Advisory Versea Advisory	Ocusoft Advisory Board TearLab Advisory Board Sight Science Advisory and Speaker RVL Advisory Board Oyster Point Advisory and Speaker Tarsus Advisory Science Based Health Advisory and Speaker Sun Advisory and Speaker Ophthalmic Resources Partner Orasis Advisory Johnson & Johnson Vision Advisory and Speaker Lumenis Advisory and Speaker

2

Milton Hom, OD, FAAO Disclosures

Any conflicts have been mitigated

Abbve Advisory Board and Speakers Bureau Avilleno Lenz Harrow	Synaxis Tarsus Scope Thea

3

Section 1.2: Diagnostics for Eyelid Margin Health

4

5

6

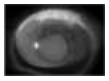
Diagnostic Tools and Tests

Tear Osmolarity

Slit-Lamp Exam

MMP-9

Vital Dyes



Meibography

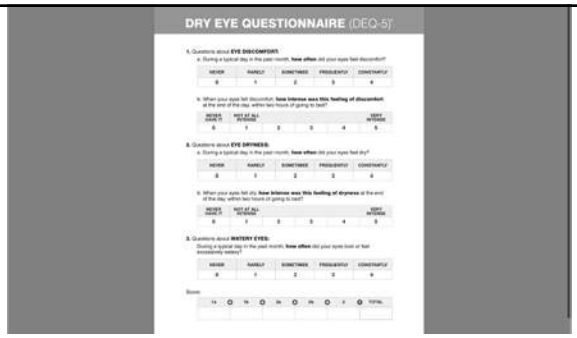
DED Questionnaire

7

Standard Patient Evaluation of Eye Dryness (SPEED) Questionnaire[1]

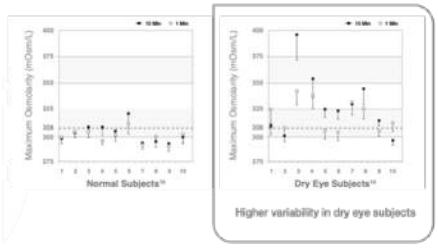
- Evaluates the frequency and severity of symptoms
- Developed as an easy to use fast screening tool for dry eye disease
- SPEED questionnaire is one of the tools used to identify candidates for LipiFlow®

8



9

Variability in Tear Osmolarity is the Hallmark of DED[1]



1. Keech A, Senchyn M, Jones, L. Impact of time between collection and collection method on human tear fluid osmolarity. Current Eye Research, Early Online, 1-9, 2013.

10

10

Mechanical MGD Treatments

- Zocular Eyelid System Treatment
- Blephex Treatment

ZEST procedure with ZocuKit (2019) YouTube. Available at: https://www.youtube.com/watch?v=g9youf3M7tk (Accessed: 04 November 2023).

Video courtesy of Doug Devries, OD, and Marc Bloomenstein, OD, FAAO

11

11

Automated Vectored Thermal Pulsation

Video courtesy of Doug Devries, OD, and Marc Bloomenstein, OD, FAAO

12

12

In-Office Osmolarity Testing

Specimen collection and analysis

Results displayed on pen right after testing

Rechargeable batteries in pen hold 8 hours or charge

Charging base, small footprint, optional wall mount

Test cards

Image credit: trukera.com

13

13

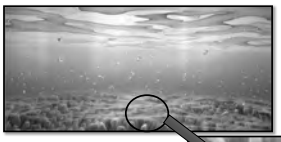
Osmolarity[1]

- **Definition:** Concentration of solutes in the tears representing the balance of water and dissolved substances on the ocular surface.
- **Importance:** Plays a crucial role in maintaining ocular surface health. Deviations from the normal osmolarity range can indicate ocular surface disease.

1. Lemp MA, Foulks GN. The definition and classification of dry eye disease. Ocul Surf. 2007 Apr;5(2):75-92.

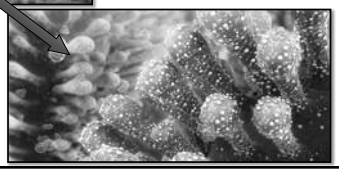
14

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 glycocalyx and microvilli help retain water on the corneal surface

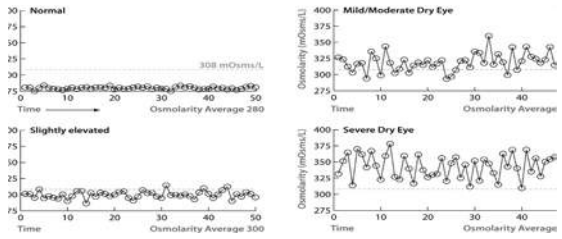
15

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

16



17

18

Hyperosmolarity May Cause Large Variance in K Readings[1]

 Normal	**40** Patients	**< 310** mOsm/L	**12.4±2.2** sec TBUT	**42.9 ± 0.7** Mean K
			Ocular findings overwhelmingly normal. You can't see osmolarity with the slit lamp.	**Excessive variance in K readings due to hyperosmolarity*
 Hyperosmolar	**41** Patients	**> 310** mOsm/L	**9.0 ± 1.8** sec TBUT	43.9 ± 1.1* Mean K

1. Kursite A, Laganovska G. Effect of tear osmolarity on postoperative refractive error after cataract surgery. J Ophthalmol (Ukraine). 2023 Apr 25(2):11-5.

19

Patients Experiencing Hyperosmolarity Are Almost 7X More Likely to be 20/20 Unhappy[1]

 Normal	**0.89 ± 0.12** UCVA	**0.28 ± 0.25** SE	**62.5%** hit < 0.5 D	**32.5%** hit 20/20	**0** >1.0 D miss
	**Hyperosmolarity lead to significantly less visual acuity and over 3X the refractive error*		**You are almost 3X as likely to hit your target in a normal patient than in a hyperosmolar patient*		**You are far more likely to have a big miss with a hyperosmolar patient than with a normal patient*
 Hyperosmolar	**0.76 ± 0.14** UCVA	**0.60 ± 0.34** SE	**26.8%** hit < 0.5 D	**9.7%** hit 20/20	**4** >1.0 D miss
	p < 0.01	**p < 0.01**			

1. Kursite A, Laganovska G. Effect of tear osmolarity on postoperative refractive error after cataract surgery. Journal of Ophthalmology (Ukraine). 2023 Apr 25(2):11-5.

20

The Role of Matrix Metalloproteinases-9 (MMP-9)

- Proteolytic enzymes that are produced by stressed epithelial cells on the ocular surface[1]
- MMP-9 in tears
  - Nonspecific inflammatory marker
  - Normal range between 3 and 41 ng/ml
  - More sensitive diagnostic marker than clinical signs
  - Correlates with clinical exam findings
  - Ocular surface disease/DED demonstrates elevated levels of MMP-9 in tears

1. Chotikavanich S, de Paiva CS, Chen JJ, Bian F, Farley WJ, Pflugfelder SC. Production and activity of matrix metalloproteinase-9 on the ocular surface increase in dysfunctional tear syndrome. Invest Ophthalmol Vis Sci. 2009 Jul 1;50(7):3203-9.

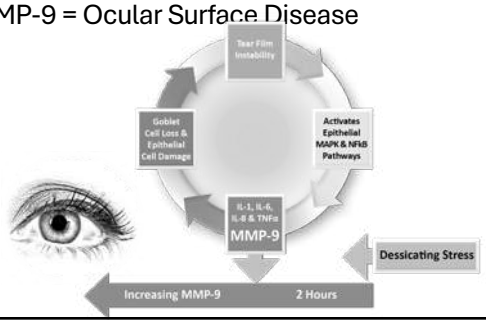
21

21

22

23

MMP-9 = Ocular Surface Disease



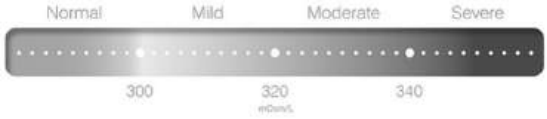
24

24

Normal Tear Film Osmolarity
Typically between 275 and 295 mOsm/L

Abnormal osmolarity is defined by:

An elevated reading > 300 mOsm/L *OR* When the inter-eye difference is > 8 mOsm/L



25

25

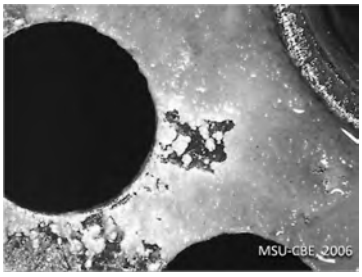
Blepharitis
= lid inflammation

26

26

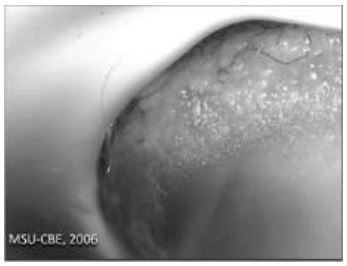
27

27



28

28



29

29

30

30

QUORUM-SENSING GENE ACTIVATION 1968

John Woodland "Woody" Hastings, (March 24, 1927 – August 6, 2014)
Professor of Molecular and Cellular Biology at Harvard University
Increase in population densities causes production of virulence factors

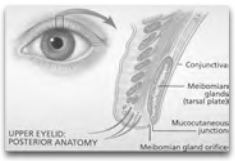
- Exotoxins
- Lipases
- Superantigens….toxic shock syndrome

31

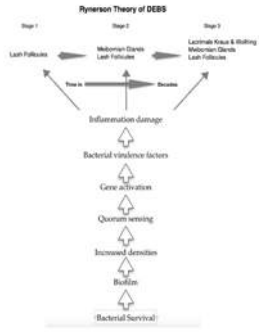
32

32

BLEPHARITIS - DEBS



Clin Ophthalmol. 2016;Dec 9;10:2455-2467.

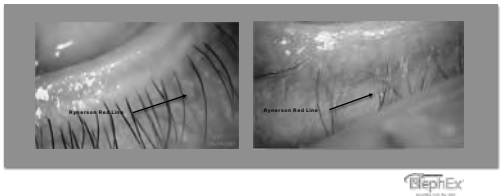


33

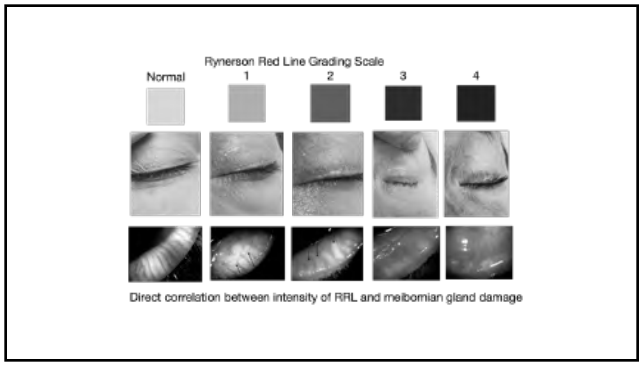
Rynerson Red Line

***Important new sign for easy and early diagnosis

below lower and above upper lash line
Sign of longstanding folliculitis & meibomianitis



34



35

MICROBLEPHAROEXFOLIATION (MBE)

Doctor centered approach to lid health

- Spins a micro-sponge 4000 RPM along margin
- Results in completely clean lids
- Repeated every 4-6 months
- Private pay procedure, typically $150-$250

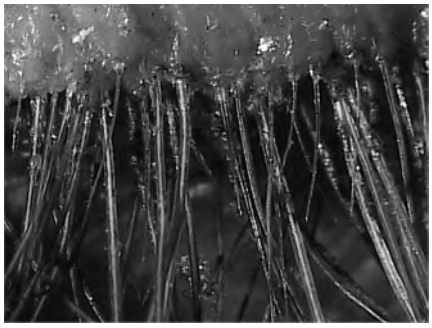
36

Video Workshop Presentation of Microblepharoexfoliation

00:52

37

37

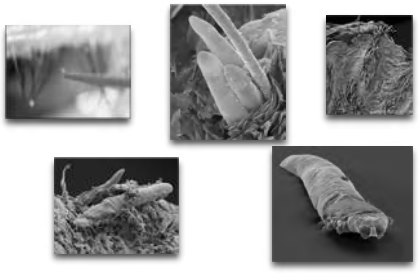


38

39

Demodex Blepharitis

40



Biofilm is a polysacharride
Perfect food source for a **Demodex** infestation

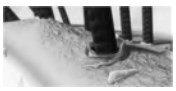
41

DEMODEX BLEPHARITIS | Mechanisms of Disease

Image courtesy of Laura M. Periman, MD, used with permission.[1]

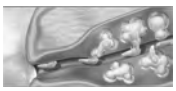
MECHANICAL

- Lash distension occurs as *Demodex* mites attach to follicles[2-4]
- *Demodex* mites deposit debris and digestive enzymes, causing further irritation to the eyelid margin[4,5]



BACTERIAL

- *Demodex* mites can contribute to blepharitis by carrying bacteria on their exterior surface that may elicit immune responses[3,6-7]



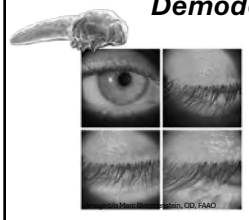
CHEMICAL

- *Demodex* mites have been associated with altered meibum composition[8]
- Debris from *Demodex* mites can potentially lead to chronic inflammation and degeneration of conjunctival tissue[9]

1. Data on file. Images courtesy of Laura M. Periman, MD; 2022. **2.** Zhang AC et al. *Ophthalmic Physiol Opt.* 2020;40(4):389-432. **3.** Liu J et al. *Curr Opin Allergy Clin Immunol.* 2010;10(5):505-510. **4.** Fromstein SR et al. *Clin Optom (Auckl).* 2018;10:57-63. **5.** Gao YY et al. *Invest Ophthalmol Vis Sci.* 2005;46(9):3089-

42

Demodex blepharitis (DB)



- Common eyelid margin disease caused by an overgrowth of *Demodex* mites
- **56%** of patients with cataracts have DB[1]
- **60%** of patients treated for dry eye also have DB[2]
- **93%** of patients with soft contact lens intolerance were found to have DB[3]
- **66%** of blepharitis cases are associated with *Demodex* mites[1]

The number of mites correlates with:
- symptom severity
- density/severity of collarettes

DB IS HIGHLY PREVALENT BUT UNDERDIAGNOSED IN CLINICAL PRACTICE[1,2]

1. Trattler W et al. Clin Ophthalmol. 2022;16:1153-1164.
2. O'Dell L et al. Clin Ophthalmol. 2022;16:2979-2987.
3. Tarkowski W et al. Biomed Res Int. 2015;2015:259109.

43

Key Signs and Symptoms of DB

- **Itching***
- Dry eyes
- Missing/misdirected eyelashes
- Lid margin inflammation
- Sensitivity to light
- Blurred vision

*Most common symptom

44

44

Diagnosing DB Is As Simple as Having Your Patients Look Down During a Routine Slit-Lamp Exam

- DB can cause eyelid redness and cylindrical deposits around the base of the eyelashes (collarettes), which are the pathognomonic sign of DB[1,2]
- If you see collarettes, then you can confidently diagnose DB[3]

1. Trattler W et al. Clin Ophthalmol. 2022;16:1153-1164. 2. Fromstein SR et al. Clin Optom (Auckl). 2018;10:57-63.
3. Gao YY et al. Invest Ophthalmol Vis Sci. 2005;46(9):3089-3094.

45

45

Video c/o Marc Bloomenstein, OD, FAAO

46

46

OTC Treatment of DB

Tea Tree Oil Compounded

Tea Tree Oil Solutions
- Scrubs
- In-Office Tx

Image credit: Tarsus

47

47

Treatment of DB

Lotilaner ophthalmic solution 0.25% (XDEMVY, Tarsus) is the only FDA-approved treatment for DB. It works by targeting and killing the *Demodex* mites that cause the condition. The active ingredient, lotilaner, is a lipophilic agent formulated in an aqueous eye drop.

The most common side effect in clinical trials was stinging and burning in 10% of patients. Other side effectsexperienced in less than 2% of patients included chalazion/hordeolum and punctate keratitis.

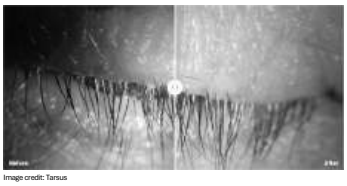


Image credit: Tarsus

48

48

Treatment of DB With Lotilaner

SATURN-1 and SATURN-2 Study Results

1. Collarette Reduction (≤2 collarettes)
   - 50% compared with 10% vehicle
2. Mite Eradication (0 mites/lash)
   - 60% compared with 16% vehicle
3. Erythema Cure (Grade 0)
   - 25% compared with 8% vehicle
4. Collarette Reduction (≤10 collarettes)
   - 85% compared with 28% vehicle

1. Yeu E, et al. Cornea. 2023 Apr 1;42(4):435-43. **2.** Gaddie IB, et al. Ophthalmology. 2023 Oct 1;130(10):1015-23. **3.** Sadri, E. Castillo, RM, and Jalalat, P. Presented at ASCRS 2023; May 5-8, 2023; San Diego, CA.

49

Key Study Data – ERSA and RHEA

ERSA and RHEA were two separate, randomized pilot studies evaluating the safety and efficacy of lotilaner ophthalmic solution 0.25% and vehicle for the **treatment of DB with MGD**. Eligibility criteria and endpoints for the ERSA and RHEA studies were identical.

ERSA: Collarette grade reduction and responder rate at day 43

Reduction to ≤2 collarettes

of patients treated with lotilaner 0.25% (n=20)

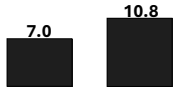
Reduction to ≤10 collarettes

of patients treated with lotilaner 0.25% (n=20)

RHEA: At Day 43, vehicle (n=10) did not show statistically significant improvement in mean collarette grade compared with baseline (*P*>.1)

ERSA: Patients treated saw ~54% improvement in mean meibomian glands yielding liquid secretion (MGYLS) at day 43 compared with baseline

Number of expressible glands



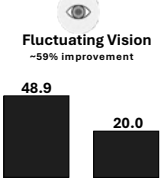
RHEA: At Day 43, vehicle (n=10) did not show statistically significant improvement in number of MGYLS compared with baseline (*P*>.1)

Data on file, Tarsus Pharmaceuticals, Inc

50

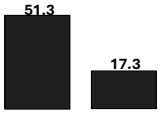
Key Study Data – Patient Reported Outcomes

Fluctuating Vision
~59% improvement



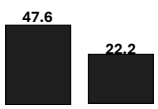
RHEA: At day 43, vehicle (n=10) did not show statistically significant improvement in patient-reported fluctuating vision compared with baseline (*P*>.1)

Itching
~66% improvement



RHEA: At day 43, vehicle (n=10) did not show statistically significant improvement in patient-reported itching compared with baseline (*P*>.1)

Redness
~53% improvement



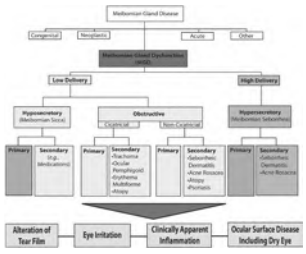
RHEA: At day 43, vehicle (n=10) did not show statistically significant improvement in patient-reported redness compared with baseline (*P*>.1)

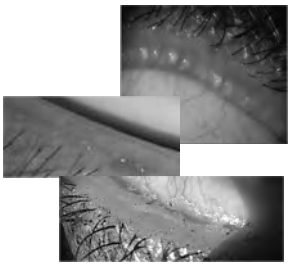
Based on 100-point visual analog scale (VAS)

Data on file, Tarsus Pharmaceuticals, Inc

51

What is Meibomian Gland Dysfunction (MGD)?





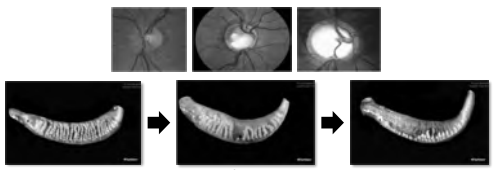
Nelson JD, et al. Investigative ophthalmology & visual science. 2011 Mar 1;52(4):1930-7.

Photos courtesy of Paul Karpecki, OD FAAO

52

52

Imaging changes everything



Dynamic Meibomian Imaging (DMI)

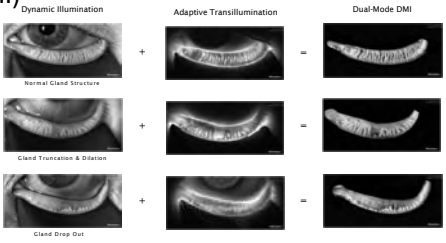
Early intervention requires early detection

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

53

53

LipiView II with Dynamic Meibomian Imaging (DMI)



54

Meibography in Your Office

- Advanced corneal topographer with a built-in keratometer and a color camera optimized for external imaging

- Portable slit lamp-mounted, cloud-based infrared non-contact camera
- Captures images of the external images of the eye, including meibomian gland structures, in black and white

- First high-definition, cloud-based external ocular camera and meibographer
- Portable and slit lamp compatible

55

Meibomian Gland Segmentation

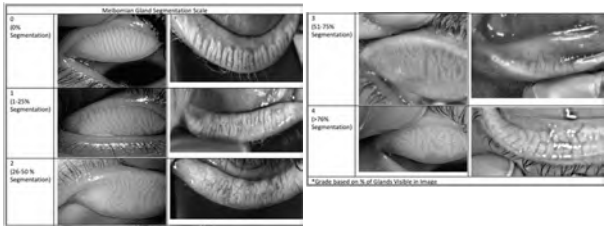
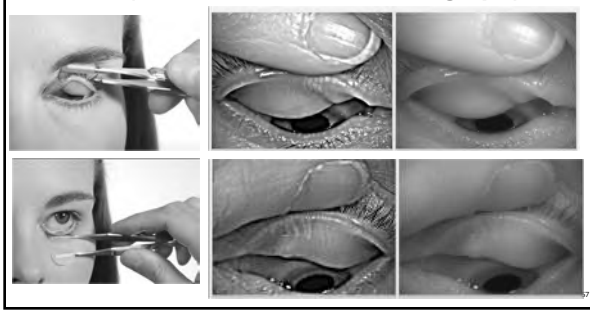


Image credit: LEO grading scale for meibomian gland segmentation.

56

56

Eyelid Inversion and Meibography



57

57

Meibography in Your Office

- Comprehensive diagnostic system for high-quality tear film analysis
- Quick and detailed examinations

- Measures objective scatter index of each patient
- Measures total optical quality, accounting for light scatter caused by pathologies

- Offers a complete diagnosis of the three tear film layers, produces images of the meibomian glands, and measures the percentage loss of the meibomian glands
- Performs four noncontact examinations (interferometry, noninvasive tear breakup time, tear meniscus, and meibography) in 4 minutes

- Portable
- Visualizes treatment zones to target blocked meibomian glands

58

58

INTEGRATE TearScience® LIPISCAN® IN EVERY SCREENING EXAM

Dynamic meibomian imager provides high-definition gland images:

- **Small footprint and lightweight** for optimal versatility
- **Fast and intuitive** operation for seamless integration into routine workups
- **Renders high-definition images** of meibomian gland structures
- **DICOM compatibility** to export image to EMR

Indications: LipiScan® Dynamic Meibomian Imager (DMI) is an ophthalmic imaging device intended for use by a physician in adult patients to capture, archive, manipulate and store digital images of the Meibomian glands.

Not approved in all eye markets.

59

59

Mechanical MGD Treatments

Low Level Light Therapy (LLLT), Quantum Molecular Resonance, and Radiofrequency Technology

- Significant improvement in upper lid meibography in LLLT group compared to baseline[1]
- Quantum molecular resonance improved symptoms, tear stability, and meibomian gland function[2]
- There are no peer-reviewed literature indexed on PubMed examining radiofrequency and their efficacy in treating MGD in a clinical setting

1. Park Y, et al. Scientific Reports. 2022 Mar 4;12(1):3575. **2.** Ferrari G, et al. Cornea. 2019;38(11):1424-1429.

60

60

THERMODYNAMIC TX TO EXPRESS AND EVACUATE MGs

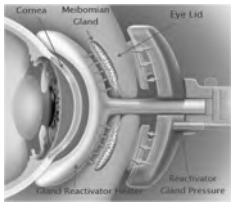
A new thermodynamic treatment to express & evacuate the MGs

Heat applied to both inner lid surfaces

Pulsatile pressure applied to outer lids

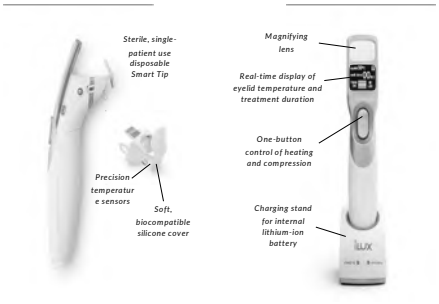
The device applies controlled heat to the inner upper and lower palpebral conjunctival surfaces and lid margins, while simultaneously applying pulsating pressure over the upper and lower (outer) eyelids.

THE LIPIFLOW (TearScience Inc., Morrisville, NC)



FDA approved LipiFlow July 2011

61



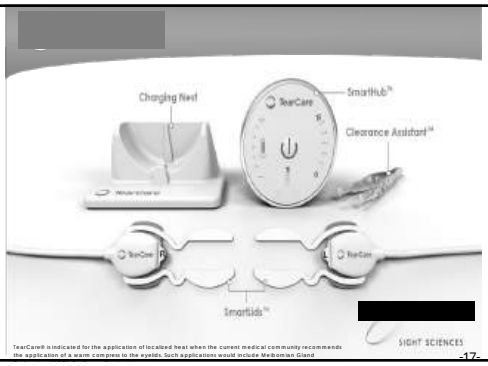
62

Heat it

Apply LED light to raise the eyelid temperature and melt the blockages.

63

64



TearCare® is indicated for the application of localized heat when the current medical community recommends the application of a warm compress to the eyelids. Such applications would include Meibomian Gland

-17-

65

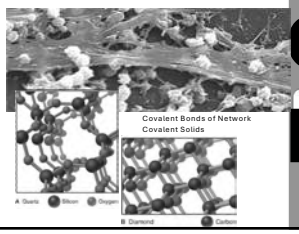
Diagnostic Meibomian Gland Expression

Video courtesy of Doug Devries, OD, and Marc Bloomenstein, OD, FAAO

66

66

Bacteria colonizing the glands produce biofilm and tightly "glue" it to the inner walls of the ducts and acini using an adhesin molecule



VAP OR RIZE

67

The doctor uses an OptiVize to deliver a 6 volt current (equivalent of 2 AA batteries) through a specialty contact lens that is harmonically tuned to blow apart the bonds of a bacterial polysaccharide biofilm

68

Relieve the Crisco-obstructed glands

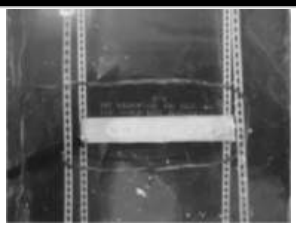
Perform heat and manual vibratory expression

Observe the expressed contents to guide future Tx intervals

MOB IL IZE

69

Biofilm has an Achilles heel



Courtesy Montana State University Center for Biofilm Engineering

70

Relieve the Crisco-obstructed glands

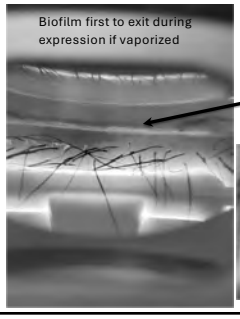
Perform heat and manual vibratory expression

Observe the expressed contents to guide future Tx intervals

MOB IL IZE

71

Biofilm first to exit during expression if vaporized



OptiVize Vaporizes Intraglandular Biofilm in Less than One Minute

Granules of polysaccharide compare to melted Crisco

72

Radio Frequency

RISKS
- Denting
  - Fat necrosis
  - Unintended fat lipolysis
  - Scarring
- Does not address inflammation in DED
- Low evidence so far
- Results are machine dependent

CONTRAINDICATIONS
- Metal device implants
- Pacemakers
- Pregnancy

73

74

INADEQUATE LID SEAL

Not just nocturnal lagophthalmos but a micro version where the lids don't seal shut during sleep

Constant desiccative stress on the cornea while sleeping night after night

8

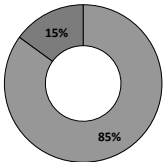
75

Targeting the Source

ILS: The Primary cause of non-Responsive Dry Eye Disease (ref: Korb et al)

76

Total ILS Prevalence: 85%



(N = 120)

ILS can be ruled out if NONE of the following are observed:
- 2+ Morning Symptoms
- Exposure Keratitis
- Positive Korb Blackie

Positive ILS	102 (85%)
Negative ILS	18 (15%)

77

INADEQUATE LID SEAL

Can be induced with loss of elasticity or surgically with a blepharoplasty

Most often an inherited trait

8

78

Most Important Question to Ask:

Do you have morning symptoms?

79

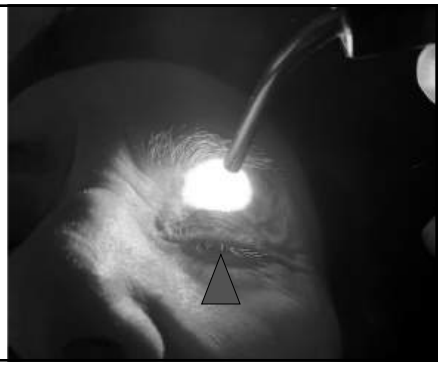
What to look for:

1)Korb/Blackie Light Test

2)Inferior staining on cornea or conjunctiva

80

ILS

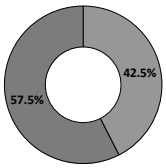


81

Korb-Blackie Test

82

Exposure Keratitis



(N = 120)

Positive Exposure Keratitis	51 (42.5%)
Negative Exposure Keratitis	69 (57.5%)

83

Signs to look for:

84

85

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

86

87

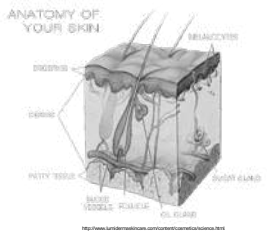
IPL – dry eye discovery

- Serendipitous discovery in 2003 by R. Toyos, MD
- Initially recommended for dermatological treatment
- Patients experienced subsequent dry eye relief

88

Intense pulse light

Three main chromophores:
- Hemoglobin
- Water
- Melanin



89

Who is a candidate for IPL treatment?

- Moderate to severe dry eye/ MGD/ Blepharitis
- Fitzpatrick Skin Type Scale types I-IV

90

My Practice Experience

Nearly 9 1/2 Years of experience with IPL
Discuss with any MGD patient with telangiectasia
4 Sessions of IPL 3 to 4 weeks apart
Cosmetic and therapeutic treatment
Package with
- BlephEx
- Optima IPL
- Thermal Pulsation (Lipiflow, Digital Heat, iLux, Tear Care)

Most rapid payback of any major piece of therapeutic equipment
Survey such as SPEED questionnaire
Mark on the back the number of patients with MGD and Ocular Rosacea
Multiply the number of candidates

91

91

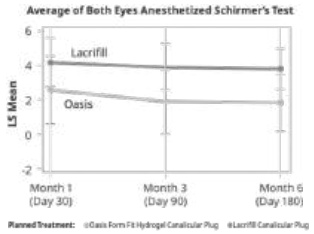
What the Research Shows

Randomized Non-Inferiority Clinical Trial

The trial randomly assigned patients 2:1 to treatment with either LACRIFILL or Oasis Form Fit.
The trial found that:

Change from Baseline of Anesthetized Schirmer's Test (Averages of Both Eyes) at all Post-Baseline Visits

ITT Population with Available Data Only



92

93

Safe & Well Tolerated:
Adverse Events Generally Consistent with Dry Eye Syndrome

	Canalicular Gel (n=103)	Control (n=54)
Adverse Events	%	%
Corneal Staining	36.9	40.7
Ocular Pain	9.7	0
Presumed Dacryocystitis	0.97	0
Conjunctivitis	4.9	1.9
Allergic Blepharoconjunctivitis	0.97	0
Epiphora	7.8	5.6

For a full listing of Adverse Events associated with LACRIFILL Canalicular Gel, please see **lacrifill.com/instructions-for-use**.

94

Selenium sulfide

"Selenium sulfide is thought to reduce keratinocyte activity and soften keratin in skin and to increase lipid secretion in sebaceous glands"

https://azuraophthalmics.com/scientific-meetings

95

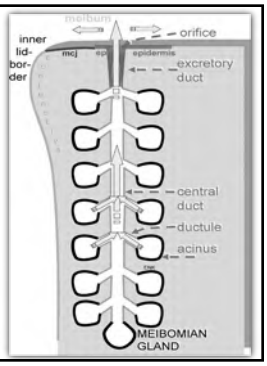
Sel... sulfide

96

"Obstructive MGD is the most common form of MGD resulting in dry eye"

Caroline Blackie
Donald Korb

Blackie, Caroline A., and Donald R. Korb. "MGD: getting to the root cause of dry eye: Review of Optometry 149.6 (2012): 30-37.
Nelson JD, Shimazaki J, Benitez-del-Castillo JM, et al. The international workshop on meibomian gland dysfunction: report of the definition and classification subcommittee. Invest Ophthalmol Vis Sci. 2011 Mar 30;52(4):1930-7.



97

Obstruction

"hyperkeratinization is one of the primary components…of obstructive MGD."

Knop, Erich, et al. "The international workshop on meibomian gland dysfunction: report of the subcommittee on anatomy, physiology, and pathophysiology of the meibomian gland." Investigative ophthalmology & visual science 52.4 (2011): 1938.

98

Obstruction

Hyperkeratinization…disorder of the cells lining the inside of a hair follicle."

Blackie, Caroline A., and Donald R. Korb. "MGD: getting to the root cause of dry eye: Review of Optometry 149.6 (2012): 30-37.
Nelson JD, Shimazaki J, Benitez-del-Castillo JM, et al. The international workshop on meibomian gland dysfunction: report of the definition and classification subcommittee. Invest Ophthalmol Vis Sci. 2011 Mar 30;52(4):1930-7.

99

Obstruction

"normal function of these cells [is] to..slough off (desquamate)…this process is interrupted…dead skin cells do not leave the follicle…[due to] excess of keratin"

Blackie, Caroline A., and Donald R. Korb. "MGD: getting to the root cause of dry eye: Review of Optometry 149.6 (2012): 30-37.
Nelson JD, Shimazaki J, Benitez-del-Castillo JM, et al. The international workshop on meibomian gland dysfunction: report of the definition and classification subcommittee. Invest Ophthalmol Vis Sci. 2011 Mar 30;52(4):1930-7.

100

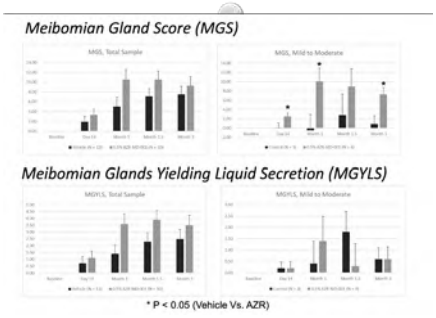
Obstruction

"cohesion of cells will block or "cap"…or clog the sebaceous/oil duct."

101

Selenium sulfide

102



https://azuraophthalmics.com/scientific-meetings

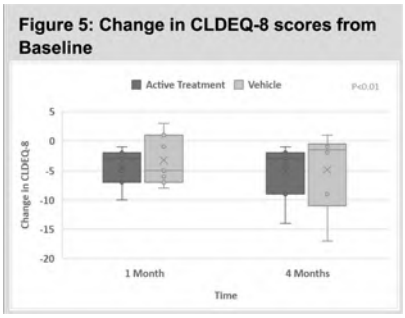
103

Selenium sulfide

"Twice weekly use of a topical ointment…selenium sulfide…appears to improve Meibomian gland[s]…by more than 30% in symptomatic CL wearers after…6 weeks"

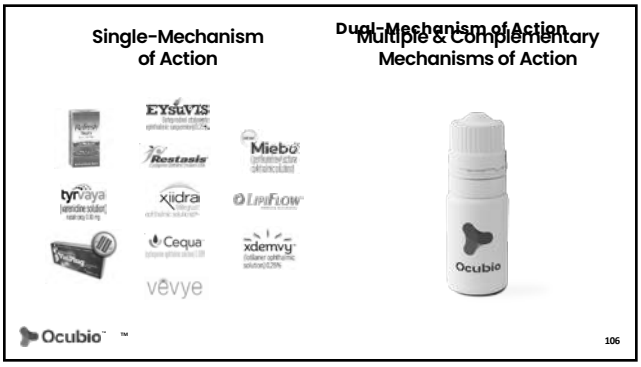
https://azuraophthalmics.com/scientific-meetings

104

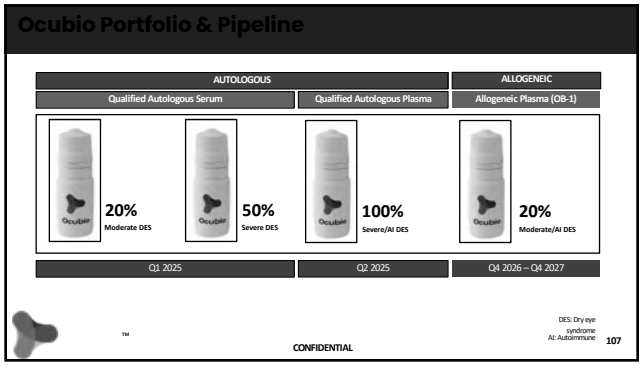


https://azuraophthalmics.com/scientific-meetings

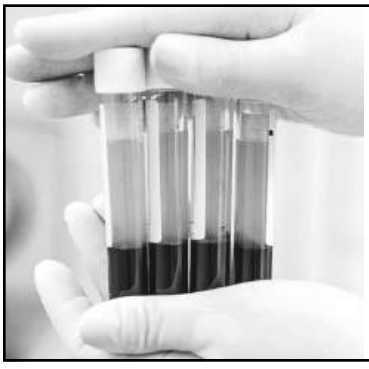
105



106



107



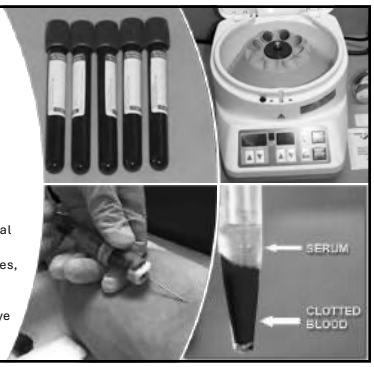
Platelet rich plasma (PRP)

108

Blood Biologics – Platelet Rich Plasma (PRP)

AS, PRP, PRGF

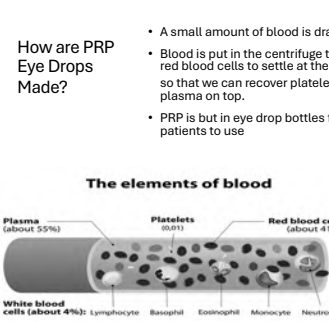
- PRP eyedrops are made from the patient's own blood.
- Most similar to natural tears. They contain high concentration of essential growth factors to help heal dry eyes.
- PRP does not contain any preservatives, additives or stabilizers.
- Unlike medications, there are no side effects or adverse reactions to PRP eye drops.

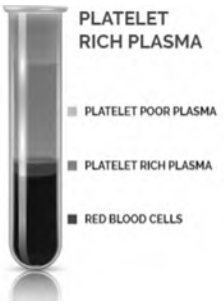


109

How are PRP Eye Drops Made?

- A small amount of blood is drawn
- Blood is put in the centrifuge to get the red blood cells to settle at the bottom so that we can recover platelets and plasma on top.
- PRP is but in eye drop bottles for patients to use





110

DES Treatments

Cyclosporine 0.05%	Inhibits T-cell activation enabling patients to produce their own tears I Decreases inflammatory cytokines I Increases Schirmer scores I Reduces corneal staining I Increases goblet cell density I Reduces the need for ATG
Lifitegrast 0.5%	Inhibits T-cell migration and secretion of inflammatory cytokines I Improves both signs and symptoms at 12 weeks with improvement as early as 2 weeks I Irritation, pain, dysgeusia greater than placebo
Cyclosporine 0.09%	Aqueous, nanomicellar formulation of unpreserved, isotonic, neutral pH fluid that is supplied in unit dose vials I Well -olerated in a 12-week phase 2b/3 study
Cyclosporine 0.1%	Solubilized in a water-free excipient I Indicated for the treatment of signs and symptoms of DED with efficacy demonstrated after 4 weeks of treatment
Topical Corticosteroids	Probably provide small to moderate degrees of symptom relief beyond lubricants I May provide small to moderate degrees of symptom relief beyond cyclosporine
Perfluorohexyloctane	First FDA-approved eye drop targeting tear evaporation in DED

1. Nelson JD, Helms H, Fiscella R, Southwell Y, Hirsch JD. A new look at dry eye disease and its treatment. Advances in therapy. 2000 Mar;17(2):84-93.
2. Baudouin C, et al. Eur J Ophthalmol. 2017 Sep 27;(5):520-30. Expert Opin Pharmacother. 2017 Jun;18(9):885-898. doi: 10.1080/14656566.2017.1329498.

111

DES Treatments

Acoltremon .003%	Neuro Modulator stimulating the TyrpM-8 receptors to stimulate a full basal tear
Varenicline	Neuro Stimulator acting on the nasal branch of the ethmoidal branch of the trigeminal nerve
Lotepredanol .25%	Solubilized in a water-free excipient I Indicated for the treatment of signs and symptoms of DED with efficacy demonstrated after 4 weeks of treatment

1. Nelson JD, Helms H, Fiscella R, Southwell Y, Hirsch JD. A new look at dry eye disease and its treatment. Advances in therapy. 2000 Mar;17(2):84-93.
2. Baudouin C, et al. Eur J Ophthalmol. 2017 Sep 27;(5):520-30. Expert Opin Pharmacother. 2017 Jun;18(9):885-898. doi: 10.1080/14656566.2017.1329498.

112

Cyclosporine ophthalmic solution 0.09%

- A calcineurin inhibitor immunosuppressant indicated to increase tear production in patients with DED
- Nanomicellar formulation (NCELL) encapsulates hydrophobic cyclosporine molecules for improved solubility and penetration through the tear film into ocular tissues
- Addresses *cause* of tear deficiency, not just *symptoms*
- Supports corneal and conjunctival epithelial integrity
- May improve visual quality in symptomatic dry eye patients

1. US Patent 9,937,225 B2. 2. Data on file. Cranbury, NJ: Sun Pharmaceutical Industries, Inc. 3. Cholkar K, Gilger BC, Mitra AK. Topical, aqueous, clear cyclosporine formulation design for anterior and posterior ocular delivery. Transl Vis Sci Technol. 2015;4(3):1-16. 4. Mandal A, Bisht R, Rupenthal ID, Mitra A. Polymeric micelles for ocular drug delivery: from structural frameworks to recent preclinical studies. J Control Release. 2017;248:96-116.

113

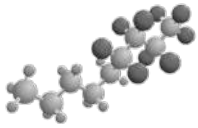
Cyclosporine ophthalmic solution 0.1% dissolved in perfluorobutylpentane

First and only Cyclosporine In PFBP

- In a semifluorinated alkane vehicle (perfluorobutylpentane)
- Approved for the treatment of the signs and symptoms of DED
- To show clinically and statistically significant improvement at day 15
- With no pH or osmolarity
- Can Improve Tear Film and Comfort after Use

114

Cyclosporine ophthalmic solution 0.1%



PERFLUOROBUTYLPENTANE
SFA in cyclosporine ophthalmic solution 0.1%

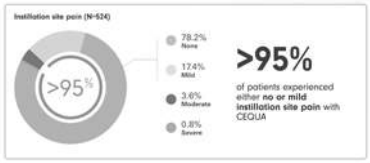
- A preservative-free solution that enhances the penetration of cyclosporine into the cornea, directly targeting inflammation
  - o High-concentration cyclosporine serves as both an **anti-inflammatory and immunomodulator**
  - o Unique semifluorinated alkane (SFA) vehicle spreads evenly across ocular surface and integrates into tear lipid layer
    - **Due to the amphiphilic nature of SFAs, perfluorobutylpentane can effectively dissolve hydrophobic drugs like cyclosporine**
    - **This helps enhanced corneal penetration of poorly soluble drugs**
    - **Detectable in tears for up to 8 hours**

https://vevye.com/hcp/vehicle

115

Cyclosporine ophthalmic solution 0.09%

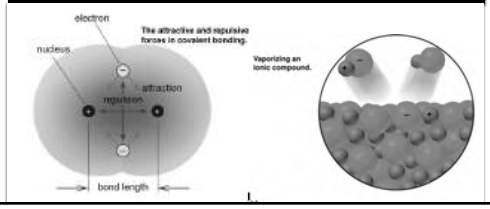
- In clinical trials, most patients found cyclosporine ophthalmic solution 0.09% to be comfortable right from the start
- The first time they tried cyclosporine ophthalmic solution 0.09%, nine of 10 patients reported no or mild discomfort after 3 minutes



1. Tauber J, Schechter BA, Bacharach J, et al. A phase II/III, randomized, double-masked, vehicle-controlled, dose-ranging study of the safety and efficacy of OTX-101 in the treatment of dry eye disease. Clin Ophthalmol. 2018;12:1921–1929.

116

The **only** way to remove the biofilm from inside the oil acini is to literally blow it off of the walls of the duct and the acini
By using DC current to VAPORIZE IT



117