

Contemporary Thoughts on OSD and Dry Eye Management... there's more than just MGD going on!

S. Barry Eiden, OD, FAAO, FSLs

North Suburban Vision Consultants / Keratoconus Specialists of Illinois

International Keratoconus Academy of Eye Care Professionals

AEG Vision

Disclosures

Dr. Eiden

(consulting, lecturer, research, or financial interest*)

Alcon
Allergan
Avellino
Bausch & Lomb / B&L Specialty Vision
Cooper Vision
Euclid
Glaukos
Heru
Lentechs
LENZ
Oculus
Nevakar
Novartis
Sight Sciences
SightGlass
Special Eyes
SynergEyes
Visible Genomics*
VTI
EyeVis Eye and Vision Research*



North Suburban Vision Consultants, Ltd.

Keratoconus Specialists of Illinois / AEG Vision Group

CEO/Co-founder:

International Keratoconus Academy

Adjunct Faculty:

University of Illinois Medical Center, Dpt. of Ophthalmology

Indiana Univ., Illinois, Midwest, UMSL, PCO and SUNY Colleges of Optometry



Ocular Surface Disease & Dry Eye

Surely an Enigmatic Clinical Challenge

- ◆ Defining Dry Eye and OSD
- ◆ Demographics of Dry Eye
- ◆ Impacts optical outcomes of Cataract & Refractive Surgery
- ◆ Quality of life
- ◆ Disease chronicity and characteristics
- ◆ Differential Diagnostic Approach

OSD and Dry Eye Definition

TFOS DEWS II: REFINED DEFINITION OF DRY EYE DISEASE

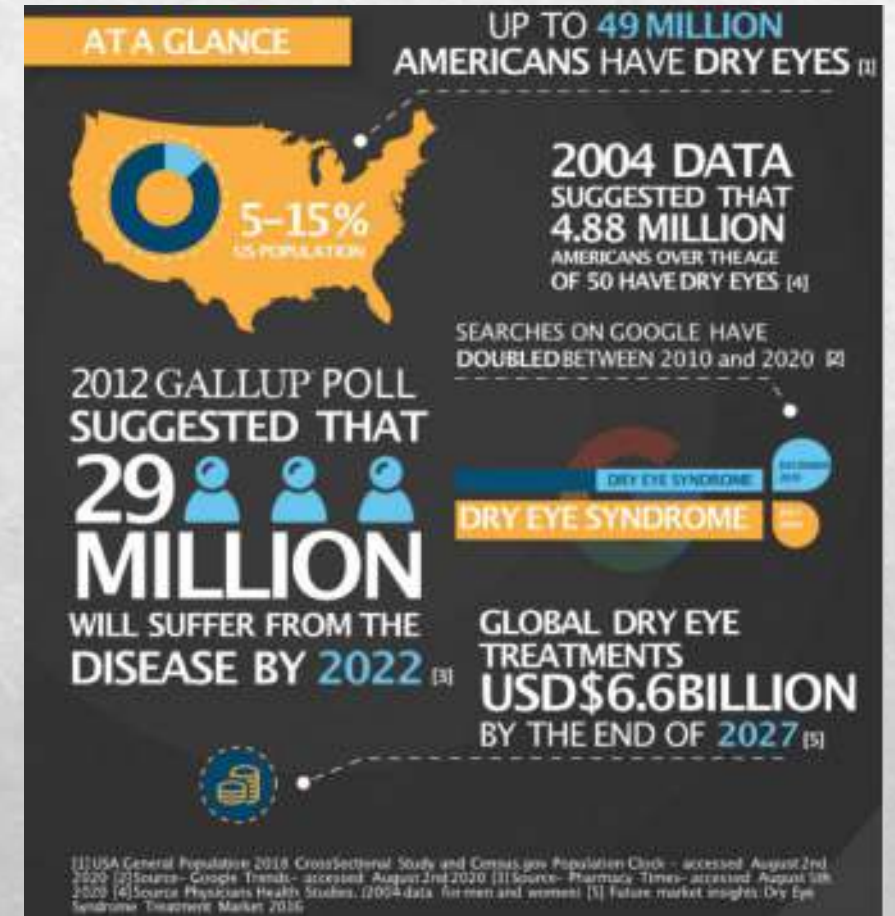
Dry Eye is a multifactorial disease of the ocular surface characterized by a **loss of homeostasis** of the tear film, and accompanied by ocular symptoms, in which **tear film instability** and hyperosmolarity, ocular surface inflammation and damage, and **neurosensory abnormalities** play etiologic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

—The Definition and Classification of Dry Eye Disease, TFOS 2017.

Demographics of Dry Eye

Dry Eye Statistics- At a Glance*:

- Current estimates between **16 million and 49 million** Americans have dry eyes. This is between **5-15%** of the population. [1]
- Dry Eye Disease in the USA **costs over \$55.4 billion to the economy each year** [10]
- Global dry eye treatments are expected to top over USD\$6.6billion by the end of 2027 [5]
- Around **one billion people have Meibomian Gland Dysfunction globally** [9]



* <https://dryeyedirectory.com/dry-eye-statistics/>

Implications of OSD and Dry Eye Disease

- ◆ Comfort Impact
- ◆ Vision Impact
 - ◆ Quality/Stability & Prescribing Implications
 - ◆ Impact on Cataract & Refractive Surgery Outcomes
- ◆ Quality of Life
- ◆ Measurement Tools re: OSD/DED



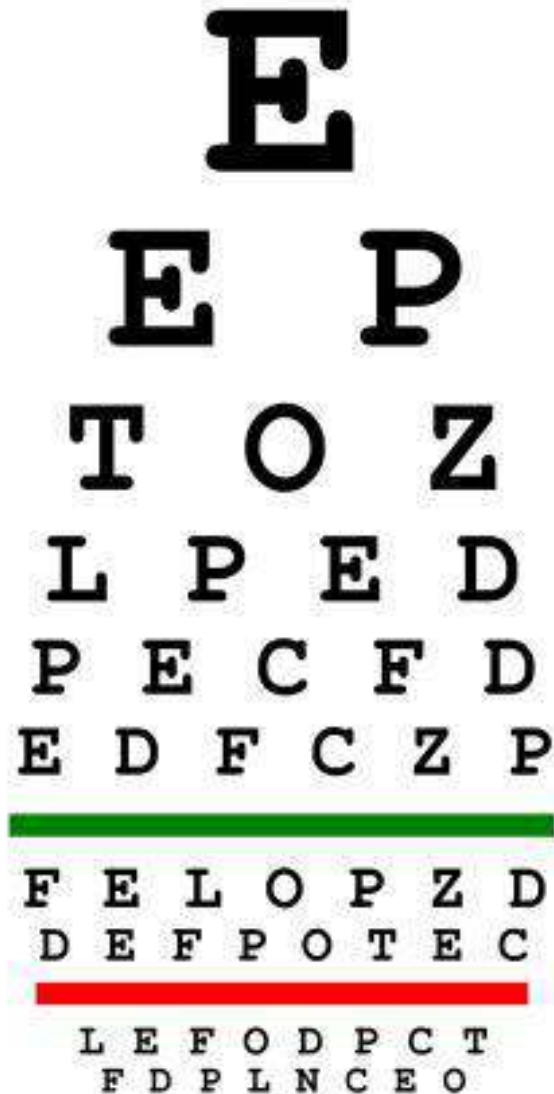
Classic Symptoms of Dry Eye

- ◇ gritty
- ◇ burning
- ◇ itchy.
- ◇ sore.
- ◇ red.
- ◇ blurry.
- ◇ sensitive to light.
- ◇ more watery than normal.
- ◇ contact lens intolerance



HOWEVER:

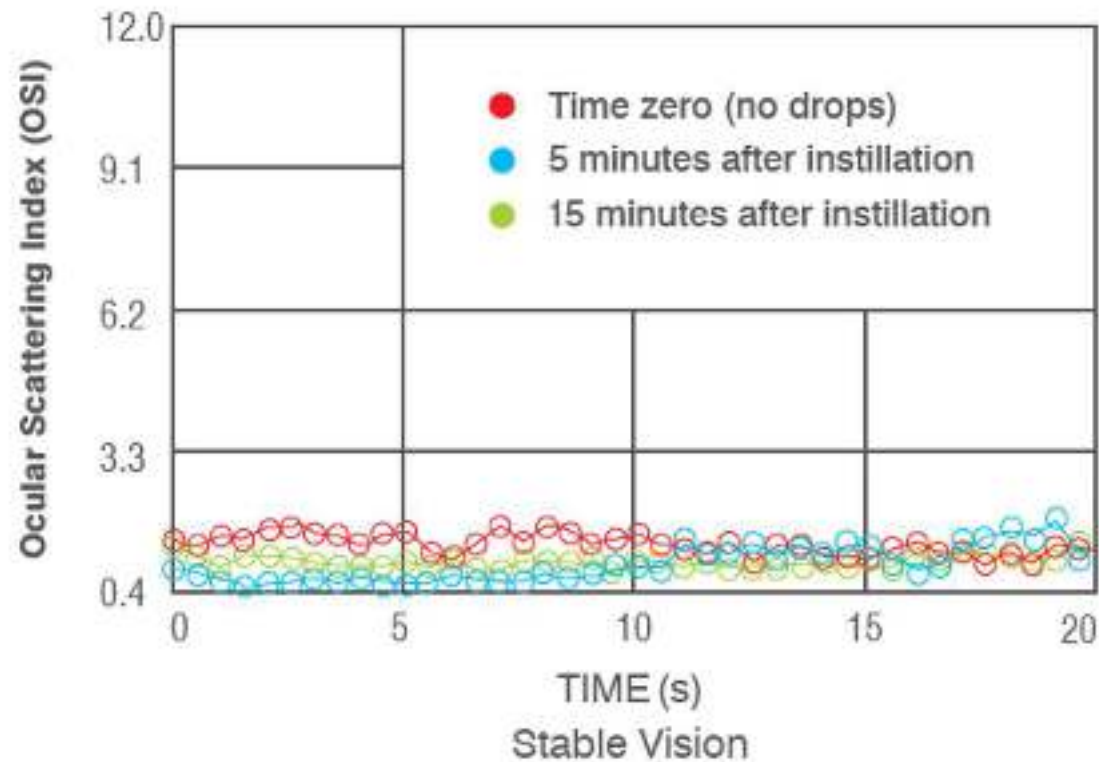
OSD/DED: Impact on Visual Function



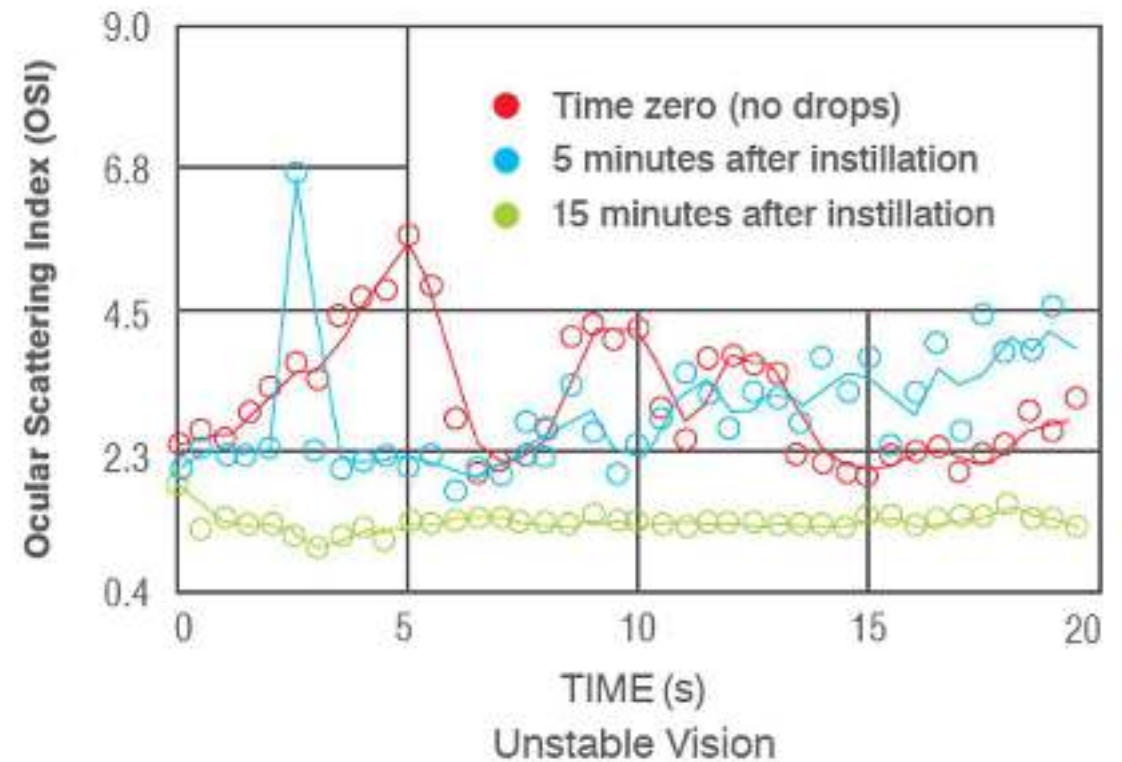
**Dry Eye/OSD
Can Decrease
Visual Acuity
and/or
Quality of
Vision**

Visual Stability & Osmolarity

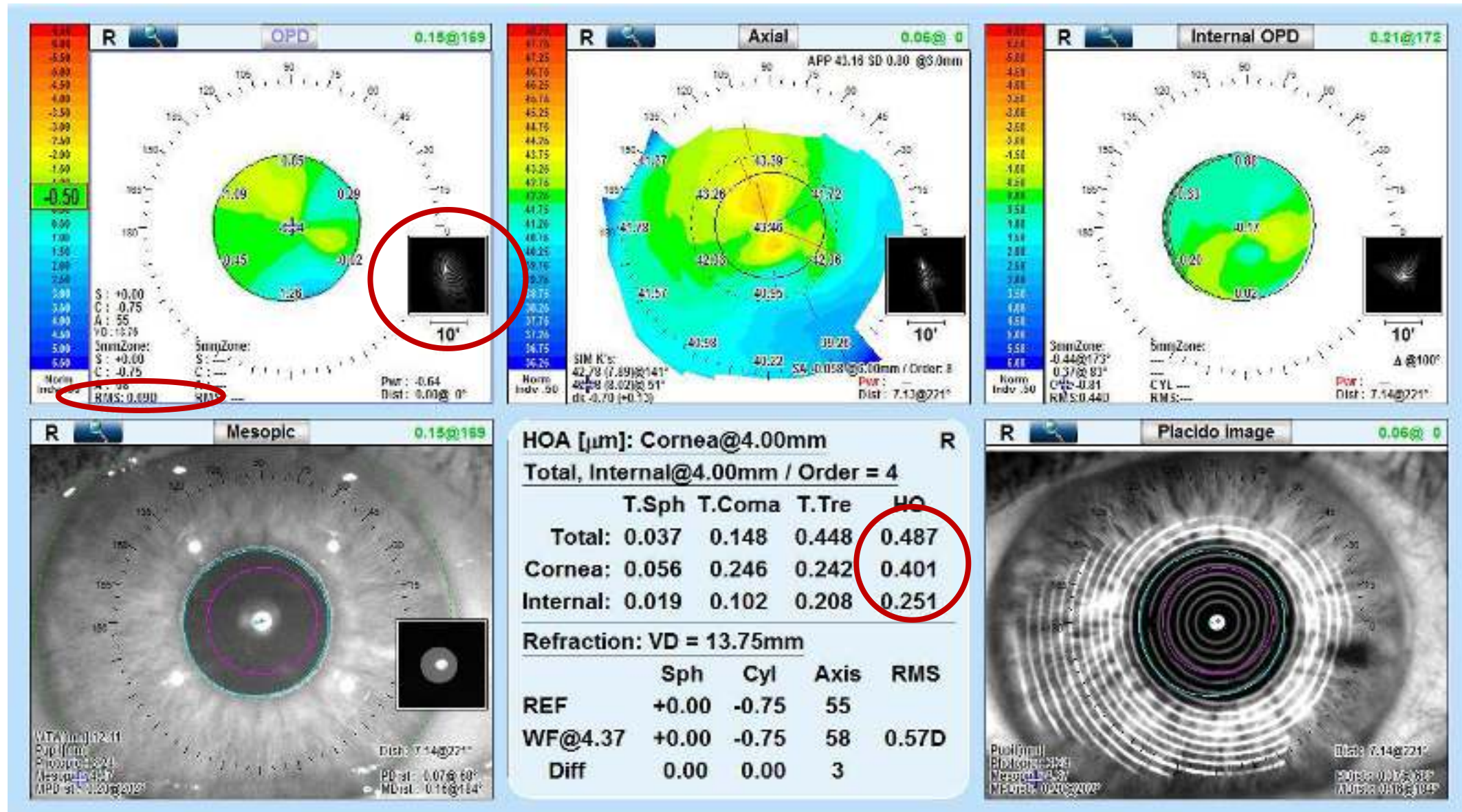
Patient with Normal Osmolarity | 284 mOsm/L



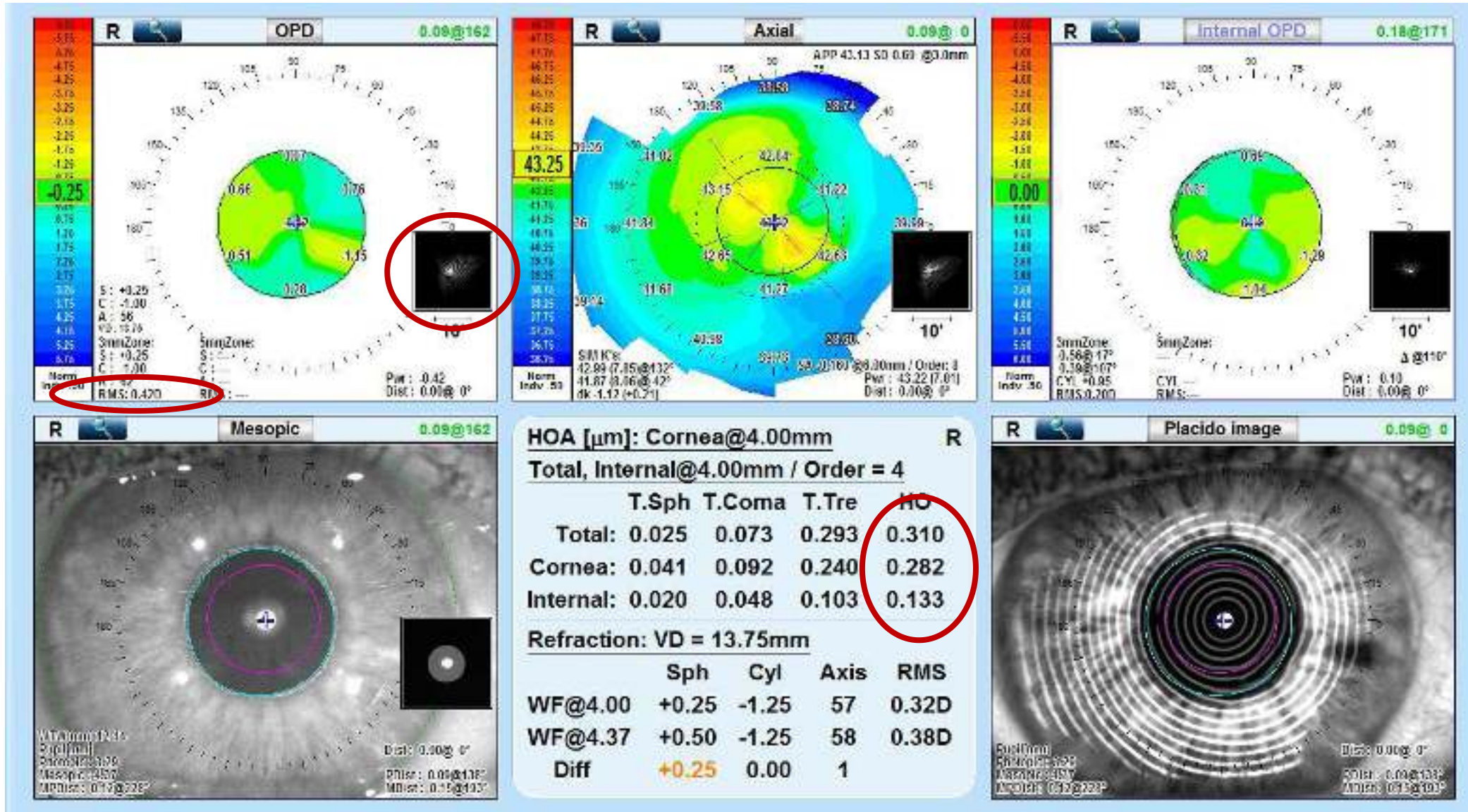
Patient with Abnormal Osmolarity | 326 mOsm/L



Aberrometry in Dry Eye



Reduced HOAs with Initial DE Tx



Impact on Cataract & Refractive Surgery Outcomes

DED / OSD Can Affect Surgical Outcomes & Expectations

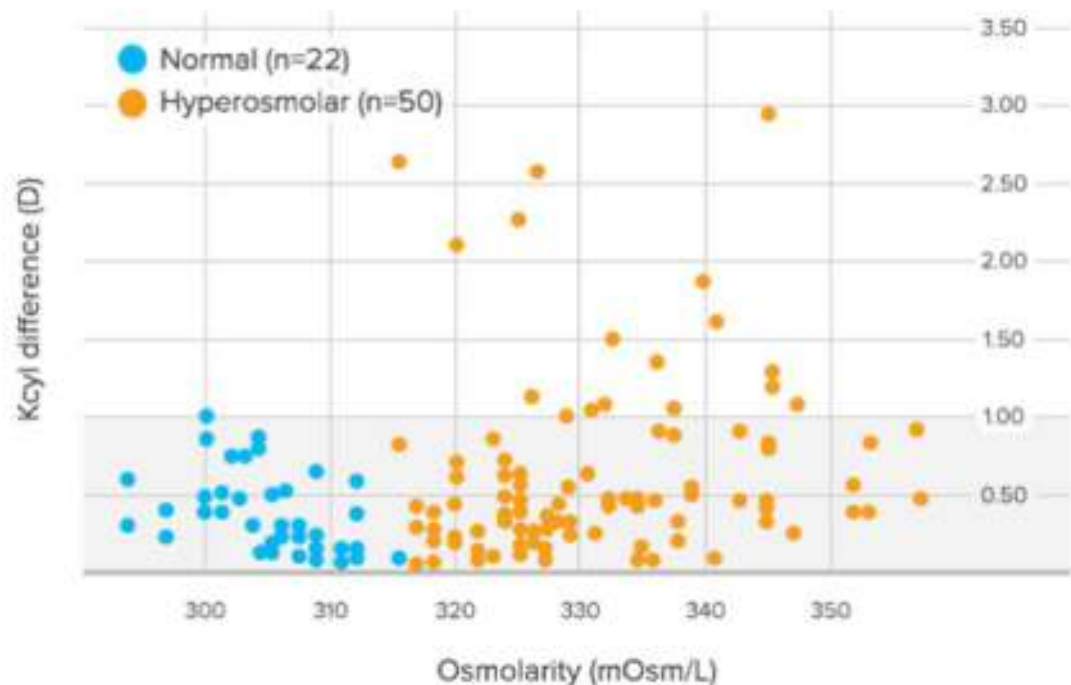


P.H.A.C.O. Study: Prevalence of Dry Eye in Patients Scheduled for Cataract Surgery

- **87% of patients scheduled for cataract surgery were diagnosed with OSD**
- Majority were asymptomatic
- Blurred vision common
- Clinical signs common

If you look.....you will find it

Impact of OSD/DED on IOL Outcomes S/P Cataract Surgery

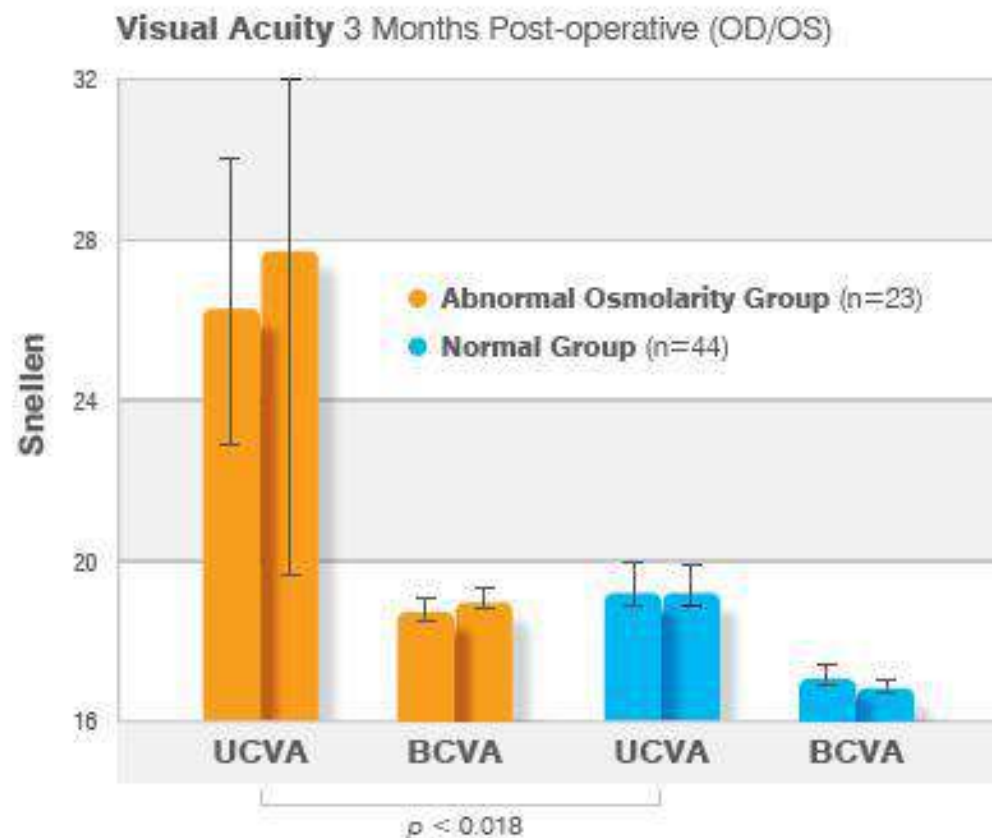


- 17% of hyperosmolar eyes had >1 D difference in K cyl
- 10% had >0.5 D change in IOL power

Undiagnosed and untreated, abnormal osmolarity predicts poor outcomes.³

The uncorrected visual acuity (UCVA) in patients with abnormal osmolarity were significantly worse than normal patients at 3 months post-LASIK.

The gain in visual acuity with post-surgical optical correction (BCVA), among subjects with abnormal osmolarity, is indicative of an unanticipated refractive outcome.³



Patients with abnormal osmolarity demonstrate significant changes in keratometry readings that could impact surgical planning and surgical outcomes.²

References

1. Dawson D, Witzky M, Geeski D, Edelhauser H, Cornad and Sclera. *Duques Ophthalmology*. New York; 2. Epiropoulos AT, Matossian C, Bedy GJ, et al. The effect of tear osmolarity on repeatability of keratometry for corneal surgery planning. *J Cataract Refract Surg*. 2015 Aug;41(8):1673-7.
3. Eldridge D, Donnerfeld E, Bue T, et al. Presurgical hyperosmolarity predicts refractive outcomes. *Association for Research in Vision and Ophthalmology*. 2012 May 6-9; Fort Lauderdale, FL.

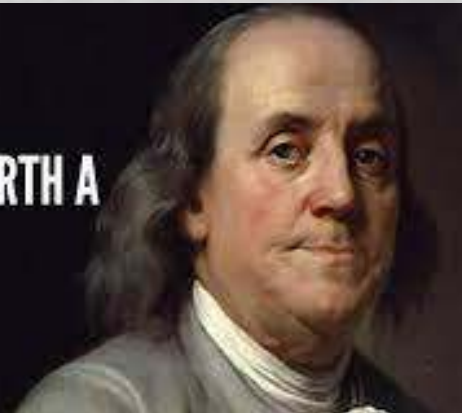


Take Home:

Pre-Surgical Treatment & Management

**AN OUNCE OF
PREVENTION IS WORTH A
POUND IN CURE**

Benjamin Franklin



OSD/DED: Quality of Life / Comorbidities

*Impact of Dry Eye...
it can be significant in many ways!*

▣ **Quality of life**

- DED hampers lives and, in some cases, severely limit activities such as reading, operating a computer, working, driving, and watching television.

▣ **Comorbidities**

- Significantly higher prevalence of medical comorbidities in patients with dry eye disease*:
 - ischaemic heart disease, hyperlipidaemia, cardiac arrhythmias, peripheral vascular disorder, stroke, migraines, myasthenia gravis, RA, systemic lupus erythematosus, asthma, pulmonary circulation disorders, diabetes with complications, hypothyroidism, liver diseases, peptic ulcers, hepatitis B, deficiency anaemias, depression, psychoses and solid tumors without metastasis.

OSD/DED – Disease Characteristics

- ◆ Chronic Disease

- ◆ Characterized by progression and exacerbation & remission episodes

- ◆ Concept of “flare ups”



Validated Questionnaires



- ▶ Repeatability
- ▶ Can track effectiveness of treatment
- ▶ Ease of administration
- ▶ Proven to support dry eye diagnosis

Subjective Measurement Tools for OSD/DED

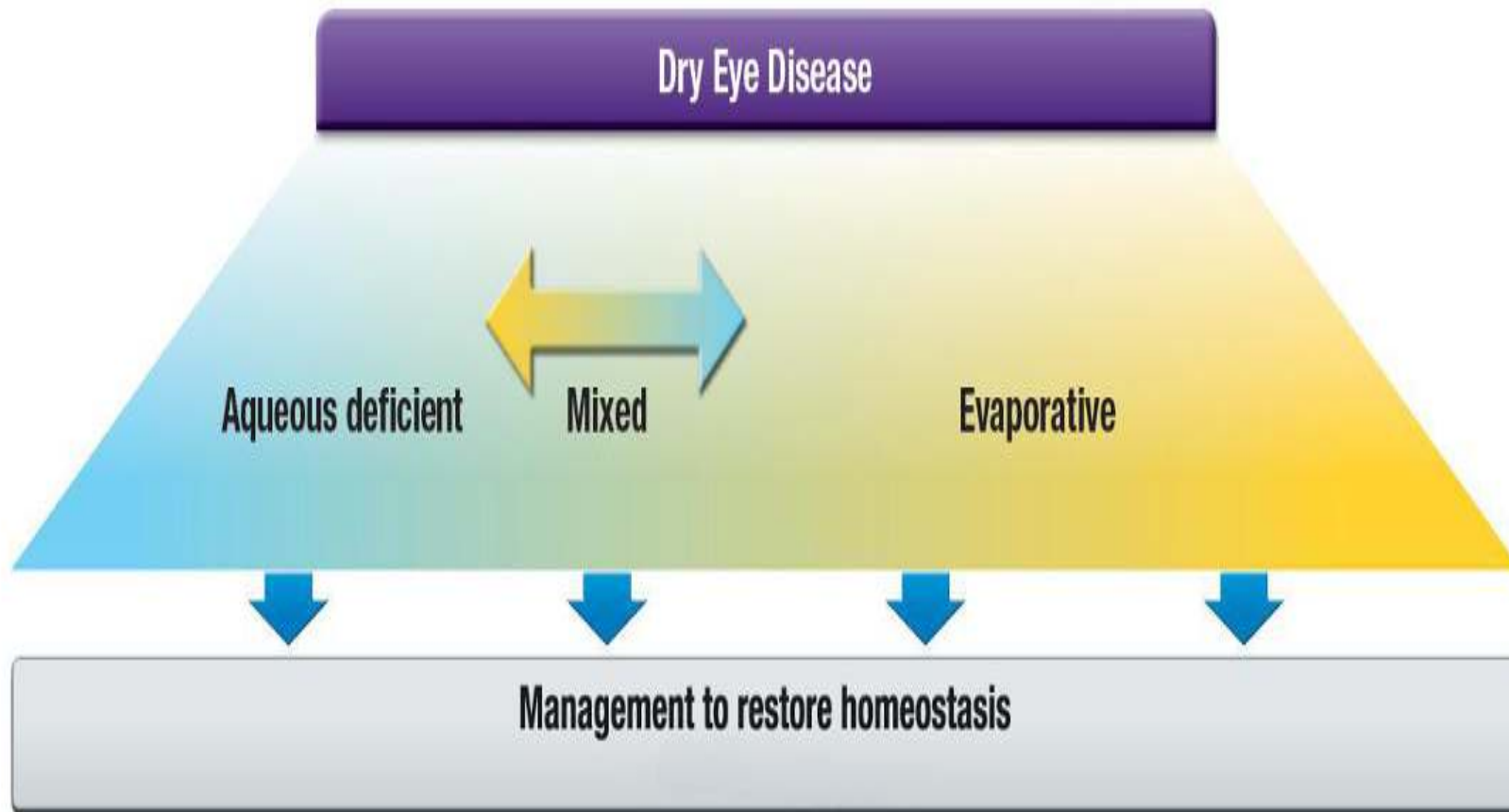
Questionnaires

Notable Standardized OSD/DE Questionnaires:

- Standardized Patient Evaluation of Eye Dryness (SPEED)
- Ocular Surface Disease Index (OSDI)
- Dry Eye Questionnaire (DEQ-5)

Review patient history and medications list

- Antihistamines
- Diuretics
- SSRIs
- +++



OSD/Dry Eye Therapy...

it should be based on the underlying cause(s)

- ◆ Is it due to exogenous causes?**
- ◆ Is it due to anatomical issues?**
- ◆ Is it assoc. w/ blepharitis / MGD?**
- ◆ Is there an inflammatory component?**
- ◆ Is there an aqueous deficiency (ADDE)?**
- ◆ Is there a lipid deficiency – evaporative component (EDE)?**

Key: treat the etiology(s)

Differential Diagnostic Approach

- ◆ Comprehensive history & use of validated questionnaires
- ◆ Detailed Biomicroscopy & anatomical analysis
- ◆ Point of care testing:
 - ◆ Osmolarity/MMP-9
- ◆ Tear Volume/Tear film stability/Meibography

Biomicroscopy & Dry Eye



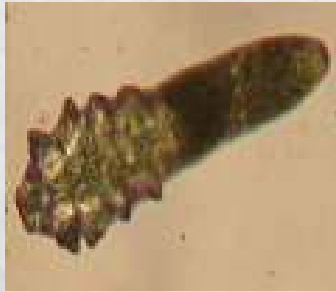
Biomicroscopy and Dry Eye

- ◆ **Blepharitis**
 - ◆ **Anterior**
 - ◆ **Posterior (MGD)**
 - ◆ **Mixed**
- ◆ **Lid Wiper**
- ◆ **Lid Closure / Blink Quality and Frequency**
- ◆ **Conjunctiva**
(Staining, Chalasis, injection patterns)
- ◆ **Tear Quality and Volume**
- ◆ **Corneal Surface**
(EBMD, irregularity, staining, etc.)



Demodex Blepharitis

- *D. folliculorum* + *D. brevis* (ectoparasite: inc. w/ age found in 100% pts over 70!)



- “Cylindrical” debris at lash roots*



*Gao YY et al High prevalence of demodex in patients with cylindrical dandruff. Invest Ophthalmol Vis Sci 2005 46(9)



Posterior Blepharitis / MGD = Primary Evaporative Dry Eye

**Posterior
Telangiactasia**



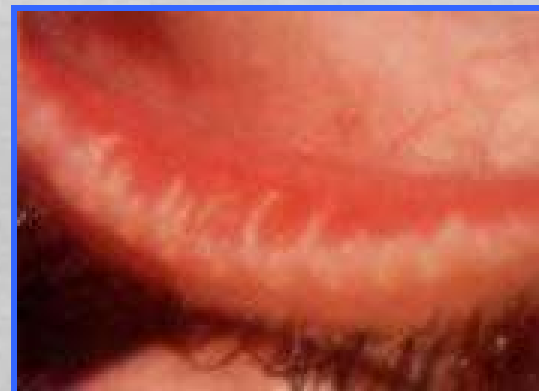
**Obstruction and “capping” of
meibomian gland orifices**



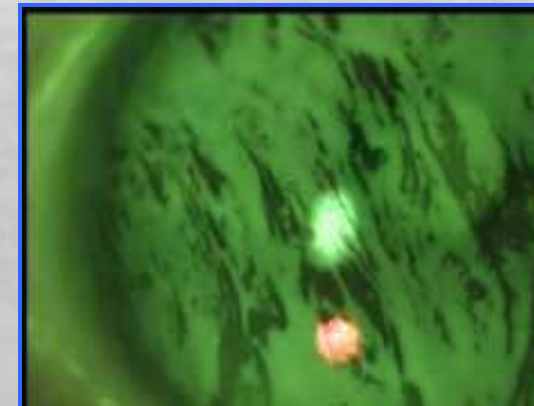
**Meibum “alterations”
•(color / composition)**



Gland drop out



Short TBUT



Untreated MGD Leads to the “Dry Eye Cascade”

Decrease in lipid secretions and LLT

Evaporation increases (4x to 16x)

Secondary decrease in aqueous layer thickness

Unstable tear film

SYMPTOMS

LLT indicates lipid layer thickness.

Advanced Technologies in MGD Evaluation

Meibography

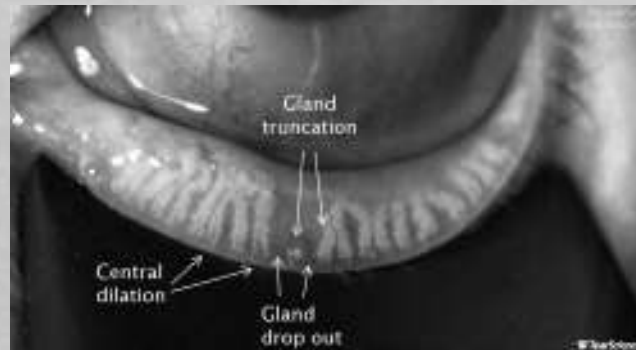
Grade 0 (no loss)

Grade 1 (0 ~ 1/3 loss)

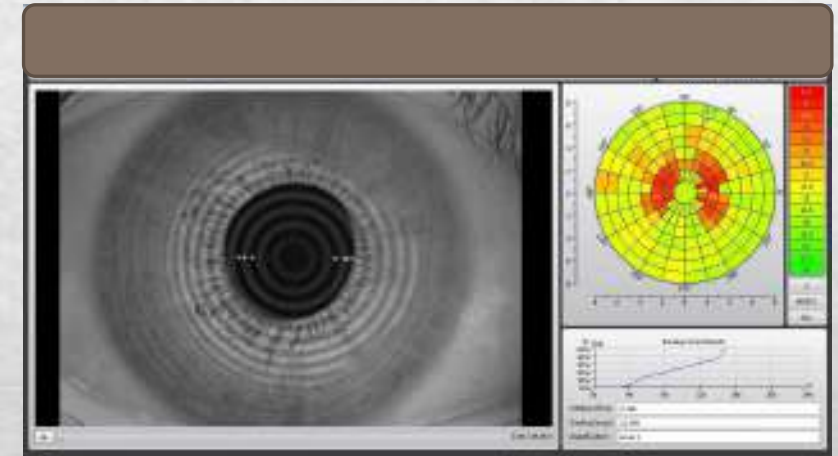


Grade 2 (1/3 ~ 2/3 loss)

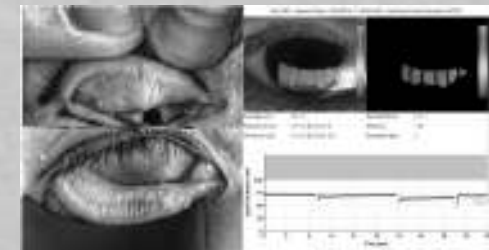
Grade 3 (loss > than 2/3)



Non-Invasive TBUT



Lipid Layer Thickness & Evaluation



Meibomian Gland Dysfunction:

A Prevalent Condition With Consequences

“Meibomian gland dysfunction (MGD) may well be the leading cause of dry eye disease throughout the world.”¹

—*The International Workshop on Meibomian Gland Dysfunction:
Executive Summary*



However:

1. Nichols KK, et al. The international workshop on meibomian gland dysfunction: executive summary. *Invest Ophthalmol Vis Sci.* 2011;52(4):1922-1929.
2. 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.

Look Beyond MGD !

There often is more

◆ Lid Anatomy & Function

- ◆ Incomplete blink, ectropion/lid laxity, lag ophthalmos, +

◆ Conjunctival Surface

- ◆ Conjunctival Chalasis, pterygium/pinguecula, +

◆ Corneal Surface

- ◆ EBMD, nodule, neurotrophic keratitits, +

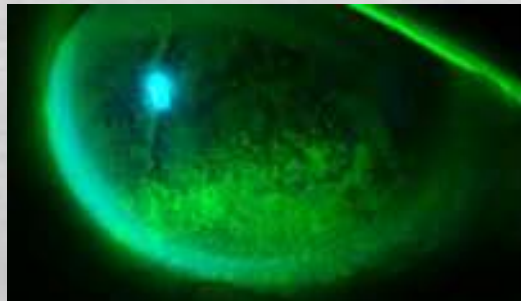
◆ Others:

- ◆ Neuropathic ocular surface pain, medications, environment, & other “masqueraders” of dry eye

Lid Anatomy and Function



Ectropion & lid distention



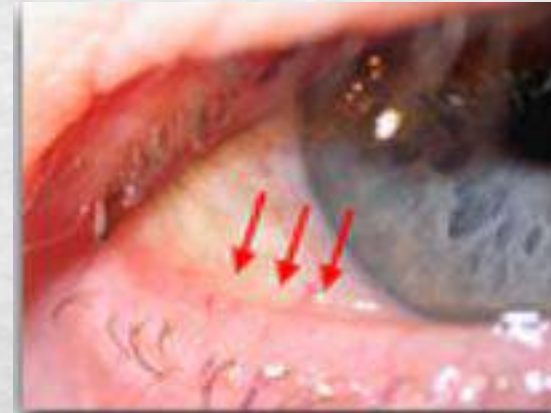
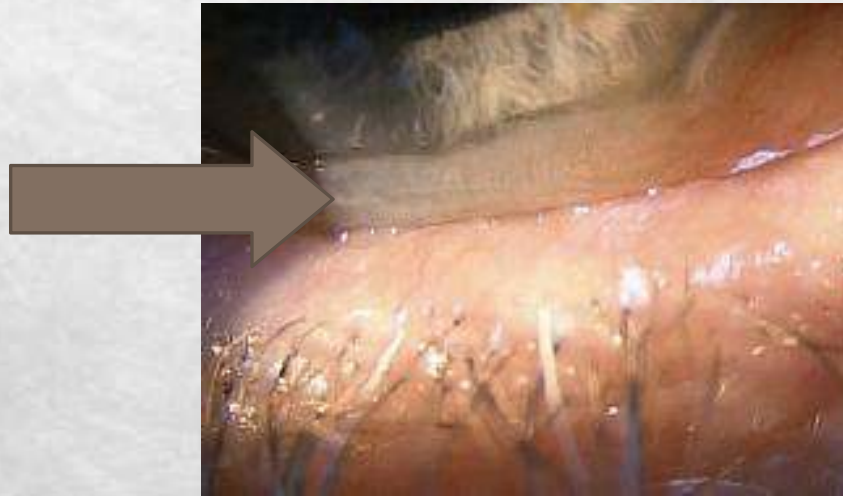
Blackie CA, Korb DR. A Novel Lid Seal Evaluation: The Korb-Blackie Light Test. Eye & contact lens. 2015 Mar 1;41(2):98-100.

Testing for incomplete closure

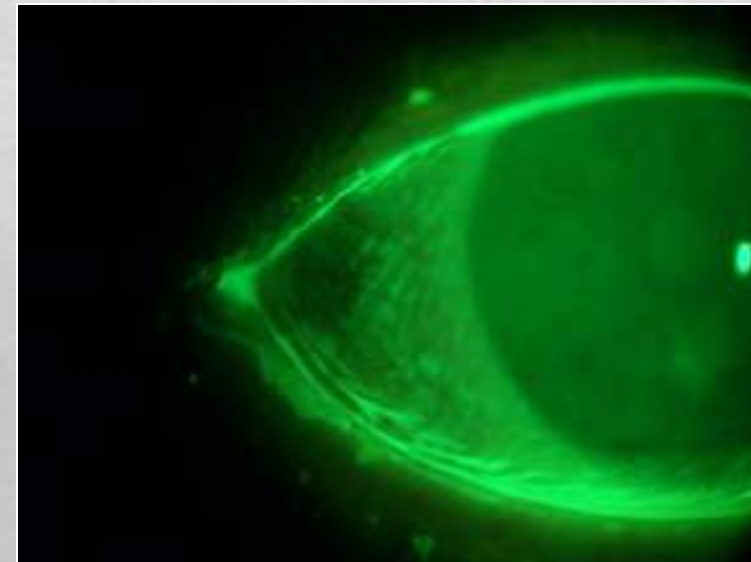
Courtesy Selina McGee OD

consider: **Conjunctivochalasis (CCH)**

(Redundant B. Conj. Folds – typically parallel to lids)

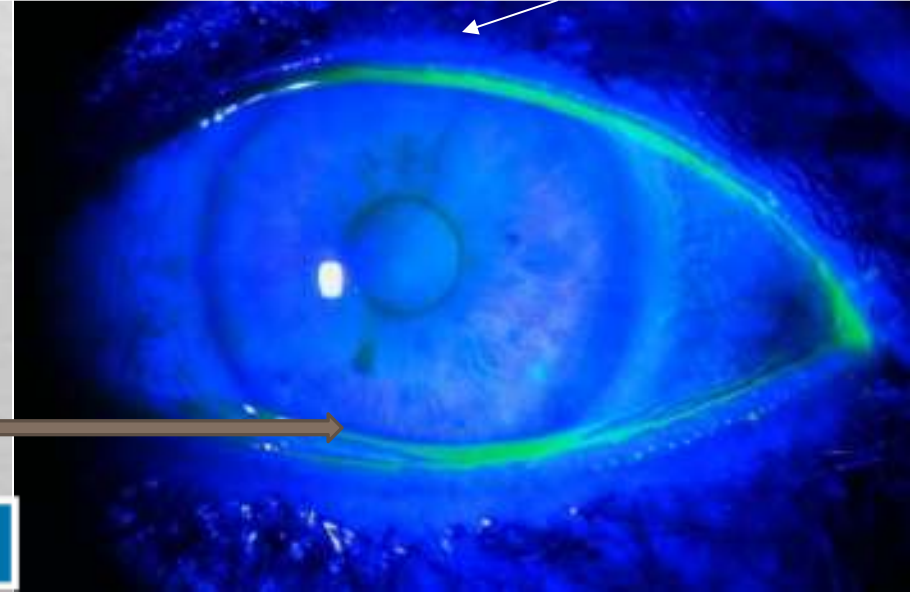
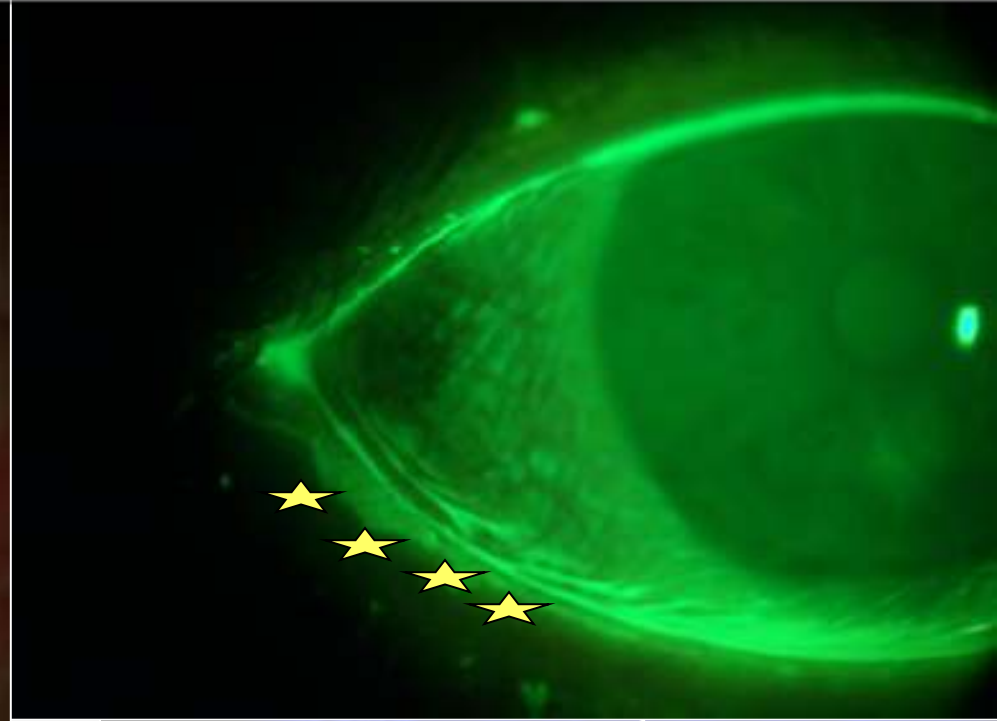
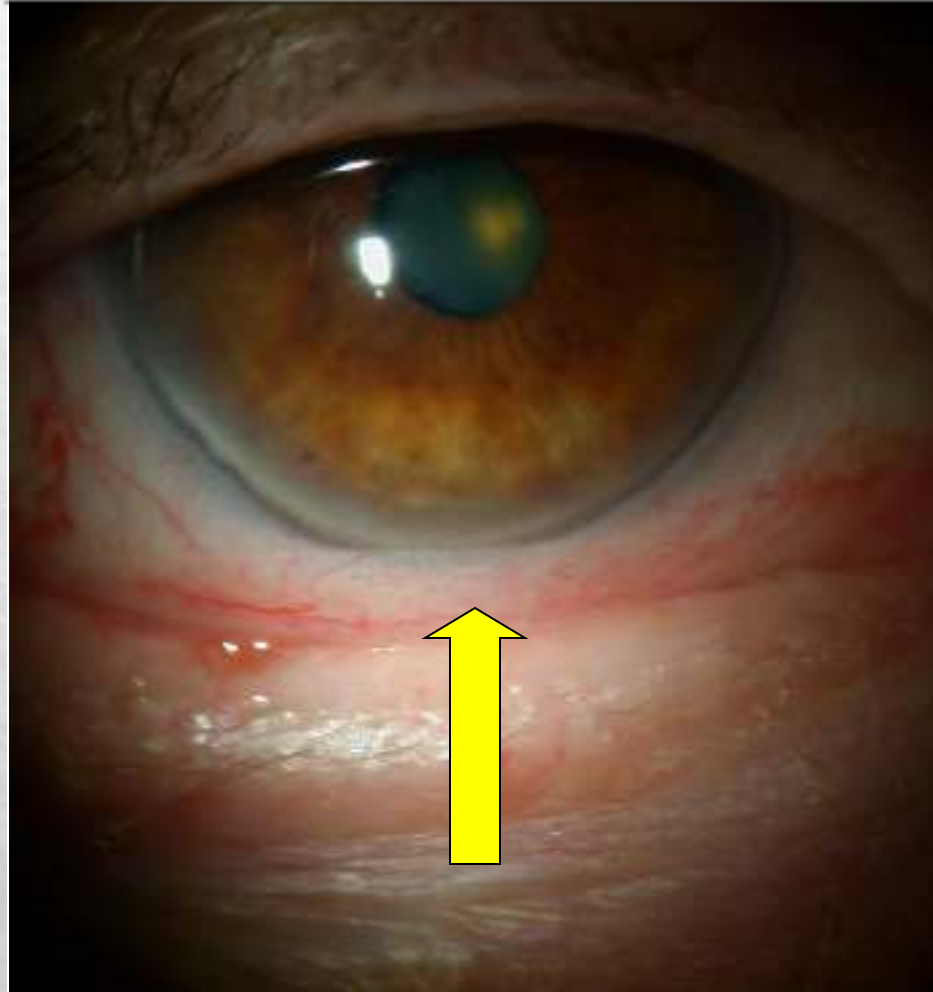


Press Finger to the Lid against the Globe



Courtesy S. C. Tseng

Conjunctival Chalasis



Detect CCh by Fluorescein

How to Verify Conjunctival Chalalasis?



Vigorous Blinking under Slit Lamp



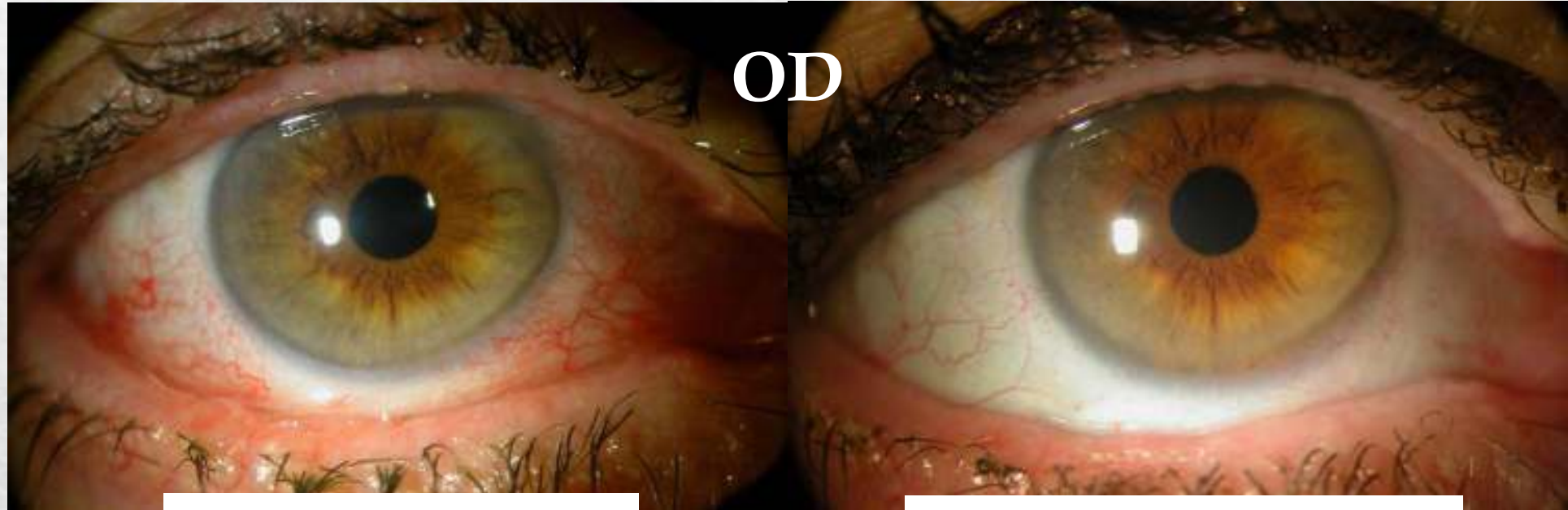
“Tenting” by 0.12 Forceps



Press Finger to the Lid against the Globe

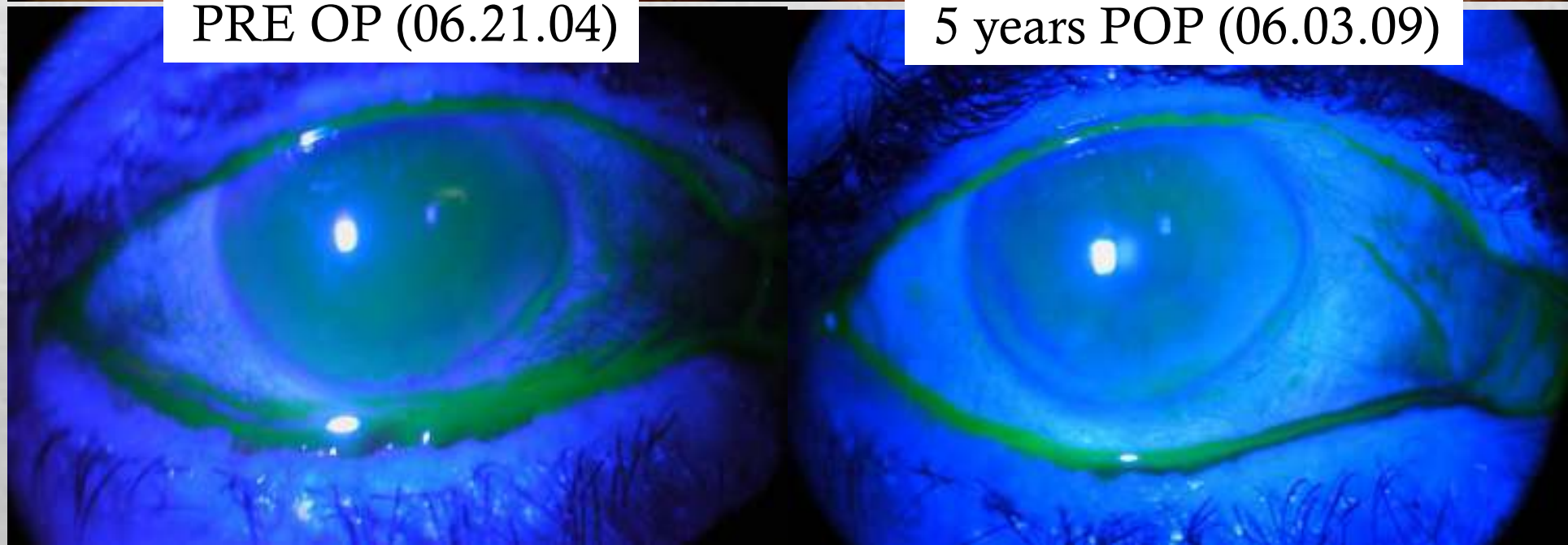


Patient's Benefit from CCh Surgery



PRE OP (06.21.04)

5 years POP (06.03.09)



“Masqueraders” of Dry Eye

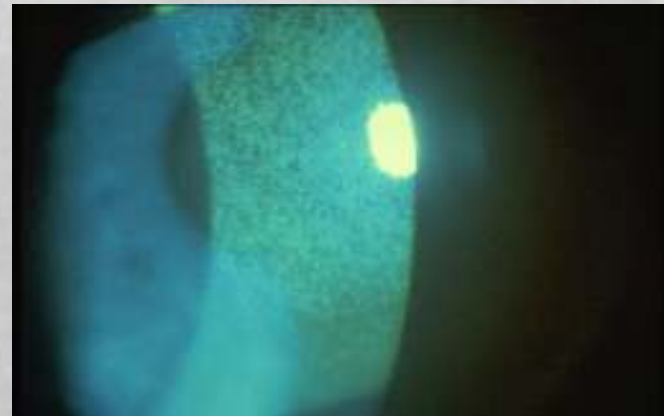
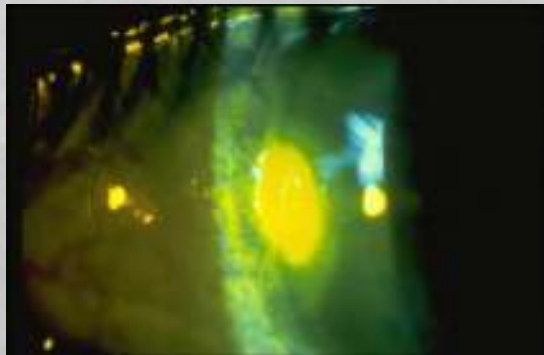
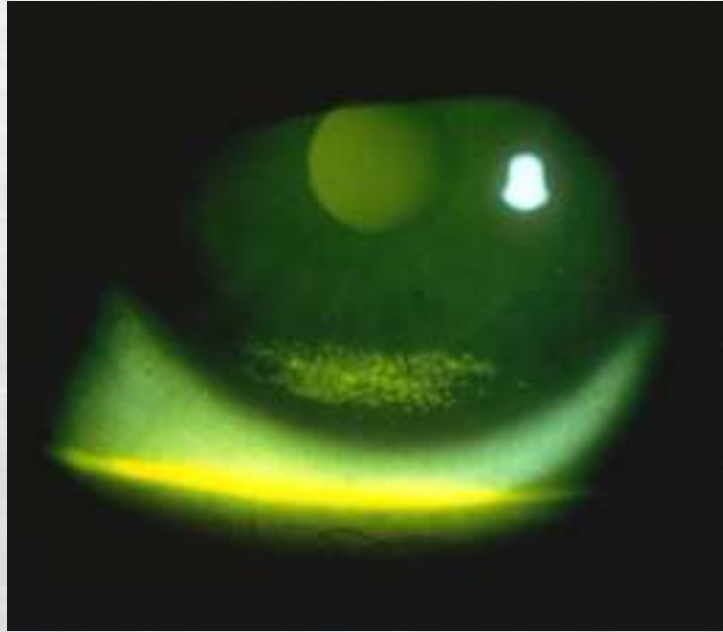
(can mimic or exacerbate sxS)

- ◆ Allergic Conjunctivitis
- ◆ Mucus Fishing syndrome
- ◆ Floppy Eyelid syndrome
- ◆ SLK
- ◆ Corneal / Conj. Disorders: EBMD, CCh, etc.
- ◆ Binocular Vision disorders / Excess Digital Device Use
- ◆ + Others...



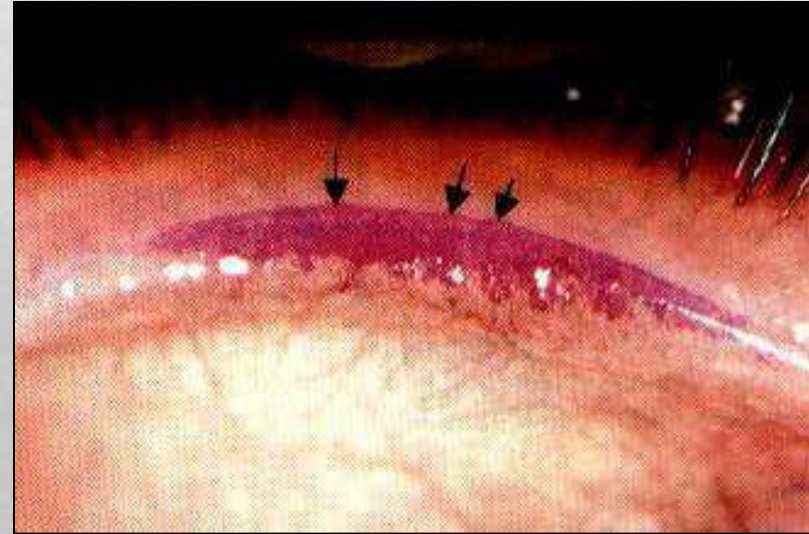
KEY: Consider it All!

Vital Staining



Lid Wiper Epitheliopathy

- **Characterized by presence of damaged epithelial cells on “lid wiper” portion of the palpebral conjunctiva**
- **Lissamine or Rose Bengal for staining in LWE**
- **Staining graded on scale of 0 to 4:
0 = no staining 4 = heavy staining**



1. Korb DR, Herman JP, Greiner JV, et. al: Lid Wiper epitheliopathy and dry eye symptoms. Eye & Contact Lens 31(1): 2-8, 2005.

2. Korb DR, Herman JP, Greiner JV, et. al: Lid Wiper epitheliopathy and dry eye symptoms in contact lens wearers. CLAO J 28: 211-216, 2002.



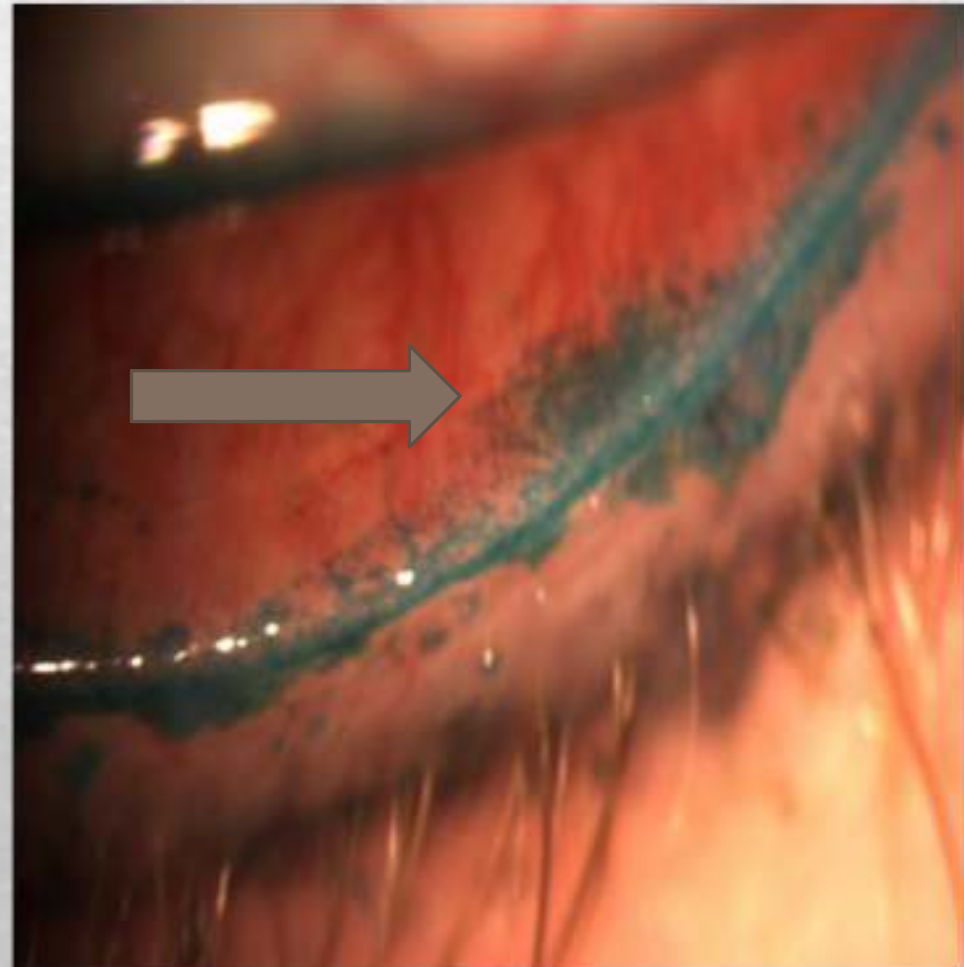
**Staining of the
“lid wiper”
portion of the palpebral
conjunctiva**

Staining of Marx line
(mucocutaneous junction)
of the lid margin
(normal finding)



LID WIPER EPITHELIOPATHY

LWE:
is a result of
friction
(due to insufficient
lubrication – common
to MGD)



Tear Volume Measurement

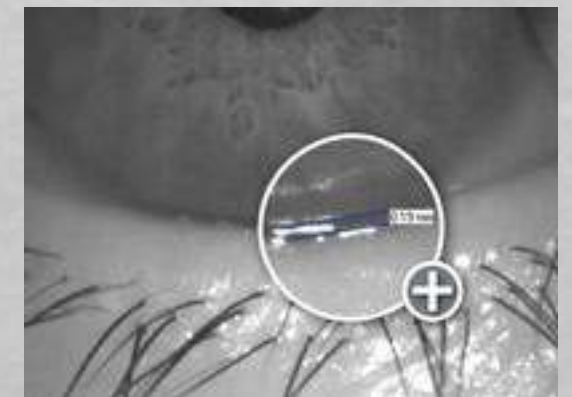
◆ Schirmer Testing



◆ Phenol Red Thread Test



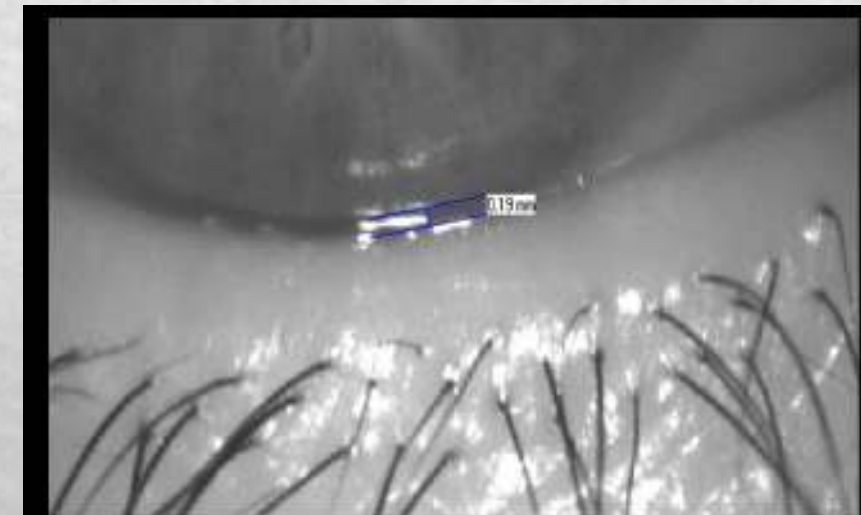
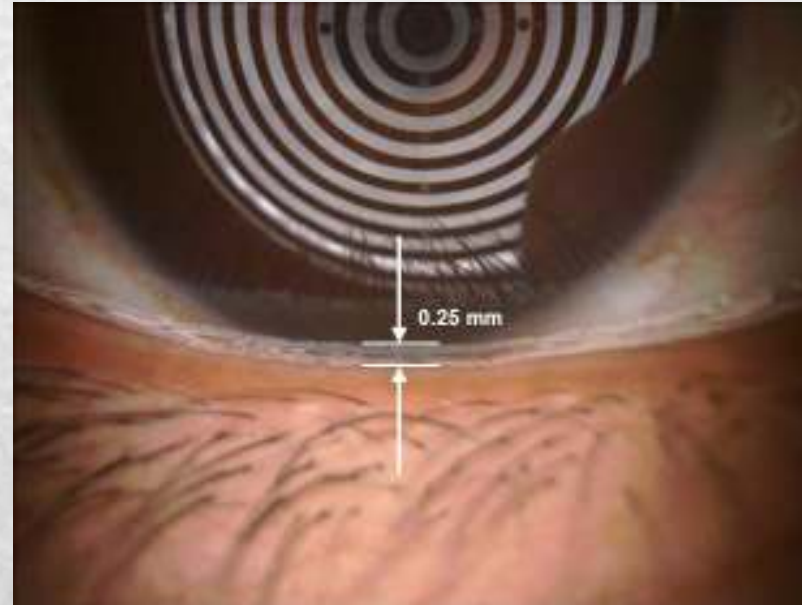
◆ Tear Meniscus Height



Objective Tear Meniscus Height



- Non invasive
- Objective measurement
- Documentation (baseline and change over time)



Normal: >0.25 mm
Abnormal <0.20 mm

Point of Care Testing in OSD/Dry Eye

◆ Osmolarity of Tear Film

◆ Inflammatory Markers (MMP-9s)

Tear Film Osmolarity

- ◆ **Osmolarity** is a measure of the concentration of active particles in a solution

$$\text{osmol/L} = \sum_i \varphi_i n_i C_i$$

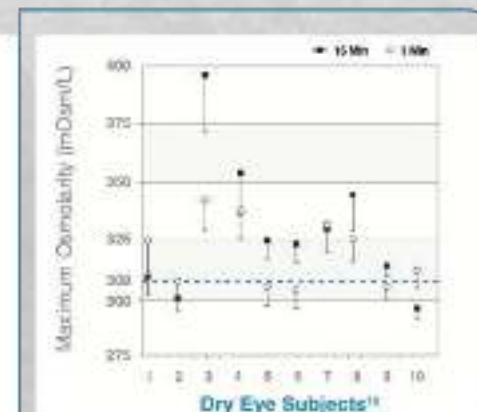
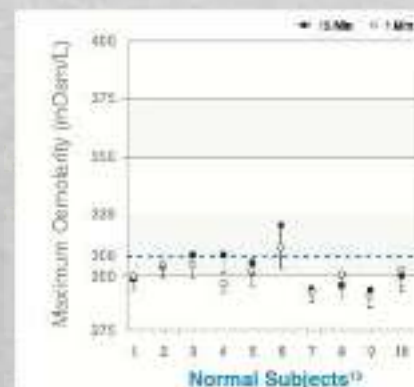
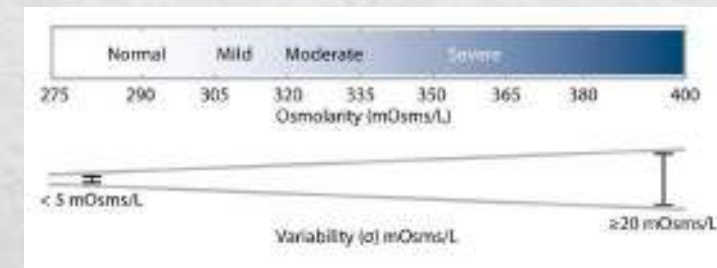
- ◆ Integral in the contemporary definition of dry eye
- ◆ High “**positive predictive value**” with dry eye



Characteristics of Osmolarity

◆ Hyperosmolarity

- ◆ Causes inflammation and apoptosis
- ◆ Leads to a breakdown of homeostatic control causing tear film instability
- ◆ Elevated osmolarity (in higher of 2 eyes) >300 mOsm/L ($>300-308$ brdln. / >308 abnl.)
- ◆ Inter-eye difference = hallmark of DED (> 8 mOsm/L Between eyes)***
- ◆ Variability is the Hallmark of DED



Higher variability in dry eye subjects

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.

Inflammatory vs. Non-Inflammatory Dry EYE

◆ InflammADry detector

◆ Detects **MMP-9** in tear sample

◆ **Matrix Mettaloproteinase (MMP-9)**: inflammatory marker that is known to be elevated in patients with dry eye disease. MMP-9 is a cytokine produced by epithelial cells experiencing inflammation.

◆ Can guide towards initial anti-inflammatory Tx and initial avoidance of punctum plugs



InflammaDry Limits of Detection

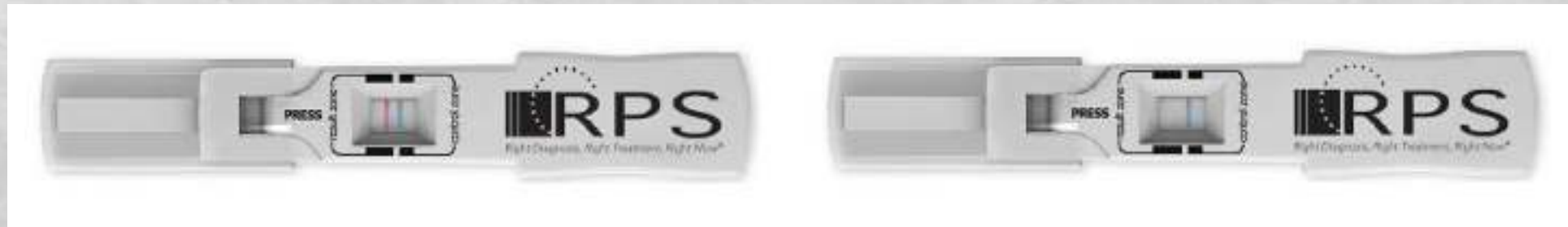
Normal levels of MMP-9 in
human tears range from
3 to 40 ng/mL

POSITIVE TEST RESULT

MMP-9 \geq 40 ng/mL

NEGATIVE TEST RESULT

MMP-9 < 40 ng/mL



*Grade as mild, moderate, and strong positive
(How red)

* Careful for “false negatives” (miss mild or insuf. sample)

Regarding Treatment of Dry Eye Disease

- ◆ **Elevated MMP-9 may predict which patients will respond to anti-inflammatory therapy.**
- ◆ Patients who test positive can be treated with one of the following:¹⁻³
 - ◆ **Cyclosporine**
 - ◆ **Lifitegrast**
 - ◆ **Steroid**
 - ◆ **Azithromycin**
 - ◆ **Doxycycline**



OK, we diagnosed dry eye,

Now what do we do about it???



Targeted Therapeutic Approach

it should be based on the underlying cause(s)

- ◆ **Is it due to exogenous causes?**
- ◆ **Is it due to anatomical issues?**
- ◆ **Is it assoc. w/ blepharitis / MGD?**
- ◆ **Is there an inflammatory component?**
- ◆ **Is there an aqueous deficiency (ADDE)?**
- ◆ **Is there a lipid deficiency – evaporative component (EDE)?**

Key: treat the etiology(s)

So Many Choices – Where to Start? Where to Go?



Inflammatory Control

- ◆ *Topical “soft” Steroids*
(Loteprednol gtt QID 1mo then BID 1 mo)
- ◆ *Cyclosporine A or Lifitegrast BID*
- ◆ *Omega-3 supplements (2gm / day)*
- ◆ *Consideration of low dose Doxy. (25mg)*



Eiden's

“Anti-inflammatory Protocol”:



- ◆ **Loteprednol gtts QID 2 weeks:**
- ◆ **If + Response: begin Lifitegrast or Cyclosporine BID**
- ◆ **Continue Loteprednol BID 1 mo. Then D/C if L, cont. to 2mo. if C – once D/Cd then cont. L or C BID ongoing.**
- ◆ **Omega 3: 1 gram 1 week then increase to 2 grams ongoing**

Punctum Occlusion / Plugs

- ◇ *After* control of inflammation
- ◇ *Diagnostic plugs (collagen)*
- ◇ *Permanent plugs (silicone)*
- ◇ *Extended duration plugs (collagen)*



MGD/Evaporative Dry Eye Therapy

- ◆ Tear Stabilizing OCT agents (hyaluronate/glycerine)
- ◆ Home Heat Tx
- ◆ In Office Deep Heat and Expression Tx
- ◆ Topical Anti-inflammatory Agents (short and long term)
- ◆ Oral Anti-inflammatory Option
- ◆ IPL / LLLT



Naso-Lacrimal Stimulation Tx



◆ Varenicline Soln. Nasal Spray

- ◆ Approved for Tx of S/Sxs of DED
- ◆ Cholinergic agonist - believed to activate the trigeminal parasympathetic pathway via the nose, resulting in increased basal tear film production
- ◆ Stimulates production of all 3 tear layers
- ◆ No known contraindications / few non-serious side effects:
Sneezing (>80%), throat or nasal irritation and cough (5-16%)
- ◆ **Synergistic with other treatment modalities**



OSD/DED “Flares”



- ◆ Acute Exacerbations / Recurrence
- ◆ Tx: Short term steroid (FDA approved for short term tx of dry eye – 2 weeks = “flares”)
- ◆ Loteprednol etabonate 0.25% suspension
(W/AMPPLIFY® NANOPARTICLE DRUG DELIVERY TECHNOLOGY for enhanced ocular surface tissue distribution)

Autologous Serum

for treatment of more severe DED

◆ **Blood serum contains critical elements found in healthy tears for epithelial health:**

- ◆ EGF (epidermal growth factor)
- ◆ Vitamin A
- ◆ TGF beta

◆ **Elements missing or highly reduced in severe dry eye (SS, SJS, etc.)**

◆ **Critical elements **NOT** found in AT's**



AUTOLOGOUS SERUM DROPS

- Closest natural tear supplement available
- Biomechanical qualities
 - Lubrication
- Hydration
- Similar biochemistry
 - pH
 - Osmolarity
 - Albumin
 - Epithelial growth factor
 - Transforming growth factor- β 1
 - Vitamin A
 - Lysozyme
 - Surface Immunoglobulin A
 - Fibronectin and cytokines

Table 1. Comparison of the biochemical properties of normal human tears and serum^(2,5)

	Tears	Serum
pH	7.4	7.4
Osmolarity	298	296
EGF (ng/ml)	0.2-3.0	0.5
TGF- β (ng/ml)	2-10	6-33
Vitamin A (mg/ml)	0.02	46
Lysozyme (mg/ml)	1.4	6
IgA (μ g/ml)	1190	2
Fibronectin (μ g/ml)	21	205

EGF= epithelial growth factor; TGF= transforming growth factor

G Quinto, M Campos, A Behrens. Arq Bras Oftalmol. 2008; 71 (6 Supl):47-54

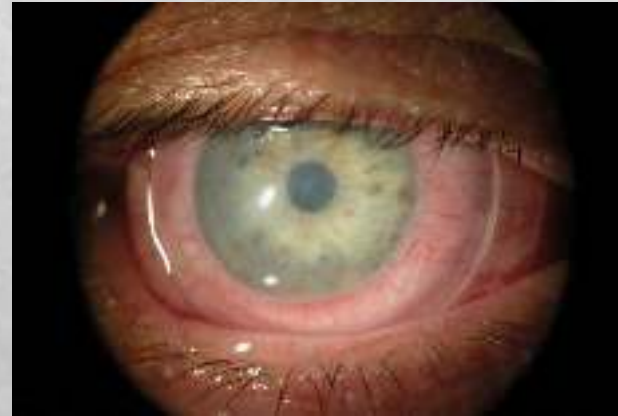
Amniotic Membrane For Tx of OSD



ProKera is a disk of amniotic membrane that is applied like a bandage contact lens.



When Used?
To promote healing
Severe Dry Eye w/Keratitis
PED's, Filaments, etc.



Tape Tarsorrhaphy



Taping the eye lid



Key Take Aways on OSD/DED

- ◆ Highly prevalent
- ◆ Highly impactful on comfort/vision/QoL ++
- ◆ Multifactorial
- ◆ Chronic disease with remissions and exacerbations
- ◆ Identify primary and secondary drivers
- ◆ R/O masqueraders
- ◆ Target therapy



Dry Eye Disease...
So common and so complex!

Thank You!

S. Barry Eiden, OD, FAAO



North Suburban Vision Consultants Ltd.
Ours is a 20/20 Commitment to Eye Care Excellence!