



#### 2018 Innovations and Updates Ocular Surface Disease

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#### isclosure

- Alcon
- CIBA
- Odyssey Medical
- Science Based Health
- Shire
- TearLab

#### Any product superiority mentioned during this presentation will be supported by scientific studies and papers

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 Having issues with simple tasks like...
 Reading
 Computer
 Driving
 Experiencing
 Tired eyes
 Unstable vision

No help in sight



### Course Objectives

Examine quality of life issues linked to DED Review basic demographics of DED Review salient data from landmark DED studies Discuss current models of pathophysiology DED Review new therapy, concepts, technology DED Informed decisions and prescribing strategies

### Do Doctors and Patients Perceive Dry Eye Differently?

Severity of Symptoms	<u>DIS. DIY EYE PIS.</u>
<ul> <li>Symptoms are severe.</li> </ul>	9% 19%
	20%
<ul> <li>symptoms moderate</li> </ul>	170/ 200/
Symptoms mild	47% 23%
<u>summa</u>	<u>п</u> Х
<ul> <li>Patients w/ dry eye experienc</li> </ul>	e more symptoms than
doctors would expect from cl	linical signs
Signs & symptoms of OSD offer	n have no correlation
• orgina a symptom a or 000 onto	<u>n nave <u>ne conciation</u></u>

### Chalmers R.L. et al. Grading Dry Eye Severity: A Comparison of Clinician Self-Assessment. ARVO 2002





### Dry Eye on C Quolity of Life 20t value for <u>mild</u> dry advector and the

- QOL value for <u>mild</u> dry eye was roughly equivalent to that of psoriasis.
  - OOL value for <u>severe</u> dry eye equivalent to that assigned to <u>severe</u> angina or <u>disabling</u> hip fracture.

end WD. The impact of dry eye on quality of li

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### Dry Eye Demographics USA

- Analyzed data from 75,000 participants in National Health and Wellness Survey
- #1- Have you ever experience dry eye ?
- #2- have you been Dx'd by physician If no, end of the evaluation
  - If yes, have you experienced ..
  - Pain, light sensitivity, a gritty sensation, a feeling of a foreign body or sand in the eye, itching, redness, and blurring of vision

Farrand KF et al. Prevalence of Diagnosed Dry Eye Disease in the United States Among Adults Aged 18 Years and Older. Am.Journ. of Ophth. October 2017









#### 1995 National Eye Institute (NEI) Industry Dry Eye Workshop

#### Definition of Dry Eye

"...a disorder of the tear film due to tear deficiency or excessive evaporation, which causes damage to the interpalpebral ocular surface and is associated with symptoms of ocular discomfort."

# 1995 National Eye Institute (NEI) Industry Dry Eye Workshop

- Disorder of the tear film Ocular surface damage Tear deficiency
- Excessive evaporatien 0
- Associated symptoms of ocular discomfort

## Industry Dry Eye Workshop



### Dry Eye Workshop 2007 **Definition Dry Eye**

.. a multifactorial disease of the tears and ocular surface that results in symptoms of discomfort, visual disturbance, and tear film instability with potential damage to the ocular surface. It is accompanied by increased osmolarity of the tear film and inflammation of the ocular surface."

Dry l	Eye Works	hop (DE'	WS) 2007
<ul> <li>Multifacto</li> <li>Affects tea surface</li> <li>Increased</li> <li>Discomfol</li> </ul>	rial disease ars & ocular l evaporation rt	<ul> <li>Tear film</li> <li>Potentia surface</li> <li>Increase osmolar</li> </ul>	n instabilit <del>);</del> al damage ocular ed tear film
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### Dry Eye Workshop II- 2017 **Definition Dry Eye**

...a multifactorial disease of the tears and ocular surface that results in symptoms of discomfort, visual disturbance, and tear film instability with potential damage to the ocular surface. It is accompanied by increased osmolarity of the tear film and inflammation of the ocular surface?" ve

### Dry Eye Workshop II- 2017

- Multifactorial disease
   Increased tear osmolarity of tears and ocular surface
- Discomfort
- Visual disturbance 0
- Tear film instability
- Homeostasis: the tendency toward a relatively
- physiological processes.
- ocular surface damage
- Ocular surface inflammation
- Impaired homeostasis of ocular surface

stable equilibrium between interdependent elements, especially as maintained by





### Homeostasis Diabetes

- Inability to maintain blood glucose within a physiologic range
- Diabetes represents a disruption of "energy homeostasis"



### Homeostasis: Dry Eye

- Inability to maintain tear film osmolarity within a physiologic range
- Dry eye results in or from "disruption of ocular surface homeostasis"



### Step 1-Determine Primary & Secondary Causes for DED

- Aqueous tear deficiency (ATD)
- Lipid anomaly dry eye (LADE) evaporative dry eye i.e. meibomian gland dysfunction (MGD)
- Allergic dry eye (ADE)
- Lipid surface/blinking anomalies dry eye (LSADE)
- Prevalence: LADE > ADE > LSADE > ATD

Albietz JM. Prevalence of dry eye subtypes in clinical optometry practice.. Optom Vis Sci. 2000 Jul;77(7):357-63.

### Strategies For Diagnosis: Conventional Testing

- Tear film break-up time (TBUT)
- Measures tear film stability
- Evaluates the relationship between tear lipids & mucins.
- Conventional (fluorescein)
- Use yellow filter
- Use non-preserved, compounded fluorescein

#### New Strategies For Diagnosis: Conventional Testing

- Tear meniscus (OCT)
- Better than SLE but no definitive levels of "normal"
- Inferior tear meniscus correlates better than superior with w/ TBUT & fluorescein staining, Schirmer test
- Corneal staining-
- Non-preserved stains in micro-filtered syringes =better reliability, ease of instillation
- Combination products reduce chair time



#### Sterile Preservative-Free Stains

- From a compounding pharmacy
- Much more consistent staining
- TBUT- No interference from preservativ
- Quicker- saves time
- 🔸 Easy

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### Tear Film Osmolarity

- 1979- Gilbard & Farris describe association between dry eye & elevated tear film osmolarity
- 1983- Gilbard & Farris propose using hypoosmolar drops to treat dry eye syndrome
- Early dry eye studies using tear film osmolarity conducted with freezing point depression
- 2010- Tomlinson et al find good correlation between tear film osmolarity measured by electrical impedance & freezing point depression









### TearLab

#### Composed of:

- Base unit
- Pens to hold test card
- Test cards
- Quality assurance materials
  - Test solutions
  - Standard test cards
- Determines Tosm using tear impedance (electrical resistance measured in Ohms)





### **TearLab Discovery**

- Determines Tosm MMP-9
- Both markers for OSD and inflammation
  - Currently in FDA approval process Expected availabilitysoon!







#### International Workshop Studiess in Dray Excention Nichols et al.

- Proposed mechanism for pathophysiology of
- MGD
   Outlined specifics @ normal composition of MG secretions
- Classified MGD based on secretion
  - Low delivery (hypo-secretory or obstructive)
  - High delivery (hyper-secretory)
- Concluded that MGD is the leading cause of DED

#### Landmark Studies in Dry Eye International workshop on meibomian gland dysfunction Nichols

"MGD is "a chronic, diffuse abnormality of the meibomian glands, commonly characterized by terminal duct obstruction and/or qualitative/quantitative changes in the glandular secretion. It may result in alteration of the tear film, symptoms of eye irritation, clinically apparent inflammation, and ocular surface disease".

#### Landmark Studies in Dry Eye International workshop on meibomian gland dysfunction Nichols

terminal duct obstruction qualitative/quantitative changes in the glandular secretion alteration of the tear film symptoms of eye irritation clinically apparent inflammation ocular surface disease

### Melbomian Gland Disease

- 👼 Diagnostic workup-
  - Standard dry eye tests plus gland expression
    - Expressibility
    - Assessment of meibum quality
- Proposed a staging system of MGD
- Proposed a treatment plan based on the disease stage

#### Approximately 117 million Americans have MGD

#### Pathophysiology of Melbomian Gland Disease

- Ductal hyperkeratinization- the key event
  - Simple MGD: plugging of meibomian gland orifices
  - Cicatricial MGD: scarring of conjunctival mucosa leads to displacement of orifices
  - Meibomian keratoconjunctivitis: MKC associated with skin conditions such as seborrhea, acne rosacea

#### Pathophysiology of Melbom Gland Disease

- Triggers for MGD
  - Bacterial toxins- mostly gram positive
  - Release of pro-inflammatory mediators
  - Reduced protective function by androgens
  - Reduced essential fatty acids and their byproducts
  - Contact lens wear

#### Important News @ Metbomian. Glands

- Applied constant force of 1.25 g/mm<sup>2</sup>
- Location is relative to meibum output
  - Medial > Central > Temporal
- Symptoms relative to meibum output
  - Mild > Moderate > Severe
- Recovery of meibomian glands
  - Total drainage by expression 20 seconds
  - Recovery to 50% = 2 hours

Korb DR, Blackie CA. Meibomian gland diagnostic expressibility: correlation with dry eye symptoms and gland location. Cornea. 2008 Dec;27(10):1142-7.

### Meibomian Gland Evaluation

Injection/

- telangiectasia
- Pouting
- Quality of secretions
- % of MG yielding lipid
- Recording
- 40% MGYLS
- Quality <u>2/4</u>





#### Evaluation for Meibomian Gland Disease

#### Meibomian gland transillumination

- Use standard transilluminator
- Flip upper or lower lid
- Position transilluminator to backlight eyelid
- Maximal illumination in dark room for best viewing
- Record location and loss if any of MG structures
- Photo document baseline and at subsequent visits
- Infrared photos gaining acceptance





#### Melbomian Gland Transillumination











### Therapeutic Strategies for MGD

- Renewing patency of MG orifices
- Reducing inflammation
- Thinning MG secretions
- Long-term changes to minimize recurrence of MGD

#### Long-term Management of Melbomian Cland Dysfunction

- Education
- Demonstration
- In office therapy
- Patient based therapy
  - 👩 Heat
  - Manual expression
- Dietary
  - supplementation

#### Long-term Management of MGD

- Lipiflow
- Disposable elements
- Maintains patency up to 9 months
- Often requires periodic retreatment



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- Handheld device for treating MGD
- Heating pads on either side of lids
- Can do general or focused treatment
- Raises temperature of the meibum inside the meibomian glands to its melting point of around 39 – 41°

etearfilm



#### MGD and Cyclosporine A: 2013

- A 3-month prospective, randomized, double-masked trial -70 patients
- CSA 0.05% vs carboxymethylcelluose
- @ 3 months improvements in
- Study group: OSDI, NIBUT, FBUT, lid margin inflammation, MG expressibility, tarsal injection showed significant improvement from baseline group
- Control group: only the OSDI improved
- A Randomized Double-Masked Study of 0.05% Cyclosporine Ophthalmic Emulsion in the Treatment of Meibomian Gland Dysfunction Prabhasawat



#### Conclusions: CSA & MGD

- CsA statistically superior to placebo
  - Decreased # meibomian gland inclusions
  - Improved fluorescein staining
  - Improved TBUT
  - Reduced inflammation
  - Increased MG expressibility
- Off-label use of topical CsA appears to be beneficial in treating MGD

In our experience, it can be very useful for advanced MGD. It may take months show



#### Dry Eeye Risk Factor: Childhood





## 

Moon JH et al. Smartphone use is a risk factor for pediatric dry eye disease according to region and age: a case control study. BMC Ophthalmol. 2016 Oct 28;16(1):188.

### **Risk Factor: Childhood**

- Evaluated pediatric DED in children
  - Region (urban vs. rural)
  - 🍯 Age
  - DED in relation to smartphone use rate

Moori JH et al. Smanphone use is a risk factor for pediatric dry eye disease according to region and age: a case control study, BMC Ophinamol, 2016 Oct 26:16(1):188. C

- 916 subjects
- Rate of smart phone use in Korea
  - Children 83%
  - Adolescents 89.8 %

	Urban	Rural	1
Diagnosis DED	8.3%	2.8%	
Smartphone use	61.3 %	50.0 %	ł
	Older children	Younger children	
Smartphone use	65.1 %	50.9 %	
Diagnosis DED	9.1 %	4 %	

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## Smartphone Use in Children

- Daily duration of smartphone use was longer in the DED group than controls
- Daily duration of outdoor activities was shorter in the DED group than controls
- 4 weeks after D/C smartphone use: DED group
  - Subjective symptoms improved
  - Objective signs improved
- Outdoor activity protective against DED

Moon JH et al. Smartphone use is a risk factor for pediatric dry eye disease according to region and age: a case control study. BMC Ophthalmol. 2016 Oct 28;16(1):188. C



### MGD in Children

- Just beginning to recognize severity and prevalence of MGD/DED in children!
- Management
  - Patient/parent education
  - Limit device time
  - Nutritional supplementation
  - Home-based expression



#### MG Loss in Children, Adolescents

- Sixty-nine patients two groups
  - Children 3 to 11 years
  - Adolescents 12 to 18 years
- Meibomian glands imaged w/ IR meibography
- Results: significant meibomian gland loss

Morphological Evaluation of Meibomian Glands in Children and Adolescents Using Noncontact Infrared Meibography. J Pediatr Ophthalmoi Strabismus, 2017 Mar 1:54(2):78-83.

- Found in both groups.
- Occurs in both children and adolescents.





### MG Loss in Children,

- Adolescents
- Primary issue: reduced blink rate!
   Muscle of Riolan "milks" Meibomian
- glands w/ every blink
   Reduced blink rate leads to stasis, ultimately loss of

meibomian glands



Lipham, WJ. Et al. A Histologic Analysis and Three-Dimensional Reconstruction of the Muscle of Riolan. Ophthal Plast Reconstr Surg. 2002 Mar;18(2):93-8.

