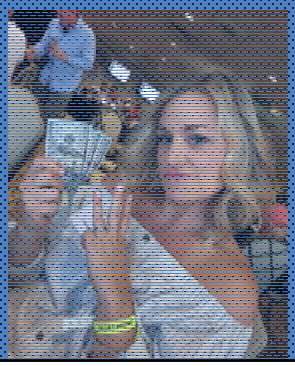
My Daughter's New Car



My Daughter's New Car

2018: Innovations and Updates In Ocular Surface Disease

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Disclosures
William D. Townsend, O.D., F.A.A.O.

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

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

Imagine…

- Having issues performing 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 diagnostic evaluation options for DED
- Review new therapy, concepts, technology DED
- Informed decisions and prescribing strategies

Do Doctors and Patients Perceive Dry Eye Differently?

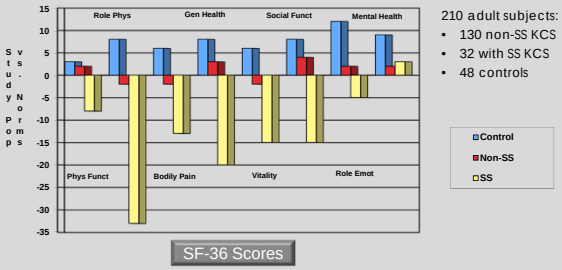
Severity of Symptoms	Drs.	Dry Eye Pts.
Symptoms are severe	9%	19%
Symptoms moderate	20%	36%
Symptoms mild	47%	23%

Summary

- Patients w/ dry eye experience more symptoms than doctors would expect from clinical signs.
- Signs & symptoms of OSD often have no correlation

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

The Impact of DED on Quality of Life



210 adult subjects:
- 130 non-SS KCS
- 32 with SS KCS
- 48 controls

Mertzanis P. The relative burden of dry eye in patients' lives: comparisons to a US normative sample. Invest Ophth & Vis Sci Jan 2005

Dry Eye and Quality of Life

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


dry eye dx and tx

The Impact of Dry Eye on Quality of Life

Townsend WD. The impact of dry eye on quality of life? Contact Lens Spectrum. September 2008

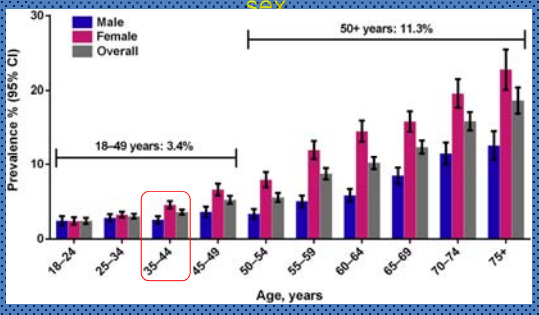
How Can We Help?

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

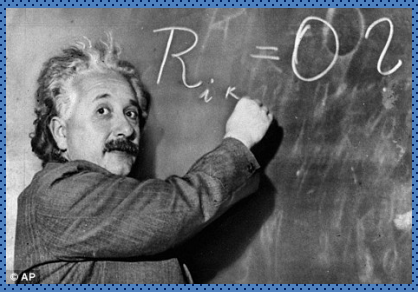
Farrand KF et al. Prevalence of Diagnosed Dry Eye Disease in the United States Among Adults Aged 18 Years and Older. Am.Journ. of Ophth. October 2017

Estimates of diagnosed dry eye disease (Diagnosed-DED) prevalence by age and sex



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

What Does Science Say?



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."

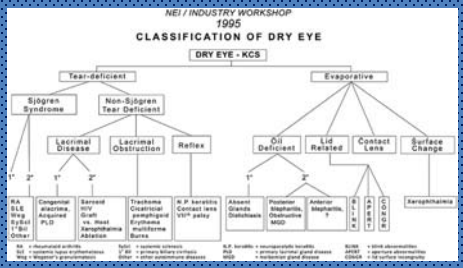
1995 National Eye Institute (NEI) Industry Dry Eye Workshop

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

"…a blueprint for clinical, translational, and basic research that would propel the field to the next level."

"…identified the relevance of tear film quality as well as tear quantity."

1995 National Eye Institute (NEI) Industry Dry Eye Workshop



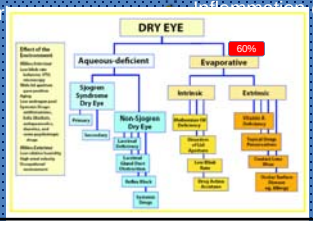
Dry Eye Workshop 2007

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 Eye Workshop (DEWS) 2007

- Multifactorial disease
- Affects tears & ocular surface
- Increased evaporation
- Discomfort
- Visual disturbance
- Tear film instability
- Potential damage ocular surface
- Increased tear film osmolarity
- Inflammation of ocular



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."

…mechanistic & shows how each cause may act through a common path.

…severity which is expected to provide a rational basis for therapy.

…DED represents a failure or inability to maintain homeostasis of the OS

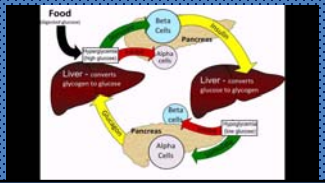
Dry Eye Workshop II- 2017

- Multifactorial disease of tears and ocular surface
- Discomfort
- Visual disturbance
- Tear film instability
- Increased tear osmolarity
- Ocular surface damage
- Ocular surface inflammation
- Impaired homeostasis of ocular surface

Homeostasis: the tendency toward a relatively stable equilibrium between interdependent elements, especially as maintained by physiological processes.

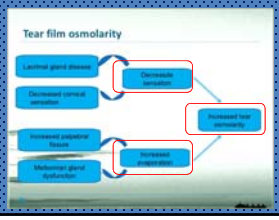
Homeostasis: Diabetes

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

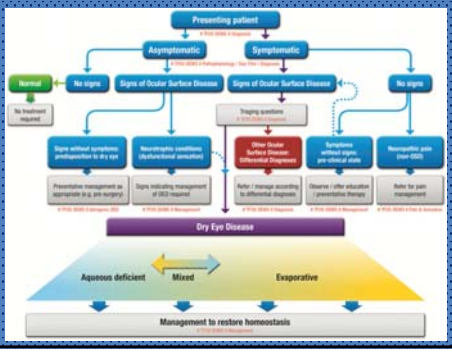


Homeostasis: Dry Eye

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



Dry Eye Workshop II 2017



Key Elements 1995-2017

- Disorder of the tear film
- Tear deficiency
- Multifactorial disease
- Increased evaporation
- Visual disturbances
- Tear film instability
- Increased tear film osmolarity
- Inflammation ocular surface
- Impaired homeostasis

DED: How Prevalent is It?

- Hospital-based study, 400 subjects, mean age 56.8 years
- Questionnaire
  - Demographic, medical Hx, lifestyle Hx,
  - Symptoms
    - Dryness, grittiness, stickiness, heaviness, burning, itching, watering
- Examination:
  - SLE + TBUT

Shah S, Jani Het al. Prevalence and associated risk factors of dry eye: our experience in patients above 40 years of age at a tertiary care center. Oman Journ. of Ophth.; 8:3, 2015

DED: How Prevalent is It?

- Incidence DED
  - Overall- 54%
  - > 71 years of age- 67%
- Gender:
  - Males 51%
  - Females 57%
- Highest incidence in outdoor workers

Shah S, Jani Het al. Prevalence and associated risk factors of dry eye: our experience in patients above 40 years of age at a tertiary care center. Oman Journ. of Ophth.; 8:3, 2015

DED: How Prevalent is It?

- Association with systemic disease
  - Diabetes 67%
  - Hypertension 51%
  - Arthritis 55%
- Meibomian gland blockage 18%
  - Prevalence of DED 95%
- Glaucoma (6%)
  - Prevalence of DED 72%

Shah S, Jani Het al. Prevalence and associated risk factors of dry eye: our experience in patients above 40 years of age at a tertiary care center. Oman Journ. of Ophth.; 8:3, 2015

Strategies For Diagnosis: Conventional Testing

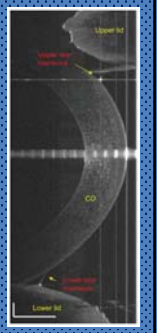
- Tear break-up time (TBUT)
  - Measures tear film stability
  - Evaluates the relationship between tear lipids & mucins.
- Conventional (fluorescein)
  - Use yellow filter
  - Use non-preserved, compounded fluorescein

Presenting Symptoms DE Patients		
Symptom	# Patients	Percentage
Watering	89	41%
Itching	43	20%
Heaviness	33	15%
Burning	32	15%
Stickiness	20	9%
Dryness	19	9%
Grittiness	19	9%
Excess mucous	7	3%

Shah S, Jani Het al. Prevalence and associated risk factors of dry eye: our experience in patients above 40 years of age at a tertiary care center. Oman Journ. of Ophth.; 8:3, 2015

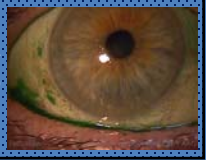
Strategies For Diagnosis: Conventional Testing

- Tear meniscus (OCT)
  - Better than SLE but no definitive levels of "normal"
  - Inferior meniscus correlates better than superior with w/ TBUT & fluorescein staining, Schirmer test



Strategies For Diagnosis: Conventional Testing

- Tear meniscus (OCT)
  - Better than SLE but no definitive levels of "normal"
  - Inferior meniscus correlates better than superior with w/ TBUT & fluorescein staining, Schirmer test
- Corneal & conjunctival staining
  - Rose Bengal- cells that have lost mucin protective layer
  - Sodium fluorescein- areas cellular degeneration or death, damage to cell membranes, epithelial cell junctions



Sterile Preservative-Free Stains

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

Tear Film Osmolarity

- 1979- Gilbard & Farris describe association between dry eye & elevated tear film osmolarity
- 1983- Gilbard & Farris propose using hypo-osmolar 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

Osmolarity in the Diagnosis of Dry Eye Disease

Clinical Test	PPV*
Osmolarity	87%
Schirmers	31%
TBUT	25%
Staining	31%
Meniscus Height	33%

- Osmolarity is the "gold standard" test for Dry Eye
  - 45 years peer reviewed research
  - Osmolarity has been added to definition of Dry Eye
  - Global marker of Dry Eye, indicating a concentrated tear film

*positive predictive value, i.e., % of time an osmolarity > 308 will actually be dry eye

Source: DEWS Report, Ocular Surface April 2007 Vol 5 No 2, &Tomlinson A, et. al., IOVS 47(10) 2006

Hyperosmolarity Causes Apoptosis/Inflammation

Hyperosmolarity-Induced Apoptosis in Human Corneal Epithelial Cells Is Mediated by Cytochrome c and MAPK Pathways

Lihui Luo, MD,*†‡ De-Quan Li, MD, PhD,* and Stephen C. Pflugfelder, MD*

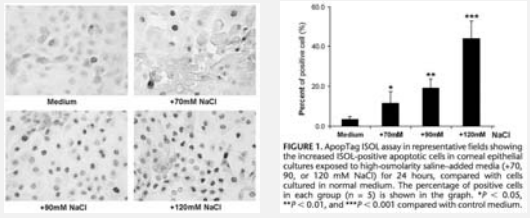


FIGURE 1. ApopTag ISOL assay in representative fields showing the increased ISOL-positive apoptotic cells in corneal epithelial cultures exposed to high-osmolarity saline–added media (+70, 90, or 120 mM NaCl) for 24 hours, compared with cells cultured in normal medium. The percentage of positive cells in each group ($n = 5$) is shown in the graph. $^*P < 0.05$, $^{**}P < 0.01$, and $^{***}P < 0.001$ compared with control medium.

Liu H. Invest Ophthalmol Vis Sci. 2009;50:3671–3679

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)

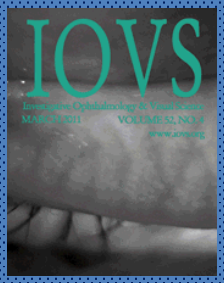
TearLab Discovery

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

- o Fluctuations in tear film osmolarity are a hallmark sign of DED
- o Represent an impaired ability to maintain ocular surface homeostasis
- o Elevated osmolarity a hallmark sign of OSD/DED

Dry Eye Workshop II 2017

International Workshop on Meibomian Gland Dysfunction Nichols et al. 2011



Landmark Studies in Dry Eye

International Workshop on Meibomian Gland Dysfunction
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".

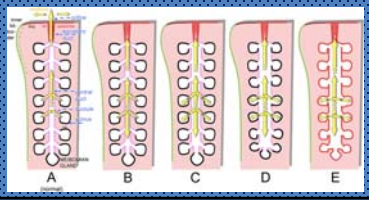
Landmark Studies in Dry Eye

International workshop on meibomian gland dysfunction Nichols et al.

- 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

Pathophysiology of Meibomian 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 Meibomian Gland Disease

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

Important News @ Meibomian Glands

- Applied constant force of 1.25 g/mm^2
- 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

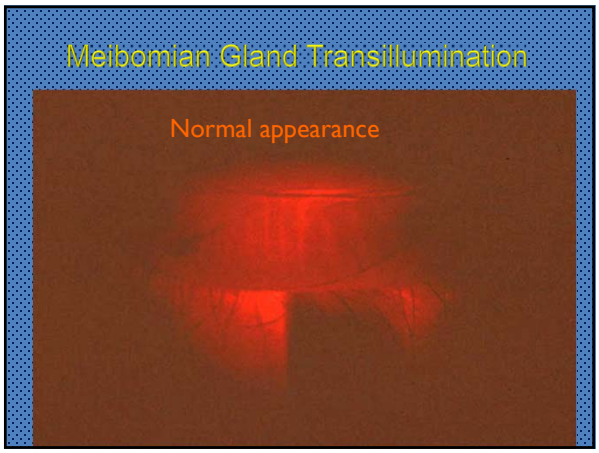
- Injection/ telangiectasia
- Pouting
- Quality of secretions
- % of MG yielding lipid
- Recording
  - 40% MGYLS
  - Quality 2/4

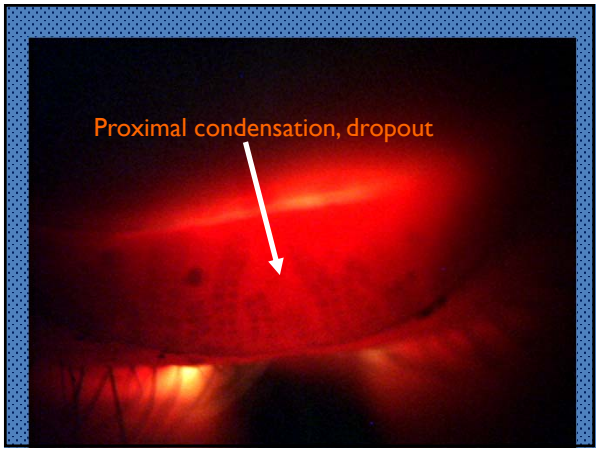
Normal Meibomian Piano Pattern

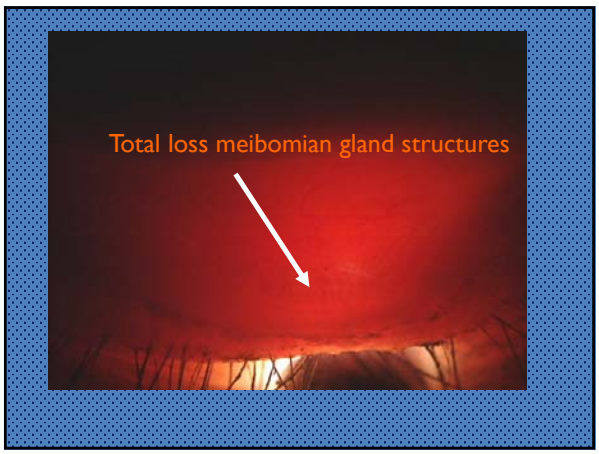
Evaluation for Meibomian Gland Disease

- 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

Meibomian gland transillumination

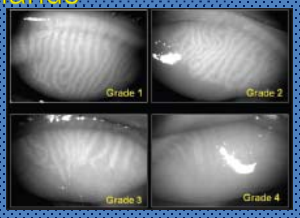

Meibomian Gland Transillumination
Normal appearance


Proximal condensation, dropout


Total loss meibomian gland structures

Infrared Imaging Meibomian Glands

Keratograph 5 (OCULUS)



Lipiscan (Tear Science)

Therapeutic Strategies for MGD

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

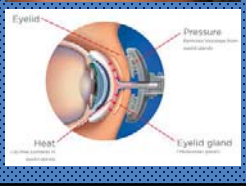
Long-term Management of Meibomian Gland Dysfunction

- 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



Ilux

- 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° C

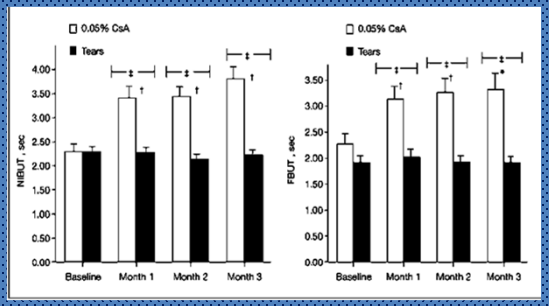
tearfilm innovations

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

Breakup Time CSA vs. CMC

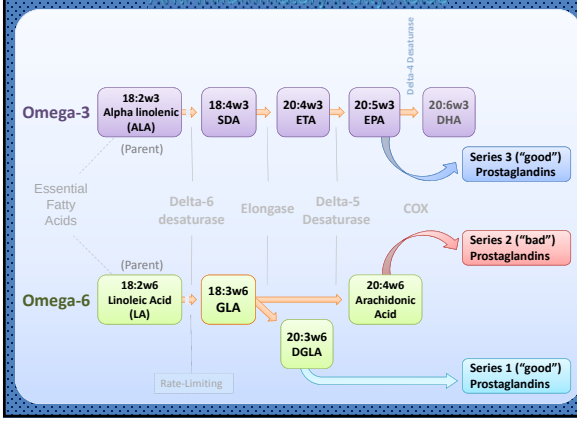


Conclusions: CSA & MGD

- 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

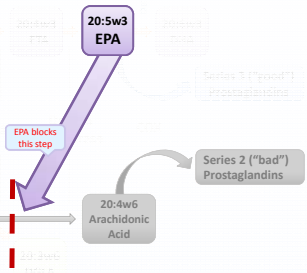
Anti-Inflammatory Fatty Acids



Anti-inflammatory Fatty Acids

1) GLA heavily favors the anti-inflammatory pathway

2) As back up, adding EPA to GLA in proper balance, blocks production of pro-inflammatory pathway



Combination N-3 + N-6 Preparations

Supplement Facts

Serving Size: 4 softgels
Servings Per Container: 30

	Amount Per Serving	% Daily Value*
Calories	30	
Calories from Fat	20	
Total Fat	2.5 g	4%
Vitamin A (from retinyl palmitate and cod liver oil)	2080 IU	42%
Vitamin E (d-alpha tocopherol)	12 IU	40%
Vitamin C (as ascorbic acid)	240 mg	300%
Vitamin B6 (from pyridoxal 5-phosphate)	12.6 mg	630%
Magnesium (from magnesium sulfate)	40 mg	10%
Black Current Seed Oil (15% gamma linolenic acid (GLA); also contains 12-15% alpha linolenic acid (ALA))	1570 mg	†
Omega-3 Fatty Acids (100 mg EPA, 70 mg DHA from USP-verified fish oil)	170 mg	†
Mucin Complex (60% mucin)	100 mg	†

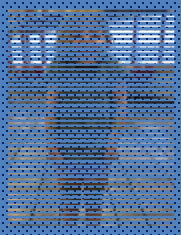
*Percent Daily Values are based on a 2,000 calorie diet.
† Daily Value not established.

Other Ingredients: Gelatin, Glycerin, Water, Beeswax, Lecithin, Titanium Dioxide, Lemon Oil and Caramel Color.

2017

- IPhone introduced 10 years ago
- Since then……

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

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

Smartphone Use in Children

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

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

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

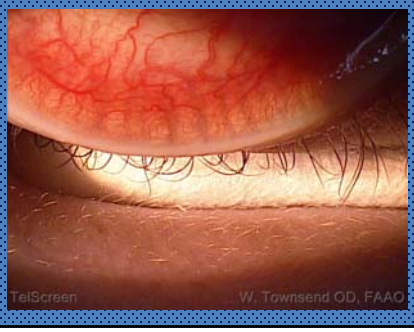
Moon JH et al. Smartphone use is a risk factor for pediatric dry eye disease according to region and age: a case control study. BMC Ophthalmol. 2016 Oct 28;16(1):188. C

Encourage Outdoor Activity

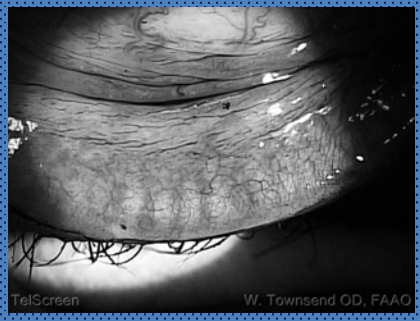
MGD in Children

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

14 year-old Male…Yesterday



14 year-old Male…Yesterday



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

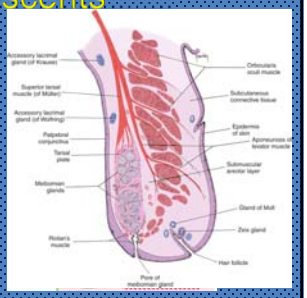
Morphological Evaluation of Meibomian Glands in Children and Adolescents Using Noncontact Infrared Meibography. J Pediatr Ophthalmol Strabismus. 2017 Mar 1;54(2):78-83.

MG Loss in Children, Adolescents

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

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.

Our Mission Statement

"To promote excellence in the care of patients and the advancement of knowledge of dry eye and ocular surface disease (OSD) for ophthalmic educators and clinicians through professional education and scientific investigation"

OSSO's members enjoy the benefit of the OSSO online newsletter and the opportunity to share clinical cases with our Executive Board and Members-at-large.

Ocular Surface Society of Optometry

Membership Details

- OSSO's goal is to serve as the "Voice of Optometry in Ocular Surface Disease"
- To join OSSO you:
  - Must have an optometric degree from an accredited school or college of optometry
  - Must be a reputable individual in good standing within their profession and community
  - Must complete and submit an application form to OSSO
  - Students, scientists, and physicians with a specific interest in dry eye and/or ocular surface disease are also welcome to join as special class members of OSSO
- Membership dues are $54.00 per year

membership@ossopt.com

Ocular Surface Society of Optometry

Conclusion

- Dry eye represents a huge opportunity for eye care providers, especially OD's
- Join TFOS or OSSO and connect w/ like minded providers who manage DES
- Give special attention to the next generation of dry eye sufferes