





Paul M. Karpecki, OD, FAAO Financial Disclosures:

Healthe Hue.AI iCare USA

Iveena Jobson/Web MD Kiora Pharmaceut Konan Medical LenTechs Mallinckrodt Mitotech

Novartis Oasis Medial Oculus OcuMedic OcuTerra Omega Ophthal mpic Ophthalmic

enerEyes chert

endia xSight



I am on the speaker panel
for:
Alcon
Allergan
Abbott Medical Optics
Bausch + Lomb
BVI
TearLab

I am a consultant for:
Akorn
Allergan
Abbott Medical Optics
BioTissue
Lunovus
OcuSoft
TearLab

I have no direct financial interest in any company or product that is mentioned in this lecture

4





vant relationships have been mi

All rel

5

Adom Al Optics Alcon Aldeyra Allergan/Abbvi Apellis Atlas Medical Aurion Aveilino Labs

Avellino Labs Azura Pharmaceutis Barti Bausch + Lomb BioTissue BlephEx Bruder Healthcare Bruno Vision Care Cambium Pharma Dompe

Cambium Dompe Eyedaptic Eyedetec G

Dry eye is not just a <u>disease</u>, it's a <u>complex, multi-</u> <u>factorial disorder</u>.

DEWS

Dry eye is 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.



7

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 abmormalities play etiologic roles.



Dry Eye /Ocular Surface Disease

- Medical Ocular condition or disease
- · Ocular manifestation of a systemic problem
- · Ocular complication from a medical Treatment

9

10

Dry Eye /Ocular Surface Disease

- Diabetes
- Thyroid Disease
- Autoimmune disease
- Hormonal changes
- Botox and Filler procedures
- Facial plastic procedures
- Graft VS Host disease (cancer Tx complications)















Restasis Xiidra Cequa Verkazia Autologous serum Platelet rich plasma. PRP Regener-eyes / biologics (amniotic enhanced) Neurostimulation iTear100 Salagen Evoxac Tyrvaya Lotemax Eysuvis Steroids Nutracueticals Bruder Mask Expression devices IPL LLT Night goggles Doxycycline



20



Lacrimal Functional Unit (LFU)

• Tear film

Barabino S et al. Prog Retin Eye Res. May 2012

- Lacrimal glands
- · Corneal and conjunctival epithelia
- · Meibomian glands
- Homeostasis controlled by nerve connections and systemic hormones



21



ClinicalTrials@PerimanEyeInstitute

OCULAR SURFACE

0

- Control Inflammation, Control desiccating stress (normalize osmolarity, control evaporation), Control tissue damage (epithelium and nerves)
- Tune up the LFU components (lacrimal, MGs, goblet cells, NLD)
- Neural Stimulation
- Mechanical extranasal (Olympic Ophthalmics)
- Chemical intranasal (Viatris)
- Neural Modulation
- TRPM8 activation (AR-15512, UMAY)
- TRPVI antagonist
- · IPL, Paraceuticals, CGRP antagonists
- ?RF plus DMSt

22



- Immunomodulators
- ⋆ steroids, CsA, LfG
- Delivery systems
- Neuralmodulators
 Mechanical (iTear)
- Mechanical (11ear)
 Chaminal (Wananialina)
- Chemical (Varenicline)
- Growth factors (Cenegermin, Enriched Tear Function Gene Therapy-ETF-GT, mesenchymal secretosomes—KPI-012)
 Neuroinflammatory modulators
- Neuroinflammatory m
 TRPV1 antagonist
- TRPV1 antagoni
 TRPM8 agonist
- CGRP antagonist

<text><text><image>





Senation Touch	Soma Mechano	Channels SA	Natural Stimuli Mechanical forces	Agonists Mechanical forces	Pipeline
Pain/Heat	Polymodal	(slowly adapting) TRPA1, TRPV1, TRPV2, SA, ASICs (transient receptor potential, acid sensing)	Noxious stimuli	Mustard oil, Icilin, Cinnamaldehyde, Capsacin, Piperene	SAF312 TRP V1 antagonist Reproxalap siRNA (Tivanisiran, Sylentis)
Temperature	Warm	TRPV3, TRPV4	Moderate temp changes	Vanillin, Thymol	
Temperature	Cold	TRPM8	Moderate temp changes	Menthol, Eucalyptol, Icilin	AR-15512 UMAY Cryosim-3 wipes











IPL OPT then RF +DMSt



32



33



• IPL with OPT

- Dermaceutical grade skincare
- Skin microbiome
- Tacrolimus

• Dysregulation of

neuronal systems

CGRP antagonists

paraceuticals) In office lines

· Paraceutical skincare that blocks C-nociceptors in the skin



















Meibomian gland dysfunction (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

















۲	Do your eyes ever feel irritated, dry or burn?
••	Are your eyes red?
۲	Do you experience blurred vision especially fluctuating vision?
Ô	Do you use or have the urge to use artificial tears?
n	. Hannan di sima da yan ayaa da sa di gita bahari sa ga sa dayi













<complex-block>

 Image: state sta

<complex-block>

58

In Chronological Order

- Symptoms (most significant and when)
- · Eyelid assessment with MG expression
- Ocular surface staining with NAFL (#15 yellow Wratten filter)
- Corneal stain
- Conjunctival stain
- ► TFBUT
- Tear meniscus height







Perflourohexyloctane

Indication

perfluorohexyloctane ophthalmic solution is a semifluorinated alkane indicated for treatment of the signs and symptoms of dry eye disease.

Important Safety Information

- Should not be administered while wearing contact lenses. Contact lenses should be removed before use and for at least 30 minutes after administration
- Instruct patients to instill one drop of PFHO into each eye four times daily
 The safety and efficacy in pediatric patients below the age of 18 have not been established
- The most common ocular adverse reaction was blurred vision (1% to 3% of patients reported blurred vision and conjunctival redness)









- Intense Pulsed Light Therapy and Low Level Light Therapy
- Clear association between DED and lid margin inflammatory disease
- Widely accepted as a treatment for dermatological rosacea
- · More than 80% of patients with rosacea have MGD
- 20% have ocular signs first



Treatment: Demodex

Consists of a PHASE 1 (With a specific blue light mask) And a PHASE 2 (With the standard supplied Red Light Mask)

PHASE 1 - BLUE MASK

Blue light stimulates porphyrins and creates an antibacterial action.

PHASE 2 - RED MASK

 Positive action on lipid layer (Graham RH. There's nothing fishy about omega-3 fatty acids for Dry Eye Syndrome.
 www.medscape.com/viewarticle/707984. Sep 3, 2010.)

· Positive action on tear volume (Roncone M, Bartlett H, Eperjesi F.

Essential fatty acids for dry eye: A review. Cont Lens Anterior Eye

Red light stimulates ATP by increasing and improving cellular activity, it reduces inflammation and oedema and works on Meibomian glands.



68



69



Increase "good" PG (PGE-1)Against ocular surface inflammation

• Help to maintain MG function (Macsai, 2008)

· Increase tear production

2010; 33(2):49-54.)



Supplementa 7 Controlled

- Supplemental GLA for Dry Eye: 7 Controlled Clinical Trials
- Aqueous-deficient (Barabino S et al. Cornea 22: 97–101, 2003.)
- PRK (Macri A et al. Graefes Arch Clin Exp Ophthalmol 241:561-6, 2003.)
- Sjögren's (Aragona P, et al. Ophthalmol Vis Sci 46:4474-9, 2005.)
- Contact lens (Kokke KH et al. Contact Lens Ant. Eye 31:141-6, 2008.)
- MGD (Pinna et al. Cornea 26:260-264, 2007.)
- Mild-moderate DE (Brignole-Baudouin et al. Acta Ophthalmologica 89:e591-7, 2007.)
- Post-menopausal women (HydroEye) (Sheppard JD, Pflugfelder SC, et al. Cornea 32 :1297-1304, 2013.)

















Aqueous Volume

- Indications:
- · Symptomatic contact lens wear
- · Dry eye related to refractive surgery
- ADDE · Dry eye associated with a rapid TBUT
- Systemic medications that reduce tear film production
- Superior limbic keratoconjunctivitis
- (SLK) Corneal irregularities or scarring that affect tear stability
- · Lid palsy or lid closure abnormalities · Toxic epitheliopathy
- · Contraindications:
- · Presence of ocular surface inflammation could prolong the presence of pro-inflammatory cytokines
- · A recent study showed that punctal occlusion resulted in:
- ↓ corneal fluorescein staining
- \downarrow symptom scores
- · With no elevation of cytokine or matrix metalloproteinase (MMP)-9 levels



80



79

Dry Heat Glass Bead Sanitizer

Suitable for all metal instruments including the Meibomian Gland Expression Instruments Fast acting and easy to use:

- Chamber size: : 1 5/8" Diameter x 2 1/2" Deep.
- · Chamber with glass beads heats to 250 °C
- in approximately 30 minutes
- · Sanitizes in 30 seconds

NOTE: Glass Beads Sanitizers are not FDA approved as sterilizers. Glass Bead sanitizers are a ouick, easy and accurate alternative to traditional methods of sterilization and sanitizing.

Electrical











Amniotic Membrane Types Cryopreserved

Pros

- FDA Approved
- · Proprietary Freezing Process
- · Ease of use (fitting a contact lens)
- Cons · Requires refrigeration and
- space in office • Has to be thawed before use
- · Ring placement can be
- uncomfortable
- · Shorter shelf-life
- Price



86



85

Neurotrophin-3/Neurotrophin-4	NT-3/NT-4
Basic fiberblast growth factor	bFGF
Beta nerve growth factor	β-NGF
Epidural growth factor/Epidermal growth factor receptor	EGF/EGF-R
Glial cell line-derived neurotrophic factor	GDNF
Heparin binding growth factor	HB-EGF
Hepatocyte growth factor	HGF
Platelet-derived growth factor	PDGF-AA/PDGF-BB
Placenta growth factor	PIGF
Stem cell factor	SCF/SCF-R
Transforming Growth Factor Alpha	TGFa/TGFb1/TGFb3
Vascular endothelial growth factor	VEGF



o	7
o	1



88



Action of Growth Factors in Serum

- · Cellular proliferation
- Migration
- Differentiation
- Apoptosis
- Intercellular communication



	TEARS	SERUM
	0	
Ph	74	74
Osmolality	298	296
Albumin (mg/l)	54	35-55
EGF (ng/ml)	1.5	0.7
TGF-b (ng/ml)	2-10	6-33
Vitamin A (mg/ml)	0.02	46
Lysaryme (mg/ml)	1.4	6
SigA (ug/ml)	1190	2
Fibronectin (ug/ml)	21	205
Hepatoryte GF, NGF, NGF, L, Substance P, Compl GF, cGRP, other lg, ecc.	iement, Fibroblast	✓
First described 1984 by For in eyes with persistent epitl	x et al (for KCS), more after success helial defects (Tsubota et al 1999)	

National Outfit for ASED

- Present in almost every major city in the US
- · Blood draw at patients home or work
- Processing
- Regular replacement
- · Doctors must specify concentration
- ► 20% for most patients
- ► 40% for GVHD etc.

92

Six Respondents	Victoria (Chin, OD, Mann Eye Institute Paul Karpecki, OD, Kentucky Eye Institute Marjan Farid, MD, University of California, Irvine Vedram Hannrah, MD, Neve England Eye CenterTufts Shachar Tauber, MD, Mercy Clinić Eye Specialists Winston Chamberlain, MD, Casey Eye Institute
Questions	
How do you decide with unspecified sys	on starting therapy with serum tears in a dry eye patient mptoms or significant MGD?
What is your prefer	red starting formulation of serum tears?
Are there particular tears?	types of patients you have found respond well to serum
What perceptage of	moderate and severe patients do you prescribe serum?

KOL Serum Tears Survey Results What is the preferred starting formulation?							
	⁰²	A	A 04	es es	M. ⁰⁶		
40 %	75%	20%	40%	50%	20%		
4	8	8	6	6	6		
Times/D	Times/D	Times/D	Times/D	Times/D	Times/Day		
ay	ay	ay	ay	ay			
Take Aways							
Survey Answers Varied							
Rx Data Average Shows:							
• >00% P	roviders in 2	020					

94



What percent of moderate and severe DED patients do you put on serum tears?

















- With progression, patients may develop MGD or blepharitis
- With further progression, desiccation stress/exposure occurs and inferior corneal staining may be noted
- Patients may eventually develop immune mediated dry eye, but the vast majority don't have dry eye, they have ILS.
- When ILS is treated they typically do not need dry eye therapies



ILS (Inadequate Lid Seal)

- · And leads to nocturnal evaporative stress, desiccation and eventually exposure keratitis
- · It is NOT lagophthalmos
- · It is a major cause of dry eye
- · Overnight eye seals Hypoallergenic
- · Oxygen permeable
- ▸ Latex-free
- · Adequate mild adhesive · Sensitive and regular



Title	
Loteprednol ointment is a new preservative-free steroid ointment.	
Loteprednol ointment is a corticosteroid indicated for the treatment of post-operative inflammation and pain following ocular surgery.	

104

103









Meibomian Gland Expression

- Fees: 99213 or 99214 OSD evaluation Pre expression
- Plus: Out of pocket expense for expression
- ABN
- Covers 2 Office visits
- · Per visit fee after initial two visits

