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Financial Disclosures

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 Orasis-Consultant
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Dry Eye Overview

- 30 million Americans suffer from dry eye
- \$3.8 billion spent on dry eye symptom relief annually in USA
- most frequent encountered disease state by eye care providers
- 43% of asymptomatic patients have clinical dry eye

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Dry Eye Definition

“Dry eye is a multifactorial, **symptomatic** disease characterized by a **loss of homeostasis** of the tear film and/or ocular surface, in which tear film instability and hyperosmolarity, ocular surface inflammation and damage, and neurosensory abnormalities are etiological factors” *-DEWS III*

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DEWS III Updates

- Start with a questionnaire → OSDI 6 (6 questions)
- Clinical Evaluation
- 10 sections of comprehensive therapies
- Emphasis on lifestyle factors
- 3 treatment algorithms

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Ocular Surface Disease Index 6: OSDI 6


Dr. Heiko Pult & Prof. Dr. James Wolffsohn

Please answer the following questions by circling the numbers in the boxes

	Constantly	Mostly	Often	Sometimes	Never
Have you experienced any of the following during a typical day of the last month?					
1. Eyes that are sensitive to light?	4	3	2	1	0
2. Blurred vision?	4	3	2	1	0
Have problems with your eyes limited you in performing any of the following during a typical day of the last month?					
3. Driving or being driven at night?	4	3	2	1	0
4. Watching TV, or a similar task?	4	3	2	1	0
Have your eyes felt uncomfortable in any of the following situations during a typical day of the last month?					
5. Windy conditions?	4	3	2	1	0
6. Places or areas with low humidity?	4	3	2	1	0

Sum of all questions: _____

Likely dry eye if total sum ≥ 4



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ALGORITHM #1

ETIOLOGIC DRIVER TESTS

Lipid

- Tear film lipid layer thickness / interferometry
- Mebomian gland expressibility
- Mebum quality

Aqueous

- Tear meniscus height
- Meniscometry / Schirmer / phenol red thread test
- Oral / cyclo-oxygenase
- Lissamine green / rose bengal staining
- Conjunctival impression cytology

TEAR FILM DEFICIENCIES

EVIDENCE-BASED INTERVENTIONS

Lipid

- Tear supplementation / stabilization (lipomimetics)
- Tear conservation devices (moisture-retaining spectacles)
- Pharmacological tear stimulation / restoration
- Device tear stimulation / restoration
- Blink therapies
- Topical lid hygiene

Aqueous

- Oral nutrition (Omega 3)
- Tear supplementation / stabilization
- Tear conservation devices
- Pharmacological tear stimulation / restoration
- Topical anti-inflammatories
- Ocular surface regenerators
- Surgical options

Muco-aqueous

- Tear supplementation / stabilization (HP guar)
- Topical anti-inflammatories
- Pharmacological tear stimulation
- Device tear stimulation (neurostimulation)

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ALGORITHM #2

ETIOLOGIC DRIVER TESTS

- Blinking / lid closure
- Incomplete blinking
- Anterior blepharitis
- Eyelid biomicroscopy - greasy (ectothelium) or flaky (staphylococcal)
- Eyelash base - cylindrical dandruff / Demodex
- Mebomian gland dysfunction
- Pouting, missing, displaced gland orifices
- Mebomian gland expressibility
- Meblography - truncated, dilated glands, slope roof
- Telangiectasia
- Lid margin keratinization

EYELID ANOMALIES

EVIDENCE-BASED INTERVENTIONS

- Blinking / lid closure
- Blink exercises
- Anterior blepharitis
- Topical lid hygiene
- Oral antibiotics
- Mebomian gland dysfunction
- Oral nutrition (vitamin D3)
- Tear supplementation / stabilization (lipid-based, androgen)
- Pharmacological tear stimulation / restoration (topical azithromycin, selenium sulfide)
- Device tear stimulation / restoration (internal and external lid heating, IPL, LLET, QMR, radio-frequency)
- Lid margin debridement for significant keratinization
- Oral antibiotics

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ALGORITHM #3

ETIOLOGIC DRIVER TESTS

- Antibiotic misapplication
- Biomicroscopy e.g. staphylococci, UPQ29 / inflammation
- Extension / extension, lagophthalmos
- Corneal sensation
- In vivo confocal microscopy
- Cellular density / fibroplasia
- Cornea (fluorescein)
- Bulbar Conjunctiva (lissamine green)
- Lid wiper epitheliopathy (lissamine green)
- Inflammation / oxidative stress
- Bulbar conjunctival hyperemia
- Inflammatory markers

OCULAR SURFACE ABNORMALITIES

EVIDENCE-BASED INTERVENTIONS

- Surgical options
- Pharmacological tear stimulation / stabilization
- Tear supplementation / stabilization
- Surgical options (punctal occlusion)
- Cellular damage / fibroplasia
- Oral nutrition (vitamin D3)
- Tear supplementation / stabilization
- Pharmacological tear stimulation / restoration
- Device tear stimulation / restoration
- Topical lid hygiene
- Topical anti-inflammatories
- Ocular surface regenerators
- Surgical options (punctal occlusion)
- Inflammation / oxidative stress
- Oral nutrition (omega 3 / vitamin D3)
- Tear supplementation / stabilization
- Pharmacological tear stimulation / restoration
- Device tear stimulation / restoration (PL)
- Topical lid margin hygiene / debridement
- Topical anti-inflammatories
- Ocular surface regenerators (amniotic membrane)
- Surgical options (punctal occlusion)

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Diagnostic Innovations

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HYPEROSMOLARITY

- Osmolarity=measure of salt concentration of tears
 - Changes in osmolarity due to fluctuations in water content
- Hyperosmolarity from increased evaporation rate or reduction of tear secretion is indicated of reduced aqueous levels
 - Hyperosmolarity stimulates epithelial cell death → inflammatory cascade → proinflammatory cytokine production → cell death via apoptosis & loss of goblet cells
 - Variability (readings & between eyes)

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INFLAMMATION DETECTION: INFLAMMADRY IDENTIFIES ELEVATED LEVELS OF MMP-9

85% SENSITIVITY
94% SPECIFICITY

InflammaDry

CUIDEL

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T-POC (Tear-Based Point-of-Care)

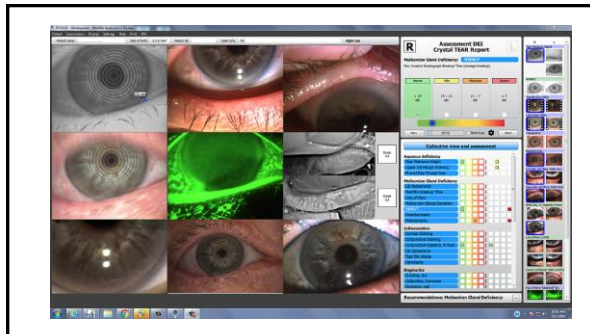
(not currently available)

- New Quantitative testing platform by Versea Ophthalmics
- Lactoferrin & IgE results (ocular surface disease & allergies)
- CLIA certified
- Is it aqueous deficient or evaporative? Is there an allergy component?
 - Lactoferrin: protein that is seen in immunological defense mechanism & can be used to assess secretory function of the lacrimal gland
- IgE: antibody that binds to allergens & triggers degranulation of mast cells that cause inflammation

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Incomplete Lid Closure

- Korb Blackie Test
- Sxs: worse in AM



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Corneal Sensitivity

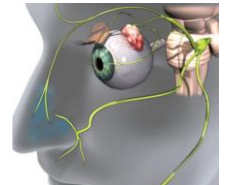
Reduced or Absent



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Neurostimulation

Why use ATs when you can make your own tears?



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Acotremon ophthalmic solution 0.003% (TRYPTYR - AR-15512)

2025
Dosed: BID
Pharmacy: Blink Rx
Mechanism:

- TRPM8 is a cold-sensing receptor in the cornea and eyelid that when stimulated has been shown to activate trigeminal nerve signaling, leading to increased basal tear production

Trials:

- COMET-2: **42.6%** versus **8.2%** of patients experienced ≥ 10 mm increase in Schirmer score from baseline at day 14
- COMET-3: **53.2%** versus **14.4%** of patients
- COMET-4: Tear production was consistently observed (12 MONTHS)
- Most common AE (50%) **instillation site pain**

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Varenicline solution 0.03 mg (Tyrvaya)

2021
Dosed: BID
Mechanism:

- Activates the trigeminal parasympathetic pathway to increase the production of basal tears.

Trials:


- ONSET-1: 52% of patients experienced ≥ 10 mm increase in Schirmer score from baseline, 47% in ONSET-2 study at day 28
- AE's: sneezing (82%), cough, throat irritation, and instillation-site (nose) irritation (5-16%)



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Neuromodulation Therapy

- Non-chemical, Neuro-stimulation treatment that comes with a USB charger and is Bluetooth enabled. It can be used with a smartphone app that allows patients to set the sensitivity level.
- Prescription only
- Increases natural tear production in adult patients



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Pharmacological Agents

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Immunomodulators

Drug	Year	Active Ingredient	Concentration
Restasis	2003	Cyclosporine	0.05%
Xiidra	2016	Lifitegrast	5%
Cequa	2018	Cyclosporine	0.09%
Veveye	2023	Cyclosporine	0.1%

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Immunomodulators

Veveye

2023

Cyclosporine 0.1%

Mechanism:
 Novel water-free vehicle (perfluorobutylpentane), which allows VEVEYE to spread evenly over the ocular surface with longer residual time and increased penetration

Trials:
 Phase 2/3 ESSENCE-1 trial, phase 3 ESSENCE-2 trial
 66% of subjects had 3 or more grades of ICFS (total corneal fluorescein staining) improvement by Day 29
 57% of patients showed at least 3 grades of improvement in ICFS at Day 15
 99.8% of patients experienced no or mild site instillation irritation*
 AE's: instillation site reactions (8%) and tem

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perfluorohexyloctane ophthalmic solution

Dosed: QID

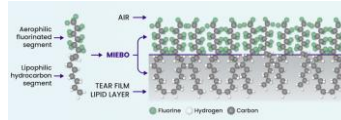
Small bottle, small drop

Mechanism:

- 100% perfluorohexyloctane
- Only drop that targets tear evaporation
- Forms a monolayer at air liquid interface of tear film

Trials:

- MOHAVE and GOBI
- 32% improvement in TCFS at day 57, 36% in ccFS
- 43% improvement in eye dryness at day 57
- **Improvements noted at day 15**
- AE's: most common blurred vision (2.1%)



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lotilaner ophthalmic solution 0.25%

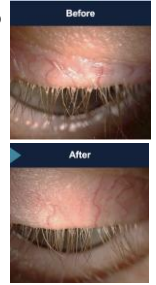
Dosed: BID x 6 weeks

Mechanism:

- Lotilaner, lipophilic agent in aqueous drop that acts via mite GABA-gated chloride channels to target, paralyze and kill demodex

Trials: SATURN 1 and SATURN 2

- 60% total eradication of mites
- 50% reduction of collarettes to 2 or less
- 85% reduction to 10 or less
- 25% erythema cure
- AE's: 10% stinging and burning, 2% chalazia/punctate keratitis



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lotilaner ophthalmic solution 0.25%

What about MGD improvement?

Ersa Phase 2 study

- Lotilaner BID or TID x 12 weeks
- Statistically significant and clinically meaningful improvements compared to baseline in two objective measures:
 - the presence and quality of liquid secretion as measured by the Meibomian Gland Secretion Score (MGSS)
 - the number of glands secreting normal (clear) liquid as measured in the central 15 glands of the lower eyelid

No statistically significant differences were observed between the BID and TID treatment arms

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0.25% loteprednol (Eysuvis)

- First ocular corticosteroid approved by the FDA for treatment of dry eye flares
- QID dosing X 2 weeks

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cenegermin-bkbj (Oxervate)

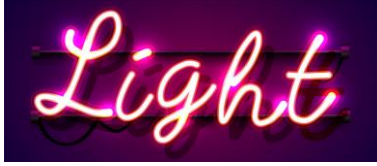
- FDA approved in 2018
- cenegermin-bkbj is structurally identical to human Nerve Growth Factor protein made in ocular tissue
- It is a recombinant nerve growth factor (protein)→this protein activates receptors that allow for differentiation & maintenance of neurons that support the innervation of the cornea
- Dosing: 6Xday (2hr Intervals) for 8 weeks
- Apply 1st if using ung/gel after
- Wait 15minutes CL insertion
- Can do another round if needed



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In Office Treatments

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Photobiomodulation "PBMT"

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$$\text{Energy} = \text{Joules}$$

$$\text{Fluence} = \text{Joules/cm}^2$$

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Terminology

- **BBL=Broadband light**
 - Uses a broader range of light spectrum → different treatment options, different range of skin conditions
- **IPL=Intense Pulsed Light**
 - Uses certain wavelengths & Fluence to target pigment or hemoglobin
- **LLLL=low light level therapy**
 - Uses red/near-infrared light energy to modulate cellular bioenergetics & increase energy production
- **Dry Eye Combo=IPL +LLLL**

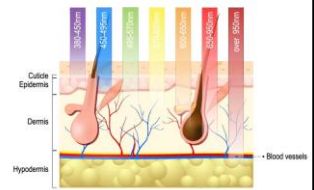
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IPL

- Uses different wavelengths
- Not a laser, IPL is
 - Non-Monochromatic
 - Non-coherent
 - Defocused



Light Therapy



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IPL Mechanism of Action

- Light is being absorbed by pigment & blood (chromophore) in skin
 - Melanin: absorption 400-750 nm range
 - Hemoglobin: absorbs 578nm
- Use different wavelengths to target skin depth, adjust power/fluence
 - Shorter wavelengths=superficial structures
 - Longer wavelengths=deeper into skin
 - 590→reaches dermis and nothing further
- Light emitted absorbed by the oxyhemoglobin→ causes blood vessels to lyse → reduces release of proinflammatory mediators

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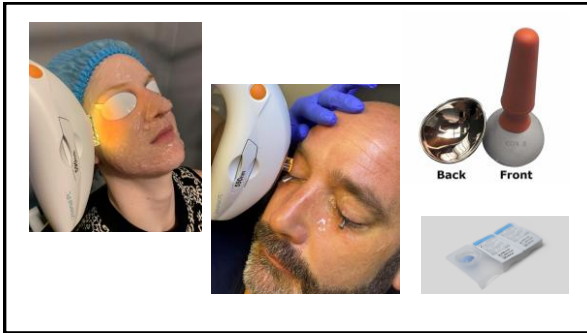
BBL/IPL Devices



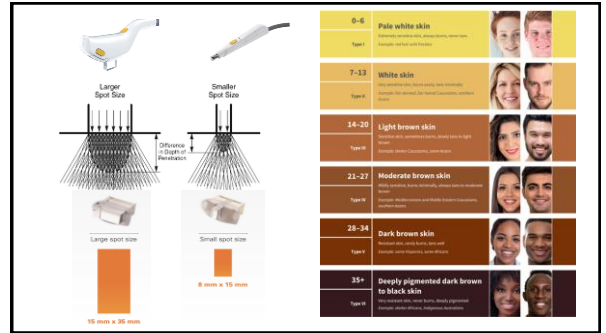
- On-Label:**
- MGD & Rosacea
 - 22yo and older
 - Moderate to severe signs & symptoms of dry eye disease
 - Fitzpatrick Skin Types I-V

- Off-Label:**
- Skin rejuvenation
 - Chalazion treatment

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IPL Protocol

- Toyo Protocol
- Periman Protocol
- # of treatments
- Lids vs no lids
- Contraindications

The diagram shows a front view of a human face with yellow horizontal bars highlighting the treatment areas on the cheeks and upper lip.

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LLLT (Low Level Light Therapy)

- Sends low incident levels of photo energy to cause photoactivation of the target cells
- Photoactivated cells increase ATP production which may better repair cellular damage and improve function

The top image shows a patient wearing red LLLT goggles. The bottom image shows the LLLT device, which is a white handheld unit with a flexible arm and a lens.

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LLLT

- Aesthetic Use: reduce fine lines, wrinkles, acne treatment, pain management, wound healing, & hair restoration
- Dry Eye
 - Treatment MGD, blepharitis, chalazion, & Hordeolum
 - Red Light = decrease inflammation
 - Blue Light = kill bacteria
 - Lower power than IPL (more inclusive for skin types & ages)
 - Treatments last 15-30min

Park Y, Kim H, Kim S, Cho K.J. Effect of low-level light therapy in patients with dry eye: a prospective, randomized, observer-masked trial. Sci Rep. 2022;12(1):3575. doi: 10.1038/s41598-022-07427-6

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What percentage of patients comply with at home warm compresses?

16%

Unlocking MGD Management Insights into Prescribing Patterns of Dry Eye Doctors in North America, O'Dell L, Garlich J, Mahdan M, Horn M. American Academy of Optometry, New Orleans October 2023

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Evaporation Treatment: In-Office

Thermal Expression

Device	Year	Method
Lipiflow	2011	Machine heat & expression
MiBo Thermoflo	2014	Heat only
TearCare	2019	Heat then doctor expression
Systane iLux2	2019	Doctor+device expression
RF	2023	Heat then doctor expression
Tixel i	2025	Heat then doctor expression

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Radio Frequency

- Generates vibrations of the tissue particles, which produce friction between tissue particles and, consequently, heat is generated
- Heat generated with RF could be useful for liquefying waxy secretions, unclogging MGS
- Activate the fibroblasts responsible for producing and repairing skin collagen and elastin.
- Stimulate periorbital skin rejuvenation
- Treatments last 30-60 min

LotusVisio

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Radio Frequency

- RF is energy delivered to the skin via applicator → applicator emits RF energy that penetrates deep within the skin converting to thermal heat
- Different thermal temps=different goals
 - When collagen is heated, reacts by producing more collagen to improve texture & elasticity
 - When fat cells are heated, it induces apoptosis of select fat cells
- RF energy is electrical (rather than light based) so melanin is unaffected
- RF for Dry Eye=40-43degrees (higher temps could cause orbital fat loss)

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Radio Frequency

- Monopolar RF
 - Applicator with 1 electrode (used on treatment area) & grounding plate/pad (usually patient's back)
 - Average depth 20mm (can affect deep dermis & subcutaneous fat)
 - Monopolar is different than unipolar devices
- Bipolar & Multipolar RF
 - Applicator has 2 electrodes (energy travels from one electrode into the skin back to the 2nd electrode on the same handpiece)
- Contraindications
 - **pacemaker, internal defibrillator, any active electrical implant in the body**
- Improvements in signs and symptoms in RF + expression patients were similar to patients treated with LipiFlow 3 months after treatment.

Jaccoma E, Litherland C, Jaccoma A, Ahmed A, Peliwé vs LipiFlow MGD-Related Dry Eye Treatment Study: The ThermalLid Procedure. Journal of Dry Eye Disease 2018; 1(1):11-421

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MG Probing


- Small, sterile probe is inserted into the openings of the meibomian glands, which are located on the eyelids.
- The probe gently breaks up and removes any blockages or scar tissue that may be obstructing the glands.
- This allows the glands to produce and release their natural oils (meibum), which are essential for maintaining a healthy tear film.

Dr. Maskin

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Muscle Stimulation



- Dynamic Muscle Stimulation Technology (DMS) to tone and tighten the periorbital area
- Uses electrical pulses to trigger nerve signals & activate muscles and inducing contractions
- Improves lower laxity & impaired blinking
- Clinical Data: 4 treatments (4-6 wk intervals)

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A GROWING OPPORTUNITY

Addressing the unmet needs of patients with lower lid laxity and impaired blinking

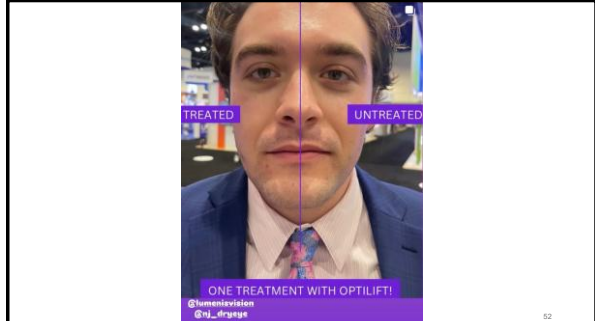


- MORE THAN **60%** of DED patients suffer from impaired lid closure*
- 78.3%** using ophthalmology clinics with eyelid-related issues*
- X2.2x** risk of developing severe ocular surface symptoms for patients with eyelid laxity*

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Microblepharoexfoliation

BlephEx



Zest



NuLids



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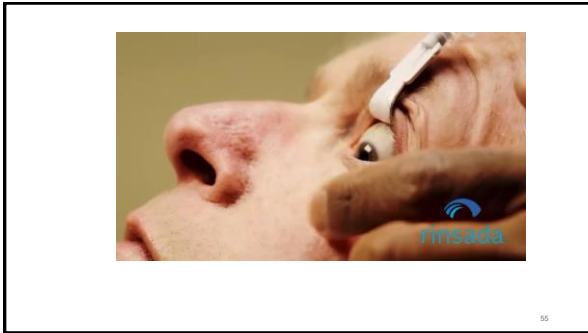
Eyelid Irrigation Device



- A device for cleaning the entire ocular surface
- Developed by Dr. Srinu Kondapalli (retina specialist)
- Able to reach undersurface of the eyelid and fornix
- Dry Eye or Allergy relief treatment

Rinsada

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Canalicular gel

- The gel is a transparent, cross-linked hyaluronic acid derivative and has been cleared by the FDA to temporarily block tear drainage by the occlusion of the canalicular system
- The gel is contained in a syringe which is packaged in a sealed tray. The device is packaged for single patient use.
- Fill up to 0.2mL per punctum

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Autologous Serum

- Using patients own blood as eye drops (red blood cells & clotting factors removed)
- Contains important growth factors & nutrients normally found in healthy tears
- 20%-40% concentrations
- Does NOT contain platelets

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PRP drops

- Platelet-rich plasma (PRP): blood-based product
- PRP has richer concentration of growth factors and other platelet-derived factors
- Not diluted
- Dosing: **The PRP Process**

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Amniotic Membranes

- Amnion: Innermost layer of the fetal membrane & placenta
- Shares the same cell origin as the fetus
- Contains anti-inflammatory cytokines & growth factors
- Harvested in a sterile environment from placental tissue obtained during elective cesarean sections from healthy mothers
- Donors are screened for transmissible disease

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Amniotic Membrane Types

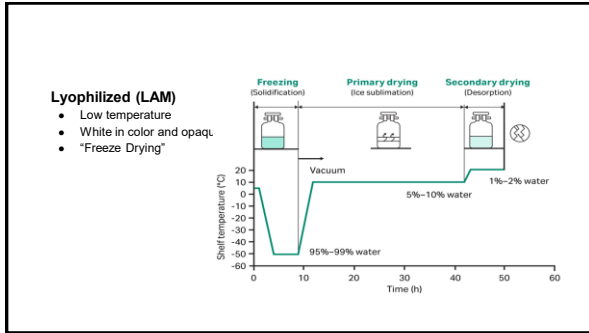
Cryopreserved

- harvest: slow freezing at -80 C using DMEM/glycerol preservation media (slow-rate freezing without ice formation)
- FDA approved for wound healing, anti-inflammatory, protective barrier
- held in place with plastic ring
- store in freezer

Dehydrated

- Preserved using vacuum with low temperature heat to retain devitalized cellular components
- FDA approved for wound healing
- Stored at room temperature-must be rehydrated to use
- Uses soft contact lens to hold in place

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Nutraceuticals

- Omega-3/6 supplementation
- Proprietary blends
 - Lutein, zeaxanthin isomers, curcuminoids, vitamin D

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Plasma Energy/Fibroblast Plasma Pens

- Plasma forms when gas is super heated
- Plasma pen device discharges an ionized gas in the air to create a small electrical arc that improves the appearance of the skin without heating surrounding tissue
- Make tissue firmer/tighter by inducing trauma that triggers skin cells called fibroblasts to produce more collagen (same logic as microneedling devices)

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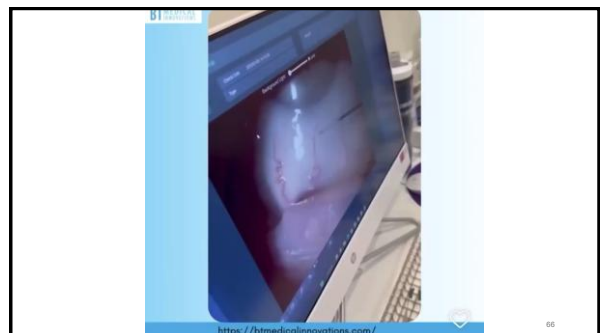
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Plasma Pen for CCH

- The plasma pen delivers plasma energy to shrink the loose tissue
- "plasma energy": superheated, ionized gas that is created by the device when it ionizes the air around it
- Essentially generates a small controlled "mini-burn" on the skin's surface, which then stimulates the skin's natural healing process to produce more collagen and elastin, resulting in skin tightening and wrinkle reduction; this process is also known as fibroblasting.
- For CCH: the procedure is performed at the slit lamp and takes about two minutes.
- Patients may experience minor irritation for a few days.

Ucar F. Alternative Approach for the Treatment of Conjunctivochalasia: Plasma-Based Conjunctivoplasty, Cornea. 2024 Feb 1;43(2):201-206.

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Ingredient resources

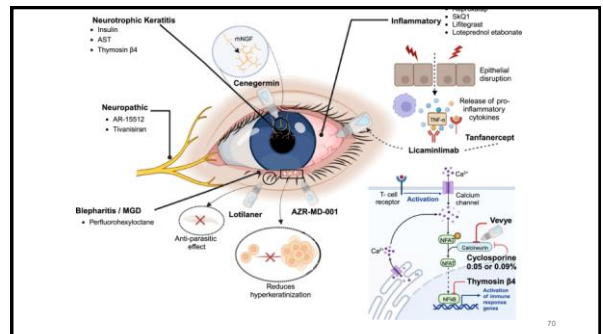
- ThinkDirty App 
- Ingredio App 
- <https://www.ewg.org/skindeep/>

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Future Dry Eye Treatments

- Reproxalap (Adeyra)
 - 0.25% topical ocular reproxalap; RASP modulator used to alleviate inflammation in DED & allergic conjunctivitis
- IVW-1001
 - TRPM8 agonist
 - Eyelid wipe that is applied over upper eyelid
- SI-614 (SEIKAGAKU)
 - Made of amphiphilic polymer produce by introducing hydrophobic group into hyaluronic acid --> stabilize tear film by utilizing mucoshesive and surface tension properties of SI-614
 - Promotes wound healing
- Visomitin (Mitotech)
 - Cardiolipin peroxidation inhibitor
 - Designed to sustain & restore mitochondrial function & interrupt apoptosis in mitochondrial conditions
- Apeita Biotechnologies (ApeitaBio); ung
 - Soil bacterium that can be toxic to insects
 - Currently available in headlice & garden pesticide products
- Azura Ophthalmics (selenium sulfide); ung
 - Reduces keratinocytic activity (softens the skin)
 - Selsun blue shampoo
- Hovione (minocycline hydrochloride); ung
- Ivermectin topical (1%)

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New Innovation Challenges

- Access to Care
- Where does it fit in your practice?
 - Office flow
 - Patient education
 - Team training
- Clinical Experience builds confidence
- Breaking out of the "hamster wheel" thinking

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THANK YOU!

  @jessilinqunt

SMART EYE CARE

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