




Optometric Education Consultants



Ocular Disease Interpretation and Utilization of New and Old Technologies

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Mackinac Island
Optometric Education Consultants
Sunday, August 28, 2022




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Disclosures- Greg Caldwell, OD, FAAO

All relevant relationships have been mitigated


- The content of this activity was prepared independently by me - Dr. Caldwell
- Lectured for: Alcon, Allergan, Aerie, BioTissue, Kala, Maculogix, Optovue, RVL, Heru
- Disclosure: Receive speaker honorariums
- Advisory Board: Allergan, Sun, Alcon, Maculogix, Dompe, Visus, Eyenovia
- Disclosure: Receive participant honorariums
- I have no direct financial or proprietary interest in any companies, products or services mentioned in this presentation
- Disclosure: Non-salaried financial affiliation with Pharmanex
- Envelope: PA Medical Director, Credential Committee
- Healthcare Registries - Chairman of Advisory Council for Diabetes
- The content and format of this course is presented without commercial bias and does not claim superiority of any commercial product or service
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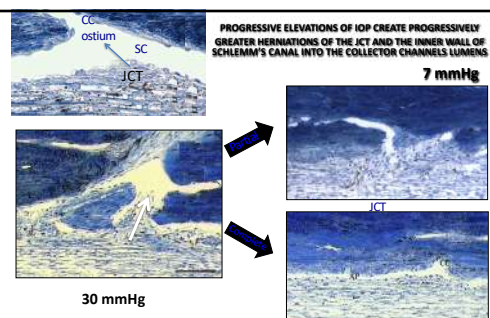
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My Goal - Today

To be able to do something better in patient care



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PROGRESSIVE ELEVATIONS OF IOP CREATE PROGRESSIVELY GREATER HERNIATIONS OF THE JCT AND THE INNER WALL OF SChLEMM'S CANAL INTO THE COLLECTOR CHANNELS LUMENS

7 mmHg

30 mmHg

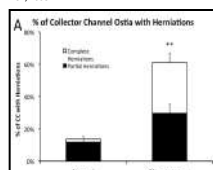
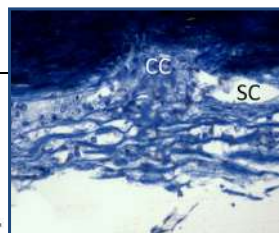
The pressure-induced herniations observed at 30 mmHg were either partially or completely reversible after the IOP was decreased to 7 mmHg in enucleated bovine eyes. So, in normal eyes, these herniations slide in and out with regular rise and fall of IOP.

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Human eyes with POAG even at 0mmHg, exhibit herniations and many more than in age-matched normal eyes

A: Significantly more herniations of the TM into CC ostia were found in POAG eyes (33 of 54), than in normal eyes (7 of 51) (61% vs. 14%, p<0.0001). In normal eyes, herniations that were present were predominantly partial (86%) rather than complete (14%). In POAG eyes, over half of the larger total number of herniations were complete (52%).

Battista SA, Luz, Hoffmann S, Freddo TF, Overby DR, Gong H: Acute IOP elevation reduces the available area for aqueous humor outflow and induces meshwork herniations into collector channels of bovine eyes. Invest. Ophthalmol. Vis. Sci., 49:5346-52, 2008.





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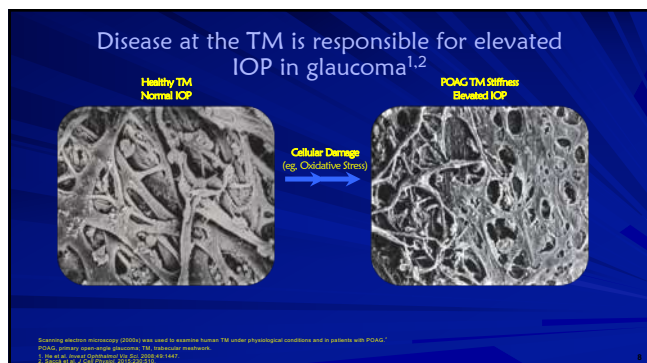
PRINCIPAL NEW FINDING

The presence of herniations, at 0 mm Hg, suggests they were permanent in-vivo obstructions in the ostia of CC, whether partial or complete. These are the only exits from Schlemm's canal. If enough of these 30 channels are fully or even partially blocked, IOP MUST go up.

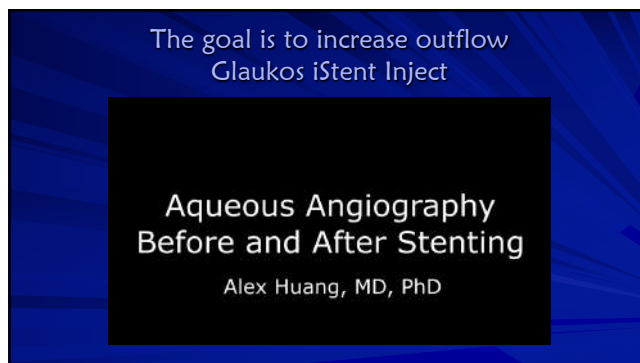
This study is the first to document the existence of permanent herniations into CC ostia in POAG. Since resistances in series are additive, it could be that these previously unreported permanent herniations, which obstruct CC ostia, represent an additional source of resistance, distal to the trabecular meshwork, in POAG.



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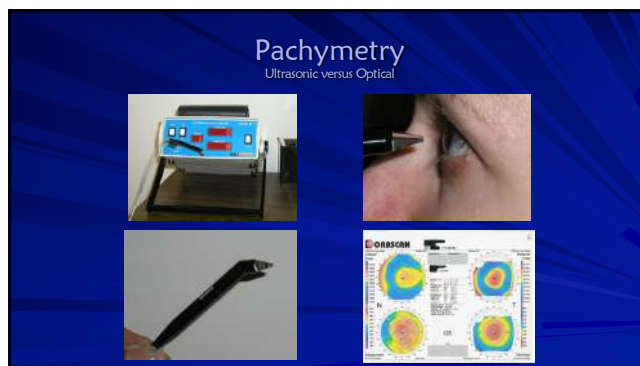
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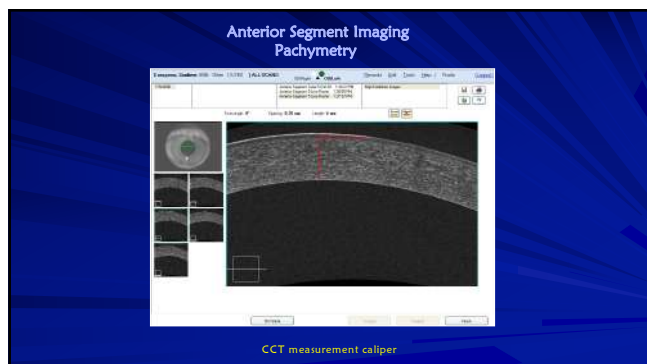
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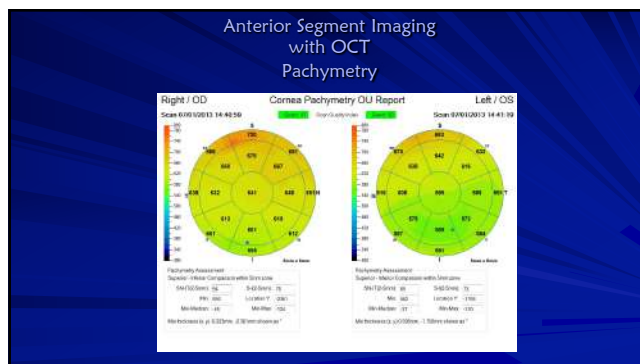
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Bonus on Visual Fields

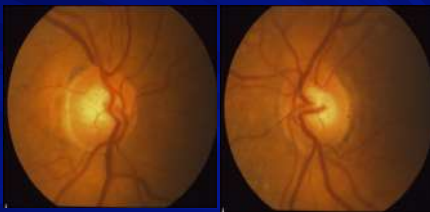
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50-year-old woman

- ☞ Recently has moved to the area and needs followed for her "ocular hypertension"
- ☞ Diagnosed 18 months ago
- ☞ Currently is using Travatan qd OU (PM)
- ☞ VA 20/15 OU
- ☞ Externals: unremarkable
- ☞ SLE: slight hyperemia OU
- ☞ IOP: 13 OD and 14 OS @ 8:30 AM

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ONH Appearance

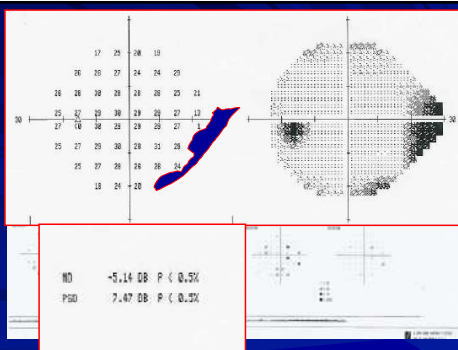


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Review of Records

- ☞ Diurnal IOP without medication
 - * OD 16-19 8:00 AM thru 5:30 PM
 - * OS 17-20 8:00 AM thru 5:30 PM
- ☞ Pachs
 - * OD 505
 - * OS 505
- ☞ VF results

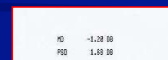
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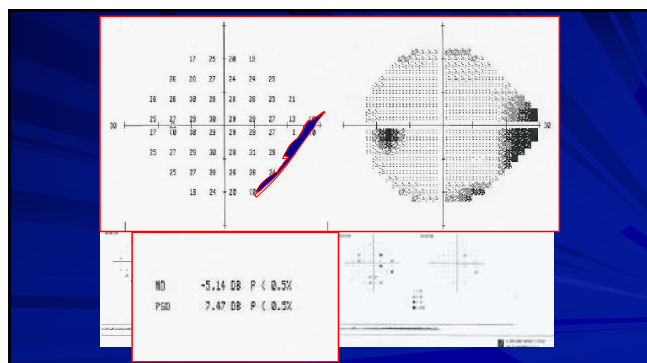
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MD and PSD

- ☞ MD
 - * 54 spots on 24-2
 - * All 54 spots reduced by 1 DB (54DB)
 - * MD 1DB
- ☞ PSD
 - * 54 spots on 24-2
 - * 27 spots reduced by 2 DB (54 DB)
 - * MD 1 DB
- ☞ Moderate PSD (More localized loss)
 - * 3.00 DB
- ☞ High PSD (Localized loss)
 - * 5.00 DB



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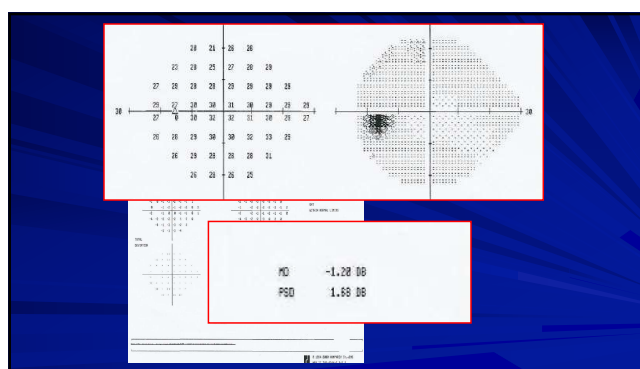
Discussion
Why is this patient being treated?

30

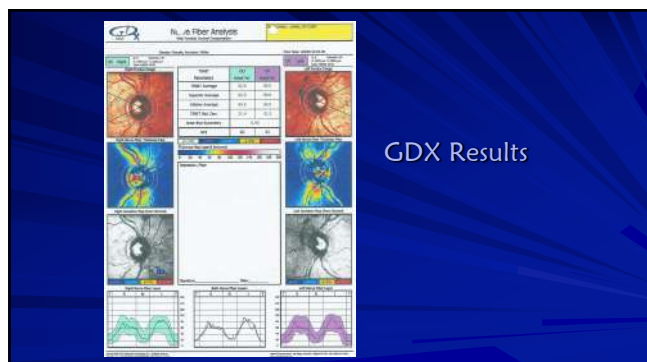
Treatment

- Repeat visual field
- Discontinue Travatan
- Get GDX nerve fiber analysis

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Cranium Keeper

- Do not back door patients into the ocular hypertension treatment study
 - Via thin pach results
- A patient needs to be suffering from ocular hypertension to use the study
- Thin pach tell us:
 - Patients with ocular hypertension are at high, medium or low risk for development
- If you have a diagnostic instrument learn how it works and make proper interpretations

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Ask Yourself

What's the Mean Deviation (MD) of a blind eye on a 24-2 Threshold Visual Field?

- * + 5 db
- * 0
- * -5 db
- * -12 db
- * -32 db
- * -50 db

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Thoughts on Mean Deviation (MD)

What is the Mean Deviation on a visual field of a blind eye?

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Thoughts on Mean Deviation (MD)

Turn on your VF let it run

- * 30 DB (decibel)

0-5	(1/6)	30% reduction
5-10	(1/3)	40% reduction
>10	(1/2)	50% reduction

How many DB difference to reliable VF should cause a RAPD?

- * 3 DB for a small APD, the larger the difference the greater the APD

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Wearable Technology

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A Wearable Technology

- Born out of the University of Miami's Bascom Palmer Eye Institute
- Their goal is to provide physicians and patients access to state-of-the-art, accurate, portable technology through real-time wearable diagnostics
- re:Vive™ by Heru™** is the modern, gamified diagnostic solution using a **lightweight, wearable headset** to aid doctors in diagnosis
- Future developments include vision augmentation applications utilizing AI algorithms to personalize vision enhancement.

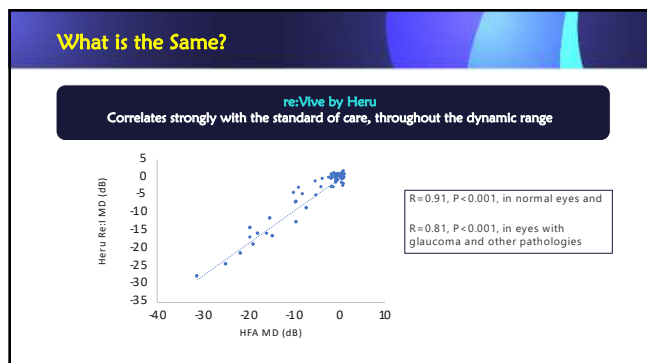
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A Decade of Research, Innovation and Clinical Validation

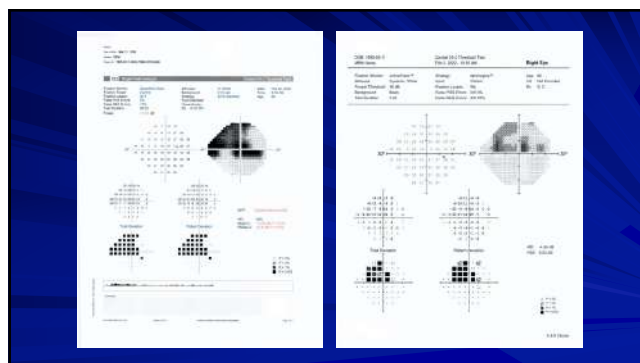
Artificial Intelligence (AI) driven diagnostics and vision augmentation platform is backed by ten years of research and clinical validation at the University of Miami's Bascom Palmer Eye Institute where it is continuously developed.

- 10 Years of Clinical and Scientific Research
- 40 U.S. and International Patents to Date
- 1,000+ Patients in Clinical Trials
- 450 Million Patients with Visual Field Defects

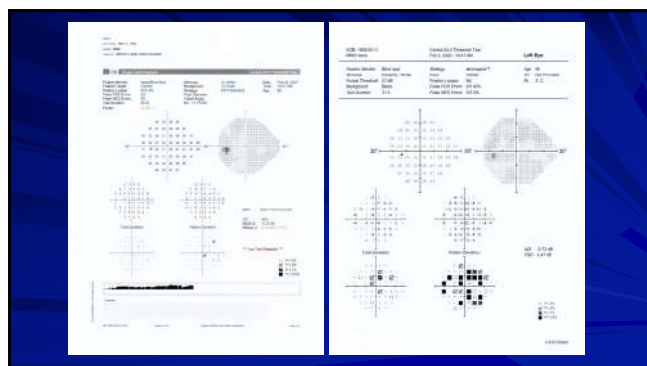
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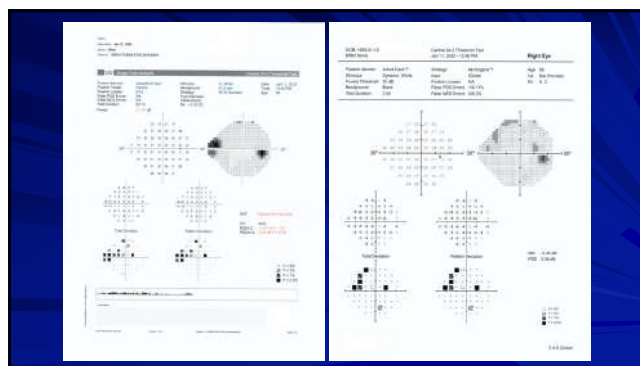
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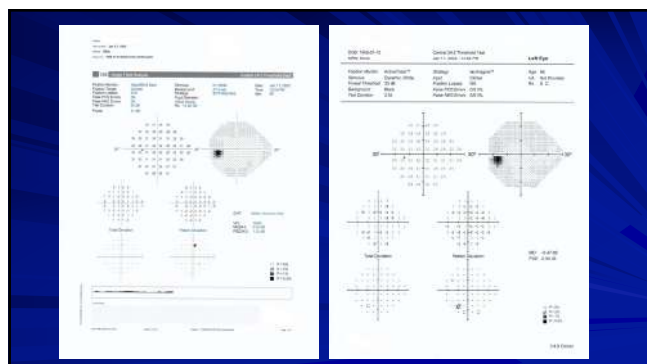
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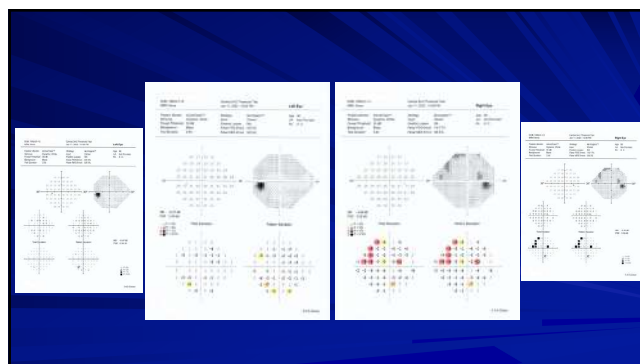
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re:Vive 2.0 – Color Vision

- ~ **Ishihara Color Vision Screening**
 - Ishihara color vision testing is a commonly used rapid, color vision screening modality.
 - This test can be completed in under 2 minutes.
 - 3 or more Ishihara plates incorrect will trigger the D-15 extended vision test using AutoWorkflow."
- ~ **Farnsworth D-15 Extended Color Vision Test**
 - D-15 color vision testing is a commonly used color vision diagnostic modality.
 - D-15 test is a **reimbursable** service: **CPT Code 92283**
 - **Average national reimbursement is \$56.16**.
 - This is more advanced than any color vision testing currently being offered by competitor goggle companies.

Technician and/or clinician not required to administer exam.

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re:Vive 2.0 - Contrast Sensitivity

- Embracing the science connecting contrast sensitivity with detecting early AMD, re:Vive provides the most efficient way to document and monitor the functional macular health in conjunction with supplementation.
- We are reporting the change over time from the last visit. The doctor can use this change to communicate the benefits of lifestyle modifications, smoking cessation.
- Moves test out of the exam lane with the screening being performed in full room lighting.
- Contrast Sensitivity (and Dark Adaptation) are part of a broader AMD screening and diagnostic portfolio.

TEST RESULTS			
Right Eye		Left Eye	
1.85	10%	0.60	85%
1.00	10%	0.60	85%

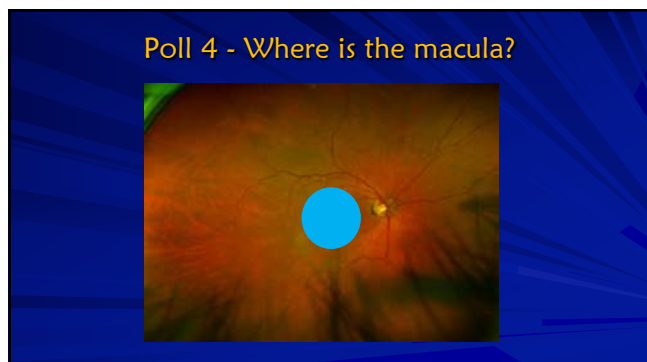
Technician and/or clinician not required to administer exam.

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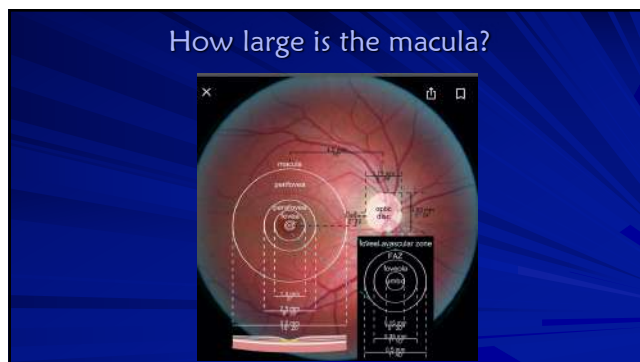
Instruments for AMD – fragmented care

- ~ Slit lamp/DFE
- ~ Camera
- ~ OCT
- ~ OCT Angiography
- ~ Dark adaption
- ~ PHP
- ~ Macula pigment eval – Scanner
- ~ Genetic testing

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Early Onset Pathogenesis

- ~ Drusen small or large are not makers for early stage AMD
 - * Visible structural evidence of a pathological process
 - Underway for quite some time
- ~ Cholesterol deposits exist beneath the surface long before drusen form
 - * Cannot be seen with structure-based methods
 - * Cholesterol produced by RPE and deposits into Bruch's membrane
 - * Continue to layer in Bruch's membrane
- ~ As this cholesterol accumulates the process unfolds with compromise to the outer retina
 - * Inflammation
 - * Oxidative stress
 - * Disruption of oxygen and nutrients
 - * Drusen formation
- ~ Impaired Vitamin A across Bruch's membrane
 - * Functional impairment can occur to dark adaptation

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Healthy choriocapillaris, Bruch's, RPE, and Photoreceptors



The diagram illustrates a healthy cross-section of the retina. At the top, the choriocapillaris is shown as a network of blood vessels. Below it is Bruch's membrane, followed by the retinal pigment epithelium (RPE) and the photoreceptors. The layers are clearly defined and healthy.

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Cholesterol barrier deposited along Bruch's and RPE



The diagram shows the progression of AMD. Cholesterol deposits, represented by yellow and orange granules, have accumulated along Bruch's membrane and the RPE. The photoreceptors are still present but the underlying layers are compromised.

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RPE Secretes even more cholesterol and degenerates



The diagram shows further progression of AMD. The RPE is now degenerating and secreting even more cholesterol, which is accumulating in larger clumps. The photoreceptors are beginning to show signs of damage.

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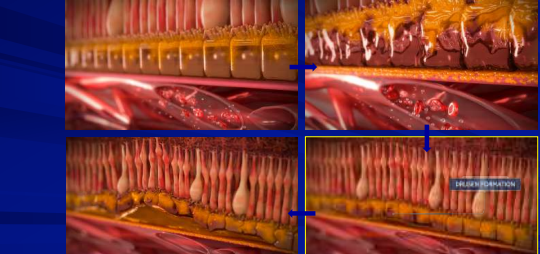
Finally, visibly evident drusen on fundus evaluation



The diagram shows the final stage of early AMD. Large, visible drusen are present on the fundus, indicated by a yellow circle. The underlying retinal layers are significantly compromised.

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AMD is a Disease Process that Starts Below the Surface



The diagram illustrates that AMD is a disease process that starts below the surface. It shows the progression from healthy layers to the accumulation of cholesterol and the formation of drusen, which are visible on the fundus.

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Beckmann Committee Classification of AMD

Based on presence of lesions within 2 DD of fovea in either eye

- No AMD**
 - None or few small drusen, < 63 microns
 - No AMD pigmentary abnormalities
- Early AMD**
 - Medium drusen, > 63 – <125 microns
 - No AMD pigmentary changes
- Intermediate AMD**
 - 1 large drusen, > 125 microns
 - Any AMD pigmentary changes
- Advanced AMD**
 - Any geographic atrophy
 - Choroidal neovascularization (CNV)

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AMD is a Disease Process that Starts Below the Surface

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Applying a Familiar Standard of Care: Two Multifactorial Diseases

	Glaucoma	AMD
Structure	Cup-to-disc Ratio	Drusen
Function	Visual Field	Dark Adaptation
Risk	Intraocular Pressure (IOP) Corneal Thickness Age/race Family history/etc. Health and Lifestyle (Diabetes)	Age Genetic Testing Health and Lifestyle (Smoking) Macular Pigment Optical Density (MPOD) Contrast Sensitivity

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Dark Adaptation in AMD Function Test

- Measures how long to recover from bright light to darkness
 - Rod Intercept line (RI) time
- Functional test that can help overcome the challenges in diagnosing AMD
- Alabama Study on Early Age-Related Degeneration (ALSTAR)
 - Able to detect subclinical 3 years before clinically visible
 - 325 adults without clinically detectable AMD
- Rod deterioration happens in earliest stages of AMD
 - Earlier detection before visual acuity
- AdaptDx 92284
 - Sensitivity 90.6%
 - Specificity 90.5%

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Dark Adaptation in AMD Function Test January 1st, 2020

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AdaptDx Pro Now Available for Clinical Use

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This Means We Now Have an *Early* Symptom
We Can Use to Help Diagnose AMD



- Night vision impacted in early AMD: 30+ studies
- AMD patients often give up driving at night
- Night vision is impaired before day vision
- Typically ECP's chalk this complaint up to cataracts

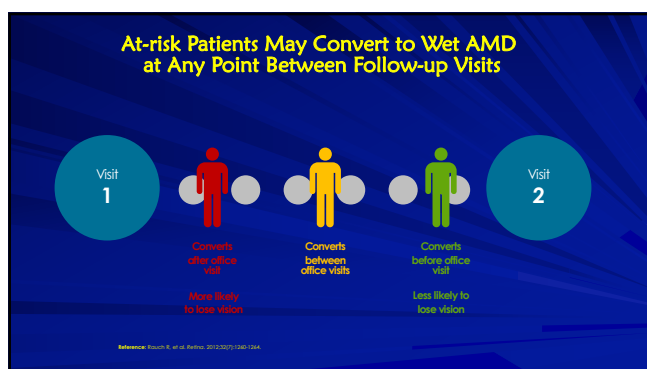
**Ask Every Patient Over 50
About Their Night Vision**

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Poll 5
**Preferential Hyperacuity
Perimetry (PHP)**

Who does this testing?

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Notal Vision - ForeseeHome® product overview



Uses **Preferential Hyperacuity Perimetry (PHP)**

Medicare covered

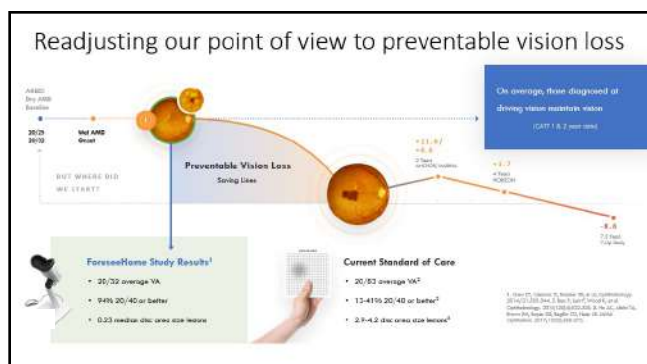
6,000+ actively testing patients

600+ active prescribers

Proven efficacy with level 1 evidence

Reference: Data on File.

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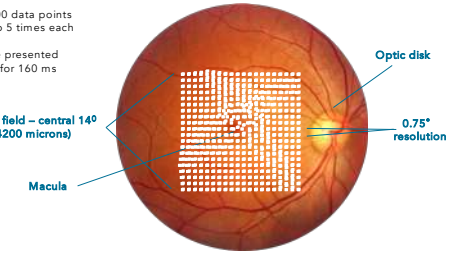


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Notal Vision- PERIMETRY: The ForeseeHome Test

Total of 500 data points tested 3 to 5 times each

Stimuli are presented on screen for 160 ms



Visual field - central 140° (4200 microns)

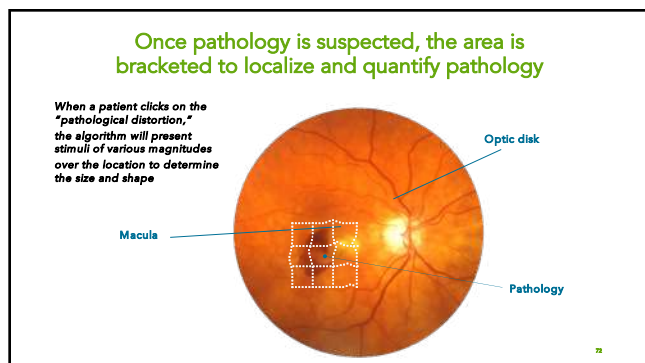
Macula

Optic disk

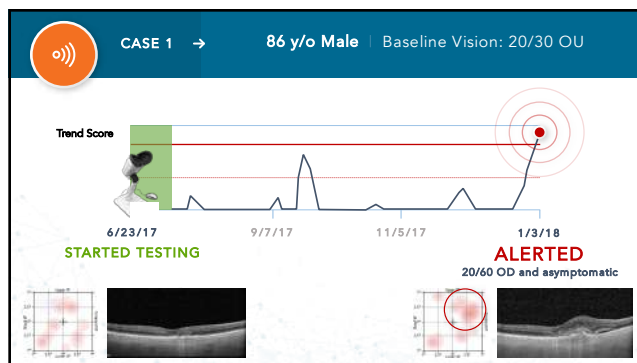
0.75° resolution

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Treatments for AMD

- Early detection and meaningful treatments with significant value, do not cure, but have been shown to slow or halt progression. Not limited to early stages but all stages of AMD
- Prescribe smoking cessation programs
 - Smoking and AMD
 - Depletes serum antioxidants
 - Decreases pigmentary density
 - Increases risk to advanced AMD
- Lifestyle changes
 - Diet
 - Exercise
- Systemic disease management
 - Cardiovascular disease, DM, obesity, high cholesterol

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Treatment for AMD

Nutritional supplements

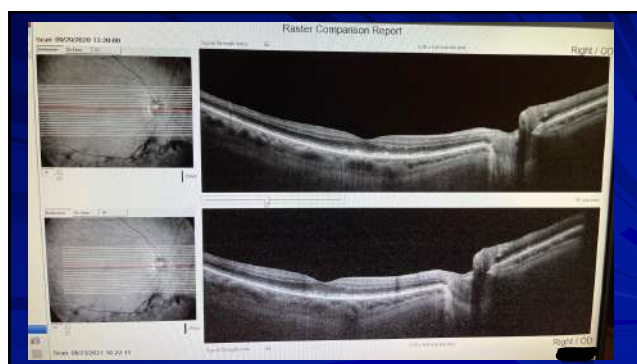
- Sub-clinical/sub-structural or early disease
 - Controversy flourishes
 - No definitive guideline exists
 - Despite consensus evidence suggests using supplements
- Intermediate - advance disease
 - No controversy on advocating for supplements
- AREDS 1
 - Contains Beta-carotene and no lutein or zeaxanthin, no longer recommended
 - Investigated early AMD, no statistically significant benefit
- AREDS 2
 - Recommended for intermediate and advanced AMD, study protocol
- The Practical Guide for the Treatment of AMD - 3 primary options
 - Macular pigment supplement
 - Carotenoids: lutein, zeaxanthin, meso-zeaxanthin
 - Carotenoids, antioxidants, zinc, and vitamins C & E
 - Carotenoid macular supplement in subclinical and early AMD. Carotenoid and antioxidant is intermediate and AMD that is progressing

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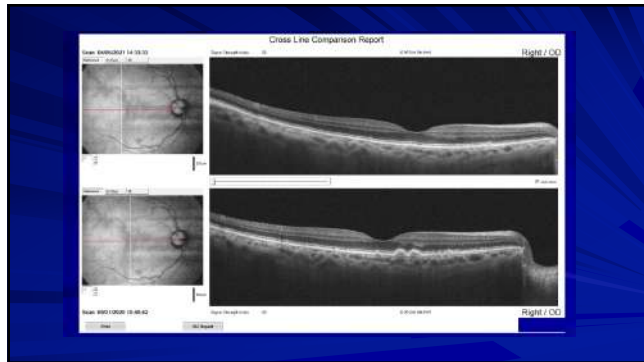
Treatment for AMD

- Retinal light protection
 - Sun exposure
- Closer follow up
 - 12 months is currently accepted as being too long to detect progression
 - 6 months or sooner based on risk of CNV
- Low vision and rehabilitation consultation

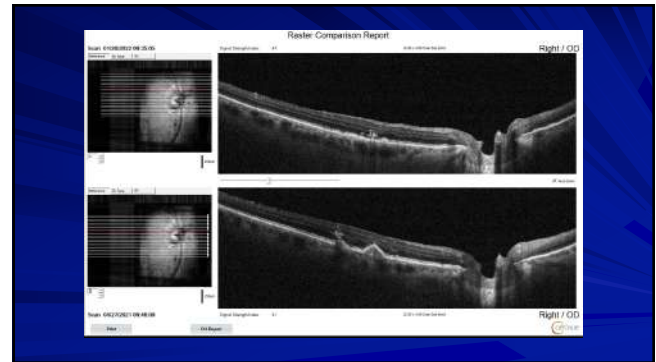
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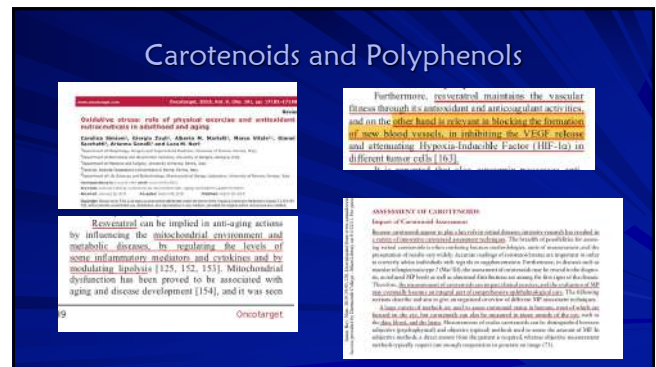
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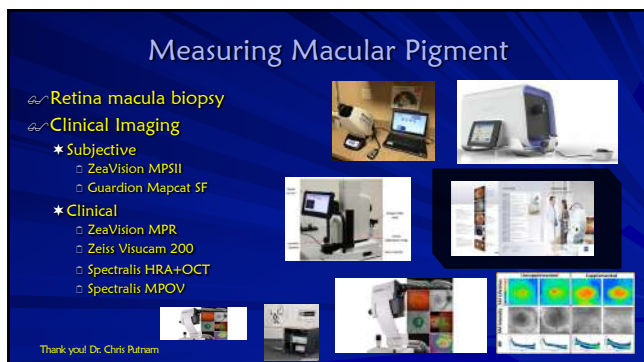
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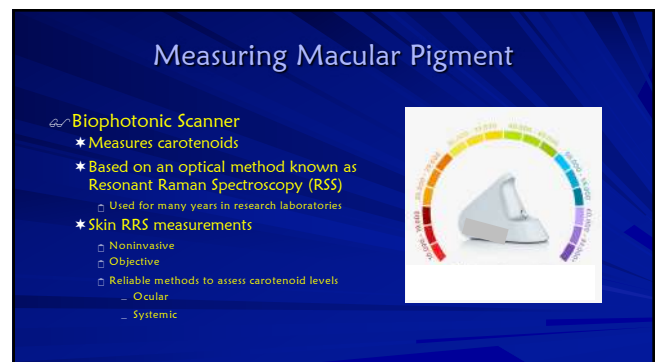
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Carotenoid Levels

Biomarker of health for diet and lifestyle

- ★ Yale University
- Phospholipid bi-layer
- Carotenoids, flavonoids, and polyphenols


Correlations Between Macular, Skin, and Serum Carotenoids

Chen, D. G. et al. (2016) *Investigative Ophthalmology and Visual Science* 55(12):3800-3808

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Carotenoid Levels


NIH National Institutes of Health
Turning Discovery Into Health



- Quick Test (approx. 30 sec)
- Portable
- Cost Effective
- Remeasure in 60 days
- Reassurance to you and patient

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Raman Spectroscopy



478nm PHOTONS ARE EMITTED FROM THE SCANNER

478nm PHOTONS STRIKE CAROTENOIDS IN THE SKIN, THEY ARE REFLECTED BACK AS 478nm PHOTONS

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Resonance Raman spectroscopic evaluation of skin carotenoids as a biomarker of carotenoid status for human studies

Susan T. Mayne^{1,2}, Brenda Cartmel³, Stephanie Scarino^{4,5}, Lisa Jahns⁶, Igor V. Ermakov⁴, Werner Gellermann⁴

90 STUDIES

Arch Biochem Biophys. PMC 2014 Nov 15.

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ARVO STUDY

Interrelationships between Macula, Skin and Serum Carotenoids- Paul Bernstein, Werner Gellerman et al ARVO May 2016

Conclusions:

"Our results emphasize the importance of measuring the total amount of carotenoids in the macula region using an objective image based modality such as AFI w Spectralis rather than subjective MPOD."

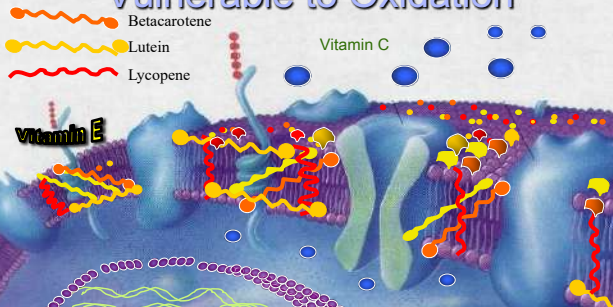
Skin resonance Raman Spectroscopy of skin carotenoids is a reasonable biomarker of macula carotenoid status, and correlates better than than subjective MPOD tests.



The objective, hand scanner is better than the subjective Macuscope, QuantREYE, and Densitometer for estimating macula pigment.

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Vulnerable to Oxidation



Betacarotene

Lutein

Lycopene

Vitamin C

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53-year-old man

- Family history of AMD
 - Dad with 43 injections for AMD
- Pre-diabetic with borderline HbA1c
- Vision 20/20 OU
- DFE- retina clear
- OCT normal
- Passes dark adaptation

CONGRATULATIONS ON TAKING THE FIRST STEPS TOWARDS OPTIMIZING YOUR SCS

Recently, on 12/10/2021, you met with me and scanned the palm of your hand with the BioPhotonic Scanner. Your score earned a Skin Carement Score (SCS) of 1000.

This score represents the current (normalized) level of your skin. The higher the score, the more consistently your body is healing.

1000

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Ingredients

Ingredients	Amount	% Daily Value
Serving Size: 1 Packet		
Vitamin A (as Beta Carotene) (875 mcg RAE from Retenol (vitamin A palmitate) (275 mcg RAE))	2750 mcg RAE	250%
Vitamin C (as Cell-U-Lin Ascorbate)	2500 mg	250%
Vitamin D (as Cholecalciferol)	5 mcg	100%
Vitamin E (as D-Alpha-Tocopheryl Acetate, D-Alpha-Tocopherols, Tocotrienols)	50.3 mg	100%
Vitamin K (as Phytylmethylsilane)	25 mcg	25%
Vitamin B1 (as Thiamine Mononitrate)	25 mg	25%
Vitamin B2 (as Riboflavin)	2.5 mg	25%
Vitamin B6 (as Pyridoxine Hydrochloride)	5 mg	25%
Vitamin B12 (as Cyanocobalamin)	500 mcg	25%
Vitamin B9 (as Folic Acid)	500 mcg	25%
Vitamin B10 (as Carnitine)	500 mcg	25%
Vitamin B11 (as Inositol)	500 mcg	25%
Vitamin B12 (as Methylcobalamin)	500 mcg	25%
Vitamin B13 (as Adenosine)	500 mcg	25%
Vitamin B14 (as Guanosine)	500 mcg	25%
Vitamin B15 (as Pantoic Acid)	500 mcg	25%
Vitamin B16 (as Panthoic Acid)	500 mcg	25%
Vitamin B17 (as Amygdalin)	500 mcg	25%
Vitamin B18 (as Salicylic Acid)	500 mcg	25%
Vitamin B19 (as Salicylic Acid)	500 mcg	25%
Vitamin B20 (as Salicylic Acid)	500 mcg	25%
Vitamin B21 (as Salicylic Acid)	500 mcg	25%
Vitamin B22 (as Salicylic Acid)	500 mcg	25%
Vitamin B23 (as Salicylic Acid)	500 mcg	25%
Vitamin B24 (as Salicylic Acid)	500 mcg	25%
Vitamin B25 (as Salicylic Acid)	500 mcg	25%
Vitamin B26 (as Salicylic Acid)	500 mcg	25%
Vitamin B27 (as Salicylic Acid)	500 mcg	25%
Vitamin B28 (as Salicylic Acid)	500 mcg	25%
Vitamin B29 (as Salicylic Acid)	500 mcg	25%
Vitamin B30 (as Salicylic Acid)	500 mcg	25%
Vitamin B31 (as Salicylic Acid)	500 mcg	25%
Vitamin B32 (as Salicylic Acid)	500 mcg	25%
Vitamin B33 (as Salicylic Acid)	500 mcg	25%
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Vitamin B36 (as Salicylic Acid)	500 mcg	25%
Vitamin B37 (as Salicylic Acid)	500 mcg	25%
Vitamin B38 (as Salicylic Acid)	500 mcg	25%
Vitamin B39 (as Salicylic Acid)	500 mcg	25%
Vitamin B40 (as Salicylic Acid)	500 mcg	25%
Vitamin B41 (as Salicylic Acid)	500 mcg	25%
Vitamin B42 (as Salicylic Acid)	500 mcg	25%
Vitamin B43 (as Salicylic Acid)	500 mcg	25%
Vitamin B44 (as Salicylic Acid)	500 mcg	25%
Vitamin B45 (as Salicylic Acid)	500 mcg	25%
Vitamin B46 (as Salicylic Acid)	500 mcg	25%
Vitamin B47 (as Salicylic Acid)	500 mcg	25%
Vitamin B48 (as Salicylic Acid)	500 mcg	25%
Vitamin B49 (as Salicylic Acid)	500 mcg	25%
Vitamin B50 (as Salicylic Acid)	500 mcg	25%
Vitamin B51 (as Salicylic Acid)	500 mcg	25%
Vitamin B52 (as Salicylic Acid)	500 mcg	25%
Vitamin B53 (as Salicylic Acid)	500 mcg	25%
Vitamin B54 (as Salicylic Acid)	500 mcg	25%
Vitamin B55 (as Salicylic Acid)	500 mcg	25%
Vitamin B56 (as Salicylic Acid)	500 mcg	25%
Vitamin B57 (as Salicylic Acid)	500 mcg	25%
Vitamin B58 (as Salicylic Acid)	500 mcg	25%
Vitamin B59 (as Salicylic Acid)	500 mcg	25%
Vitamin B60 (as Salicylic Acid)	500 mcg	25%
Vitamin B61 (as Salicylic Acid)	500 mcg	25%
Vitamin B62 (as Salicylic Acid)	500 mcg	25%
Vitamin B63 (as Salicylic Acid)	500 mcg	25%
Vitamin B64 (as Salicylic Acid)	500 mcg	25%
Vitamin B65 (as Salicylic Acid)	500 mcg	25%
Vitamin B66 (as Salicylic Acid)	500 mcg	25%
Vitamin B67 (as Salicylic Acid)	500 mcg	25%
Vitamin B68 (as Salicylic Acid)	500 mcg	25%
Vitamin B69 (as Salicylic Acid)	500 mcg	25%
Vitamin B70 (as Salicylic Acid)	500 mcg	25%
Vitamin B71 (as Salicylic Acid)	500 mcg	25%
Vitamin B72 (as Salicylic Acid)	500 mcg	25%
Vitamin B73 (as Salicylic Acid)	500 mcg	25%
Vitamin B74 (as Salicylic Acid)	500 mcg	25%
Vitamin B75 (as Salicylic Acid)	500 mcg	25%
Vitamin B76 (as Salicylic Acid)	500 mcg	25%
Vitamin B77 (as Salicylic Acid)	500 mcg	25%
Vitamin B78 (as Salicylic Acid)	500 mcg	25%
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Vitamin B80 (as Salicylic Acid)	500 mcg	25%
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Vitamin B87 (as Salicylic Acid)	500 mcg	25%
Vitamin B88 (as Salicylic Acid)	500 mcg	25%
Vitamin B89 (as Salicylic Acid)	500 mcg	25%
Vitamin B90 (as Salicylic Acid)	500 mcg	25%
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Vitamin B96 (as Salicylic Acid)	500 mcg	25%
Vitamin B97 (as Salicylic Acid)	500 mcg	25%
Vitamin B98 (as Salicylic Acid)	500 mcg	25%
Vitamin B99 (as Salicylic Acid)	500 mcg	25%
Vitamin B100 (as Salicylic Acid)	500 mcg	25%

92

SUPPLEMENT FACTS

Supplement Facts	Amount Per Serving	% Daily Value
Vitamin A (as Beta Carotene) (875 mcg RAE from Retenol (vitamin A palmitate) (275 mcg RAE))	2750 mcg RAE	250%
Vitamin C (as Cell-U-Lin Ascorbate)	2500 mg	250%
Vitamin D (as Cholecalciferol)	5 mcg	100%
Vitamin E (as D-Alpha-Tocopheryl Acetate, D-Alpha-Tocopherols, Tocotrienols)	50.3 mg	100%
Vitamin K (as Phytylmethylsilane)	25 mcg	25%
Vitamin B1 (as Thiamine Mononitrate)	25 mg	25%
Vitamin B2 (as Riboflavin)	2.5 mg	25%
Vitamin B6 (as Pyridoxine Hydrochloride)	5 mg	25%
Vitamin B12 (as Cyanocobalamin)	500 mcg	25%
Vitamin B9 (as Folic Acid)	500 mcg	25%
Vitamin B10 (as Carnitine)	500 mcg	25%
Vitamin B11 (as Inositol)	500 mcg	25%
Vitamin B12 (as Methylcobalamin)	500 mcg	25%
Vitamin B13 (as Adenosine)	500 mcg	25%
Vitamin B14 (as Guanosine)	500 mcg	25%
Vitamin B15 (as Panthoic Acid)	500 mcg	25%
Vitamin B16 (as Panthoic Acid)	500 mcg	25%
Vitamin B17 (as Amygdalin)	500 mcg	25%
Vitamin B18 (as Salicylic Acid)	500 mcg	25%
Vitamin B19 (as Salicylic Acid)	500 mcg	25%
Vitamin B20 (as Salicylic Acid)	500 mcg	25%
Vitamin B21 (as Salicylic Acid)	500 mcg	25%
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93

53-year-old man

CONGRATULATIONS ON TAKING THE FIRST STEPS TOWARDS OPTIMIZING YOUR SCS

Recently, on 12/10/2021, you met with me and scanned the palm of your hand with the BioPhotonic Scanner. Your score earned a Skin Carement Score (SCS) of 1000.

This score represents the current (normalized) level of your skin. The higher the score, the more consistently your body is healing.

1000

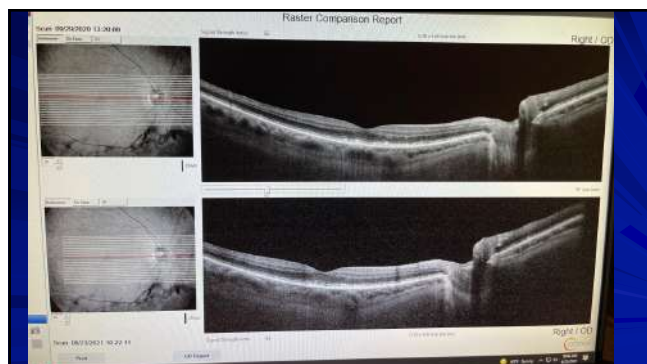
CONGRATULATIONS ON TAKING THE FIRST STEPS TOWARDS OPTIMIZING YOUR SCS

Recently, on 12/10/2021, you met with me and scanned the palm of your hand with the BioPhotonic Scanner. Your score earned a Skin Carement Score (SCS) of 1000.

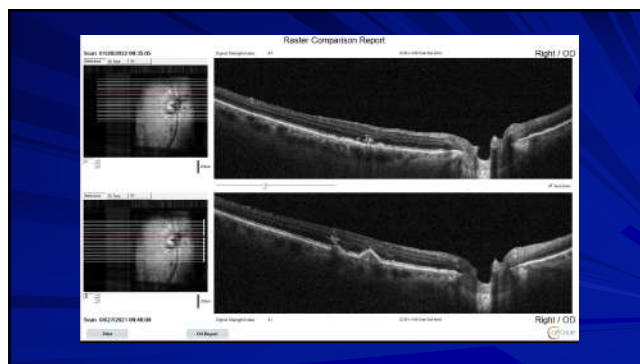
This score represents the current (normalized) level of your skin. The higher the score, the more consistently your body is healing.

1000

94



95



96

Keratoconus

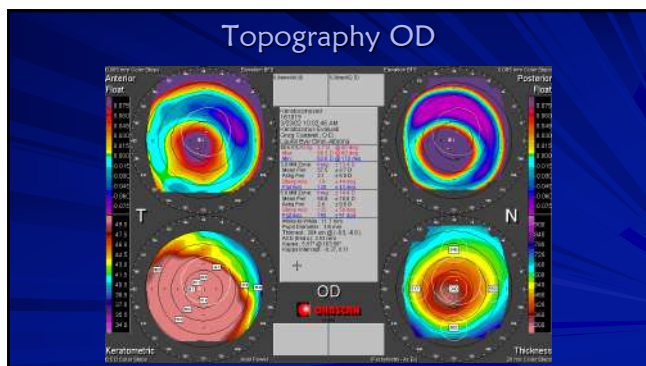
97

Advanced Keratoconus



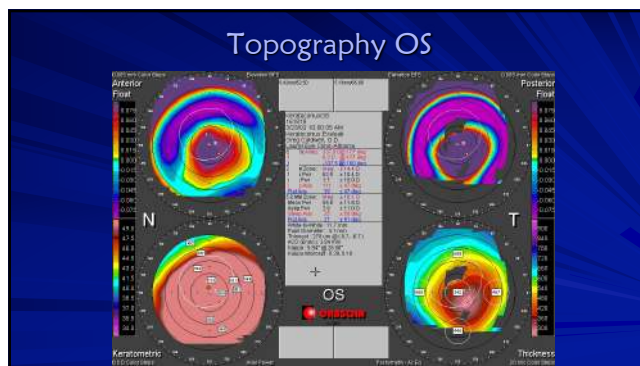
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Topography OD



99

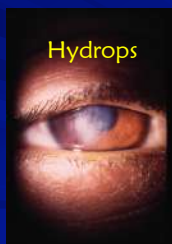
Topography OS



100

What happens when the posterior cone gets
too steep and Descemet's membrane
ruptures?

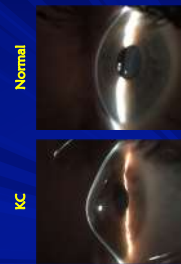
Hydrops



101

Keratoconus

- Progressive corneal disease
 - Focal thinning, steepening, bulging, and irregular shape
 - Loss of biomechanical strength
 - Bilateral, asymmetric, clinically non-inflammatory
- Caused by a combination of genetic and environmental factors
 - Allergies and eye rubbing
- Onset in puberty
 - Typically progressive to 4th decade of life
 - Previously estimated 1:2000 (1986 US), more recent estimate 1:375 (2017 Netherlands)



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Importance of Early Diagnosis in Keratoconus

- As keratoconus progresses, it becomes more challenging to manage
- Progressive keratoconus often results in:
 - Loss of visual acuity
 - Decreased tolerance to contact lens wear, caused by the ongoing changes in the cornea
- The earlier progressive keratoconus is diagnosed, the sooner treatment can be provided that may slow the progression of the disease.¹
- Important to diagnose and educate patients before visual function is lost**
- CXL is an early intervention intended to slow or halt the progression of keratoconus

1. Gelles, J. D., OD, FRCO, FCLSA. (2017, April). The Optometrist's Role in Keratoconus Management. Advanced Ocular Care.

104

Watch Out for Keratoconus!

8 Potential Signs & Symptoms

Typically onset occurs in teenage years or early twenties

- Frequent Changes in Refraction or Increasing Cylinder
- Reduced Best Corrected Visual Acuity
- Progressive Headaches
- Miles and Distortion
- Family History of Keratoconus
- Excessive Eye Rubbing
- Difficulty Seeing at Night
- Increased Light Sensitivity

LOOK OUT FOR KC!

- Look out** for warning signs in medical history
 - History of eye rubbing
 - Family & genetic predispositions
- Look out** for visual complaints
 - Blurred vision
 - Distortion of images
- Look out** for refractive anomalies
 - Distortion of mires on keratometry
 - Error messages on autorefractors
 - Unsatisfactory attempts at vision correction & progressive loss of UCVA & BCVA
 - Increasing astigmatism

If you believe a patient may have keratoconus, perform a diagnostic search or FIM. An Expert at Cornea (KCC) can refer them for a KC screening.

105

Cross-linking Procedure Summary

1. Remove epithelium
2. Soak cornea Photrexa® Viscous (riboflavin 5-phosphate in 20% dextran ophthalmic solution) for 30 minutes
3. Check for flare
4. Once flare is observed, measure corneal thickness. If corneal thickness is less than 400 µm, instill 2 drops of Photrexa (riboflavin 5-phosphate in ophthalmic solution) until the corneal thickness increases to at least 400 µm
5. Irradiate for 30 minutes. Continue applying Photrexa Viscous (riboflavin 5-phosphate in 20% dextran ophthalmic solution) during irradiation.

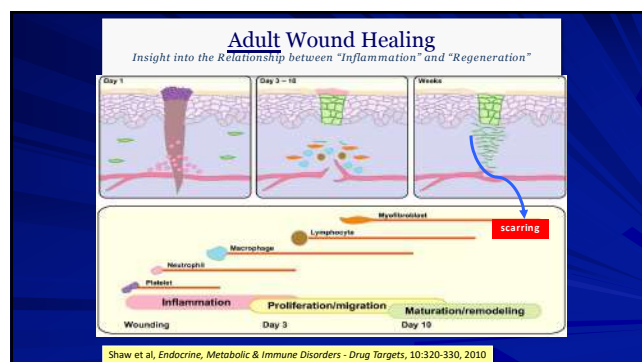
* Refer to prescribing information for entire FDA-approved procedure

106

Amniotic Membrane History

- Amniotic membrane transplantation (AMT) in ophthalmic surgery
 - ★ First documented in 1940
- 1995 Kim and Tseng used AMT for ocular surface reconstruction
- 1997 AmnioGraft (BioTissue), first in USA
 - ★ Surgical AMT, sutured
- 2005 ProKera (BioTissue), single sheet, self retained, polycarbonate, in-office and sutureless
- 2012 AmbioDisk (Katena/IOF), sutureless
- 2013 BioD Optix (BioD), sutureless

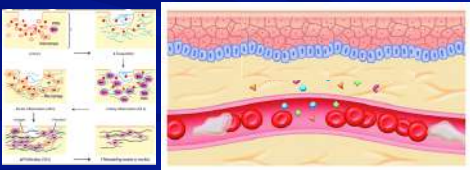
107



108

Regeneration vs. Repair


- Regeneration = cells/tissue reproduction = NO SCAR
- Repair = Healing by granulation tissue / scar formation
 - Scarring correlates directly with Inflammation
 - Controlling Inflammation → Reduces Scarring



109

The Amniotic Membrane

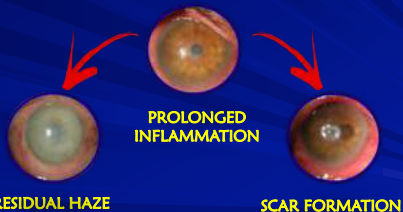
- ~ The amniotic membrane is the innermost lining of the placenta (amnion)
- ~ Are from planned Caesarean section births



110

Normal Adult Wound Healing

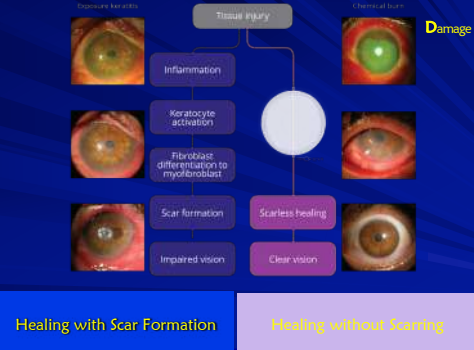
Our body does not achieve state-of-the-art healing on its own...



PROLONGED INFLAMMATION

RESIDUAL HAZE **SCAR FORMATION**

111




Healing with Scar Formation **Healing without Scarring**

112

Ocular Surface Disease Challenges

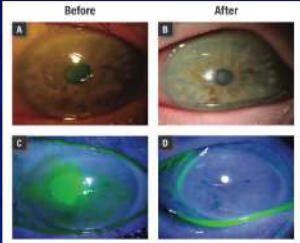
- ~ **D**EFFECT
- ~ **D**ELAYED HEALING
- ~ **D**YSTROPHY
- ~ **D**EGENERATION
- ~ **D**AMAGE



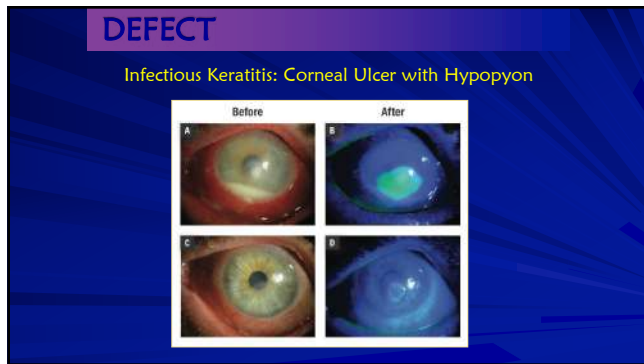
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DEFECT

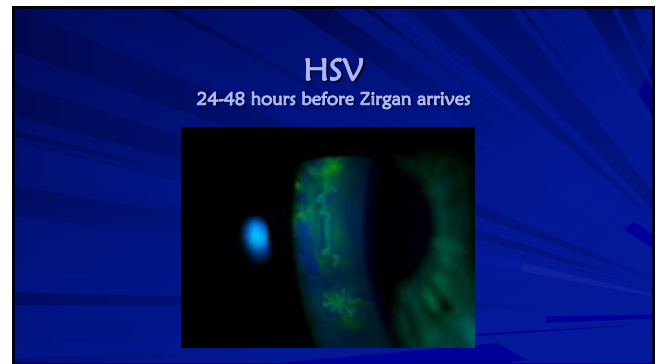
Neurotrophic Persistent Epithelial Defect



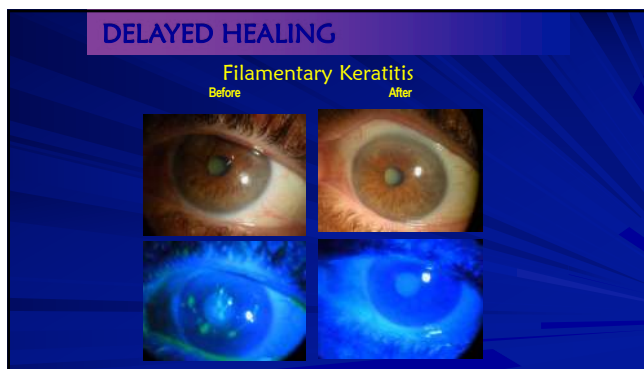
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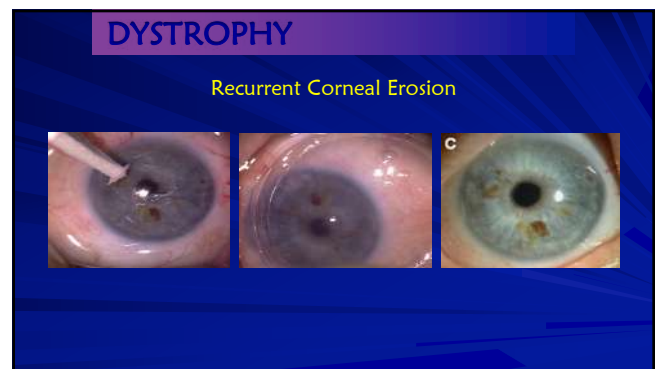
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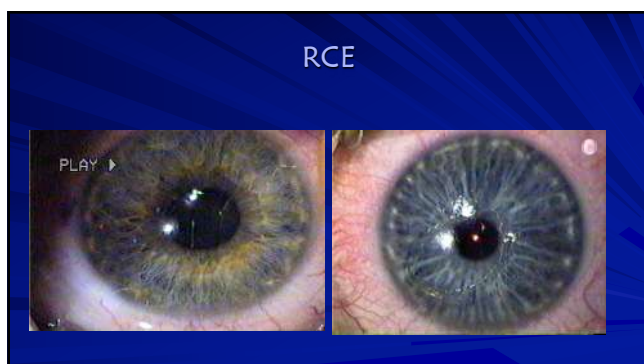
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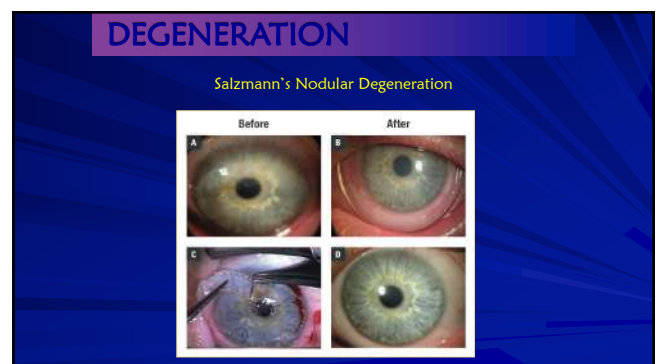
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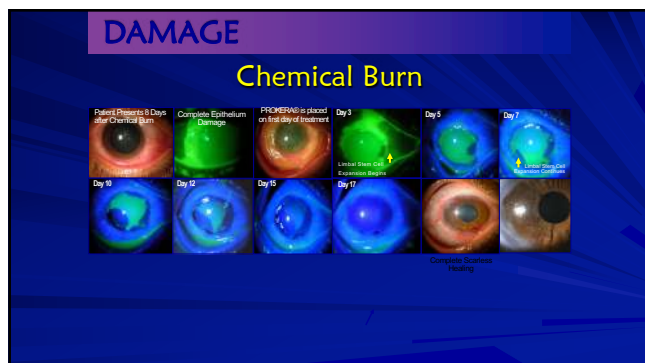
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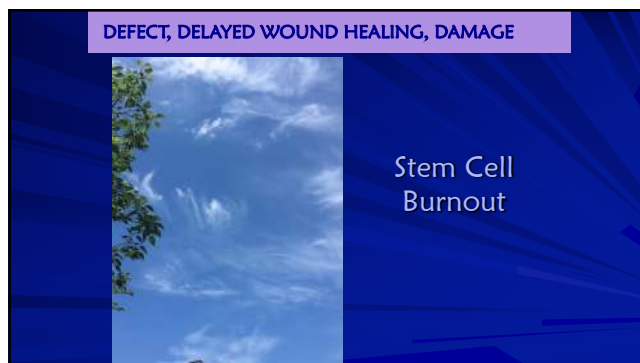
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120



121



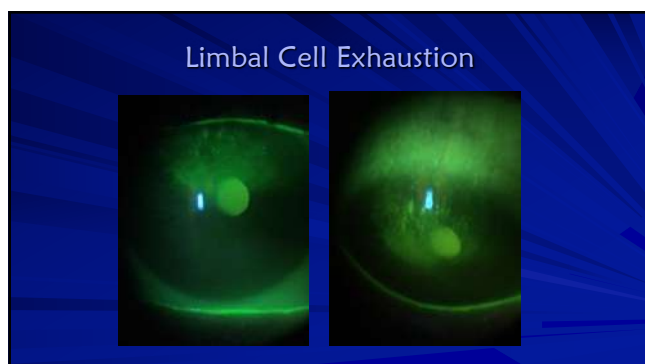
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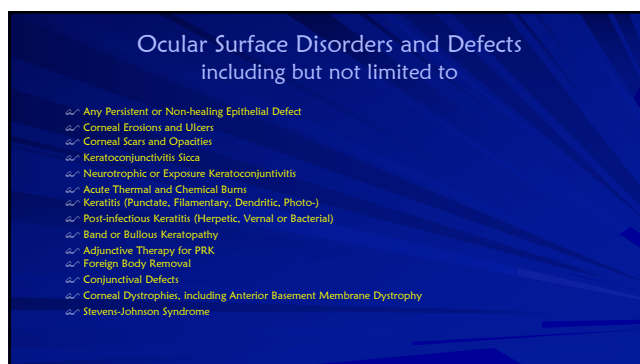
123



124



125



126

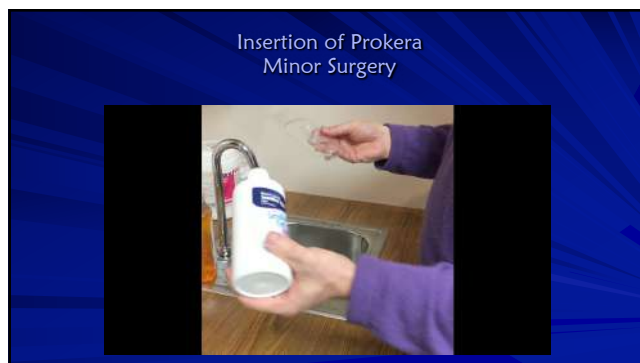
Amniotic Membrane Components

- Proteoglycans
- Growth factors
- Collagens (types I, III, IV, V and VI)
- Fibronectin
- Laminin
- Heavy chain hyaluronic acid (HC-HA)
- PTX 3 (HC-HA Complex)
 - Pentraxin 3

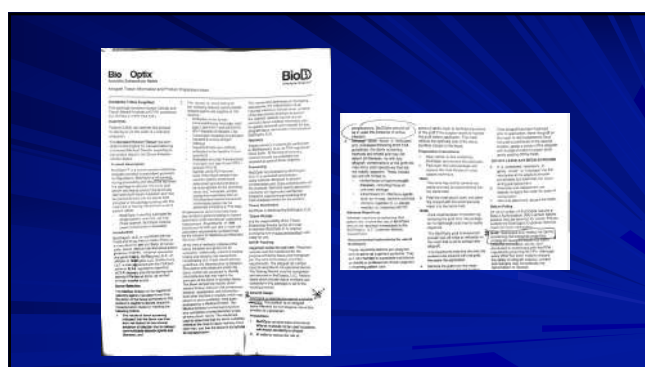
Direct inhibition of pro-inflammatory cells¹⁴

- Suppresses T-cell activation
- Inhibits giant cell formation
- Controls MMP production¹⁵

127



128



129

Prokera

Indications:

- PROKERA is intended for use in eyes in which ocular surface cells are damaged or underlying stroma is inflamed or scarred. Acting as a self-retaining biologic corneal bandage, PROKERA effectively treats superficial corneal surface diseases by suppressing inflammation and related pain, promoting epithelial healing, and avoiding haze.
- PROKERA is inserted between the eyeball and the eyelid to maintain space in the orbital cavity and to prevent closure or adhesions. Displacement of the conformer also enables application of the cryopreserved amniotic membrane to the ocular surface without the need for sutures.
- PROKERA is for single-use only in one patient by an ophthalmologist or optometrist.

Contraindications:

- PROKERA should not be used in eyes with glaucoma drainage devices or filtering blebs.

Precautions:

Location & Temperature	Use After Receipt
Unopened, sealed, shipping container	Within the expiration date printed on outer shipping box
-80°C ± 2°C (-112°F ± 36.2°F) Example: ultra-low temperature freezer, standard freezer, or standard refrigerator	Within the expiration date printed on product packaging (over 2 years from date of manufacture)

130

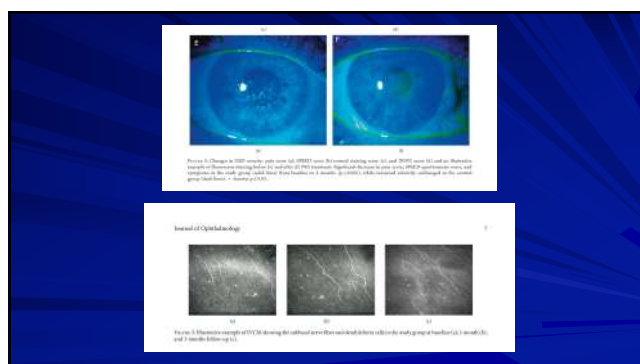
Clinical Study Corneal Nerve Regeneration after Self-Retained Cryopreserved Amniotic Membrane in Dry Eye Disease

Thomas John,^{1,2} Saeed Tighu,^{1,3} Hosam Shaha,^{2,4,5} Pedram Hamrah,^{6,7} Zafra M. Salem,^{8,9} Amy M. S. Cheng,^{3,4} Ming X. Wang,^{3,4} and Nathan D. Rock³

¹Thomas John Vision Institute, Oakley Park, Cook County, IL, USA
²Northwestern University, Chicago, Illinois, USA
³Yonkers Harbor Center for Vision Care, Yonkers, NY, USA
⁴Florida International University Herbert Wertheim College of Medicine, Miami, FL, USA
⁵Research Institute of Ophthalmology, Cairo, Egypt
⁶Boston Image Reading Center, Tufts Medical Center, Tufts University School of Medicine, Boston, MA, USA
⁷Center for Translational Ocular Research, Department of Ophthalmology, Tufts Medical Center, Tufts University School of Medicine, Boston, MA, USA
⁸King Vision Institute, San Jose, CA, USA

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 Received 12 May 2021; Accepted 18 June 2021; Published 10 August 2021
 Academic Editor: Saeed Tighu

131



132

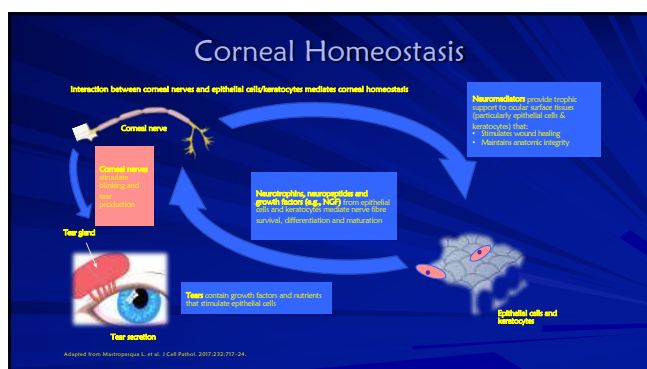
Oxervate™ (cenegermin-bkbj)

- Approved 2018 (August 28, 2018)
- Dompe farmaceutici SpA
- Ophthalmic solution indicated for the treatment of neurotrophic keratitis
- Dosing: Instill 1 drop in affected eye 6 times per day (at 2-hour intervals) for 8 weeks
 - Used as eye drop
 - Not infused or injected
- Storage issues: in the freezer at the pharmacy
 - Patient keeps the individual vials in the fridge – once “actively ready” for use, then it is only stable for 12 hours
- Contraindications
 - None

133



134



135

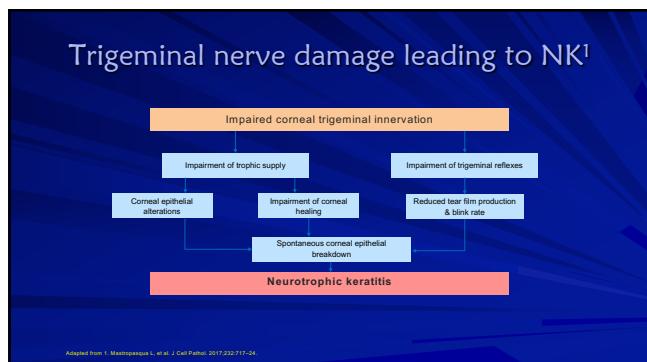
Pathophysiology of NK¹

- The loss of corneal sensory innervation via damage to the trigeminal nerve reduces release of neuromodulators that provide trophic (nutritional) support to the ocular surface tissues, stimulate wound healing and maintain anatomic integrity
- Impairment of corneal sensitivity also affects tear film production and blink rate due to the reduction of trigeminal reflexes
- Impairment of trigeminal innervation leads to decreased corneal epithelium renewal and healing rate, and ultimately the development of NK.

Penetration of nerves into the epithelium

S. Montanopole S, et al. J Cell Physiol. 2017;232:717-24; 2. Miller LJ, et al. Exp Eye Res. 2005;76:521-42.

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Etiologies Associated with NK

Ocular <ul style="list-style-type: none"> Herpes (simplex or zoster) infection Other infections e.g. acanthamoeba Chemical or physical burn Abuse of topical anaesthetics Drug toxicity Chronic ocular surface injury or inflammation Ocular surgery Cataract surgery LASIK, PRK PK and DALK Collagen crosslinking for keratoconus Vitrectomy for retinal detachment Photocoagulation for diabetic retinopathy Postsurgical or laser treatment Routine laser for proliferative diabetic retinopathy Contact lenses Orbital neoplasia Corneal dystrophies 	Central nervous system <ul style="list-style-type: none"> Neoplasm Aneurysms Stroke Degenerative CNS disorders Post-neurosurgical procedures <ul style="list-style-type: none"> For acoustic neuroma For trigeminal neuralgia Other surgical injury to trigeminal nerve 	Systemic <ul style="list-style-type: none"> Diabetes mellitus Leprosy Vitamin A deficiency Amyloidosis Multiple sclerosis
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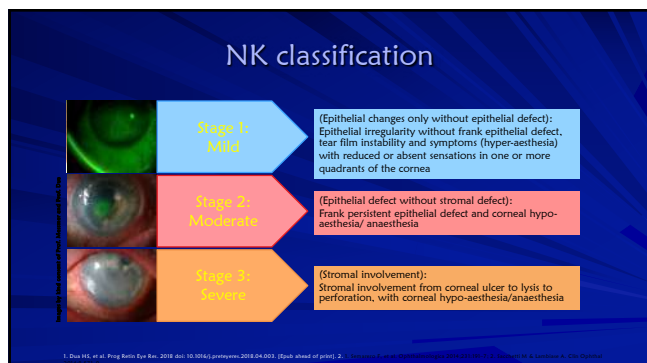
Genetic

- Riley-Day syndrome (familial dysautonomia)
- Goldenhar-Gorlin syndrome
- Mobius syndrome
- Familial corneal hypoaesthesia

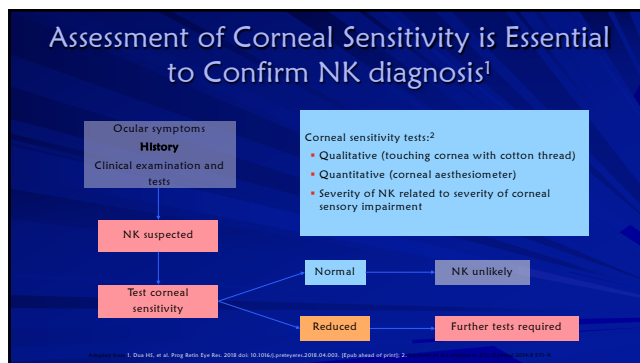
DALK=deep anterior lamellar keratoplasty; LASIK=laser in situ keratomileusis; PK=penetrating keratoplasty; PRK=photorefractive keratectomy

S. Montanopole S, et al. Prog Retin Eye Res. 2018;64:101061; Montanopole S, et al. 2018;64:101061.

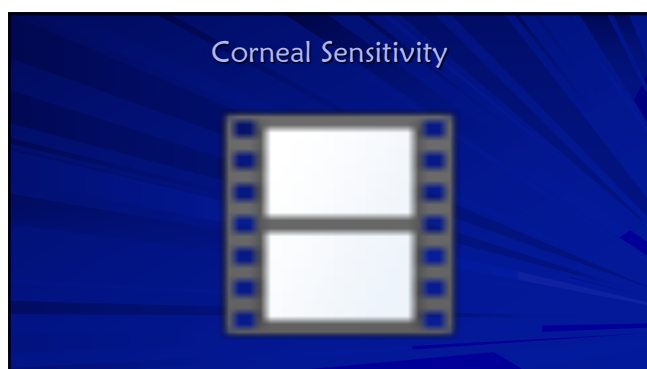
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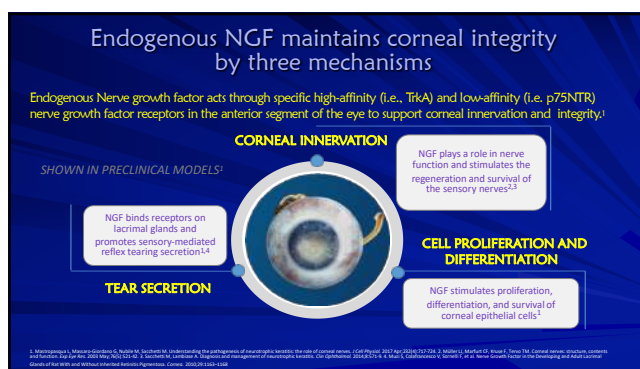
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Active ingredient structurally identical to human nerve growth factor produced in ocular tissues

- Naturally occurring neurotrophin is responsible for differentiation, growth, and maintenance of neurons¹
- The regenerative potential of nerve growth factor (NGF) was discovered by Nobel-prize winning scientists in the early 1950s¹
- Cenergermin-bkbj, a novel recombinant human nerve growth factor (rhNGF), is **STRUCTURALLY IDENTICAL** to the NGF protein²

1. Lantieri A, Remy P, Borel S, Caporaso G, Remy L. Topical treatment with nerve growth factor for corneal neurotrophic ulcers. N Engl J Med. 1996;335:1274-80. 2. Vachon R. New Drug Treatments: Debilitating Neurotrophic Keratitis. JAMA. 2016;320(13):1305.

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OXERVATE™ (cenergermin-bkbj) ophthalmic solution 0.002% Weekly Device Kit

- OXERVATE™ is supplied in a weekly carton containing 7 multiple-dose vials⁴
- A separate weekly Delivery System Kit contains the supplies needed to administer treatment¹

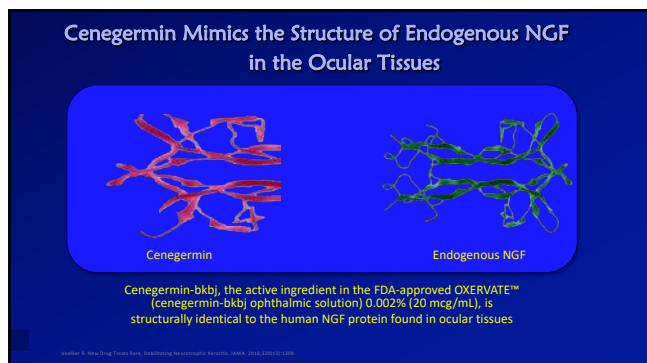
The Delivery System Kit Contains:

- 7 vial adapters
- 42 pipettes
- 42 sterile disinfectant wipes
- 1 dose recording card
- 1 extra adapter, 3 extra pipettes, 3 extra wipes are included as spares

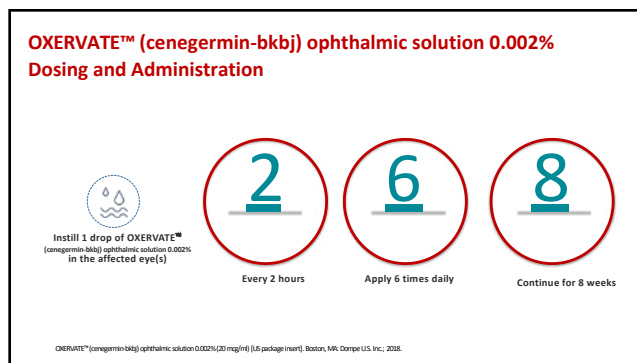
1. "Extra drug is available in each vial to take into consideration for loss or spillage during treatment administration"

OXERVATE™ [cenergermin-bkbj] ophthalmic solution 0.002% (20 mg/mL) [0.5 package insert], Boston, MA, Dorco U.S. Inc., 2018.

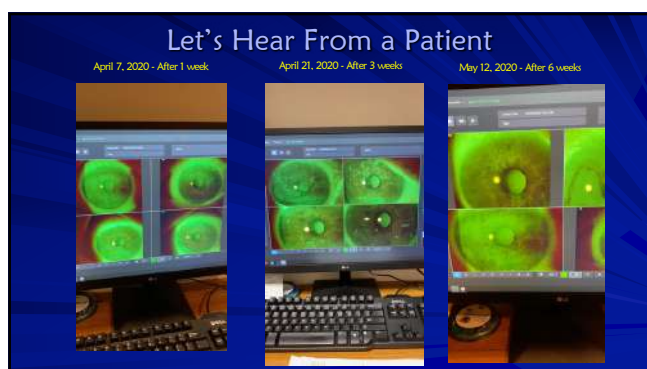
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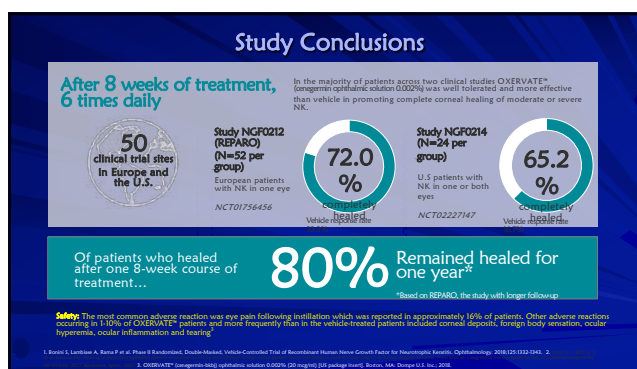
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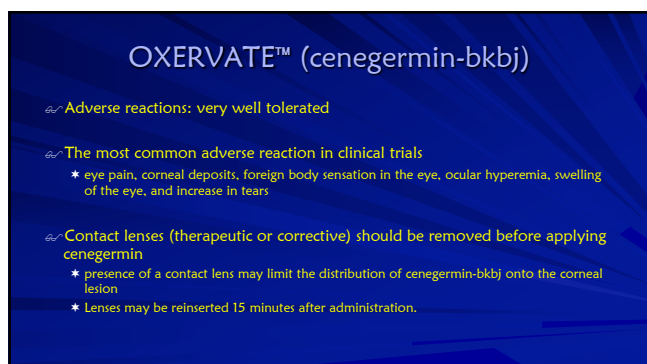
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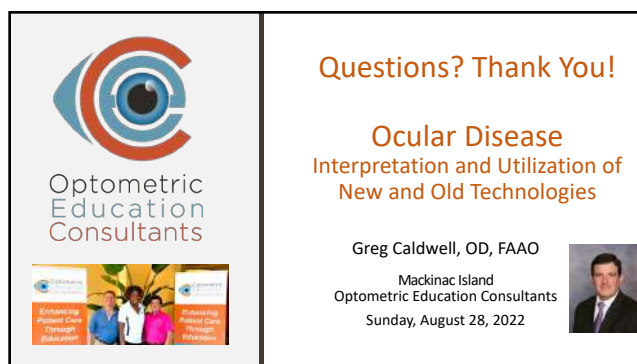
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