

Preparing for the Future of Glaucoma

Paula R Newsome, OD,MS,FAAO, FAARM,CHC
September 2023



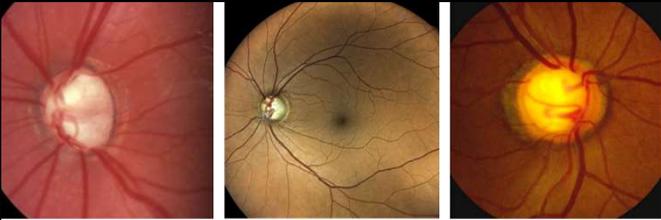
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Financial Disclosures

Paula Newsome, OD,MS, FAAO, FAARM, CHC



2



Course Objectives

- Discuss the current demographics and prevalence of glaucoma
- Discuss future trends on managing glaucoma
- Review some case studies where glaucoma was managed using some future trends

3

Did you know that Glaucoma



- About 3 million in the US have glaucoma
- About half of them do not know they have it
- Affects 1 in 200 age 50 and younger
- Affects 1 in 10 people age 80 and over
- The second leading cause of blindness in the world
- Aging population is increasing
- Glaucoma is more prevalent in people as they age
- Statistics from the Glaucoma Research Foundation



4

Glaucoma Data

- 350 million in the US
- Behind cataracts worldwide, glaucoma is the leading cause of blindness in the world
- In the US, glaucoma affects African Americans and Hispanic Americans disproportionately
- By 2040, the projected increase is to 74% or double the number of patients currently with glaucoma



5

Risk Factors for Glaucoma



- Family history
- Hypertension
- Smoking
- Sleep Apnea
- Utilization of Corticosteroids
- Some medications
- Trauma
- High Myopia

6

Glaucoma

- Neurodegenerative disease
- Progressive loss of ganglion cells and the axons in the ON
- Lowering of the IOP is the only proven treatment strategy
- Some patients continue to show loss and diminishing visual fields even with controlled IOP which suggests that lowering IOP is not the only dynamic

7

Pathophysiology of Glaucoma

PATHOPHYSIOLOGY

Etiological factors
 ↓
 Disturbance in circulation of aqueous humor
 ↓
 Leads to increased IOP
 ↓
 Which damages the retinal layer as it passes through the optic nerve head
 ↓
 Compression on the optic nerve head
 ↓
 Resulting in cell injury & death

8

Glaucoma Therapies Where we are now

- IOP lowering drops
- SLT
- MIGS
- None of these have worked in all cases

PATHOPHYSIOLOGY

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 ↓
 Compression on the optic nerve head
 ↓
 Resulting in cell injury & death

9

Other modifying factors for POAG

- Alter IOP
- Modifying ON Blood Flow
- Vary the rate of Retinal Ganglion apoptosis
- Positive Family History only accounts for less than 5% of all POAG in the general population

Data from NEI on occurrence of glaucoma in the general population

10

PATHOGENESIS OF GLAUCOMA

Outside of monitoring IOP, other factors that may be implicated in glaucoma are:

- Oxidative stress
- Axonal transport failure
- Neurotrophic factors
- Nutritional factors

11

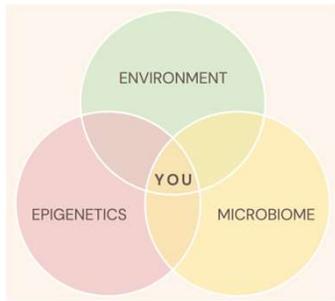
Effectiveness of Options

- Topical Antihypertensive Medications have proven effective in reducing IOP
- Most of the studies done thus far do not follow long enough to mimic long term usage and duration of therapy

Relationship of Lifestyle, Exercise, and Nutrition with glaucoma by Claudio Perez, Kuldev Singh and Shan Lin

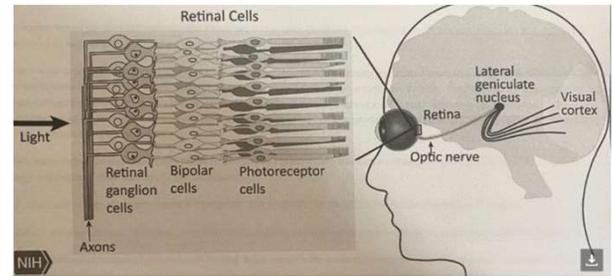
12

Connection between Microbiome and Epigenetics



13

Glaucoma and Gene Therapy



14

Neuroprotection

"If we make retinal ganglion cells more resistant and tolerant to the insults that cause cell death in glaucoma, they might be able to survive longer and maintain their function."

Dr. Chen at Mt Sinai Hospital, New York, NY

15

Found in mouse models

In different types of glaucoma, in mouse models, there was neuroprotection CaMKII

Found that CaMKII was injured and damaged when exposed to toxins or injury

Found that if they presented gene therapy to the CaMKII prior to the exposure that the insult did not occur and the RG cells were protected

Gun X, Zhou, et al, Preservation of Vision after CaMKII-mediated protection of RGC-Published in Cell, July 22, 2021

16

Glaucoma and Cannaboids

Studies were done in the 1970's

Found that IOP was lowered in both normal tensive and glaucomatous eyes

In 1978, found that the lowering was not any better than available therapies on the market

Glaucoma and Marijuana Use, June 21, 2005 Report to the Director by the Ad Hoc Group of Experts, NIH

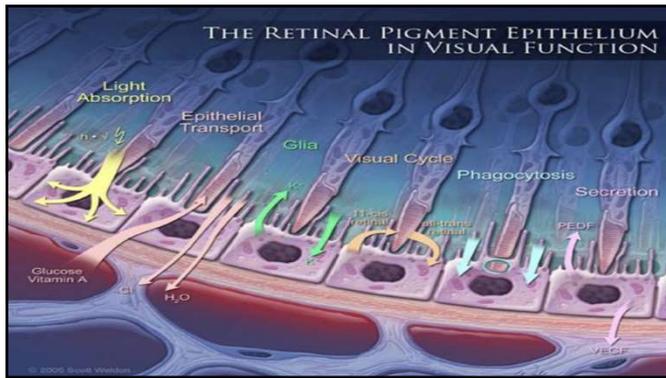
17

Glaucoma and Cannaboids

However, none of these studies demonstrated that marijuana--or any of its components--could lower IOP as effectively as drugs already on the market. In addition, some potentially serious side effects were noted, including an increased heart rate and a decrease in blood pressure in studies using smoked marijuana.

Glaucoma and Marijuana Use, June 21, 2005 Report to the Director by the Ad Hoc Group of Experts, NIH

18



19

Glaucoma and Generating RGC

Scientists are now looking to develop efficient protocols to develop a method for generating retinal ganglion cells from pluripotent stem cells.

Very new and not in humans yet but the science is there.

Focus on Axonal Mitochondria
Focus on Ischemia of the white matter
Focus on ganglion cell body

None of these one methods has gained more traction than the others but all are being worked on.

NIH-Glaucoma and Generating Retinal Ganglion Cells

20

Although we know that the current theory is to reduce IOP

There is increasing evidence during the last decade that environmentally modifiable factors may help to prevent glaucoma or its progression through different mechanisms that may or may not involve lowering IOP.

Additionally, patients are interested in maintaining a healthy lifestyle and taking an active role in the management of their disease.

Modifiable Factors in the management of glaucoma: A systematic review of current evidence. Hecht I

21



Possible modifiable risk factors

- Smoking Cessation
- Less Nutrients
- The mean reported intake of vitamin A was below the DRI for smokers and adequate for nonsmokers with a greater percentage of smokers not meeting the DRI for vitamin A.

22

Association between Smoking and glaucoma

Extensive evidence of various detrimental physiological effects of cigarette smoking on our body exists in the literature.⁷ Many active compounds found in tobacco smoke are toxic to ocular tissues, affecting the eye through ischemic or oxidative mechanisms.

Among cigarette smokers, heavy smoking defined by greater number of pack of cigarettes smoked per day is associated with higher odds of glaucoma. Health care providers should include this association when counseling patients on their smoking habit.

Smoking has been shown to be an important risk factor in the development of eye diseases such as cataract, age-related macular degeneration (AMD), Graves' ophthalmopathy, diabetic retinopathy, and dry-eye syndrome.^{1, 2, 3, 4, 5, 6} Because of the strong associations between smoking and AMD, the latest 2014 United States (U.S.) Surgeon General report calls on all eye health-care providers to assess and address the smoking status of their patients.

Eye (Lond). 2014 Apr;32(6):716-725.
Published online 2014 Jan 5. doi: 10.1093/eye/nyt129.
Cigarette smoking and glaucoma in the United States population
B.M. Lian, S. Li, F. Yu, F. Zhang, S. B. Lian, and A. L. Cotterman¹

23

What was known before

- Even though there is compelling evidence that smoking is associated with some common sight-threatening diseases such as cataract and age-related macular degeneration, the relationship between smoking and glaucoma remains unclear.
- Glaucoma is one of the leading causes of global blindness and there are approximately 1 billion smokers in the world, or about 13.5% of the world's population.
- Even if smoking is only associated with a small increase of odds of glaucoma development or in a subtype of glaucoma patients, an alteration of cigarette-smoking behavior may have a significant impact globally.

What this study adds

- Multiple factors of smoking on ocular health and our body and the complexity of the relationship between smoking and glaucoma may be the reason of discrepancies among studies on their association.
- Among smoker, heavy smoking defined by greater pack/ day of history of cigarette smoking is shown to have a statistically significant association with higher likelihood of a diagnosis of glaucoma.
- Eye-health care providers should consider this association when counseling patients on their smoking habit.

24



Moderate Aerobic Exercise

Robert Ritch, MD, at New York Eye & Ear Infirmary of Mount Sinai in New York City, tells his patients, "It's simple. If it's good for your heart, it's good for glaucoma. If it's good for your brain, it's good for glaucoma."

25

NIH-PubMed-2021

- Aerobic exercise reduces intraocular pressure and expands Schlemm's canal dimensions in healthy and primary open-angle glaucoma eyes.
- aerobic exercise (such as walking, swimming, biking, or working out on stationary machines) at a brisk level for 30 to 45 minutes three to four times a week lowered intraocular pressure (IOP) and improved blood flow to the brain and the eye.

Man. Tmoshy P H Un. KalGro.Bound ZDoM. Misheat V. Becksa. Decaia S. C Lam. ans Xiulan Zhang Schmidt KG et al. Graefes Arch Clin Exp Ophthalmol.

26

Exercise Studies

- In a recent study, all measures of physical activity—average steps per day, minutes of basic (non-sedentary) movement, and greater time spent doing moderate-to-vigorous physical activity—were associated with slower rates of visual field (VF) loss in a treated group of glaucoma patients.
- At baseline, participants walked an average of 5,313 steps and averaged 148 minutes of non-sedentary activity and 11 minutes of moderate-to-vigorous activity per day. Each incremental increase in activity was associated with less decline in VF, although the observed effects were small. But significantly boosting those levels each day—walking an additional 5,000 steps, engaging in an additional 2.6 hours of non-sedentary activity, or exercising for 120 minutes at a moderate-to-vigorous level—decreased the average rate of VF loss by approximately 10%.

Lee MJ et al. Ophthalmology. Published online Oct. 10, 2018.

27



Exercises studied to reduce IOP

- Going for a walk
- Jogging on a treadmill or outside
- Riding a bike (stationary or outdoor)
- Swimming
- Taking a Zumba class
- Using an elliptical machine

AAO, Eyelet, March 2019, Cole, OU, and Ritch

28

Avoid These Exercises

- Lack of Clarity on Strength Caution
- Yoga No to headstands

Take-Home Message

- The last thing a clinician wants to do is discourage patients from exercising. Rather, it's critical to ask patients about their activities and discuss limits and modifications when necessary.
- Finally, what about Dr. Ritch's patient, who had been standing on her head for 20 minutes a day for 20 years? She stopped doing headstand pose—and her glaucoma stopped progressing.



5 Chrysostomou V et al. Exp Eye Res. 2017;162:104-109.

29



Reducing BMI

•Body mass index (BMI), a major anthropometric indicator of obesity, has been linked to elevated IOP in many cross-sectional and longitudinal studies on healthy subjects. The exact pathophysiology of elevated IOP in obesity remains unclear. Possible mechanisms that can explain such association include: Obesity-related oxidative stress leading to trabecular meshwork malfunctioning, increased orbital fat impeding aqueous outflow, and dysregulation of retrobulbar blood flow.

30

Balanced Diet

- Leafy green vegetables
- Reducing BMI
- Anti-Inflammatory Diet
- Tea
- Ginkgo Biloba Extract



31

Tea Anyone?

- Flavonoids, a major polyphenol in tea, are thought to play a role in glaucoma owing to their various physiological actions that are proposed to affect non-IOP-dependent mechanisms. Studies have shown that flavonoids demonstrate their protective effect by reducing oxidative stress and improving blood flow.



32

More Modifiable Environmental Factors

- Managing Stress
- Avoiding Stressors
- Gratitude



33

More Studies

J Clin Biochem Nutr. 2021 Jan; 68(1): 67-72.
Published online 2020 Jul 10. doi: [10.3164/jcbn.20-50](https://doi.org/10.3164/jcbn.20-50)

PMCID: [PMC7844666](https://pubmed.ncbi.nlm.nih.gov/33536714/)
PMID: [33536714](https://pubmed.ncbi.nlm.nih.gov/33536714/)

Effects of French maritime pine bark/bilberry fruit extracts on intraocular pressure for primary open-angle glaucoma

Kaoru Manabe,¹ Sachiko Kaidzu,¹ Aika Tsutsui,¹ Mihoko Mochiji,¹ Yotaro Matsuoka,² Yasutaka Takagi,³ Etsuyo Miyamoto,³ and Masaki Tanito^{1,*}

> *Int J Mol Sci*. 2019 Aug 22;20(17):4110. doi: [10.3390/ijms20174110](https://doi.org/10.3390/ijms20174110).

Neuroprotective and Anti-Inflammatory Effects of a Hydrophilic Saffron Extract in a Model of Glaucoma

Jose A Fernández-Albarral¹, Ana I Ramírez^{1,2}, Rosa de Hoz^{1,2}, Nerea López-Villarín¹, Elena Salobrar-García¹, Inés López-Cuervo¹, Ester Licastro¹, Antonio M Inarejos-García³, Paula Almodovar³, Maria D Pinazo-Durán⁴, José M Ramirez^{5,6}, Juan J Salazar^{7,8}

Affiliations + expand
PMID: 31443568 PMCID: [PMC6747458](https://pubmed.ncbi.nlm.nih.gov/31443568/) DOI: [10.3390/ijms20174110](https://doi.org/10.3390/ijms20174110)
Free PMC article

34

MIRTOGENOL

Pycogenol and Bilberry

Mirtogenol® supplementation in association with dorzolamide-timolol or latanoprost improves the retinal microcirculation in asymptomatic patients with increased ocular pressure.

C Gizzi, P Torino-Rodriguez, G Belcaro, S Hu, M Hosoi, B Feragalli
2017 Oct;21(20):4720-4725. *EurRevMed Pharmacol Sci*



35

J Clin Biochem Nutr. 2021 Jan; 68(1): 67-72.
Published online 2020 Jul 10. doi: [10.3164/jcbn.20-50](https://doi.org/10.3164/jcbn.20-50)

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36

MORE STUDIES

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Affiliations + expand

PMID: 31443568 PMCID: PMC6747458 DOI: 10.3390/ijms20174110

Free PMC article

37

The ocular hypotensive effect of saffron extract in primary open angle glaucoma: a pilot study

• The progressive nature of glaucoma and its growing incidence make its therapy an important target for research. The role of oxidative damage in the pathogenesis of glaucoma makes antioxidants such as saffron extract an attractive target for potential clinical use. Herein, we evaluate the effect of aqueous saffron extract on intraocular pressure (IOP) in eyes with primary open-angle glaucoma (POAG).

Methods

• Thirty-four eyes of 34 clinically stable POA patients receiving treatment with timolol and dorzolamide eye drops were enrolled in this prospective, comparative, randomized interventional pilot study. Eligible subjects were randomized to receive 30 mg/day aqueous saffron extract orally (17 subjects, 17 eyes) or placebo (17 subjects, 17 eyes) for one month as an adjunct to timolol and dorzolamide. Following treatment, both study groups entered a one-month wash-out period. The main outcome measure was IOP during o treatment and after the wash-out period.

Mohammad Hossein Jabbarpoor Bonyadi, Shahin Yazdani, and Saeed Saadat

38

Mean baseline IOP was 12.9 ± 3.7 versus 14.0 ± 2.5 mmHg in the saffron and control groups, respectively ($p = 0.31$). After three weeks of treatment, IOP was significantly decreased to 10.9 ± 3.3 mmHg in the saffron group as compared to 13.5 ± 2.3 mmHg in the control group ($P = 0.013$). At four weeks, IOP was still significantly lower in the saffron group (10.6 ± 3.0 versus 13.8 ± 2.2 mmHg, $p = 0.001$). At the end of the wash-out period, IOP was 12.9 ± 3.0 in the saffron group versus 14.2 ± 2.0 mmHg in the control group ($p = 0.175$). None of the patients experienced side effects during the study and wash-out period.

Conclusions

Oral aqueous saffron extract seems to exert an ocular hypotensive effect in primary open-angle glaucoma. This effect became evident after three weeks of therapy.

39

Glaucoma and Microbiome

Oral microbiome link to neurodegeneration in glaucoma

Abstract

Background:

Glaucoma is a progressive optic nerve degenerative disease that often leads to blindness. Local inflammatory responses are implicated in the pathology of glaucoma. Although inflammatory episodes outside the CNS, such as those due to acute systemic infections, have been linked to central neurodegeneration, they do not appear to be relevant to glaucoma. Based on clinical observations, we hypothesized that chronic subclinical peripheral inflammation contributes to neurodegeneration in glaucoma.

Conclusions:

The above findings suggest that the oral microbiome contributes to glaucoma pathophysiology. A plausible mechanism by which increased bacterial loads can lead to neurodegeneration is provided by experiments in animal models of the disease and involves activation of microglia in the retina and optic nerve, mediated through TLR4 signaling and complement upregulation. The finding that commensal bacteria may play a role in the development and/or progression of glaucomatous pathology may also be relevant to other chronic neurodegenerative disorders.

Konstantin Astafurov, Eman Elhawary, Lishen Ren, Cecilia Q Dong, Christina Igborn, Leslie Hyman, Ann Griffin, Thomas MBag, John Dorcas

40

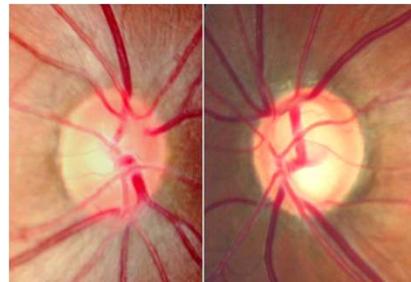
Glaucoma and Microbiome

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41

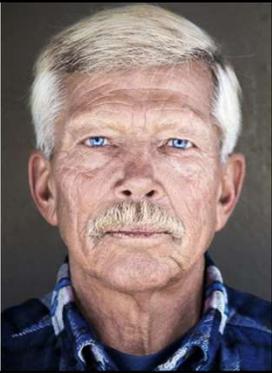
GLAUCOMA



42

Patient 1-ES

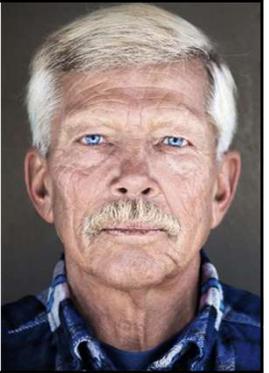
- Came in for a refractive exam
- 72 yo CA male who appears to be fit
- Still works daily and works for the hospital in accounting
- His wife died a few years ago and he also has care of his mother-in-law and lives with an adult daughter who is clinically depressed



43

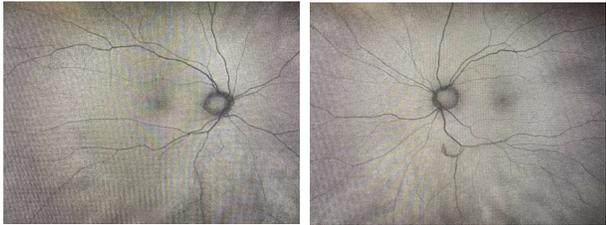
Pt ES

- We got suspicious of glaucoma in 2011 when his IOP's were 25 and 23 on the right and left eyes respectively
- We started testing him for glaucoma roughly every 6 months although he did not fit our typical glaucoma suspect model
- After OCT, we labeled him a suspect as there was no appreciable disc affectionation



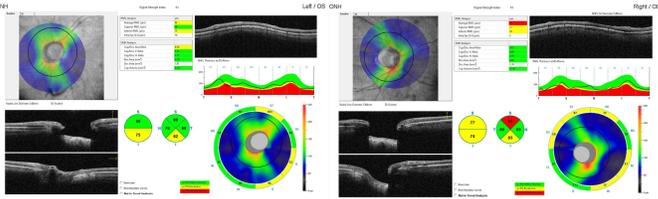
44

Current Day-Fundus Photos



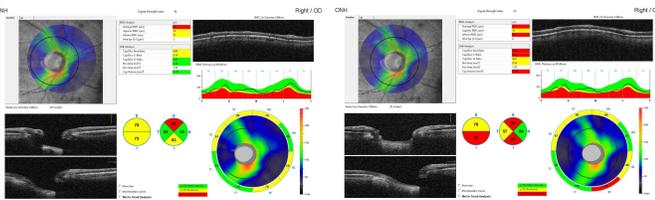
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Early in the Disease Process



46

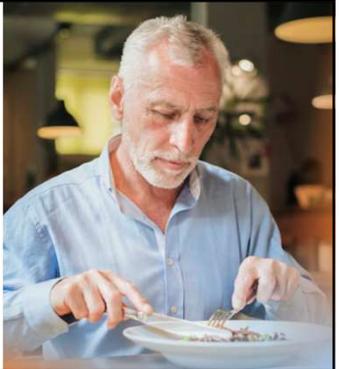
Notice the Progression



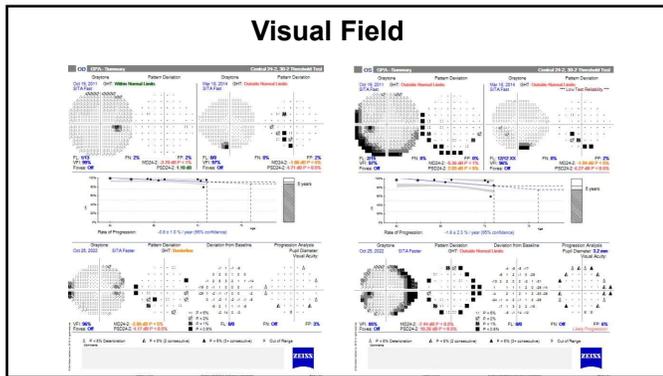
47

ES-Patient 1

- We see this patient on a quarterly basis
- His IOP's were not under control so I asked about diet and activity
- He shared that his daughter was doing the cooking and that he was consuming a lot of carbohydrates and eating fast food or delivery



48



49

So we changed his meds

- Put him on Vyzulta
- Ask him to increase activity
- Lower his carbohydrate intake
- He is also taking Mirtogenol
- Just asked him to start taking Saffron capsules

50

ES

- Came in on 3/24/22 roughly 1 month after his last visit
- IOPS had dropped to 12/13 at 8:07 am
- When I showed him the graph of his IOPS, he was happy and also skeptical

51

Patient 1 Questions



He is quite happy and promised to behave most of the time



He vowed to return to hiking



He vowed to quit eating so many prepared foods

52

The Real Dilemma

- He also reported that he had dropped 5 pounds
- But he asked the question, when could he go back to drinking his one beer per week and eating sweets.

53

What would you say? What would you do?

- Smart Goals**
- Specific
- Measurable
- Achievable
- Realistic
- Time Dependent

54

Setting Realistic Goals

- On a weekly basis
- 15 good consistent meals
- 3-4 that I don't monitor
- After doing that for several years, I really don't even want junk most of the time
- Concluded that I would rather eat my calories than drink them which is another area to question patients about

The Nourishing Home's Weekly Meal Plan for July 8-14

MON-7	TUES-8	WED-9	THURS-10	FRI-11	SAT-12	SUN-13	SUN-14
<ul style="list-style-type: none"> • Pineapple • Chicken Noodle • Brown Rice • Broccoli 	<ul style="list-style-type: none"> • Grilled Salmon w/ Asparagus • Spinach Salad 	<ul style="list-style-type: none"> • Grilled Pork Chops • Wild Rice • Asparagus 	<ul style="list-style-type: none"> • Grilled Turkey • Chicken Salad • Spinach • Apple Slices 	<ul style="list-style-type: none"> • Grilled Turkey • Bacon Sweet Potatoes • Asparagus • Creamy Berry Custard 	<ul style="list-style-type: none"> • Grilled Turkey • Bacon Sweet Potatoes • Asparagus • Creamy Berry Custard 	<ul style="list-style-type: none"> • Veggie Stir Fry w/Chicken • Grilled Chicken 	
<ul style="list-style-type: none"> • Turkey & Rice • Cheese Sandwiches • Clementines 	<ul style="list-style-type: none"> • Leftover Pineapple • Chicken Noodle 	<ul style="list-style-type: none"> • Greek Hummus • White Muffins • Lentils & Tomatoes 	<ul style="list-style-type: none"> • Leftover Chicken • Potato • Spinach Salad 	<ul style="list-style-type: none"> • Grilled Turkey • Bacon Sweet Potatoes • Asparagus • Apple Slices 	<ul style="list-style-type: none"> • Leftover Turkey • Salad and Baked w/Butter 	<ul style="list-style-type: none"> • Veggie Turkey Quinoa • w/Cucumbers 	
<ul style="list-style-type: none"> • Strawberry Smoothie • Apple • Egg w/Avocado • Fruit Smoothie 	<ul style="list-style-type: none"> • Leftover Strawberry • Spinach • Avocado • Scrambled Egg 	<ul style="list-style-type: none"> • Greek Yogurt • Fruit Parfait • Scrambled Egg 	<ul style="list-style-type: none"> • Baked Salmon • Egg • Greek Tzatziki 	<ul style="list-style-type: none"> • Homemade Gnocchi • Sauce with Fresh Herbs • Almond Milk 	<ul style="list-style-type: none"> • Banana Split • Creamed Turkey • Breakfast Butter 	<ul style="list-style-type: none"> • Egg Omelet • Berry • Banana • Smoothie • Fruit Smoothie 	
<p>Tasks to do to prep for next day</p>	<ul style="list-style-type: none"> • Save extra muffins for breakfast • Make extra rice and save for later ones • Turn dinner into breakfast • Make extra meals 	<ul style="list-style-type: none"> • Save leftover smoothie & salad for tomorrow's lunch • Bake granola 	<ul style="list-style-type: none"> • Make and save extra chicken for his lunch & Sunday dinner 	<ul style="list-style-type: none"> • Save extra bread, salad & soup for tomorrow's lunch • Cook soup for tomorrow's breakfast 	<ul style="list-style-type: none"> • Save extra creamed turkey for tomorrow's breakfast 	<ul style="list-style-type: none"> • Save extra smoothie for tomorrow's breakfast 	

55

Patient 2-RB



- Retired police officer who came in with Davis for routine eye exam
- His initial visit, he shared that he had been an NYPD during 9/11 and had moved to PTL afterwards to retire
- His wife is a holistic medication person

56

Hx-2014

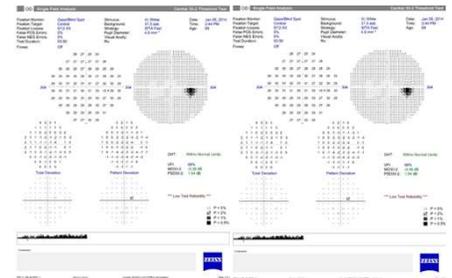
- Heart disease, Glaucoma suspect
- Meds: Pataday, Lisinopril, Zocor, Zylet for a red eye
- Allergies: Sulfur
- Social: Denies history of any
- Presented with a right red eye.
- IOP 19/17 at 11/17am
- Patient put on Zylet and RTC in 1 week for pressure check



57

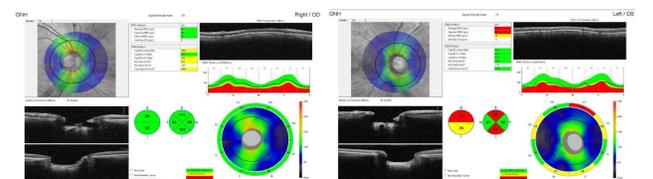
Visit 2-RB

- Most pertinent IOP's 21/20 repeated over a 2-hour period
- Left eye red eye was resolved however, we did do a glaucoma workup and found out that he has glaucoma



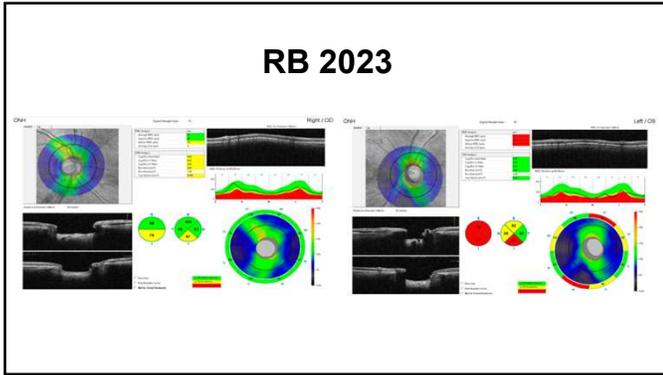
58

RB OCT 2014

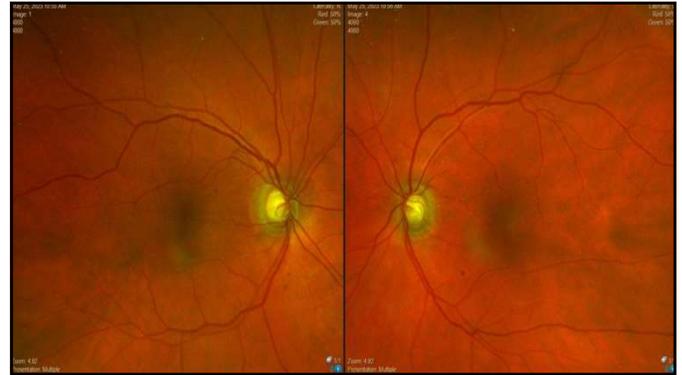


59

60



61



62

So some 9 years later

- We are holding some steady
- He has not had cataract surgery
- Seems to be depressed
- Having circulation issues
- Wife died so now, he has no joy
- Visual Fields are worse

63

What would you say? What would you do?

Smart Goals

- Specific
- Measurable
- Achievable
- Realistic
- Time Dependent

64

Course Objectives

- Discuss the current demographics and prevalence of glaucoma
- Discuss future trends on managing glaucoma
- Review some case studies where glaucoma was managed using some future trends

65

Questions?

drpnewsome@gmail.com

66