The Glaucoma Puzzle: When the Pieces Don't Always Fit

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Mark Dunbar OD: Financial Disclosure

- Optometry Consultant
  - Carl Zeiss
  - Allergan
  - Regeneration
- Advisory Board for:
  - Allergan
  - Carl Zeiss
  - Regeneron
  - Genentech

Mark Dunbar does not own stock in any of the above companies

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Why does glaucoma matter?

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Glaucoma: 2nd leading cause of blindness in developed nations[1]

~40%
of patients have **moderate-to-severe visual field loss** by the time they are diagnosed[2]

~10%
of people with glaucoma lose vision over time, even if they are treated[3]

1. NEI/NIH.10 Things you should know about glaucoma. 2017. Available at http://nei.nih.gov/10-things-you-should-know-about-glaucoma
2. Gillespie BW, et al. Invest Ophthalmol Vis Sci. 2003;44:2613-2620. 3. GRF. Glaucoma Facts and Stats. Available at http://www.glaucoma.org/glaucoma/glaucoma-facts-and-stats.php

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More People Will Need Help Lowering IOP Due to a Growing and Aging Population

- The US population is aging

  10,000 people will turn 65 every day through 2030[2]

Patient populations who have higher risk of glaucoma will also be increasing[3]

African-American and Hispanic populations: Projected to increase from **17%** of the US population in 2012 to **34%** by 2050[3]

1. Colby SL, Ortman JM. US Census Bureau. 2015. Available at http://www.census.gov/prod/cen2010/briefs/c2010br-03.pdf. 2. Pew Research Center. 2010. Available at http://www.pewresearch.org/pubs/1722/baby-boomers-retire. 3. Liu D, et al. Glaucoma's growing prevalence in the US. Available at http://www.eyenet.com/articles/2014/jun/glaucoma-2014-6-12-increase-prevalence-in-the-unite.pdf

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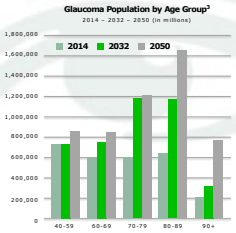
Glaucoma Is on the Rise, With 3x More Cases by 2050[1,2]

2015[1]
2.2 million people in the US ≥40 yrs old had glaucoma

2030[2]
4.3 million

2050[2]
6.3 million will have glaucoma



1. CDC. Vision Health Initiative. 2015. Available at http://www.cdc.gov/visionhealth/pdf/vision-health-initiative.pdf. 2. NEI. Glaucoma Projections. Available at http://www.nei.nih.gov/eyedata/glaucoma/glaucomaprojections.htm#1. 3. Liu D, et al. Glaucoma's growing prevalence in the US. Available at http://www.eyenet.com/articles/2014/jun/glaucoma-2014-6-12-increase-prevalence-in-the-unite.pdf

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Underdiagnoses of Open-Angle Glaucoma

- Population studies suggest **over half** of all glaucoma cases in the US have not been diagnosed
  - Percentage of patients with undiagnosed glaucoma
    - Baltimore Eye Survey: 56%[1]
    - Proyecto VER: 62%[2]
- Many suffer severe visual field (VF) loss before diagnosis[3]

1. Sommer et al. *Arch Ophthalmol.* 1991.
2. Quigley et al. *Arch Ophthalmol.* 2001.
3. Gillespie et al. *Invest Ophthalmol Vis Sci.* 2003.

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Primary Open-Angle Glaucoma: Definition

From the American Academy of **Ophthalmology's** (AAO's) Preferred Practice Pattern for Primary Open-Angle Glaucoma:

"Primary open-angle glaucoma (POAG) is a chronic, progressive optic neuropathy in adults in which there is a characteristic acquired atrophy of the optic nerve and loss of retinal ganglion cells and their axons…"

Preferred Practice Guideline: Primary Open-Angle Glaucoma. San Francisco, CA: American Academy of Ophthalmology; 2015.

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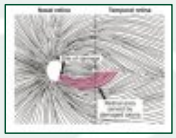
What does that mean?

- Acquired disease that affects the optic nerve
- Loss of the ganglion cells and their axons
- Characteristic "cupping" of the optic nerve
- Results in visual field loss
  - Starts peripheral (nasal field)
  - But can be paracentral
  - Can result in blindness
- Traditionally – thought to be from IOP that is too high



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How do we diagnose glaucoma?

- Measure the IOP
  - Is it normal?
    - Traditionally 10-21 mmHg
  - Is it elevated?
- Look at the optic nerve
  - Does it look normal?
  - Is there "cupping?
  - Is there asymmetry between the R and L eye?

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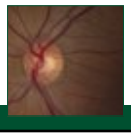
Here are the difficulties?

- Individual variability of the optic nerve



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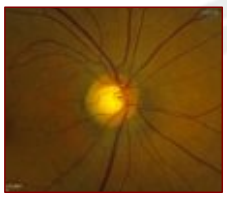
Difference in the Size Between Each Eye

Berta: 65 y/o Hispanic Female: Followed for OHTN



2005-2014: TA 20-24

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Optic Nerve Cup

- Highly variable even in normal patients
- Most people are 0.3 to 0.4
  - Jonas .42 (0 - .79) V; .50 (0 - .84) H
- Racial differences in disc size
  - Baltimore .56 (blacks) .49 (whites)
- Larger discs larger cups

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Physiologic vs. GL Damage

Physiologic
- Smaller
- Horizontally oval
- Uniform rim
- Similar to shape of nerve
- R=L

GL Cupping
- Larger
- Vertically oval
- Non uniform rim
- May be asymmetric

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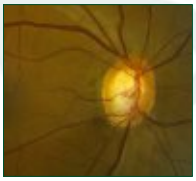
Classic Optic Nerve Findings Suggestive of Glaucoma

- Obvious large cup
- Vertical elongation of the cup
- Focal Notch
- Thinning of neuroretinal rim
- Superficial splinter hemorrhage
- Baring of vessels
- Cup/disc ratio asymmetry



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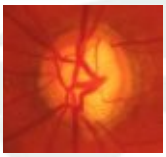
- Focal thinning of rim at superior and inferior poles



- Disc hemorrhage

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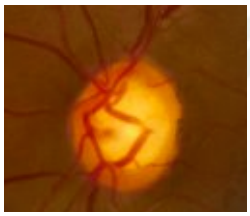
Size of the disc



- Large Optic Disc
- Large C/D
- No focal thinning
- Superior and Inferior poles are thickest part of rim

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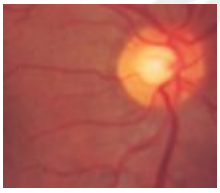
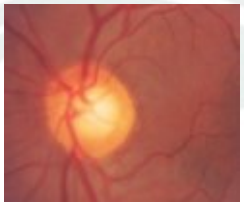
Asymmetry

- Larger nerve and cup





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How do we diagnose it?

If we are suspicious or concerned…

- Fundus photograph
- Visual field
- OCT: RNFL and ganglion cell layer

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Diagnosing Glaucoma Until Mid-1990's

- Stereoscopic evaluation of the optic nerve

- Goldmann visual field -> Automatic visual fields
  - Humphrey visual fields

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Sounds simple

1 + 1 = 2

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Here are the difficulties with IOP?

- Patients can have glaucoma when the pressure is **"normal"**
  - Beaver Dam Eye Study: 1/3 of glaucoma patients had IOP at a normal pressure[1]
  - Baltimore Eye Study: ~ 50% of glaucoma patients had IOP < 21 mmHg
- Not every with "high" IOP develops glaucoma

1. Klein, B. E. et al. *Ophthalmology* 1992;99(10):1499–1504

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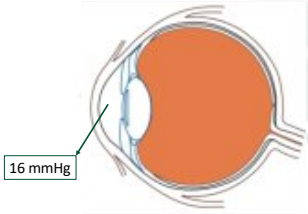
What Does a Pressure of 16 really mean?



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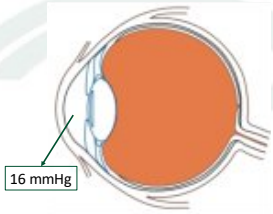
What are we measuring when we measure the IOP?

Conventional wisdom

- The intraocular pressure
- The pressure **INSIDE** the eye



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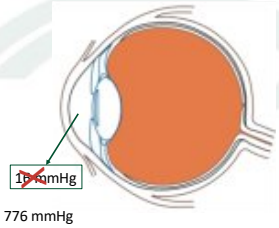

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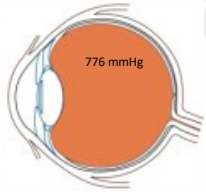
IOP = 16

What Does That Really Mean?

Normal Atmospheric Pressure = 760 mmHg



Sea level

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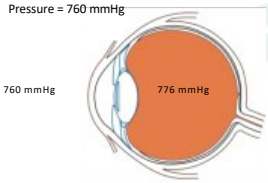
IOP = 16

What Does That Really Mean?

Normal Atmospheric Pressure = 760 mmHg



Sea level

776 mmHg - 760 mmHg = **16 mmHg**

Atmospheric pressure (inside) – normal atmospheric pressure = Intraocular pressure

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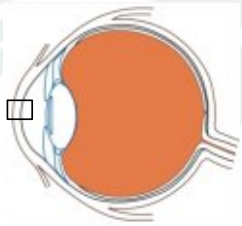
What is IOP?

- When we measure the IOP, we are really measuring the **"trans-corneal"** pressure
  - **Pressure difference across the cornea**
- The pressure inside the eye minus the atmospheric pressure that surrounds the eye.



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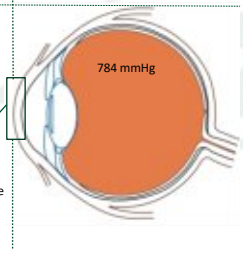
High IOP = 26 Glaucoma

Atmospheric | Intraocular

Absolute Pressure

760 mmHg



Trans-Corneal Pressure Difference 26 mmHg

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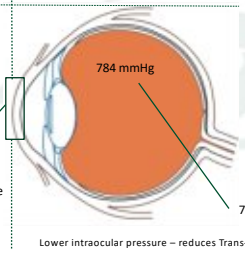
High IOP = 26 Glaucoma

Atmospheric | Intraocular

Absolute Pressure

760 mmHg



Trans-Corneal Pressure Difference 26 mmHg

774 mmHg = IOP 16

Lower intraocular pressure – reduces Trans-Cornea difference

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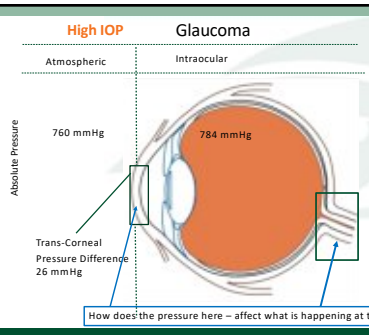

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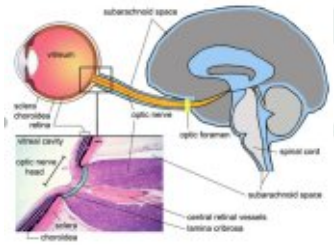
Cerebral Spinal Fluid Pressure (SFp) and Glaucoma



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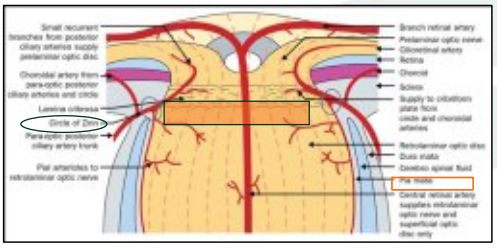

CSF (ICP) causes more displacement of the lamina then IOP

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CSF and Glaucoma

45 Years ago: (1976) Volkov pointed out that cerebrospinal fluid pressure (CSF-P) could pathogenetically be associated with glaucomatous optic neuropathy

Volkov VV. Essential element of the glaucomatous process neglected in clinical practice [in Russian]. Oftalmol Zh 1976;31: 500–4.

- 1979: Yablonsky et al postulated that an abnormally **low CSF-P around the optic nerve** may be the reason for a barotraumatically **induced optic nerve damage** in normal-pressure glaucoma.

Yablonski M, Ritch R, Pokorny KS. Effect of decreased intracranial pressure on optic disc. Invest Ophthalmol Vis Sci 1979;18(Suppl):165.

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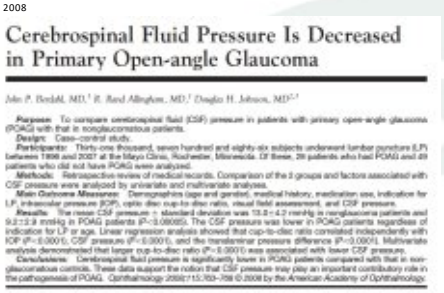
2008



Cerebrospinal Fluid Pressure Is Decreased in Primary Open-angle Glaucoma

John P. Berdahl, MD,[1] R. Rand Allingham, MD,[1] Douglas H. Johnson, MD[2,3]

Purpose: To compare cerebrospinal fluid (CSF) pressure in patients with primary open-angle glaucoma (POAG) with that in nonglaucomatous patients.

Design: Case–control study.

Participants: Thirty-one thousand, seven hundred and eighty-six subjects underwent lumbar puncture (LP) between 1996 and 2007 at the Mayo Clinic, Rochester, Minnesota. Of these, 28 patients who had POAG and 49 patients who did not have POAG were analyzed.

Methods: Retrospective review of medical records. Comparison of the 2 groups and factors associated with CSF pressure were analyzed by univariate and multivariate analysis.

Main Outcome Measures: Demographics (age and gender), medical history, medication use, indication for LP, intraocular pressure (IOP), optic disc cup-to-disc ratio, visual field assessment, and CSF pressure.

Results: The mean CSF pressure ± standard deviation was 13.2 ± 4.2 mmHg in nonglaucoma patients and 9.2 ± 3.9 mmHg in POAG patients ($P<0.00005$). The CSF pressure was lower in POAG patients regardless of indication for LP or age. Linear regression analysis showed that cup-to-disc ratio correlated independently with IOP ($P<0.0001$), CSF pressure ($P<0.0001$), and the translaminar pressure difference ($P<0.0001$). Multivariate analysis demonstrated that larger cup-to-disc ratio ($P<0.0001$) was associated with lower CSF pressure.

Conclusions: Cerebrospinal fluid pressure is significantly lower in POAG patients compared with that in non-glaucomatous controls. These data support the notion that CSF pressure may play an important contributory role in the pathogenesis of POAG. Ophthalmology 2008;115:763–768 © 2008 by the American Academy of Ophthalmology.

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Mayo Clinic Study: CSF and Glaucoma

- Retrospective review of 31,786 patients that had lumbar punctures over a 11-year period
- Determined # who had complete eye exams
- 28 met inclusion criteria of POAG, 49 controls
- **ICP was significantly lower** in patients with POAG compared to the non-glaucoma control

Berdahl JP, et al. *Ophthalmology*. 2008;115(5):763-768.

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Berdahl 2nd Mayo Clinic Study: CSF and Glaucoma
POAG vs. NTG vs OHT

- Retrospective review of 62,468 patients that had lumbar punctures over a 20-year period
- 189 met inclusion criteria of complete eye exam
- **ICP** was significantly **lower** in patients with POAG and NTG and **significantly higher in OHT**

Berdahl JP, Fautsch MP, Stinnett SS, et al Intracranial pressure in primary open angle glaucoma, normal tension glaucoma, and ocular hypertension: a case-control study. Invest Ophthalmol Vis Sci. 2008;49(12):5412-5418

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Cerebrospinal Fluid Pressure in Glaucoma

A Prospective Study

Ruoyi Ren, MD,[1,2] Jost B. Jonas, MD,[1,3] Guoghong Tian, MD,[1] Yi Zhen, MD,[1] Ke Ma, MD,[1] Shuning Li, MD,[1] Hongyan Wang, MD,[1] Bin Li, MD,[1] Xiaojun Zhang, MD,[1] Ningli Wang, MD[1]

Purpose: To assess whether a low cerebrospinal fluid pressure (CSF-P) is associated with open-angle glaucoma in eyes with normal intraocular pressure (IOP).
Design: Prospective, interventional study.
Participants: The study included 43 patients with open-angle glaucoma (14 with a normal IOP, and 29 with an elevated IOP) and 71 subjects without glaucoma.
Intervention: All patients underwent standardized ophthalmologic and neurologic examinations and measurement of lumbar CSF-P.
Main Outcome Measures: Cerebrospinal fluid pressure and IOP.
Results: Lumbar CSF-P was significantly ($P<0.001$) lower in the normal IOP glaucoma group (8.5±2.2 mmHg) than in the high IOP glaucoma group (11.7±2.7 mmHg) or the control group (12.9±1.8 mmHg). The trans-lamina cribrosa pressure difference (IOP minus CSF-P) was significantly ($P<0.001$) higher in the normal IOP glaucoma group (6.6±3.6 mmHg) and the high-IOP glaucoma group (12.3±4.1 mmHg) than in the control group (1.4±1.7 mmHg). The extent of glaucomatous visual field loss was negatively correlated with the height of the CSF-P and positively correlated with the trans-lamina cribrosa pressure difference. In the control group, CSF-P was significantly correlated with both systolic blood pressure ($P = 0.04$) and IOP ($P<0.001$). The trans-lamina cribrosa pressure difference was not significantly associated with blood pressure ($P = 0.87$).
Conclusions: In open-angle glaucoma with normal IOP, CSF-P is abnormally low, leading to an abnormally high trans-lamina cribrosa pressure difference. Pathogenetically, a low CSF-P in normal-IOP glaucoma may be similar to a high IOP in high-IOP glaucoma. Consequently, the glaucomatous visual field defect is positively correlated with the trans-lamina cribrosa pressure difference and inversely correlated with the CSF-P. In nonglaucomatous subjects, CSF-P, blood pressure, and IOP are significantly associated with each other.
Financial Disclosure(s): The authors have no proprietary or commercial interest in any of the materials discussed in this article.

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Lumbar CSF Pressure in NTG, POAG and Non GL

Ophthalmology Volume 117, Number 2, February 2010

Table 3. Measurements of Lumbar Cerebrospinal Fluid Pressure in Patients with Normal-Pressure Glaucoma, High-Pressure Glaucoma, and Nonglaucomatous Subjects

	Normal-Pressure Glaucoma Group	P-Value	High-Pressure Glaucoma Group	P-Value	Control Group
N	14		29		71
Cerebrospinal fluid pressure (mmHg)	8.5±2.2	0.001	11.7±2.7	<0.001	12.9±1.8
Median	12.1		12.1		12.9
Range	3.7–12.9		6.8–19.1		7.0–18.9

P value: Statistical significance of the difference between the group in the preceding column and the group in the next column (Mann-Whitney U test).
The difference in cerebrospinal fluid pressure was statistically significant ($P<0.001$) also for the comparison between the normal-pressure glaucoma group and the control group.

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Trans-Lamina Cribrosa **Pressure Difference**

Table 4. Measurements of the Trans-Lamina Cribrosa Pressure Difference (Intraoperative Pressure Minus Cerebrospinal Fluid Pressure) in Patients with Normal-Pressure Glaucoma, High-Pressure Glaucoma and Nonglaucomatous Subjects

	Control Group	P-Value	Normal-Pressure Glaucoma Group	P-Value	High-Pressure Glaucoma Group
N	71		14		29
Trans-lamina cribrosa Pressure difference (mmHg)	1.4±1.7	<0.001	6.6±3.6	<0.001	12.3±4.1
Median	1.8		6.2		11.9
Range	−3.6 to 4.5		1.6–13.3		6.6–24.9
Trans-lamina cribrosa Pressure difference (mmHg) (highest recorded values)	5.0±3.6	<0.001	9.0±2.8	<0.001	18.8±4.8
Median	1.8		9.4		15.3
Range	−2.2 to 6.9		4.1–15.3		8.9–27.9

P value: Statistical significance of the difference between the group in the preceding column and the group in the next column (Mann-Whitney U test).
The difference in the trans-lamina cribrosa pressure difference was statistically significant ($P<0.001$) also for the comparison between the high-pressure glaucoma group and the control group.

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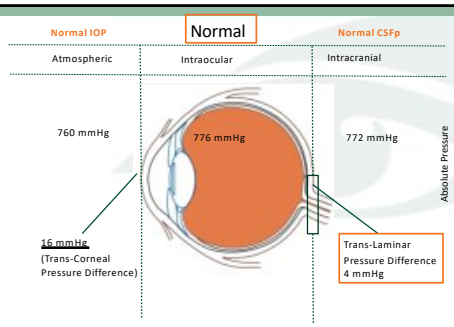

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Relationship between IOP and CSF

- In the normal state IOP and CSF have **minimal trans-laminar pressure differences**
- Increasing the difference **alters the homeostatic balance** and results pressure gradient difference at the lamina

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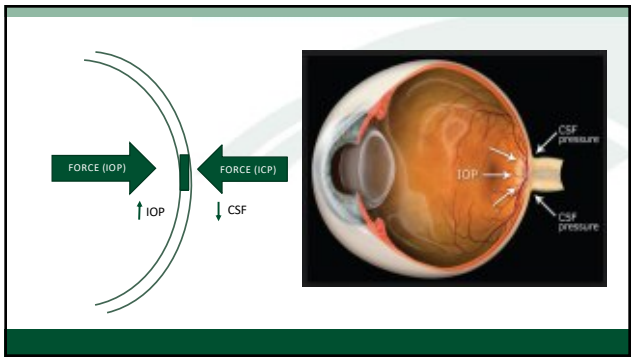

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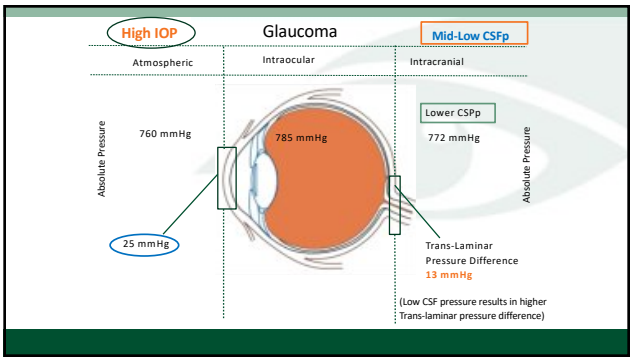

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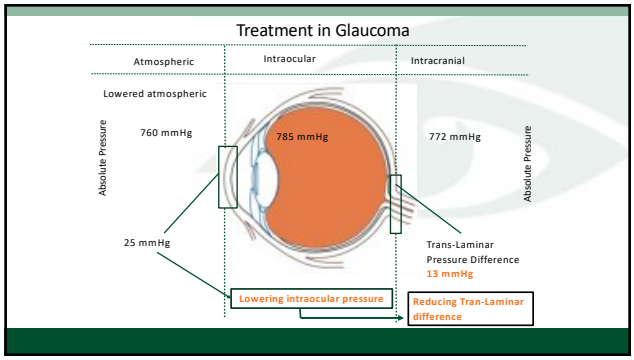

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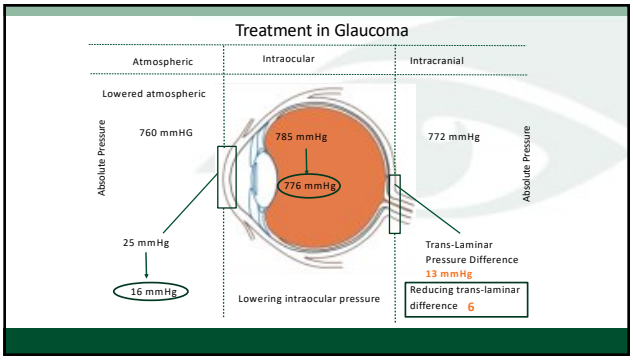

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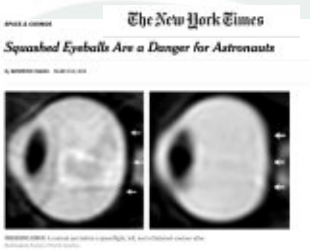
60% of astronauts suffer ocular problems related to prolonged space travel

- Globe flattening
- Hyperopic shift
- Choroidal folds
- Disc swelling



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Spaceflight Associated Neuro-ocular Syndrome: (SANS)

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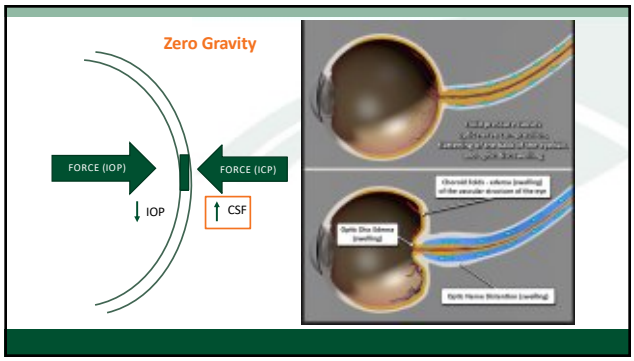

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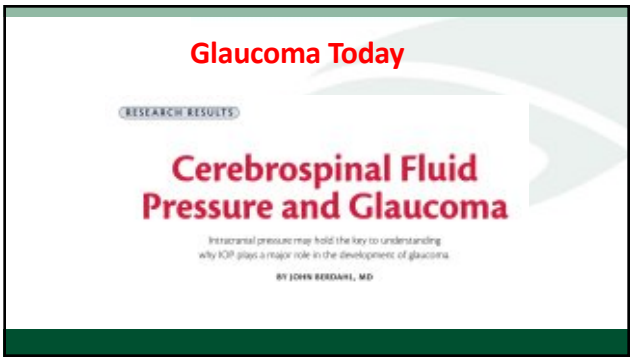

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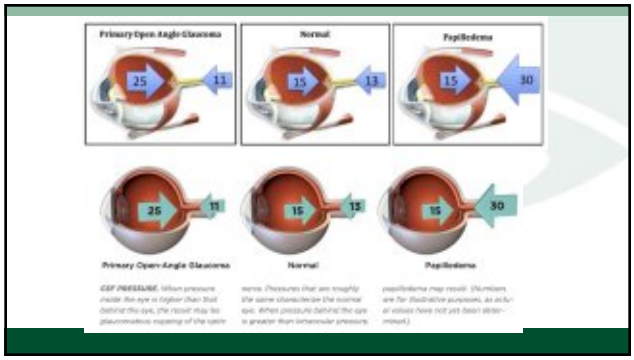

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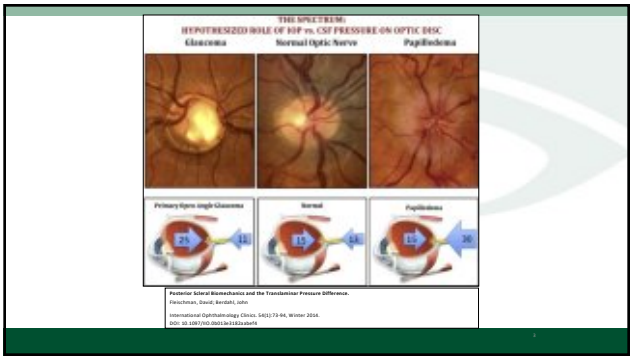

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What other factors besides IOP contribute to glaucomatous ON damage?

- Intracranial pressure (ICP)
- Blood pressure
  - High vs Low blood pressure (BP)
- Reduced ocular blood flow
  - Lower ocular perfusion pressure (OPP0

53

Where Does Blood Pressure Fit In?

54

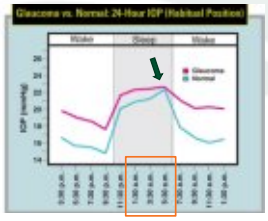
Where Does Blood Pressure Fit In?

- Not high blood pressure…but low blood pressure
- 1990's: Hayreh, Drance, and others 1st raised the important issues of **systemic hypotension** and **nocturnal blood pressure dips** in the progression of glaucoma
- The problem: difficult to measure systemic BP during sleeping hours

55

When is the highest IOP during the 24-hour cycle?

- IOP is a dynamic physiological parameter that doesn't remain constant over the course of 24 hours
- **Peak IOP is usually recorded at the end of the nocturnal sleep period**
- Trough IOP levels tend to occur at the end of the waking period



Liu JH, Kripke DF, Twa MD, et al. Twenty-four hour pattern of intraocular pressure in the aging population. Invest Ophthalmol Vis Sci 1999;40:2912-2917.

56

Risk Factors For Progression

- **BP is lowest** at night
- **IOP is highest** during the night time
  - Highest prior to waking
- Combination of ↑ IOP and ↓ BP may result in a critical ↓ ocular perfusion pressure (OPP) in susceptible people
  - Patients with faulty autoregulation

Mosaed S, Liu JH, Weinreb RN. Correlation between office and peak nocturnal intraocular pressures in healthy subjects and glaucoma patients. Am J Ophthalmol 2005;139:2-320-4.

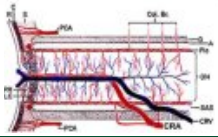
57

Ocular Perfusion Pressure (OPP)

- **OPP is the relative pressure at which blood enters the eye**
- Defined as the ocular arterial pressure minus the IOP
- OPP is a delicate balance between **IOP** and **blood pressure**
- Low ophthalmic perfusion pressure (OPP) is a risk factor for progression
  - Low BP and/or high IOP

MOPP = 2/3 X [DBP + 1/3 X (SBP – DBP)] – IOP

Simple: Diastolic BP – IOP = OPP



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Low OPP and Glaucoma

Epidemiologic Studies Linking Diastolic Perfusion Pressure and Glaucoma

Study	Design	Participants	Glaucoma Risk From Low DPP vs Normal DPP
Baltimore Eye Survey[1]	Cross-sectional	Non-Hispanic Whites and African Americans	2-6-fold
Egna-Neumarkt Study[2]	Cross-sectional	Non-Hispanic Whites	2.5-fold*
Proyecto VER[3]	Cross-sectional	Hispanics	4-fold
Los Angeles Latino Eye Study[4]	Cross-sectional	Hispanics	1.9-fold
Barbados Eye Study[5]	Longitudinal	Afro-Caribbeans	3.2-fold (4 years)

1. Tielsch JM, et al. *Arch Ophthalmol.* 1995;113(913):16-201. 2. Bonomi L, et al. *Ophthalmology.* 2000;107(7):1287-1293.
3. Quigley HA, et al. *Arch Ophthalmol.* 2001;119(10):1819-1826. 4. Memarzadeh F, et al. *Invest Ophthalmol Vis Sci.* 2010;51(6):2873-2877.
5. Leske MC, et al. *Arch Ophthalmol.* 2002;120(7):954-959.

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Low OPP and Glaucoma

Table 1 Low diastolic ocular perfusion pressure and prevalence of open-angle glaucoma

Study	n	Diastolic OPP <50–55 mmHg
Baltimore Eye Survey	5308	↑ Prevalence: 2–6-fold
Egna-Neumarkt Study	4297	↑ Prevalence: 3-fold only in high-tension glaucoma*
Proyecto VER	4774	↑ Prevalence: 4-fold
Barbados Eye Study	4631	↑ Prevalence: >3-fold
Rotterdam Eye Study (only participants receiving treatment for systemic hypertension)	1329	↑ Prevalence: >4-fold only in high-tension glaucoma (mainly probable glaucoma)

Adapted from [10–13,14**]. OPP, ocular perfusion pressure.
*Low OPP was defined as <68 mmHg in this study.

60

Risk Factors for Visual Field Progression in the Low-pressure Glaucoma Treatment Study

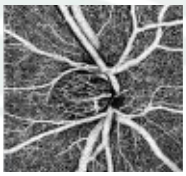
CARLOS GUSTAVO DE MORAES, JEFFREY M. LIEBMANN, DAVID S. GREENFIELD, STUART K. GARDINER, ROBERT RITCH, AND THEODORE KRUPIN, ON BEHALF OF THE LOW-PRESSURE GLAUCOMA TREATMENT STUDY GROUP

We determined that a lower MOPP during follow-up was significantly associated with visual field progression in our model and this effect was not significantly affected by other covariates, such as use of systemic antihypertensives and randomization arm (Table 4). An imbalance between

61

OPP and Glaucoma – The Reality

- Perfusion pressure is **difficult to accurately measure**
- There is currently **no widely accepted consensus** regarding **which techniques** should be used to evaluate blood flow or how the results should be interpreted
- **None of the methods** used to estimate blood flow **have been standardized** or externally validated for humans
- Ocular blood flow measurements are not currently used in the diagnosis or management of patients with glaucoma



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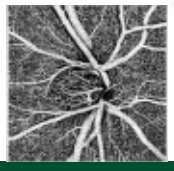
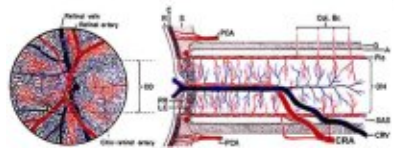
Vascular Supply to the ON

- COMPLEX arterial supply and an even more complex venous drainage system
- Which vascular network is most critical for development of glaucoma?





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Putting it all together…

64

Compromised Autoregulation in Glaucoma

- **Autoregulation: The body's ability to regulate itself in the presence of change: The ability to maintain homeostasis**
  - Vascular factors
    - Cardiovascular disease
    - Vasospasm
  - Postural changes
  - Atmospheric pressure
  - Temperature
  - Fatigue can lead to **abnormal pressure-flow relationship**
- Periods of ischemia are then more likely to occur
  - Can result in reduced or fluctuating OPP

65

Autoregulation

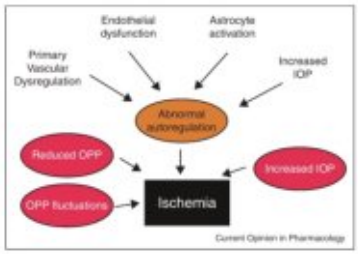
Or Vascular Dysregulation…?

Inability to maintain homeostasis

- Can lead to over/under perfusion
- Chronic under perfusion can lead to tissue necrosis and death
- Unstable perfusion leads to oxidative stress

66

Autoregulation in Glaucoma



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Case

68

80 yo White Female

- Presented for "annual eye exam"

HPI

80 yrs old, female New Patient here for annual check
Feels vision at distance was not as good as it has been, especially the LE

She uses glasses to see small prints, reports good vision at distance OU.
Denies pain, floaters or flashes of light.
S/p: CEIOL OU, YAG laser posterior capsulotomy OD (Baptist Hospital)
LEE: 02/2017 by M.D (w/DFE)

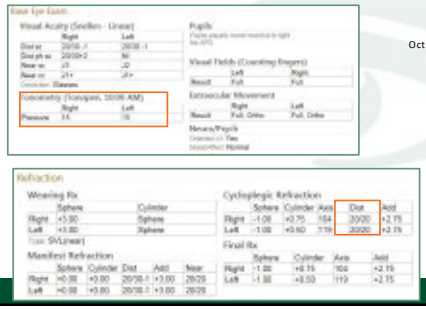
Mom had glaucoma and used drops

Generally does not wear glasses for driving

69

80 yo White Female

Oct 2017



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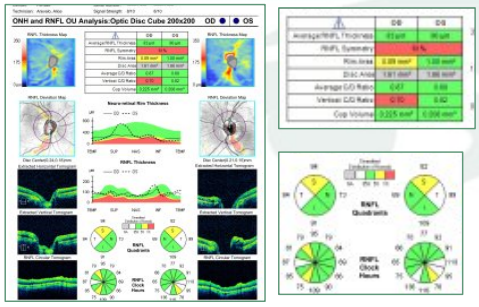

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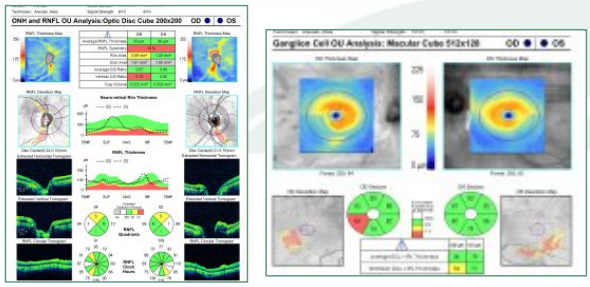

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So now what?

Is this low/normal tension glaucoma?

Would you begin treatment today?

74

Would you begin treating on this visit?

1. Yes
2. No
3. I would refer to ophthalmologist

75

This is what I did…

Impression
1) Probable Normal Tension Glaucoma OU
   Inferior thinning OU
   Disc hemorrhage RE inferior
   OCT and GCC thin corresponding to clinical presentation
   TA ~ 15 OU
2) Pseudophakia OU
3) PVD OU

Plan
1) Ed and reassure
2) RTC 1-2 weeks for VF and IOP measurement
3) Will start Tx at next visit
4) Rx given for specs

76

1 week later: 10/25/17

Base Eye Exam

Visual Acuity (Snellen - Linear)

	Right	Left	Both
Dist cc	20/20	20/20 -2	20/20
Dist ph cc		NI	

Tonometry (Tonopen, 12:06 PM)

	Right	Left
Pressure	15	14

Pupils
OU: 3/2 mm, round, reactive to light
No APD seen

Neuro/Psych
Oriented x3: Yes
Mood/Affect: Normal

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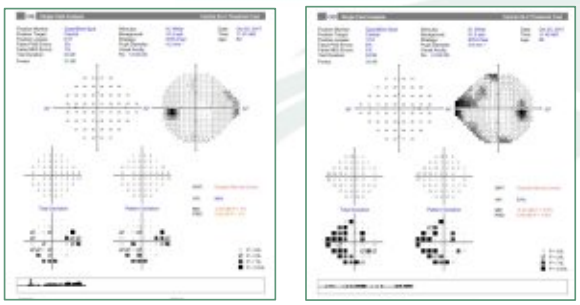

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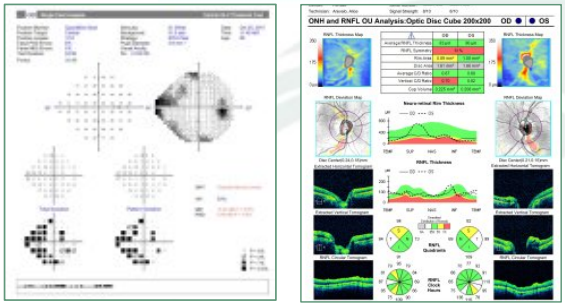

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Putting the Pieces of the Puzzle Together…

- The IOP is normal
- Abnormal optic nerve
  - Disc hemorrhage
- OCT shows RNFL thinning
  - Ganglion cell complex also shows thinning
- Visual field defect in a location where we see ON damage

80

How do you manage this patient?

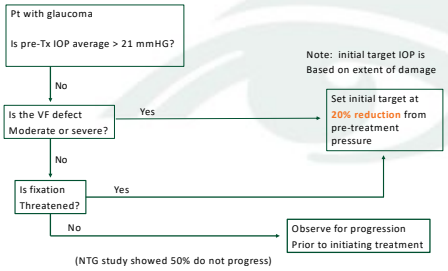
Normal Tension Glaucoma

Treatment?

- This is what I did
  - Latanoprost qhs OU
  - RTC 3 months
    - Should I bring her back sooner to check IOP?

81

Setting an Initial Target Pressure: Normal Tension Glaucoma



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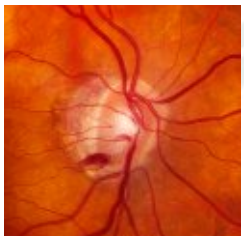
A Few Thoughts on Disc Heme



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Detection and Prognostic Significance of Optic Disc Hemorrhages during the Ocular Hypertension Treatment Study

- Disc hemorrhages detected in 128 eyes of 123 participants
- 21 cases detected by both doctor and photos
- **107 cases (84%) were detected only by a review of photography**

Ophthalmology Dec 2006

84

Of Note:

glaucoma, and smoking status. The occurrence of a disc hemorrhage increased the risk of developing POAG 6-fold in a univariate analysis (P=0.001; 95% confidence interval, 3.6–10.1) and 3.7-fold in a multivariate analysis that included baseline factors predictive of POAG (P<0.001; 95% confidence interval, 2.1–6.6). The 96-month cumulative incidence of POAG in the eyes without optic disc hemorrhage was 5.2%, compared with 13.6% in the eyes with optic disc hemorrhage. In eyes with a disc hemorrhage in which a POAG end point developed, the median time between the 2 events was 13 months.

Incidence of Progressing to POAG

- No Disc Heme: 5.2%
- **+ Disc Heme: 13.6% -> at 10 years 25.6% vs. 13%**
- Presence of a disc heme increase risk of developing POAG 6 fold

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13 Year Follow Up of Disc Hemorrhages in the OHTS

- ODH 179 eyes of 169 participants
- Incidence of POAG in eyes with ODH was **25.6% vs. 12.9%** in eyes without ODH
- ODH increased the risk of developing POAG
- Risk Factors for ODH:
  - Older age, thinner central corneal thickness, larger vertical cup to disc ratio, higher intraocular pressure, and self-reported black race

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Perhaps the Bigger Question?

- How is it that a patient can continue to "progress" or develop a disc hemorrhage with a pressure ~ 12?
- What are the factors that result in progression?

87

Compromised Autoregulation in Glaucoma

- **Autoregulation: The body's ability to regulate itself in the presence of change: The ability to maintain homeostasis**
  - Vascular factors
    - Cardiovascular disease
    - Vasospasm
  - Postural changes
  - Atmospheric pressure
  - Temperature
  - Fatigue can lead to **abnormal pressure-flow relationship**
- Periods of ischemia are then more likely to occur
  - Can result in reduced or fluctuating OPP

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Autoregulation

Or Vascular Dysregulation…?

Inability to maintain homeostasis

- Can lead to over/under perfusion
- Chronic under perfusion can lead to tissue necrosis and death
- Unstable perfusion leads to oxidative stress

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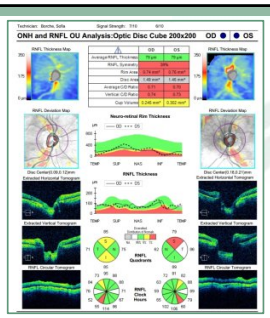
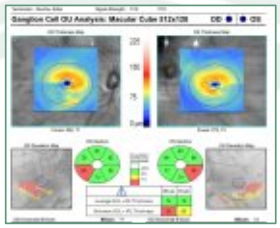


1/6/21
Ta: 13/11

Latanoprost
Alphagan P



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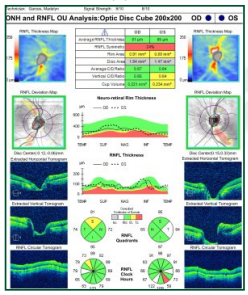
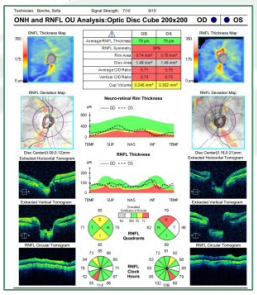
2018



2021



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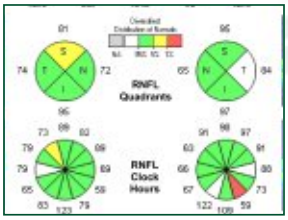
2018



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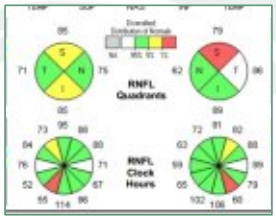

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Jan 2021

- NTG: Stable
  - No Disc heme
  - Good IOP today at 13/11 on Latanoprost and Alphagan P
  - OCT done today is "stable" but poor quality scans
- Plan
  - Continue with Latanoprost and Alphagan P
  - Follow 6 mo
  - Repeat VF
  - No need to dilate at next visit

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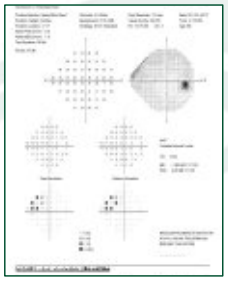
Visual Field

- Various testing methods
- Standard automated perimetry
  - SAP or White on White most commonly used
- It is a difficult test to perform
- It relies on the patient being able to provide subjective input on what they see
  - Many patients have extreme difficulties



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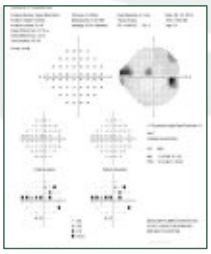
Some Things to Keep in Mind

- GL visual field loss shows more variability than normal fields
- There tends to be **high variability and reductions in sensitivity preceding definite field loss**
- Local depressions of sensitivity frequently come and go before finally resolving into stable repeatable VF defects



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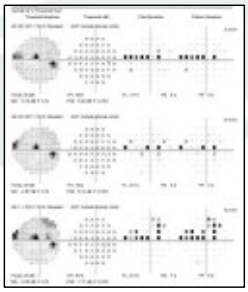
Visual Fields in OHTS

- 86% of retests had normal visual fields
- Abnormal confirmed in 14%

96

Visual Fields and Glaucoma

- Visual fields can be **difficult** to perform
- Visual fields can be **variable**
  - Some days better and some days worse
- Determining progression can be very difficult
  - Because of long term fluctuations



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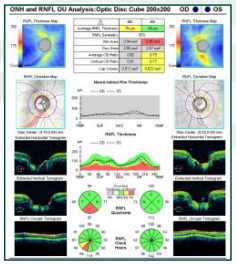
OCT: The missing piece of the puzzle?



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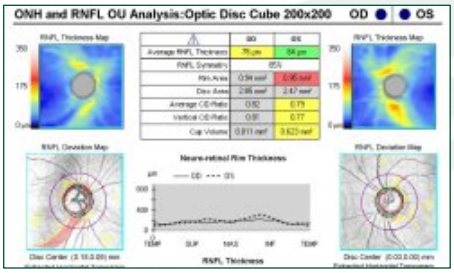

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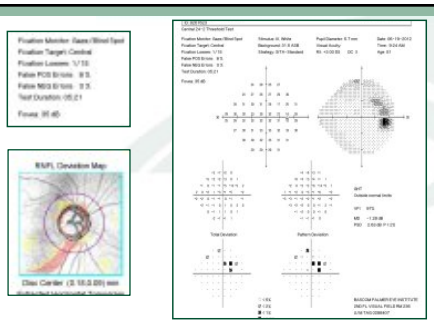


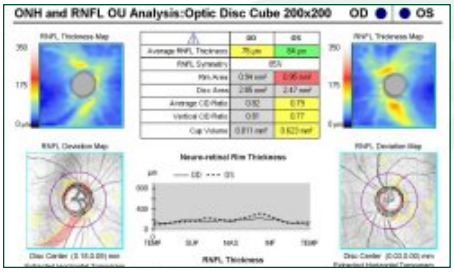
100

51 y/o Hispanic Female

- Reports shadow peripherally in her **LE**
- TA: 16-17 on 3 visits

101

102



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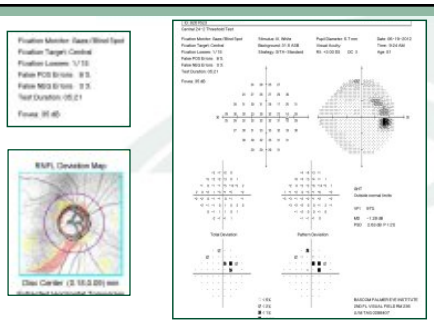

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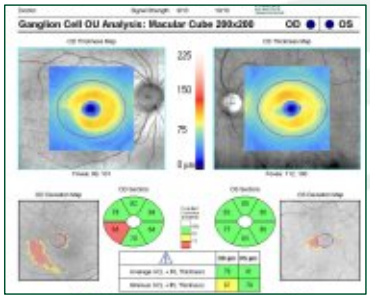

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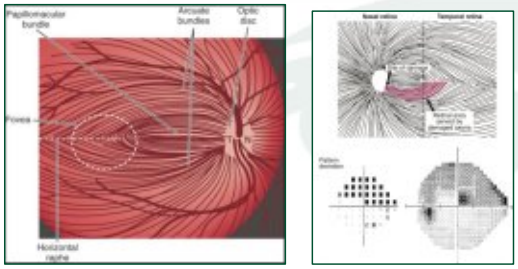

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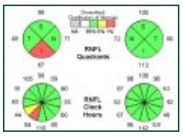
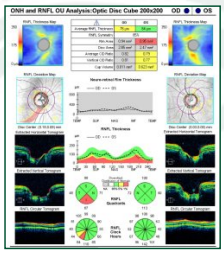
The RNFL thickness measurements are based on a "normative data base"

Can the optic nerve of this patients be compared to the normative data base?





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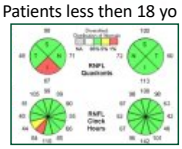
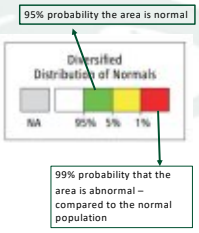
Can the RNFL/optic nerve of your patient be applied to the normative data base?

- High myopia
- Tilted disc
- Extremely large cups (and small)
- Patients less then 18 yo





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The OCT can show glaucomatous change
BEFORE it is seen on visual fields

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Estimating the Lead Time Gained by Optical Coherence Tomography in Detecting Glaucoma before Development of Visual Field Defects

Tanmay M. Kuang, MD,[1,2,3] Chaoxun Zhang, MD,[1,4] Linda M. Zangwill, PhD,[1] Robert N. Weinreb, MD,[1] Felipe A. Medeiros, MD, PhD[1]

- At 95% specificity, up to **35% of eyes had abnormal average RNFL thickness** 4 years before development of visual field loss and **19% of eyes had abnormal results 8 years before field loss**.
- **Conclusions:** Assessment of RNFL thickness with OCT was able to detect glaucomatous damage before the appearance of VF defects on SAP. In many subjects, significantly large lead times were seen when applying OCT as an ancillary diagnostic tool.

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When is it glaucoma?

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Case MC

- 73 yo female presents for follow up: GL Suspect
- Past history single elevated IOP
- BCVA 20/25 and 20/20
- IOP 21 RE 19 LE;
  - CCT 560u R 565u L
- Anterior segment normal
- Mild NS and cortical cataracts

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The ON

- Small optic discs OU
- RE c/d ~ 0.6 but
  - Appeared saucerized infero temporally
  - Broadening of a vein as it crossed edge disc
  - ? Small disc hemorrhage
- LE c/d .35

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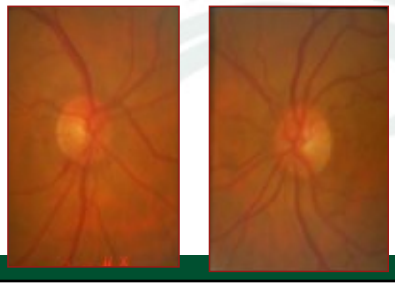
Photos



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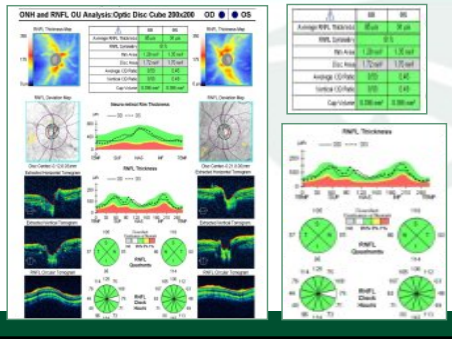

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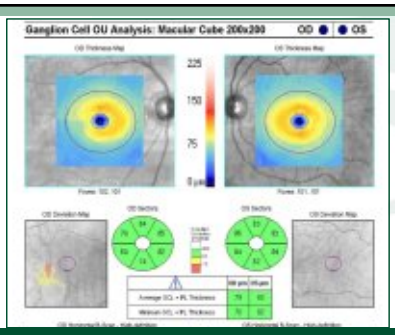

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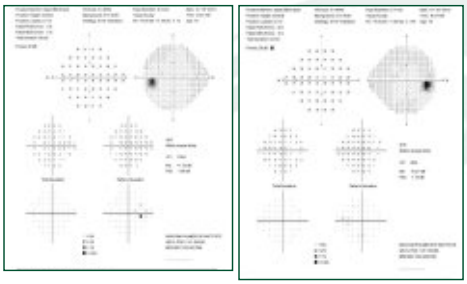

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Summary

- Suspicious disc
- Borderline IOP
- Normal visual field
- Normal OCT *
- What did I do? Observed (but did discuss tx)
  - Patient education
  - Importance of follow up

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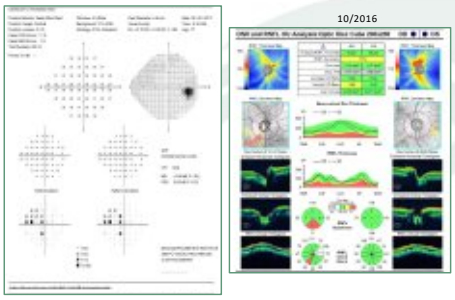

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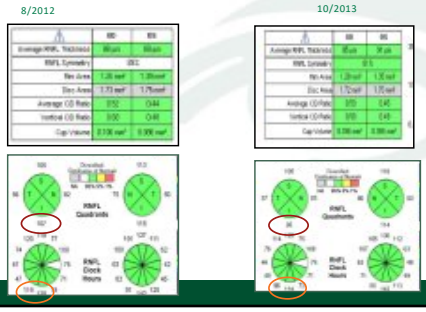
This was her 15 months earlier



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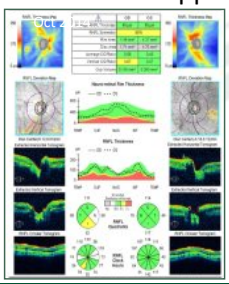
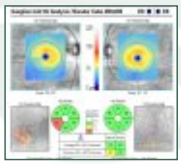
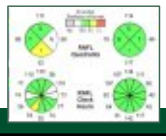
See what happens the next year







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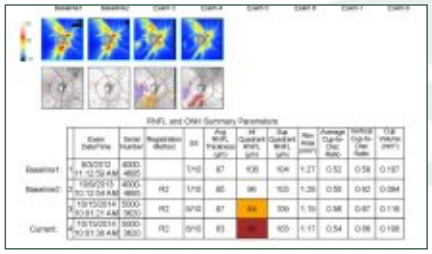

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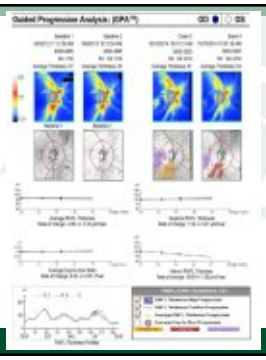

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Case MC progression

- Clinical suspicion proved true
- Initial progression in normal range and continued
  - Rate is important consideration
- Treatment initiated
- Subtle corresponding VF defect evolved
- Currently stable in short term on well tolerated meds

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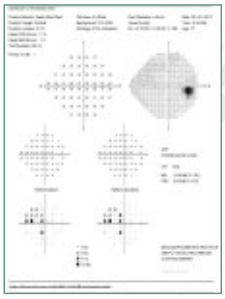
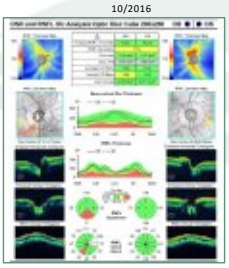


10/2016



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It Takes a Village to Manage Glaucoma Patients

- All the data that is gathered is critical!
  - IOP measurement
  - Optic nerve evaluation
  - Visual fields
  - OCT
- The data needs to be accurate and reliable
- Even though the patient comes to see **"their doctor"** for glaucoma
- Everybody who sees these patients along the way plays a critical role in the care of a glaucoma patient

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