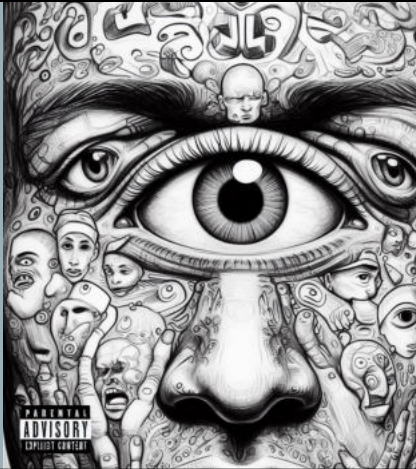


**WILL THE REAL
GLAUCOMA,
PLEASE STAND UP**

Cecelia Koetting OD FAO DipABO
Assistant Professor
University of Colorado School of Medicine





1

CECELIA KOETTING FINANCIAL DISCLOSURES

"All relevant relationships have been mitigated."

- Ocular Therapeutix -C
- Horizon-C
- Quidel-C
- Ivantis-C
- Orasis-C
- Otto-C
- Trukera-C
- LENZ-C
- Tarsus-C,S,R
- + Glaukos-C
- + B +L- C,S
- + Iveric-C
- + Aldura-C
- + Claris Bio-C
- + Aldeyra-C
- + Twenty Twenty Therapeutics-C
- + Dompe-C,S,R
- Oyster Point/Viartis-C, S,R
- Allergan/Abbvie -C,S,R
- Alcon-C,S
- Visus-C,S
- Harrow-C,S
- Thea-C,R
- Bruder-C
- Blinkjoy-C
- SCOPE-C

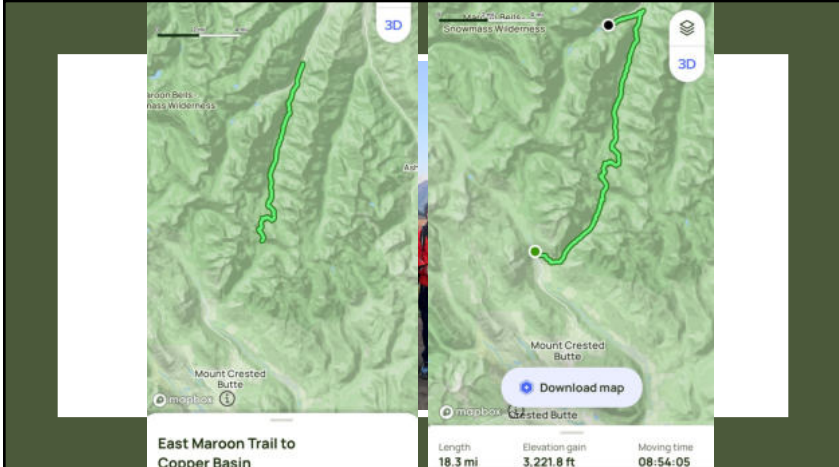



3

[POLLEV.COM/CECELIAKOETTING876](https://pollev.com/ceceliakoetting876)



4



East Maroon Trail to Copper Basin

Length: 18.3 mi | Elevation gain: 3,221.8 ft | Moving time: 08:54:05

5

GLAUCOMA DISEASE BURDEN

- Approximately 76 million people will suffer from all types of glaucoma
- Estimated to reach 111.8 million by 2040
- At least, half of those with glaucoma are unaware that they are affected. In some developing countries, 90% of glaucoma is undetected.
- In many cases, glaucoma may be asymptomatic.
- It is estimated that more than 11 million individuals will be bilaterally blind due to glaucoma in 2020 (around 13% of the cases).

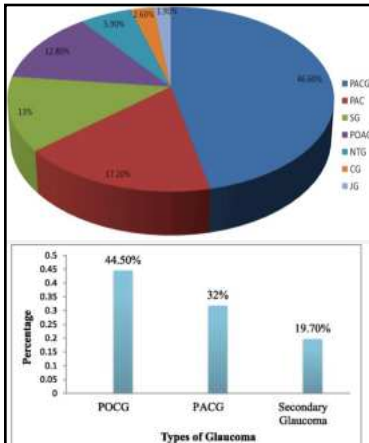
6



PROJECTION OF ALL GLAUCOMA PATIENTS

Glaucoma Market is growing with the CAGR of 7.05% during the forecast period of 2021 to 2028

7



SECONDARY GLAUCOMA PREVALENCE

Wubet, G.M., Assefa, A.A. Glaucoma and its predictors among adult patients attending ophthalmic outpatient department: a hospital-based study, North West Ethiopia. *BMC Ophthalmol* 21, 400 (2021). <https://doi.org/10.1186/s12886-021-02168-y>

8

BUT WHEN IS IT SECONDARY GLAUCOMA?



- Optic Nerve cupping
- Medical history
- Visual field analysis
- Angles
- Other clinical clues

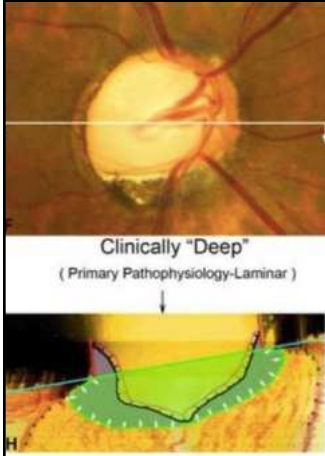
9

ONH CUPPING

Primary glaucoma vs Secondary glaucoma

10

PATHOPHYSIOLOGY OF "CUPPING"

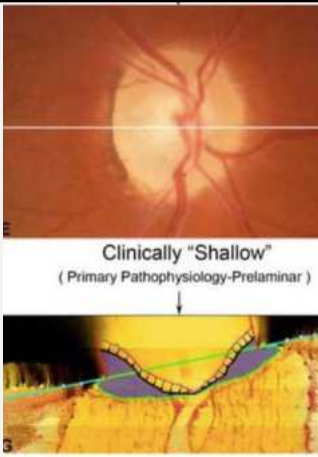


- Glaucomatous
- Cupping is believed to occur from laminar deformation
- Deep cupping from laminar insult
- Deep cups is largely IOP related

11

PATHOPHYSIOLOGY OF "CUPPING"

- Non-Glaucomatous: AION
- Non-glaucomatous cupping believed to occur as pre-laminar tissue thinning
- Appears as shallow cupping, occurs from pre-laminar insult



12

CLINICAL FINDINGS

- OAG is not typically quick onset with visual symptoms
- AION and ON will occur acutely
- Compression will be variable
- Non glaucomatous ON will have a dimming or decreased/blurred vision
- Poor visual acuity
- Non glaucomatous ON will often be asymmetric and may have pain
- Non glaucomatous ON will most often have reduced color vision
- APD more often present in non glaucomatous

13

OTHER FACTORS

Patients medical history

- HTN, DM, trauma, MS, ED drugs

Visual field defects

- More classic glaucomatous defects
 - Nasal steps
 - Temporal wedges
 - Arcuate defects
 - Paracentral defects

14

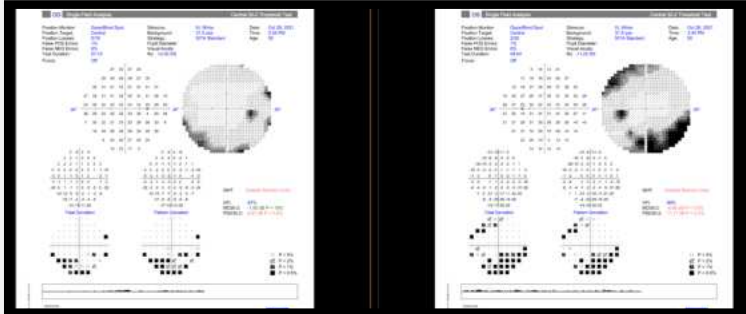


PATIENT CASES: DO YOU THINK THEY HAVE GLAUCOMA?

PollEv.com/ceceliakotting876

15

PATIENT #1
42 YEAR OLD MALE



16

DOES THIS PATIENT HAVE GLAUCOMA?

17

Does this patient have glaucoma

Yes, for sure 0%

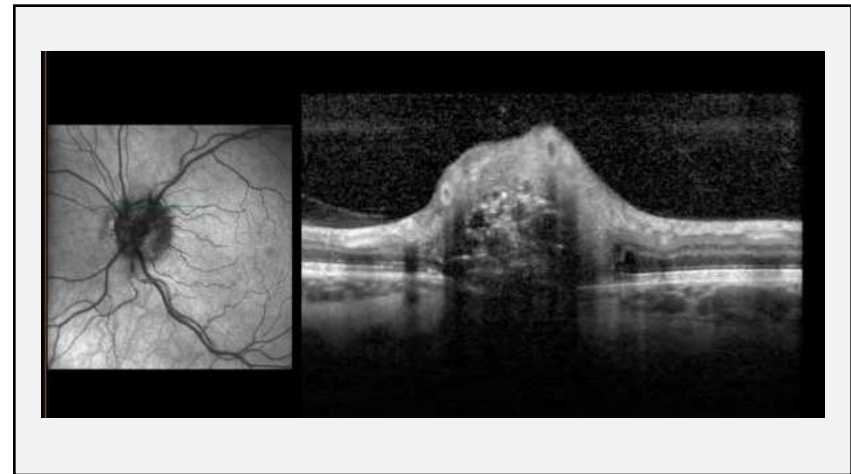
Maybe? 0%

NO, for sure 0%

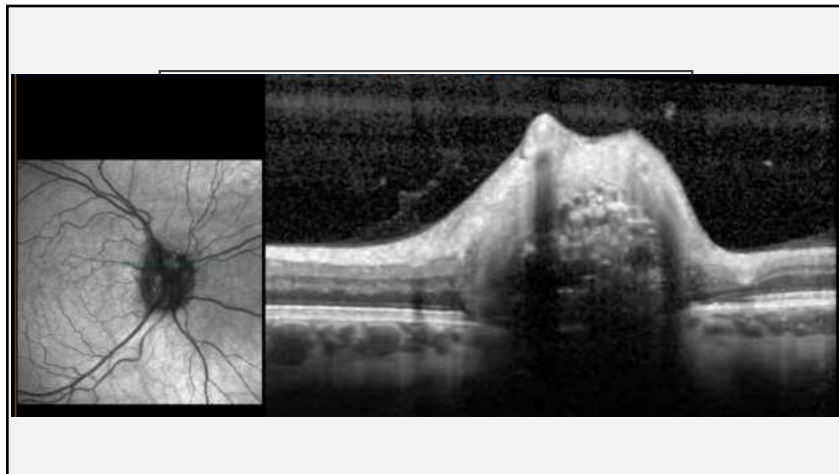
We don't have enough information 0%

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18



19



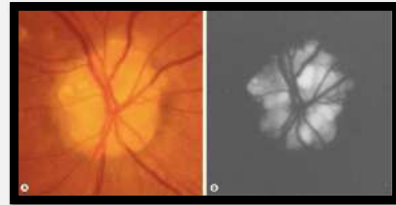
20

PSEUDOEDEMA

21

OPTIC NERVE HEAD BURIED DRUSEN

- ODD are acellular deposits of calcium, amino acids, nucleic acids, and mucopolysaccharides
 - Form in theory from impaired axonal metabolism in genetically predisposed individuals
 - Presence of narrow scleral canals are factors believed to play a role in drusen development
- Located within ONH
 - In front of lamina cribrosa
- Approximately 0.3-2% of the population
- Continue to grow over time



22

OPTIC DISC DRUSEN STUDIES CONSORTIUM

- ODD may cause sudden-onset painless vision loss through a variety of mechanisms including
 - non-arteritic anterior ischaemic optic neuropathy (NA-AION),
 - central retinal artery occlusion
 - central retinal vein occlusion,
 - choroidal neovascularization
- In two recent retrospective studies of young individuals (aged 50 years or less) with NA-AION, 51% to 53% of NA-AION eyes had ODD

23

PREVIOUS STANDARD OF DIAGNOSTICS

- B-Scan ultrasonography or CT imaging
 - Limitation is that detection requires adequate calcification of the ODD (ergo, less calcified drusen may be missed)
- Fluorescein Angiography and Fundus autofluorescence
 - Intravenous FA and fundus autofluorescence are insensitive to deeper lying ODD



24

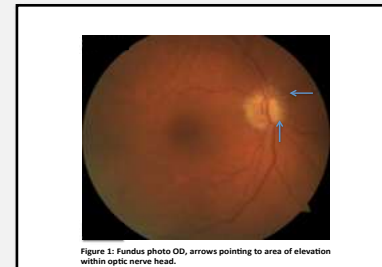


Figure 1: Fundus photo OD, arrows pointing to area of elevation within optic nerve head.



Figure 3: B-scan of OD with arrow pointing to area of hyper-reflectivity within optic nerve head

25

WHEN IS CT HELPFUL?

- Good to view
 - Bone abnormalities
 - Calcification
 - Bony involvement from soft tissue mass
 - Metallic foreign bodies
 - Fresh blood
- Indicated when:
 - Orbital trauma
 - Proptosis, swelling of eyelids (orbital cellulitis, abscess, etc)
 - Some instances MRI may still be preferred
 - Intraocular or intraorbital foreign bodies
 - Graves patients (can also use MRI)
 - Avoid if possible in pregnant patients

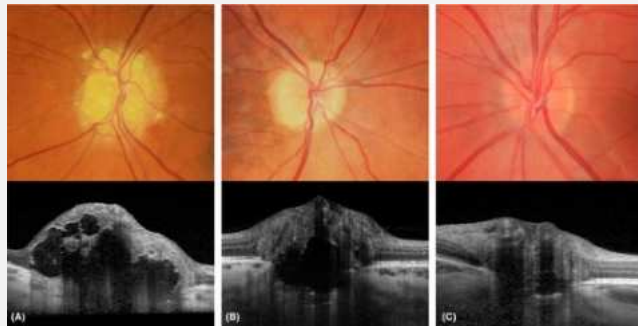
26

CURRENT DIAGNOSIS PROTOCOL FROM ODDSC

Prior to Scanning	Optimise scan quality by dilating pupils as needed, measuring corneal curvature and refraction
Acquisition	To visualize deeper structures, use EDI mode, then type in corneal curvature and refraction in the operator system
Dense optic nerve head (ONH) scan	To identify ODD, select EDI mode and high-resolution acquisition, centre a scan area of 15 × 10 degrees covering the entire optic disc area, scan with 97 sections in that area (30 μm between scans), average at least 30 frames, and perform the volume scan in horizontal (axial) direction only
Radial ONH scan	Assess scleral canal size by using EDI mode, select 20-degree 6-line radial scan, and centre scan at optic disc
Peripapillary scan	Evaluate RNFL thickness by deselecting EDI mode, select 12-degree peripapillary scan, and centre scan at optic disc
Macular scan	To exclude macular pathology, deselect EDI mode, centre scan area of 20 × 20 degrees over macula, scan with at least 25 sections (240 μm between scans), and average at least 9 frames
Autofluorescence	To identify autofluorescence, centre scan at optic disc, and average 100 frames

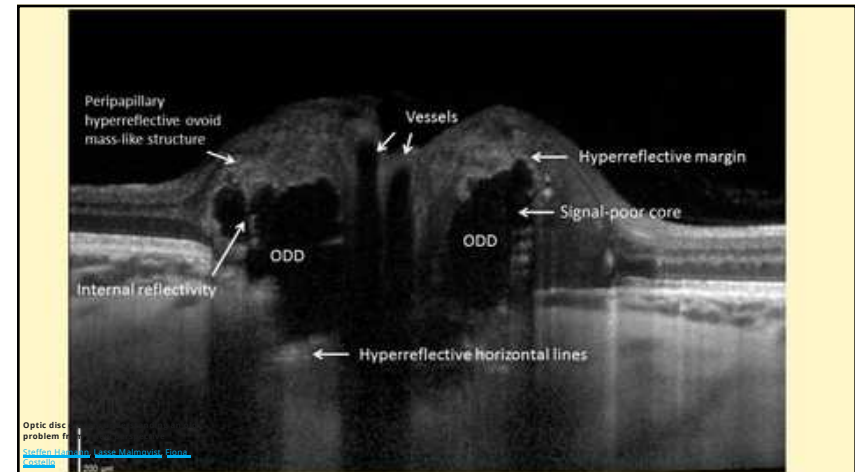
Enhanced depth imaging (EDI) optical coherence tomography and autofluorescence protocol specifications for identifying optic disc drusen (ODD)

27



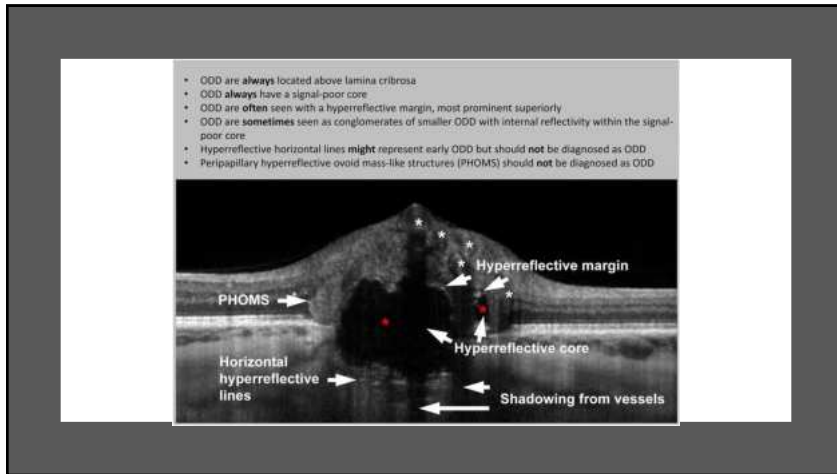
Optic disc drusen: understanding an old problem from a new perspective
[Optic Disc Drusen](#) [Optic Disc Drusen](#) [Optic Disc Drusen](#) [Optic Disc Drusen](#)

28



Optic disc problem for
[Identifying](#) [Using](#) [Using](#) [Using](#)
[Identifying](#) [Using](#) [Using](#) [Using](#)
 702 μm

29



30

VISUAL FIELDS AND PROGNOSIS

- Up to 87% of ONHD have a visual field defect
- ODDSC study
 - Larger ODD volume was associated with worse visual field defects, not location within ONH
- Most common visual field defect
 - Inferior nasal step
 - Sectoral arcuate scotoma
 - Enlarged blind spot
 - Concentric peripheral constriction

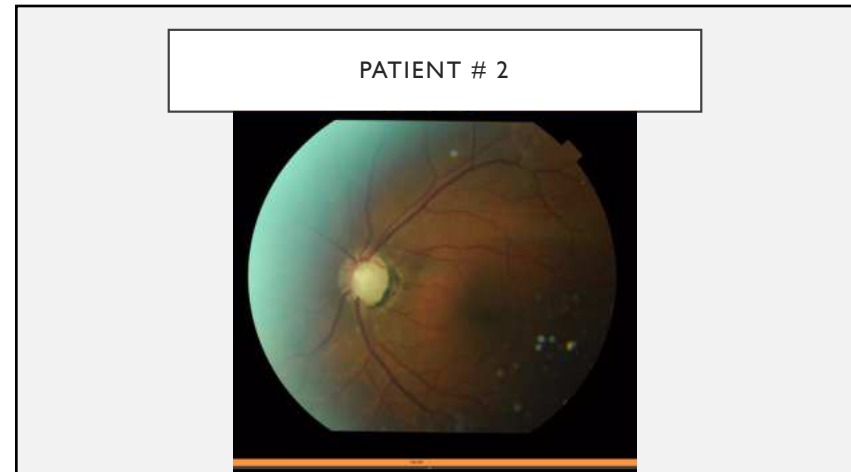
Figure 3

31

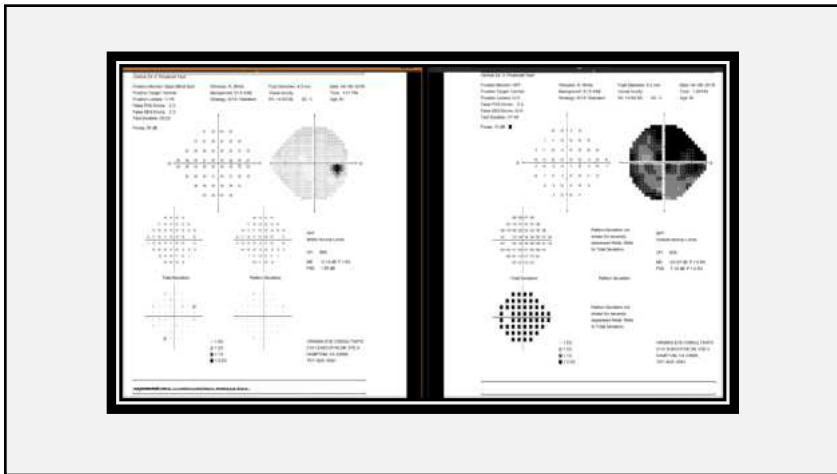
TREATMENT

- Monitor with visual fields and OCT optic nerve
- If vision becomes compromised can treat with topical IOP lowering medications
 - Secondary glaucoma
 - There are no controlled clinical studies to support this approach
- 2018 study
 - Higher IOP was not associated with greater VF loss or thinner RNFL at the time of presentation
 - This suggests that lowering IOP may not be beneficial in preventing visual loss in normotensive eyes with ONHD.

32



33



34

MORE QUESTIONING

- No history of diabetes
- HTN controlled with oral medication
 - BP normal in office that day
- **Does currently use sildenafil and has used for the last several years**
- No Hx of major surgeries with complications or blood loss/significant BP drop
- Does not report excessive alcohol use

35



36

What is the next step for this patient

- MRI of head and orbit w/ and w/o contrast 0%
- Blood work including CBC A1C ESR CRP 0%
- Both MRI and blood work 0%
- No thank you!! Refer that patient to Dr. Bozung 0%

Start the presentation to see live content. For screen share software, share the entire screen. Get help at pollin.com/app

37

HOW TO ORDER AN MRI

- If it is emergent (in the case of possible Optic Neuritis or CN 3 Palsy)
 - Refer to local ER within 24-48 hours for MRI
 - Can send with a written script for MRI of head and orbits with and without contrast
 - Include why you are ordering it
 - Sudden decrease in vision OD with pain, possible optic neuritis
 - Include a phone number to reach the doctor at and be ready for a call
 - They will likely ask for treatment suggestion if confirmed diagnosis
 - Can send with standing order for how to treat if positive diagnosis

38

HOW TO ORDER AN MRI

- In a non-emergent situation (papilledema likely IHH)
 - Order an MRI of the head and orbits with and without contrast within a few weeks
 - Can be scheduled with out patient clinics or at MRI centers
 - Your front desk staff can help the patient with this.
- MRA vs MRV
 - Artery vs veins
 - Aneurysms, dissections, cerebral venous sinus thrombosis

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- MRI of Head vs MRI of Orbits
 - Do you really need both?
 - When should you order both
- Pregnancy ok but no contrast
- Do NOT order in patients with metal implants or pins, pacemakers, or implanted cardiac defibrillators
- Claustrophobia patients consider open MRI if option
 - Valium helps

40

Imaging Requisition Form
(PLEASE FAX RESULTS TO: 1-757-793-4691)

Patient's Name: _____ Today's Date: ____/____/____

Patient's DOB: ____/____/____

Diagnosis:

<input type="checkbox"/> G45.1 Anisocoria Pupae	<input type="checkbox"/> U70.00 Myeloma Crania
<input type="checkbox"/> G48.21 CN3 Palsy, Right	<input type="checkbox"/> I01.00 Noninfective Endocarditis, Bicuspid
<input type="checkbox"/> G48.22 CN3 Palsy, Left	<input type="checkbox"/> I03.00 Nystagmus
<input type="checkbox"/> G49.0 CN7 Palsy (Bell's)	<input type="checkbox"/> I08.89 Other Neuritis
<input type="checkbox"/> H02.241 Oculophthalmic, Right	<input type="checkbox"/> I07.10 Papilloedema
<input type="checkbox"/> H02.242 Oculophthalmic, Left	<input type="checkbox"/> I07.11 Papilloedema (IHH)
<input type="checkbox"/> H03.00 Cornea Unknown	<input type="checkbox"/> I06.89 Retinopathy
<input type="checkbox"/> H03.01 Homonymous Chiasm, Right	<input type="checkbox"/> M01.6 Traumatic Strabismus
<input type="checkbox"/> H03.02 Homonymous Chiasm, Left	<input type="checkbox"/> H03.40 Visual Field Defect

Other ICD 10: _____

Description: _____

Special Studies:

CT scan of the orbits with contrast

CT scan of the orbits without contrast

MRI of the head, with and without contrast, per radiology

MRI of the orbits, with and without contrast, per radiology

MRI / MRV of the head with and without contrast, per radiology

X-ray of the chest PA and Lateral

Other: _____

Physician Signature: _____ Date: ____/____/____

The information below is to be filled out by the front desk staff, and then entered into the patient's chart:

Location/Address: _____

Arrival Time: _____ Date: ____/____/____

Other Instructions: _____

VEC Apt. Scheduler: _____

PLEASE FAX RESULTS TO: 1-757-793-4691

41

TESTING

- Blood work CRP/ESR
 - **NORMAL**
- MRI Orbit and head w/ and w/o contrast
 - MRI head **NORMAL**
 - **MRI ABNORMAL**
 - Asymmetric hyperintense signal in left optic nerve without enhancement with associated volume loss of optic nerve
 - indicating possible etiology of optic neuropathy

42

NON-ARTERITIC ISCHEMIC OPTIC NEUROPATHY

- Localized ischemic event at junction of optic nerve
- May be younger in age than AION (40-60 YOA)
- Signs and symptoms
 - Sudden painless vision loss
 - 30-2 severe defect
 - VA decreased
 - Less severe than AION
 - APD
 - Pale disc swelling
 - Flame shaped heme

43

NAION

- Diagnosis of exclusion
 - Normal MRI
 - May find chronic microvascular changes on MRV
 - Normal ESR/CRP
- 40% show some improvement in vision over the next 6 months
 - Monitor with visual fields
- Optic nerve edema will resolve within 8 weeks
 - Can monitor with OCTG
- Risk of contralateral eye involvement

44

NAION AND SILDENAFIL

- 2006 study monitoring 13000 men showed no increase risk of NAION in patients on sildenafil when compared with similar population not on the medication.
- Incidence of 2.8 patients per 100,000 men >50YOA

45

NAION AND SILDENAFIL

- 2015 study of 1109 cases of NAION also showed no increased correlation with use of sildenafil or a PDE-5inhibitor within 30 days of onset
- Cases were more likely to have hyperlipidemia, diabetes, hypertension, myocardial infarction and cerebrovascular accident

46

NAION TREATMENT

- It has been suggested in a study by Foulds in the 1970's that the patients may benefit long term visual recovery from the use of 40-60mg of oral prednisone for 1 month.
- 85% of patients treated with 60mg oral prednisone showed visual acuity improvement compared to those untreated

47

NAION TREATMENT

- More recent study, 2008, Hayreh and Zimmerman 696 eyes
 - Treated within 2 weeks of onset with 70mg oral prednisone tapered
 - 69.8% of eyes treated had an improvement in visual acuity
- Only 40.5% of eyes untreated had an improvement in visual acuity

48

LEVODOPA

Optic Nerve Clin Exp Ophthalmol. 2018 Apr;25(4):757-64. doi: 10.1007/s00417-018-3191-z. Epub 2018 Oct 25.

Levodopa as a possible treatment of visual loss in nonarteritic anterior ischemic optic neuropathy.

Lalla DN¹, Johnson LN^{2,3}, Margolin EA⁴, Madsen RW⁵.

© Author information

Abstract

PURPOSE: To determine the clinical effectiveness and potential neuroprotection of levodopa in improving visual acuity, visual field, and retinal nerve fiber layer (RNFL) thickness in eyes affected by NAION.

METHOD: Retrospective cohort study involving 59 eyes of 59 participants with NAION who were evaluated within 15 days of NAION onset. Participants received 25 mg carbidopa/100 mg levodopa three times daily with meals for 12 weeks (levodopa group) or were untreated (control group). Best-corrected visual acuity converted to logMAR, mean deviation (MD) threshold sensitivity on automated perimetry, and mean RNFL thickness on optical coherence tomography (OCT) were assessed. The primary outcome was the categorization of eyes into improved visual acuity (by 0.3 logMAR difference), worsened visual acuity (by 0.3 logMAR difference), or no change in visual acuity. The proportions in each category were compared between the levodopa and control groups.

RESULTS: Among participants with 20/60 or worse initial visual acuity, levodopa-treated participants had significant improvement ($P < 0.0001$) in the mean change from initial to final logMAR visual acuity of -0.74 ± 0.56 [95% CI, -0.58 to -0.50], while the mean change for the control group at -0.37 ± 1.09 (95% confidence interval estimate, -1.00 to $+0.26$) was not significant ($P = 0.23$). A significant difference between groups was observed ($P = 0.0098$) such that 19(23.8%) in the levodopa group improved and none got worse, as compared with 0(4.3%) in the control group improving while four (29%) worsened. The change in visual field MD and RNFL thickness on OCT showed no significant difference at $P = 0.23$ and $P = 0.75$ respectively. No levodopa-treated participant had any adverse event from the levodopa.

CONCLUSIONS: Treatment within 15 days of onset of NAION with levodopa improved central visual acuity by an average of 6 lines on Snellen acuity chart. Levodopa may promote neuroprotection of the maculopapular retinal ganglion cell fibers in NAION.

KEYWORDS: Dopamine, Levodopa, NAION, Neuroprotection, Nonarteritic anterior ischemic optic neuropathy, Optic nerve

PMID: 30461748 DOI: 10.1007/s00417-018-3191-z

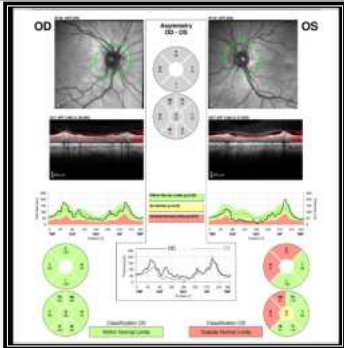
49

LEVODOPA FOR NAION

- 59 patients within 15 days of onset NAION
- Either untreated or given 25mg carbidopa/100mg levodopa PO TID
- 19/23 in the levodopa group BCVA improved and none got worse
- 6/14 in control group BCVA improved and 4/14 got worse

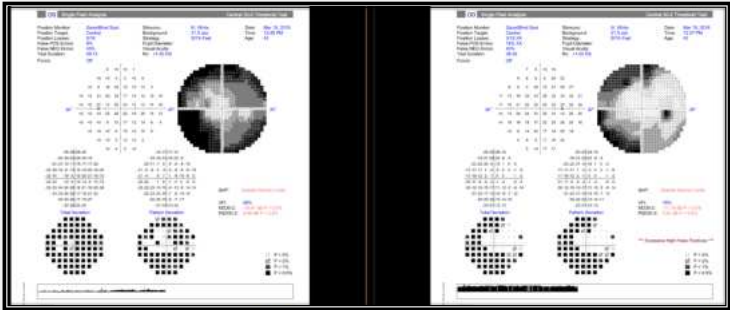
50

PATIENT #3 3/19/19



51

CURRENT VISUAL FIELD



52

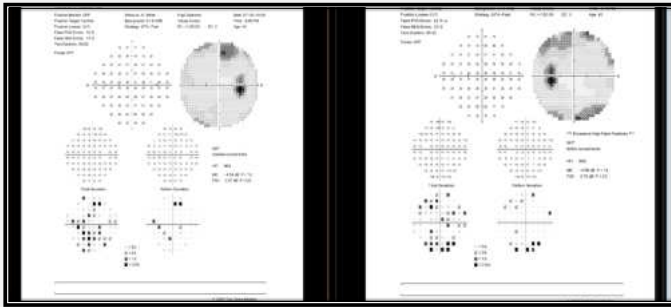
Is this glaucoma?

- Yes - POAG 0%
- Yes - secondary glaucoma 0%
- No - something else might be causing visual loss 0%
- I don't have enough information 0%

Start the presentation to see live content. For screen share software, share the entire screen. Get help at pediaw.com/app

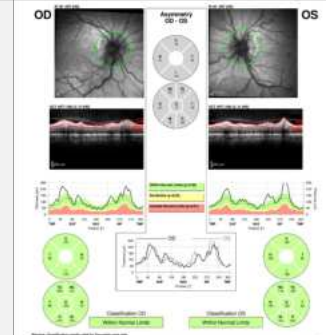
53

HOW IT STARTED (JULY 2ND, 8 MONTHS PRIOR)



54

HOW IT STARTED (JULY 2ND, 8 MONTHS PRIOR)



55

Imaging and LP Obtained July 19th, 17 days later

Show images for MRI Orbits per Radiology

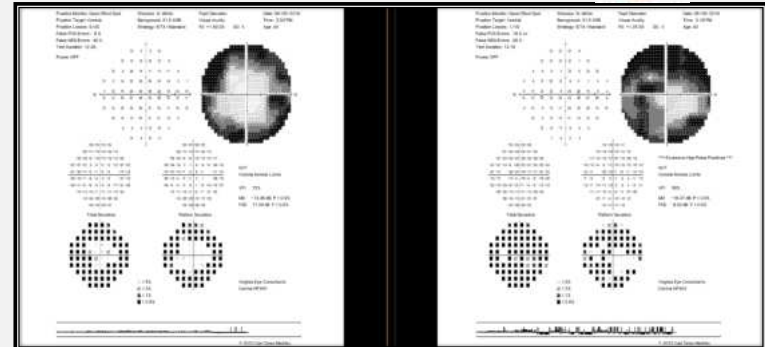
Impression

1. Normal MRI orbits.
2. No acute or other significant brain finding.
3. Partial empty sella which is usually clinically insignificant although can be related to benign intracranial hypertension.

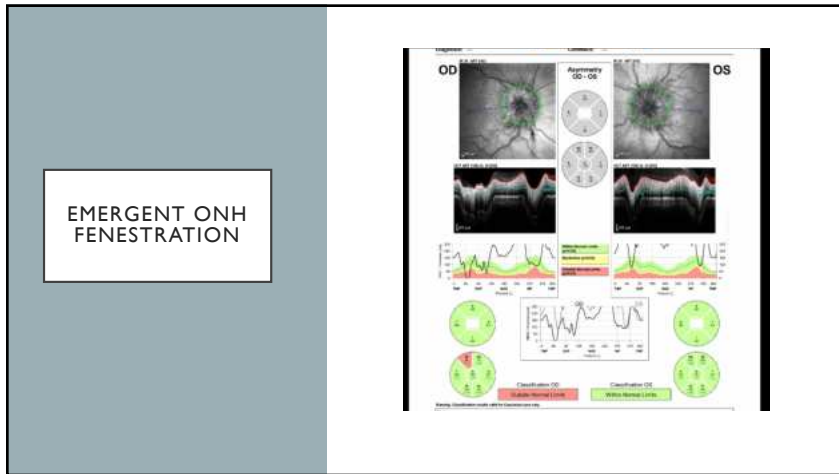
Opening pressure was obtained in a left lateral decubitus position and measured [18 cm H₂O.] CSF was clear and colorless. 27cc of CSF was withdrawn for the requested laboratory evaluation. The patient tolerated the procedure well.

56

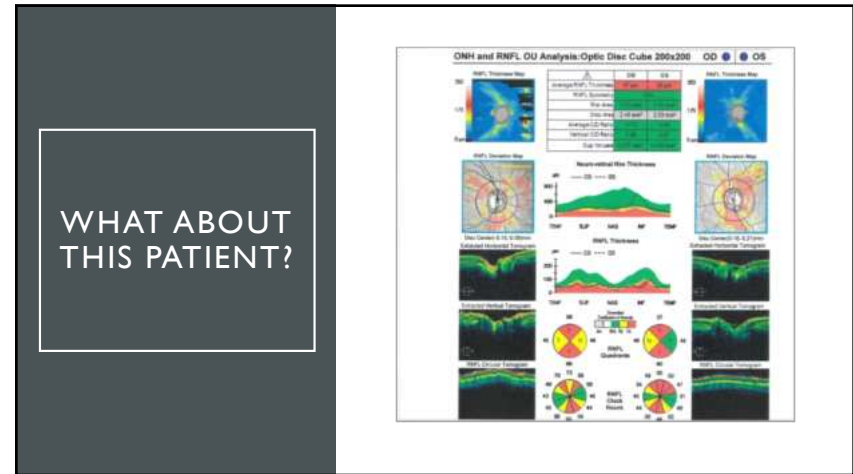
I WEEK AFTER MRI.....
OK THAT ESCALATED!



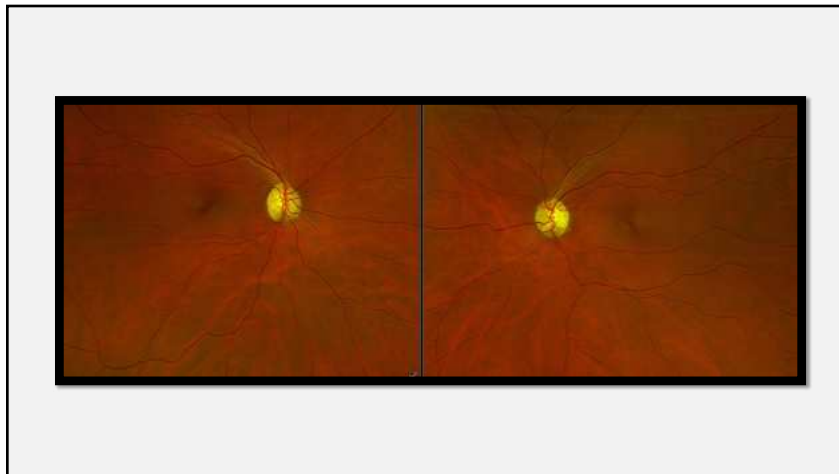
57



58



59



60

- 49 YOA. Caucasian female
- ONH atrophy progressive thinning starting in 2018 when identified by exam for LASIK consult.
- Sent to neurology.
 - Multiple tests performed.
 - Unknown cause
- Continued thinning over the next 4 years
 - Seeing patient 1 x year
 - Progression of ONH thinning, no treatment.

PRIMARY VS SECONDARY?

61

ADDITIONAL INFORMATION

(+) ringing/whooshing in ears

(+) HA

(+) weight fluctuation

(+) PCOS with ablation 2019

(+)perimenopausal

LP performed exiting pressure 17 two years prior

62

MR ORBIT W/NO CONTRAST - 06/15/2022

Optic Nerves/Chiasm:
 Unchanged prominent CSF around optic nerves. Unchanged right greater than left optic nerve atrophy, greatest at the prechiasmatic and chiasmatic area. No suprasellar mass.

Orbits:
 No masses, infiltration or enhancement of orbital fat.

Extraocular Muscles:
 Normal in size, shape, and enhancement.

Lacrimal:
 Normal lacrimal glands. No abnormality at the location of lacrimal sacs.

Extra-Orbital:
 Mild sequential mucosal thickening of the paranasal sinus. The imaged mastoids are clear. The pituitary gland is mildly flattened within the sella that is partially filled with CSF, unchanged from prior.

MRV CRANIAL
 Mild sequential mucosal thickening of the paranasal sinus. The imaged mastoids are clear. The pituitary gland is mildly flattened within the sella that is partially filled with CSF, unchanged from prior.

63

ORDERED A SECOND LUMBAR PUNCTURE

- Normal Opening pressure 18-20cm
- cerebrospinal fluid (CSF) pressure of above 25.0 cm H₂O is one of the diagnostic criteria of IIH
 - If the CSF opening pressure is below 25.0 cmCSF, but there is strong clinical suspicion of IIH, then repeating LP examination may be informative
- Opening pressure on repeat was 20cm.....

64

MODIFIED DANDY CRITERIA 2017

- No other causes of increased intracranial pressure present with CSF opening pressure of 20cm to 25 cm water, required at least one of the following:
 - Pulse-synchronous tinnitus (pulsatile tinnitus)
 - Cranial nerve VI palsy
 - Frisen Grade II papilledema
 - Echography for drusen negative and no other disc anomalies mimicking disc edema present
 - MRV (Magnetic Resonance Venography) with lateral sinus collapse/stenosis preferably using ATECO technique
 - Partially empty sella on coronal or sagittal views and optic nerve sheaths with filled out CSF spaces next to the globe on T2 weighted axial scans

65

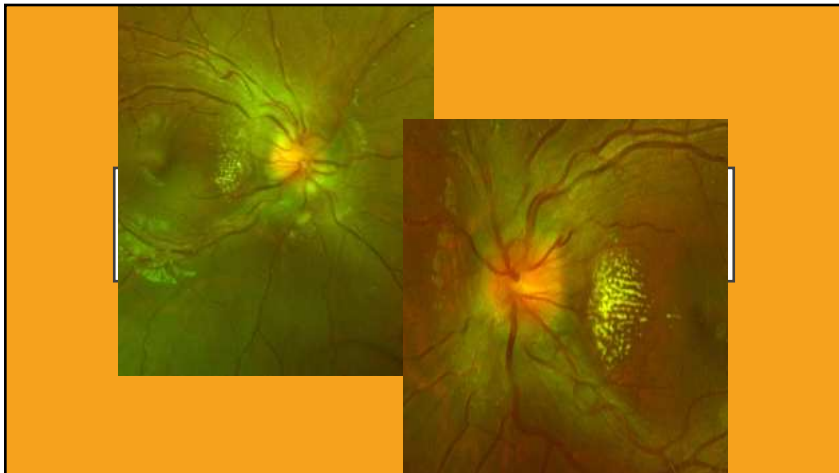
IDIOPATHIC INTRACRANIAL HYPERTENSION

66

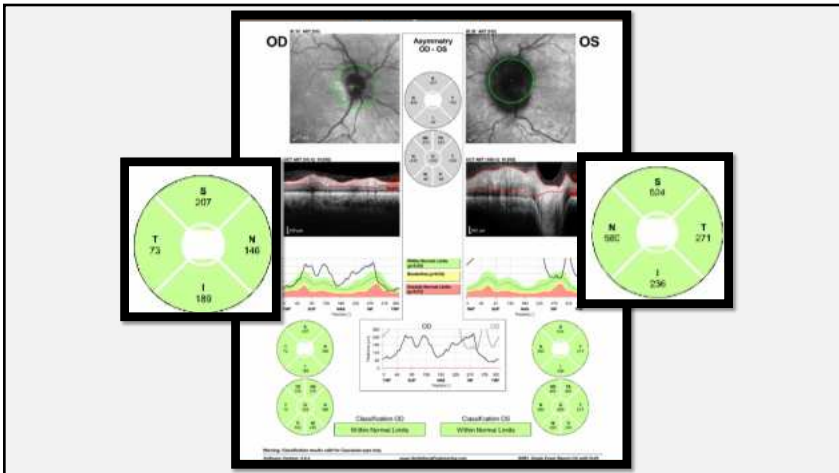
PAPILLEDEMA

- Bilateral swollen optic nerves secondary to increased intracranial pressure
- OCT-G and 30-2 HVF
- Most common VF defect
 - Enlarged blind spot
 - Peri-cecal scotoma
- Often no visual field defect
- Quickly accompanied by and MRI of head and orbit to rule out space occupying lesion
- Must be confirmed with a lumbar puncture to check the ICP

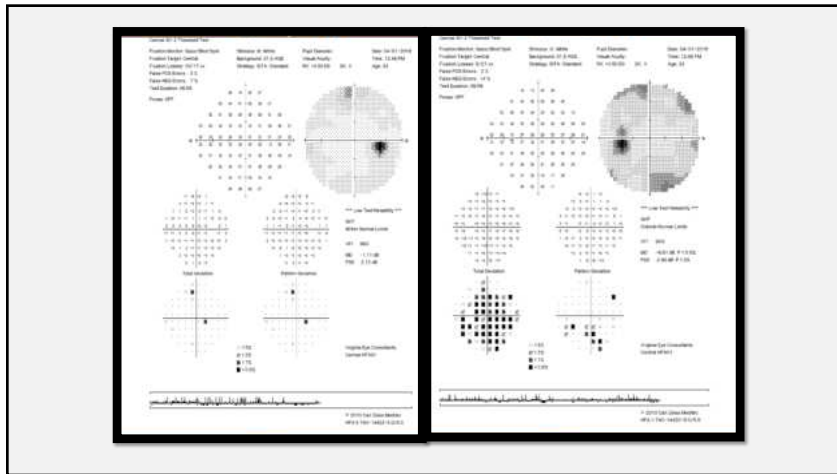
67



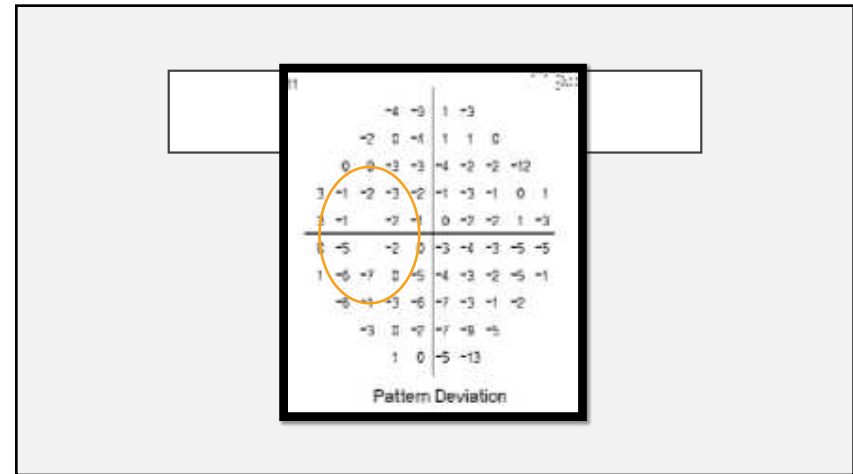
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IIH

AKA Benign intracranial hypertension and pseudotumor cerebri

Increased intracranial pressure with unknown cause

Diagnosis of exclusion

Signs and symptoms

- Headaches, tinitis,
- tingling in fingers and toes

Diagnosis

- EOM, OCT-G, 30-2, color vision, red cap SVP?
- MRI
- Within 1-2 weeks
- Lumbar puncture
- Increased exiting pressure with normal fluid
- Pregnant patients
- Usually not treated

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IIH CONTINUED

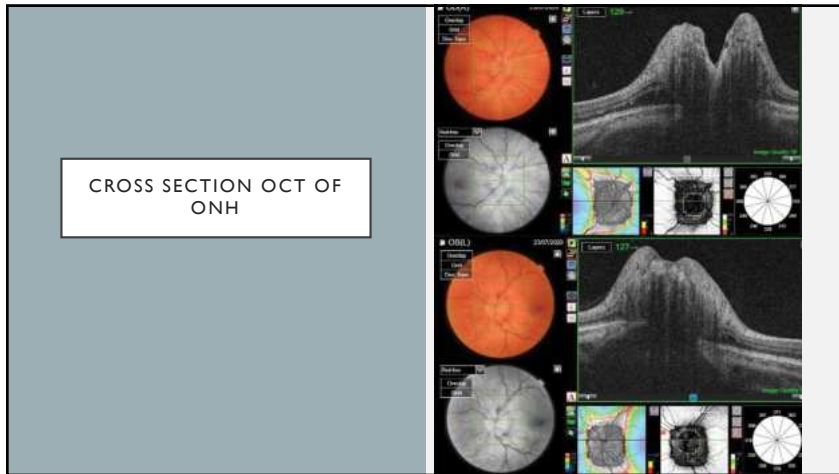
Causes

- Weight
- Birth control
- PCOS
- Minocycline, doxycycline, etc

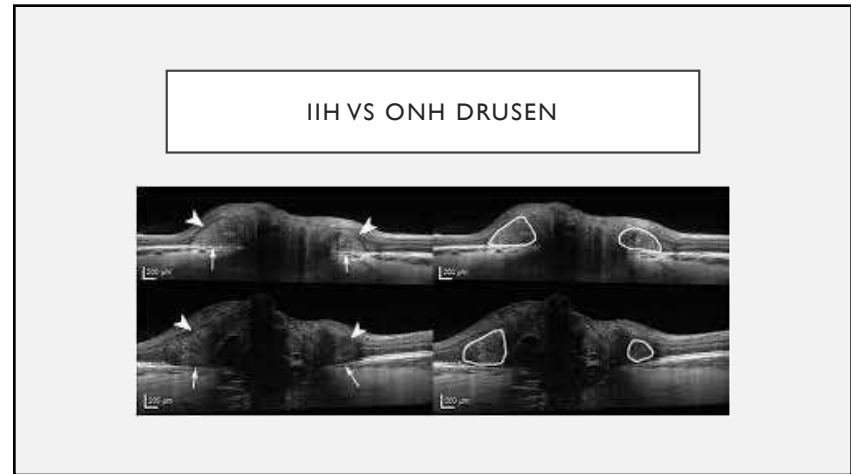
Long term concerns and treatment

- Diamox (acetazolamide)
- Topamax
- Shunt
- Optic nerve fenestration
- Weight loss
- Approx. 10% body weight loss has been show to reverse

73



74



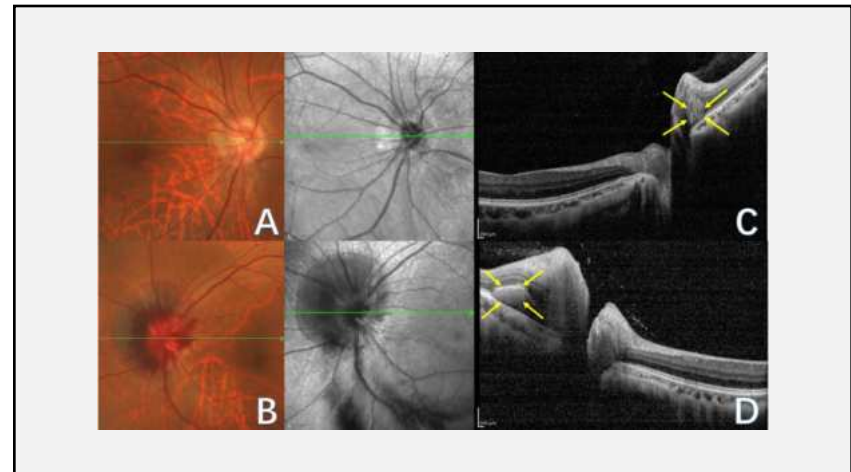
75

PERIPAPILLARY HYPER-REFLECTIVE OVOID MASS-LIKE STRUCTURES: POHMS

- Non-specific OCT finding present in various other conditions
- multiple sclerosis (MS)-related optic neuritis
- NA-AION
- Tilted disc syndrome (TDS)
- Myopic optic discs
- ODD

- Presently believed to originate from localized distortion and folding of optic nerve fiber bundles as they exit the lamina cribrosa and extend toward the surrounding retina

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CO-MANAGING IIH

- Monitor the patient closely along with neurology
- Patient sees neurology within a month for remaining testing, diagnosis, and treatment
 - Can't start Diamox prior to this or LP will be inaccurate
- Should see the patient back within 1-2 months of neurology for repeat OCT-G and 30-2 to monitor
- Follow patient every 3-6 months for repeat testing to aid neurologist in determining if medication is working adequately.

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LONG TERM OCULAR CONCERNS

- Secondary glaucoma and ONH RNFL damage
- Monitor with OCT of ONH
- HVF 24-2
- Treat similar to normal tension glaucoma

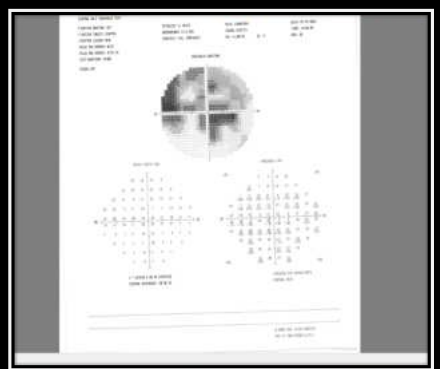
79

PATIENT #4

- The 30 year old female presents for reduced vision OD referred by optometrist. First noticed vision was blurry in the past 2 months, didn't check which eye was worse, referred to our clinic because of reduced VA in right eye to 20/200.
- gets occasional migraines, uses computer all day and eyes get watery.
- Pt is not using any drops.
- Reports migraines are more frequent and are more severe possibly since last year.
- OD CF@4ft
- OS 20/20

80

PATIENT #4



81

Procedures Performed: Exam
 MR ORBITS WWO CONTRAST Date/Time: 07/29/2019 9:01 PM
 MR19073927147

EXAM: MR ORBITS WWO CONTRAST
 CLINICAL HISTORY: H33.40. Visual field defects
 COMPARISON: MR head 7/29/2019

A T2 hyperintense lesions on the posterior pituitary measures 3.4 mm AP x 6.3 mm transverse x 3.4 mm craniocaudal, may represent a tiny Rathke's cleft cyst.

A T2 hyperintense lesions on the posterior pituitary measures 3.4 mm AP x 6.3 mm transverse x 3.4 mm craniocaudal, may represent a tiny Rathke's cleft cyst.
 Trace mucosal thickening within the left maxillary sinus. Trace mucosal thickening within the left sphenoid sinus.

IMPRESSION

82

PATIENT #5

83

Based on the visual field only, what do you think may be happening?

The patient may have had a stroke 0%

Maybe a pituitary tumor 0%

Maybe a retina problem 0%

The patient was just a bad test taker 0%

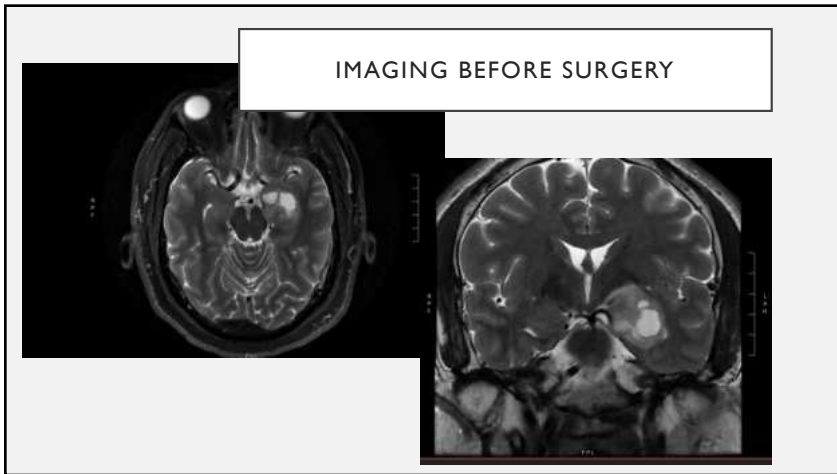
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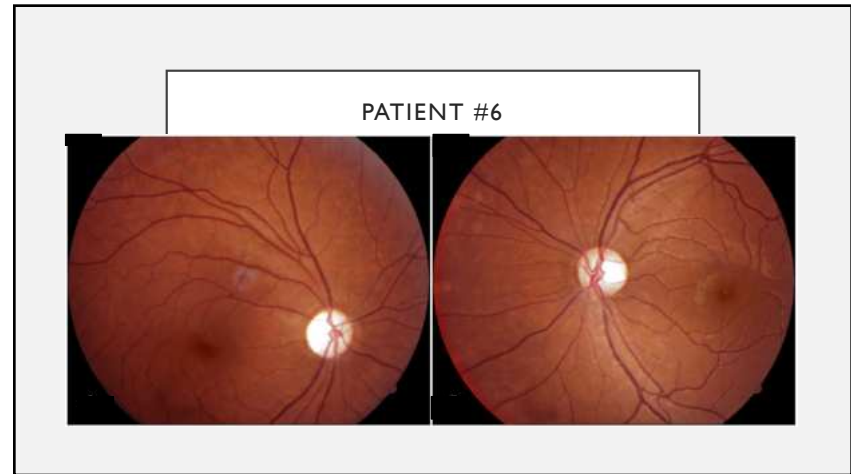
POST SURGICAL MONITORING:
 GLIOBLASTOMA REMOVAL LESS THAN 1
 MONTH PRIOR

Reason for Visit	History of Present Illness
blurry vision	The 36 year old male presents for evaluation of blurry vision in the right eye and left eye. It affects OU. The symptom is constant. The condition is significant. Pt presents in clinic today for glioblastoma. Pt states that he underwent a surgical procedure for brain cancer on 10/1/2021 and since, he states that his VA has not been the same. Pt states he is able to see simple things but when trying to focus when reading something, it becomes blurry. Pt was told by his cancer MD David Jared Kobilnicky to wait and see if his VA progress and to get his eye checked if no changes. Pt states that he does get HA once daily and takes tylenol. Pt states that his VA looking straight forward is clear but anything other than that is blurred. Pt states that he is to start chemo tomorrow. Red DESAT: OU 100% Brightness: OD 95%/OS 100%

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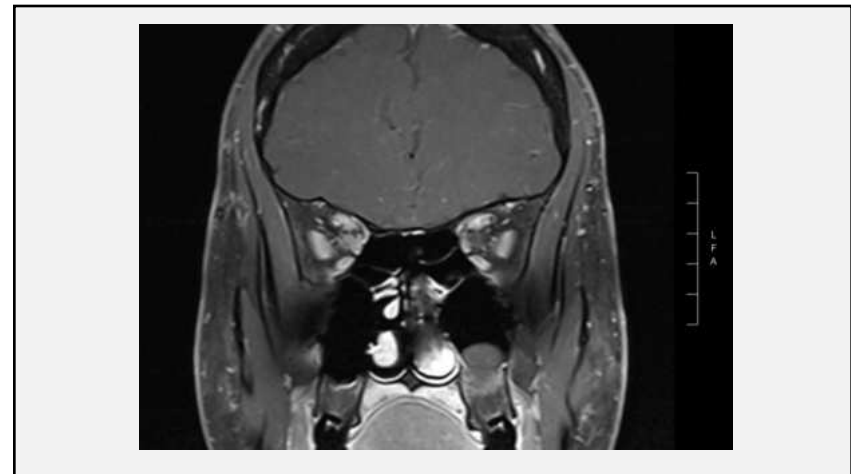


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MORE ABOUT OUR PATIENT

- 46 Year old AA Female
- Significant vision loss and atrophy OU
- Multiple occurrences of bilateral optic neuritis x 5 years.

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CC: R eye pain/blurry vision

ASSESSMENT:
#Optic perineuritis, with R eye pain/blurry vision
 Onset of R eye pain with lateral movement and blurry vision on 9/15/21 that gradually worsened. Pt presented to ED on 10/12/21. MRI orbits w/wo contrast showed enhancement involving the perioptic nerve sheath as well as the intraconal optic nerve. Findings may represent orbital lymphoma given nerve and perineural involvement. CSF studies from LP are pending. Pt has completed 3/5 days of IV Solumedrol and reports slight improvement in visual sx's. Pt will need to complete course of steroids and have close f/u with ophthalmology/neurology.

PLAN:
 -Pt needs to complete 5 day course of IV Solumedrol, today is day 3/5
 -CSF studies pending
 -Continued f/u with ophthalmology
 -Pt will need close OP neurology f/u, referral placed
 -Final recommendations per neurology attending

NMO, IgG, Serum
 Status: Final result Visible to patient: Yes (seen) Next appt: 04/08/2022 at 09:00 AM in Neurology

0 Result Notes

NMO IgG Serum	Ref Range & Units	4 d ago
Comment:	0.0 - 3.0 U/ml	48.6*
Negative:	0.0 - 3.0	
Positive:	>3.0	

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NEUROLYELITIS OPTICA SPECTRUM DISORDER (NMOSD)

- Previously thought of as variant of MS
- Demyelination of optic nerve and spinal cord
- Associated with aquaporin-4 (a water channel present in glial cells) antibodies.
- Testing for NMO-IgG should be considered in those patients with bilateral ON or ON coupled with longitudinally extensive transverse myelitis (LETM), recurrent ON, or brain MRIs atypical for MS
- No cure, but similar treatment to MS
- Poor prognosis, loss of muscle function, often death occurs 2/2 respiratory complications

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NMOSD VS MS

- Higher likelihood to have ON vs MS
 - Bilateral vs unilateral more often
- More likely to present as bilateral ON or to occur in both eyes during separate times
- More likely to have permanent vision loss
 - Minimal to no improvement after resolution of ON
- More likely to exhibit ONH atrophy after ON

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73 YOA MALE

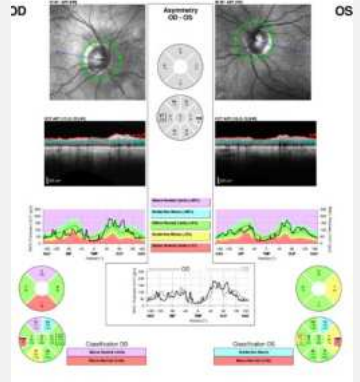
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HISTORY OF BILATERAL OPTIC NEUROPATHY

Does not have MS
Does not have NMOSD
No Immune disorders or inflammatory

MRI findings: demyelination versus other (sarcoid)

Neuro Ophthalmologist at last appointment: patient being referred to glaucoma today because of the extensive cupping despite the fact that we know he has bilateral optic neuropathy current with potential neurosarcoid v. Other



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Assuming a decrease in VA, some worsening on HVF and stable OCT of optic nerve, what else should be done?

- Look at the ocular surface 0%
- Look at the macula and the rest of the retina 0%
- Double-check the refraction 0%
- All of the above 0%

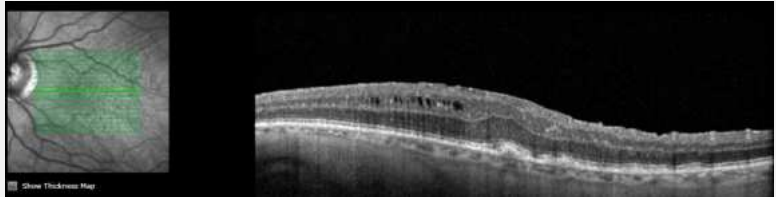
Start the presentation to see live content. For screen share software, share the entire screen. Get help at [pellax.com/app](https://www.pellax.com/app)

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WHY THE DECREASED VISION IN OS IF EVERYTHING IS STABLE?

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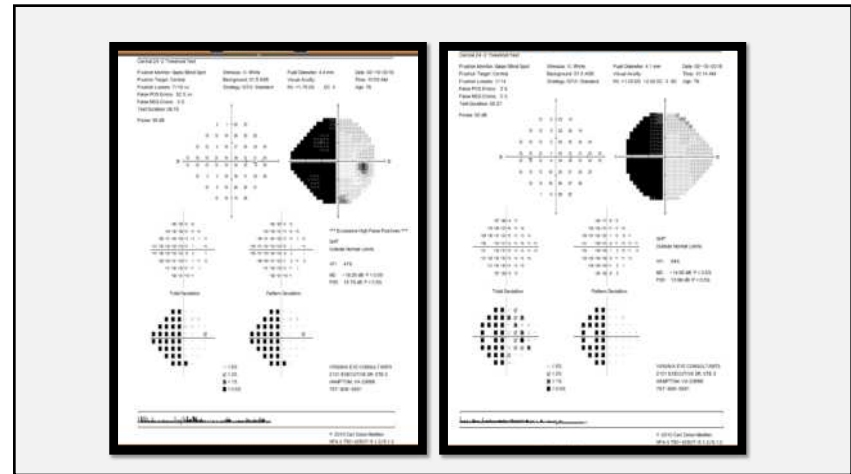
DON'T FORGET THE MACULA



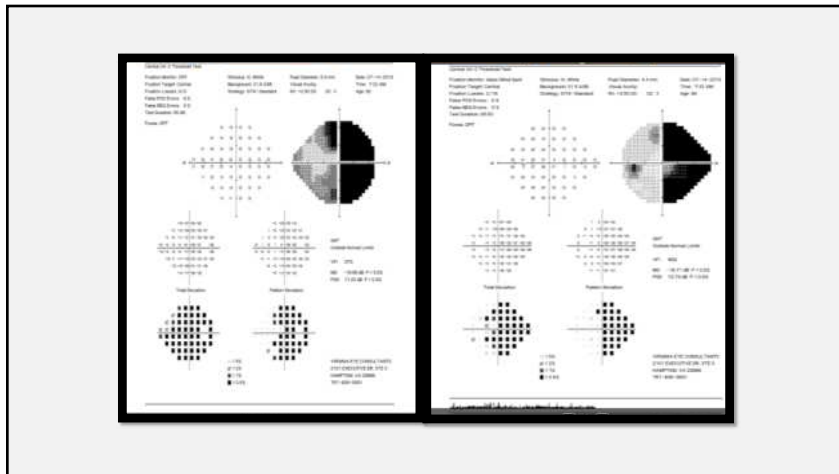
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STROKES

- Brain cells deprived of oxygen and begin to die
 - Brain aneurysm → hemorrhagic
 - Blood clot → ischemic
- Most easily identifiable defect is a bilateral homonymous hemianopsia
 - Appearance depends on location of the infarct and severity of damage

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Food for thought:

WHAT IF THEY HAVE PRIMARY GLAUCOMA BEFORE?

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OTHER FACTORS?

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MIGRAINES

Research Article
The Impact of Migraine on Posterior Ocular Structures

Süleyman Demircan,¹ Mustafa Atay,¹ Sevgi Arık Yükoel,¹ Melek D. Ünsoy,¹ İsa Yuvacs,¹ Hasan Basri Arifoğlu,¹ Burhan Başkan,¹ and Gökmen Zararsız²

¹Kayseri Training and Research Hospital Eye Clinic, 38100 Kayseri, Turkey
²Kayseri Training and Research Hospital Neurology Clinic, 38101 Kayseri, Turkey

different between the groups. **Conclusions:** This study suggests that migraine leads to a reduction in the peripapillary RNFL thickness and to thinning in choroidal structures. These findings can be explained by a chronic ischemic insult related to migraine pathogenic mechanisms and these findings are considered supportive of the relationship between glaucoma and migraine.

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Purpose: To investigate the thickness of the retinal nerve fiber layer (RNFL) and choroid in patients who have migraines in comparison to healthy controls. *Methods:* This study included 78 eyes and patients in the migraine group, 36 with aura (MWA) group and 40 without (MNA) group, and 38 eyes as control subjects. The RNFL and macular thickness were analyzed with standard OCT protocol while choroidal thickness was analyzed with EDI protocol in all subjects. Choroidal thickness was measured at the fovea, 1000 µm nasal and 1000 µm temporal to the fovea in a horizontal section. *Results:* The mean RNFL thickness for nasal and nasal inferior sectors was significantly thinner ($P < 0.010$) in the migraineur eyes than in those of the controls, as was the mean choroidal thickness at the fovea and measured points ($P < 0.0001$). However, the mean macular thickness was not significantly different between the groups. *Conclusions:* This study suggests that migraine leads to a reduction in the peripapillary RNFL thickness and to thinning in choroidal structures. These findings can be explained by a chronic ischemic insult related to migraine pathogenic mechanisms and these findings are considered supportive of the relationship between glaucoma and migraines.

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TOXIC AND NUTRITIONAL OPTIC NEUROPATHY

- Vitamin B-12
- Folate
- Copper
- Amiodarone

- Tobacco
- Methanol
- Ethambutol
- Alcohol

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TREATMENT: LOWER IOP

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POTENTIAL CANDIDATES IN NEUROPROTECTION

<p>SUSTAIN RETINA GLIAL CELL VIABILITY</p> <ul style="list-style-type: none"> • Promote non-amyloidogenic beta pathway <ul style="list-style-type: none"> • Brimonidine • Decrease glutamate-induced excitotoxicity <ul style="list-style-type: none"> • Memantine • Brimonidine • Suppress oxidative stress <ul style="list-style-type: none"> • Ginkgo biloba extract • Omega 3 • Inhibit mitochondrial dysfunction <ul style="list-style-type: none"> • Coenzyme Q10 and Vitamin E • Ginkgo biloba extract • Stimulate cell survival pathway <ul style="list-style-type: none"> • Valproic acid 	<p>PROMOTE REGENERATION</p> <ul style="list-style-type: none"> • Replace neurotrophin <ul style="list-style-type: none"> • Brain-Derived Neurotrophic Factor, • Nerve Growth Factor, Ciliary Neurotrophic Factor • Mesenchymal stem cells • Umbilical cord serum • Stimulate non-glutamatergic neurotransmitter synthesis <ul style="list-style-type: none"> • Citicoline <p>NEUROENHANCEMENT</p> <ul style="list-style-type: none"> • Block sodium channel <ul style="list-style-type: none"> • Phenytoin
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Ophthalmology
Volume 125, Issue 12, December 2018, Pages 1874-1885

Original article

Oral Memantine for the Treatment of Glaucoma: Design and Results of 2 Randomized, Placebo-Controlled, Phase 3 Studies

Robert N. Weinreb MD^{1,2,3,4}, Jeffrey M. Liebmann MD², George A. Cioffi MD¹, Ivan Goldberg MBBS, FRANZCO¹, James D. Brandt MD⁴, Chris A. Johnson PhD, DSc⁵, Linda M. Zangwill PhD¹, Susan Schneider MD⁶, Hanh Badger PharmD⁵, Marina Bajaran PhD⁶

Results

The proportion of patients who completed the studies was similar among groups (80%–83%). Compared with placebo, daily treatment with memantine 10 mg or 20 mg for 48 months did not delay glaucomatous progression significantly in the individual studies and pooled analyses. The pooled risk reduction ratio (95% confidence interval) assessed by SAP was -0.13 (-0.40, 0.09) and -0.17 (-0.46, 0.07) for memantine 10 mg and 20 mg, respectively. Results were similar per FDT and stereoscopic optic disc photographs. The most common AEs leading to treatment discontinuations were dizziness, headache, fatigue, and nausea.

Conclusions

With technologies available when the studies were conducted, daily treatment with memantine over 48 months was not shown to prevent glaucomatous progression in this patient population.

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NEURODEGENERATIVE DISEASES

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INVITED REVIEW

Optic neuropathies: the tip of the neurodegeneration iceberg

Valerio Carelli^{1,2,*}, Chiara La Morgia^{1,2}, Fred N. Ross-Cisneros³ and Alfredo A. Sadun^{1,4}

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*To whom correspondence should be addressed at: Neurology Unit, Department of Biomedical and Neuromotor Sciences, IRCCS Institute of Neurological Sciences of Bologna, University of Bologna, Bellaria Hospital, Via Azzurra 3, 40139 Bologna, Italy. Tel.: +39 051496747; Fax: +39 051496326; Email: valerio.carelli@unibo.it

Abstract

The optic nerve and the cells that give origin to its 1.2 million axons, the retinal ganglion cells (RGC), are particularly vulnerable to neurodegeneration related to mitochondrial dysfunction. Optic neuropathies may range from non-syndromic genetic entities, to rare syndromic mitochondrial diseases with optic atrophy such as mitochondrial encephalomyopathy, to age-related neurodegenerative diseases such as Alzheimer's and Parkinson's disease where optic nerve involvement has, until recently, been a relatively overlooked feature. New tools are available to thoroughly investigate optic nerve function, allowing unprecedented access to this part of the central nervous system. Understanding the molecular pathophysiology of RGC neurodegeneration and optic atrophy, is key to broadly understanding the pathogenesis of neurodegenerative disorders, but monitoring their progression in describing the natural history, and ultimately as outcome measures to evaluate therapies. In this review, the different layers, from molecular to anatomical, that may contribute to RGC neurodegeneration and optic atrophy are tackled in an integrated way, considering all relevant players. These include RGC dendrites, cell bodies and axons, the unmyelinated retinal nerve fiber layer and the myelinated post-laminar axons, as well as oligodendrocytes and astrocytes, involved in unconventional functions. Dysfunctional mitochondrial dynamics, transport, homeostatic control of neurogenesis and mitophagic removal, as well as specific propensity to apoptosis may target differently cell types and anatomical settings. Ultimately, we can envisage new investigative approaches and therapeutic options that will speed the early diagnosis of neurodegenerative diseases and their cure.


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ALZHEIMER'S DISEASE (AD)

- 60-80% of all dementia
- 50% Alzheimer's are only AD, the other 50% have mixed dementia
- 6.5% prevalence in North Americans 60 YOA or older
- Increased prevalence with age
- 32% > 85 YOA

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ALZHEIMER'S

- Progressive neuronal cell death in the brain from amyloid protein plaques and neurofibrillary tangles accumulating in the CNS
 - Interfere with communication between neurons
 - Leads to atrophy within cerebrum and hippocampus
- Incurable and difficult to study and definitively diagnose
- Estimated that neuronal damage may be present for up to 20 years prior to cognitive decline

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RNFL

- Study by Ascaso et al compared OCT measured RNFL in AD patients to mild cognitive impairment (MCI) and healthy patients
 - Significant reduction in RNFL thickness in AD patients and those with MCI
- Decreased RNFL thickness from loss of retinal neurons and axons
 - All quadrants
 - Confirmed decreased retinal function with pattern electroretinograms
 - Possible predictive value for earlier detection of AD?

Ascaso FJ, Cruz N, Modrego PJ, et al. Retinal alterations in mild cognitive impairment and Alzheimer's disease: an optical coherence tomography study. *Journal of Neurology*. 2014;261(8):1522-30.

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MACULA

- Macular thickness may be related to the stage of MCI and AD patients
- Increased macular thickness and volume in some MCI patients
- Reduced macular thickness and volume in AD patients, increase in severity correlating with degree of AD
- Other researchers have noted similar findings without correlations in dementia severity

<https://www.reviewofoptometry.com/article/all-eyes-on-neurodegenerative-disease>

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OPTIC NERVE CUPPING

- RGC loss in AD may mimic that seen in glaucoma at biochemical level
- Neurotoxicity from amyloid deposits
- 5x greater risk of VF defects and ON disc cupping in patients with AD
- Overall higher prevalence of glaucoma in AD population
- How to differentiate?

MICROVASCULAR ABNORMALITIES

- Patients identified as probable AD showed retinal blood vessel alterations associated with brain plaque deposits
- Venous branching pattern asymmetry
- Increased arteriolar length to diameter ratio values
- Theory: Retinal vasculature changes consist of amyloid deposits from the CNS to retina resulting in vessel wall destruction

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PUPILLARY ABNORMALITIES

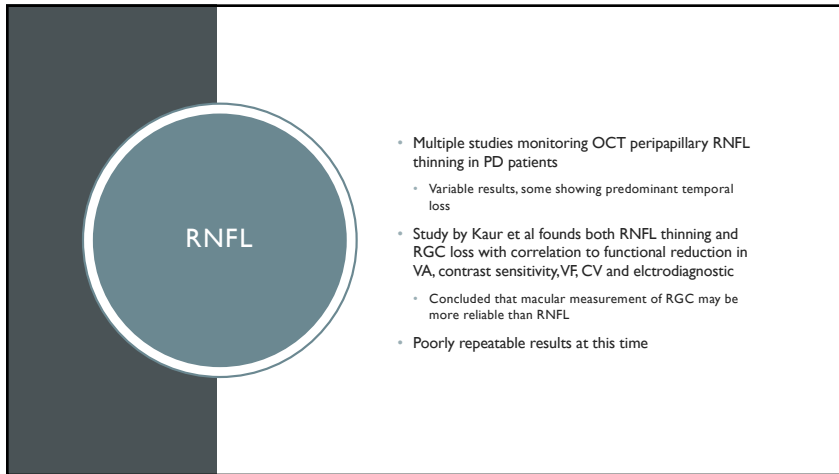
- Hypersensitivity to pupillary dilation with cholinergic antagonists and agonist
 - Diluted tropicamide and pilocarpine
- Pupil flash response decreased in AD patients
 - Pupil reactions to lights of varying intensity and durations

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PARKINSON'S DISEASE (PD)

- Neurodegenerative disorder affecting the basal ganglia of the brain
- Loss of dopamine-producing cells
 - Needed for signal transmission w/in the CNS
- Abnormal protein deposits within nerve cells
 - Lewy bodies
- Can affect other areas: hypothalamus, nuclei of thalamus, cerebral cortex, amygdala, hippocampus
- Loss of dopamine leads to impairment of cognitive, motor, and sensory functions

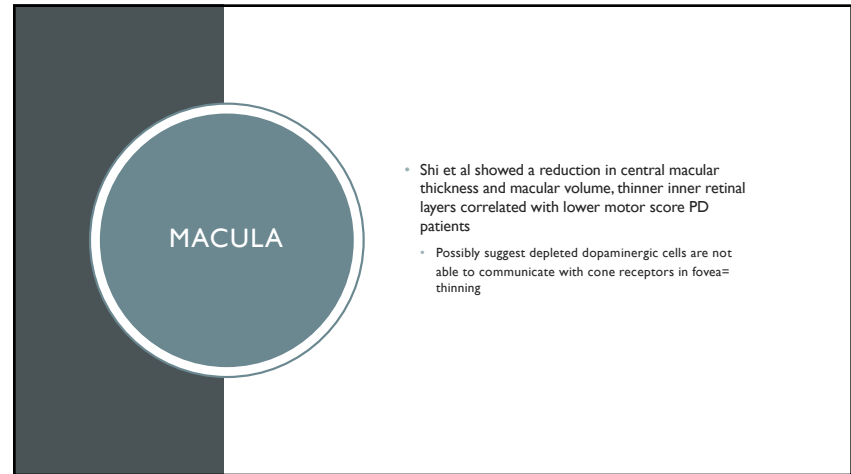
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RNFL

- Multiple studies monitoring OCT peripapillary RNFL thinning in PD patients
- Variable results, some showing predominant temporal loss
- Study by Kaur et al founds both RNFL thinning and RGC loss with correlation to functional reduction in VA, contrast sensitivity, VF, CV and electrodiagnostic
- Concluded that macular measurement of RGC may be more reliable than RNFL
- Poorly repeatable results at this time

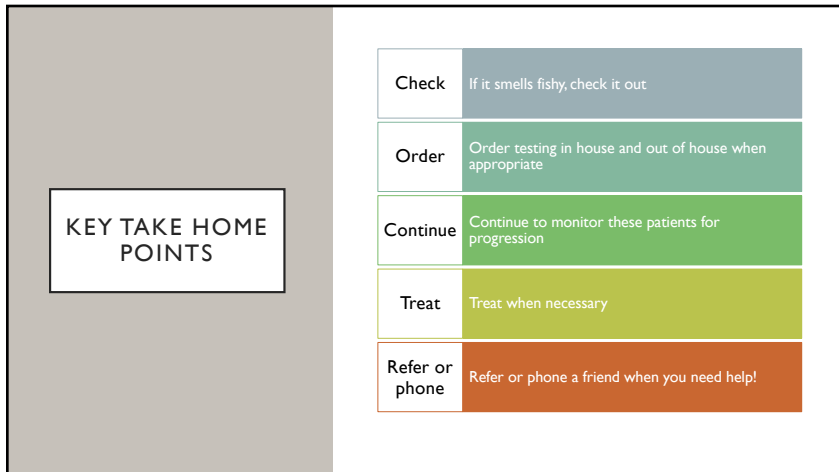
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MACULA

- Shi et al showed a reduction in central macular thickness and macular volume, thinner inner retinal layers correlated with lower motor score PD patients
- Possibly suggest depleted dopaminergic cells are not able to communicate with cone receptors in fovea= thinning

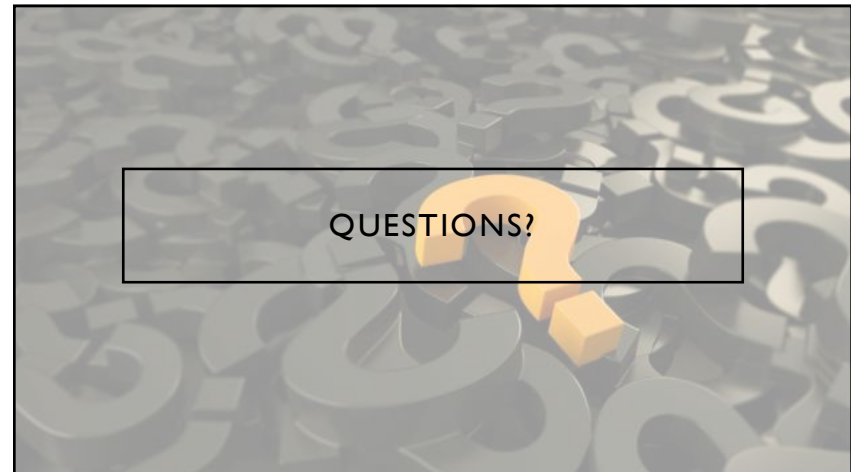
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KEY TAKE HOME POINTS

Check	If it smells fishy, check it out
Order	Order testing in house and out of house when appropriate
Continue	Continue to monitor these patients for progression
Treat	Treat when necessary
Refer or phone	Refer or phone a friend when you need help!

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QUESTIONS?

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