Don't Let Swollen Optic Nerves Make You Nervous

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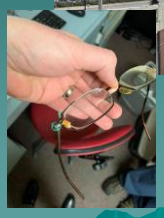
Financial disclosures

- No financial disclosures

Examination Techniques

- Stereoscopic viewing essential
- VA and VF: SVP
- Pupil testing and color vision
- Brightness comparison and red cap test



Etiologies for optic nerve swelling

- Papilledema
- Compressive neuropathy
- Drug induced neuropathy
- NAION
- Arteritic ION
- Optic neuritis
- Infectious causes such as: syphilis, Lyme disease, HIV, etc.
- Other inflammatory such as Sarcoidosis, Crohn's, etc.

Papilledema

- Bilateral (but can be sequential with one nerve becoming swollen before the other, thus unilateral at presentation) optic nerve head swelling secondary to increased ICP
- Swollen, blurred margins with splinter hemorrhages and exudates as well as nerve fiber layer edema. Patton's folds may be seen

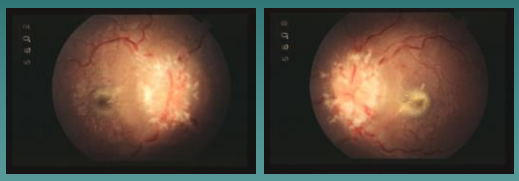
Papilledema

- May be asymmetric
- VA varies but typically mild reduction only or no loss at all
- May get diplopia secondary to abducens nerve compression
- With increased ICP, can get choroidal folds only (before papilledema) at lower pressure levels

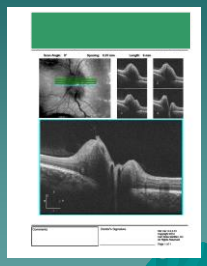
Papilledema

- VF usually shows enlarged blind spot
- No pupillary defect. Normal color vision
- SVP absent with obliterated cup

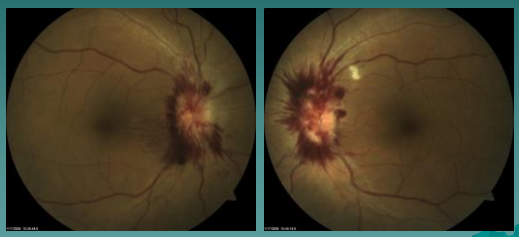
Papilledema (IIH)



OCT



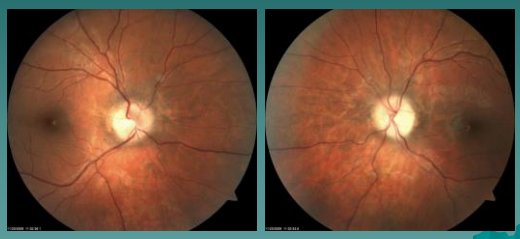
Terson's and papilledema



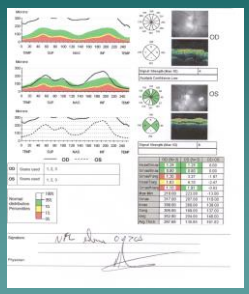
Patton's folds: RNFL thickness 231in OD, 295 in OS

Patton's folds

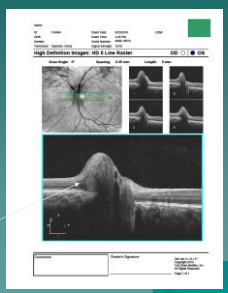
Longstanding papilledema with optic atrophy (IIH)



Papilledema OCT NFL



Papilledema OCT



What is this? We will find out later!

Papilledema OCT

This eye has one too

Increased ICP

- Variations are due to anatomical considerations
- If the channels connecting the central cavity and optic nerve sheath allow equal flow on both sides and in both directions, papilledema will occur and will improve with decreased ICP

Increased ICP

- If there is a difference in the communications, then the edema will be asymmetric. May be the result of a smaller bony canal opening on one side limiting the swelling.
- If the valves are one-way, then the swelling will not improve rapidly with treatment

Increased ICP

- An acute rise in ICP that resolves rapidly is not typically associated with papilledema. Elevation must be chronic
- Increased pressure is transmitted from the sub-arachnoid space to the optic nerve head via the nerve sheath. Venous pressure in CRV increases
- Disruption in axoplasmic flow at lamina cribosa leads to swelling

Increased ICP

- Studies show that ONH swelling as measured by OCT can decrease (but not instantly resolve) immediately after lumbar puncture
- Measured in lateral decubitus position with OCT sideways!
- Shows that reduction of ONH compression is very rapid
- Shows that pressure in spinal column is associated with pressure at ONH

Etiologies of Increased ICP

- Space occupying lesion ; must always be ruled out!
- Infection or anatomical abnormality
- Malignant hypertension
- IIH
- Certain medications
- ? Sleep apnea (obesity): ICP may be elevated only at night! Men especially
- Must order MRI in all cases

Increased ICP with papilledema in eye care practices

- 2020 study and others……

- IIH 67%
- Intracranial mass 16%
- Intracranial hemorrhage 7%
- Venus Sinus Thrombosis 7%

Idiopathic Intracranial Hypertension (IIH)

- Older term is "pseudotumor cerebri"
- Young overweight females (F 8-10 X M)
- 1/ 100,000 in population as a whole ; 20 / 100,000 in 20 to 44-year-old women 10% over ideal weight
- May be related to medications including TCN (minocycline especially), HRT, lithium, high dose Vitamin A supplementation, steroid withdrawal. But then not really "idiopathic"
- Sleep apnea link, especially in males
- Can affect children, often overlooked
- Doubles cardiovascular risk in females

IIH

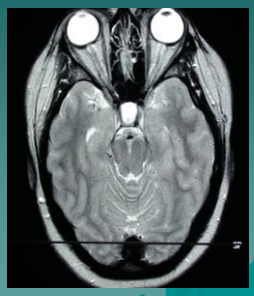
- Symptoms of transient blur, diplopia , tinnitus (intracranial noises, not just ringing) , headaches , etc.
- ICP usually severely elevated ; normal is 50 – 200 mmH20. Over 25 cm (250 mm) considered definitively abnormal. Single measurement can be misleading : levels can vary over 24 hours
- Very rare variant of normal pressure IIH. S/S, but repeatedly normal ICP

IIH more rare over age 50

- Less often female
- Fewer headache complaints
- More frequently discovered incidentally due to papilledema with no symptoms
- Lower opening CSF
- More likely to have concomitant medical conditions
- Less likely to use tetracycline family antibiotics

IIH

- Diagnosis involves normal MRI / MRV and CSF studies with elevated ICP
- Watch for spinal chord tumors
- Differential: Cerebral Venous Sinus Thrombosis
- MRV



CVST(cerebral venous sinus thrombosis)

- Young women and some men
- Often not overweight
- Can be life threatening
- Treat with blood thinners, Diamox
- Can be seen with MRI, but potentially missed if MRV not performed
- Stenosis may be secondary to IIH, but may also contribute to causing IIH

Optic atrophy post CVST induced papilledema

IIH Management

- Refer to a neurologist
- Medical management includes Diamox, Topamax
- Weight loss

IIH Management

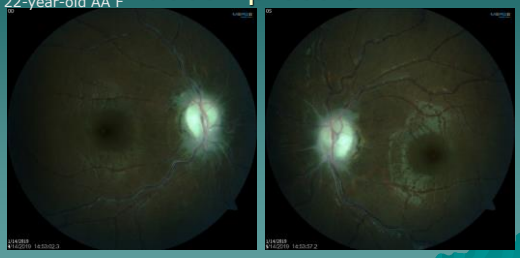
- If recalcitrant….
- Repeated lumbar taps (ugh!)
- Lumbo-peritoneal shunt
- Ventricular shunt
- Venous sinus stent

IIH Management

- If progressive changes in visual acuity or visual field occur , consider an optic nerve sheath decompression
- Several small fenestrations in the optic nerve sheath are created to allow room for expansion
- Performed by a neuro-ophthalmologist. Often do worse eye only because 50% get improvement in the fellow eye

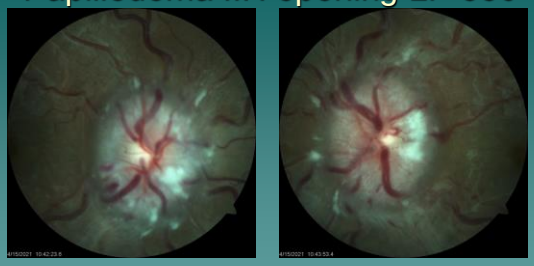
Chronic IIH induced edema leading to atrophy: S/P decompression

22-year-old AA F

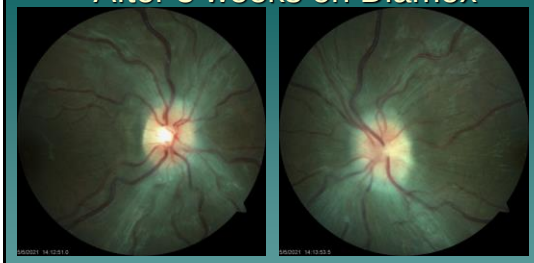


Light perception 10/700

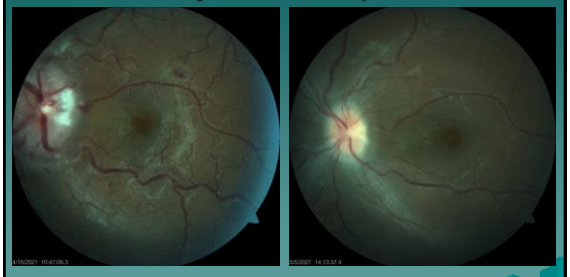
Papilledema IIH opening LP 550



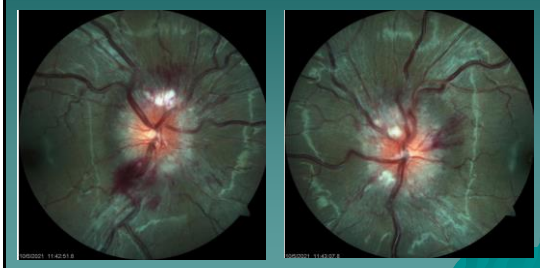
After 3 weeks on Diamox



Side by side comparison



Minocycline induced elevated ICP papilledema



Foster Kennedy Syndrome

- Swollen optic nerve on one side , advanced optic atrophy on the other
- Advanced optic atrophy prevents swelling making a bilateral problem appear to be unilateral
- Often seen in chiasmal tumors

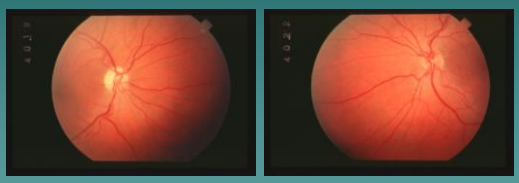
Compressive Optic Neuropathy

- Compression leads to axoplasmic stasis and retrograde death of nerve fibers
- Pale, choked, swollen nerve
- Rarely see hemes; + APD

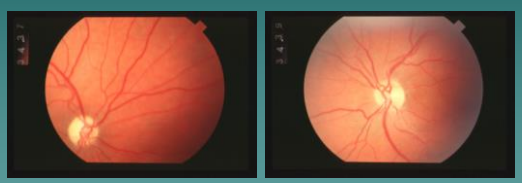
Compressive Optic Neuropathy

- Optic atrophy and severe vision loss with time
- MRI with and without contrast: neurosurgery referral

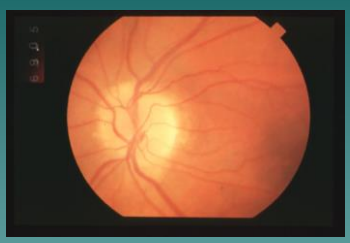
Pituitary tumor



Pituitary tumor post surgery

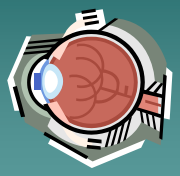


Sphenoid wing meningioma



ION

- Nonarteritic
- Arteritic



Nonarteritic ION

- Swollen , hyperemic nerve with splinter hemes and exudates
- Often sectoral
- Ischemic / hyoperfusion event caused by interruption of micro-vascular circulation, often at night.
- Highly associated with sleep apnea (75-90% in several studies)
- NAION has 5x risk of sleep apnea, 8x risk in women

NAION

- No systemic symptoms; normal ESR / CRP
- Most common cause of ONH swelling over the age of 55 (2-10 cases per 100,000 per year)
- 45-60 year-olds most commonly (any age possible) with no sex predilection)

NAION etiology factors

- Sleep apnea! Up to 90%
- Hypertension (likely med related)
- Idiopathic
- Diabetes
- Atherosclerosis
- Migraine
- Increased Homocysteine / Decreased vitamin B6
- HIV infection: distinct entity, not "pure" NAION
- ED drug use
- Possible increased risk with use of semaglutide (Wegovy, Ozempic, etc.). 9% risk vs. matched 2% risk in one study

Nonarteritic ION

- Typically seen in "disc at risk" patients with very small cups. Therefore 70 + % Caucasian
- Approximately 15% of cases will involve the fellow eye in 5 years (more common with VA < 20/200 in first eye, diabetics, and platelet polymorphisms). Repeat attacks in same eye < 5%

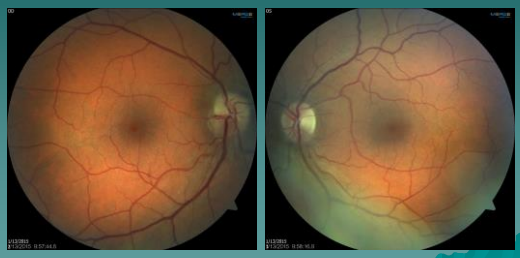
NAION

- VA varies widely from normal to severe loss: 45% 20/40 or better but 33% 20/200 or worse
- VA loss progresses over 2-4 weeks
- VA improves by up to three lines at six months in 40%
- In patients under 50 years of age, there is a higher rate of bilateral involvement and more visual recovery

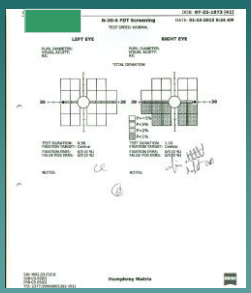
Nonarteritic ION

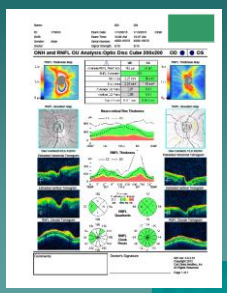
- Often APD , color vision usually normal
- Most frequent visual field defect is inferior nasal / partial altitudinal but may get essentially any type.
- After swelling resolves the nerve is pale but often not cupped-cupping may occur, however
- Why does area of swelling not always match VF defect?

NAION 2 weeks after onset of symptoms



NAION





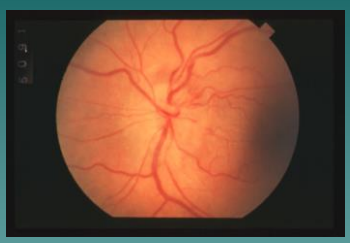
Nonarteritic ION Treatment

- No treatment other than managing the underlying cause has proven to be consistently effective
- Blood thinners may debatably protect the fellow eye but will not alter the course of recovery.
- SS Hayreh proposed oral steroids if VA 20/70 or worse, never widely adopted
- Order CBC , ESR and CRP , lipid profile , hemoglobin A1C. Check BP
- Check for sleep apnea!

Incipient ION

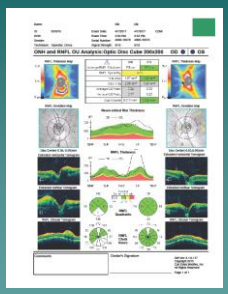
- Early swelling, but no impact yet on VA or VF
- May resolve without loss of vision or VF, may become full blown NAION with loss
- Can only impact by treating underlying condition

NAION



NAION

NAION secondary to OSA

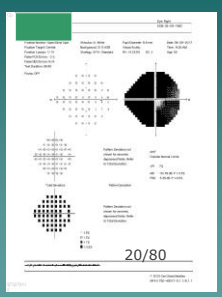


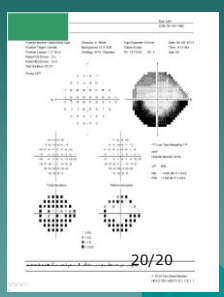
HIV optic neuropathy

Another HIV induced optic neuropathy

Bilateral NAION secondary to OSA (40% blood oxygen level)

Accompanying VF





Arteritic ION

- Pale disc swelling with splinter hemorrhages
- Average age 76 (80% over 70), F>M 3:1
- Increased ESR,C-Reactive protein, platelet
- ESR normal in about 25%!
- VA 20/200 or worse in 60% of cases
- Traditional thinking from past studies of a high predilection for Caucasians, but a large 2019 study showed only a slight predilection for Caucasians over African Americans.

Arteritic ION

- Sudden, painless loss of vision with APD
- Altitudinal VF loss most common, others possible
- Symptoms of GCA but about 1/3 are symptom free
- Very high five-year mortality rate

Giant Cell Arteritis

- GCA is a disease of unknown etiology affecting the large and medium arteries including the temporal , ophthalmic , and posterior ciliary arteries
- Symptoms include HA , scalp tenderness , jaw claudication , malaise , fever , and fatigue
- Possible link to Zoster, but unclear

GCA

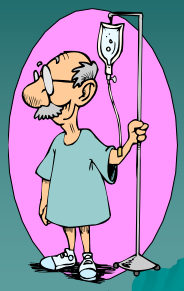
- May also see CWS, CRAO, and amaurosis fugax
- 20% of cases with ocular involvement are CRAO, 80% ION
- Obtain stat Westergren ESR, CRP, CBC with platelets

Giant Cell Testing

- Normal ESR is age/2 for men and age +10/2 for women
- C-Reactive protein testing is not specific for GCA but it is nearly 100% sensitive so very useful test
- Temporal artery biopsy when indicated. Ultrasound may be nearly as sensitive and is non-invasive

Giant Cell Arteritis

- 25% of untreated patients develop AION
- 2/3 will develop in the second eye within weeks if not treated, up to 50% within one week
- Rheumatology referral



Giant Cell Treatment

- IV hydrocortisone followed by long term oral prednisone. Maintenance dose of 10mg daily for years. Follow ESR, other markers
- Average cumulative steroid dose over course of treatment…….over 5000 mg of prednisone!

Temporal (Giant Cell) Arteritis

- Subcutaneous Tocilizumab (Actemra)
- Used with steroids (not in place of): makes steroid dose much lower
- Immunosuppressant
- Risk of infections, no live vaccines
- Delivered IV
- Also used with RA and other forms of arthritis

Amiodarone induced optic neuropathy

- Mimics NAION in nerve appearance but bilateral instead of unilateral
- Afflicts 2% of patients taking it
- Slow, insidious onset of visual loss
- Slow, complete recovery over many months after medication is discontinued (very long half-life)

Viagra / Cialis / Levitra and NAION

- ? Under reported
- These medications also occasionally used for pulmonary HTN
- Visual loss most often noted upon awakening the morning after use
- Is the association real or coincidence?
- Likely the "straw that broke the camel's back" in those with risk factors. But……

ED drugs and NAION

- Very interestingly, has been reported in a 7-month-old infant, 28-year-old, and 33-year-old, presumably all taking them for pulmonary HTN
- At those young ages, not as likely to have other NAION risk factors
- Also, 2 reported cases of PION with Sildenafil, one in a 39 YO female with pulmonary HTN

Viagra / Cialis

- Nitrous oxide release dilates vessels…..but drops blood pressure.
- Ask all males with NAION about ED drug use. D/C if using due to fellow eye risk.
- 2024 study showed over 3 X risk with Ozempic and Mounjaro use.

Optic Neuritis

- Unilateral (usually) swollen nerve. Often retrobulbar (2/3) with no visible abnormality. Hemorrhages uncommon
- Diffuse visual field loss or enlarged blind spot. Subtle defects often present in the fellow eye
- Centro-cecal defect with Goldmann perimetry
- About 5% in US bilateral, but 30% in Asia

Optic Neurits

- Younger patients (20-40 peak), F > M: more common in Caucasians
- APD, wide range of VA loss, decreased color vision; pain on eye movement (less common in Asian patients)
- Vision bottoms out at around 2 weeks

Optic Neuritis

- Often associated with post viral syndromes or demyelinating diseases such as MS (90% of demyelinating optic neuritis-initial symptom in 20% of cases-usually retrobulbar)
- VA recovers over weeks to months to near baseline level but often seems dim or washed out to the patient
- Get MRI in most cases, brain and spinal column
- May represent form fruste MS
- Several cases reported linked with use of TNF (tumor necrosis factor). Used for RA & JA: etanercept, infliximab, etc. Post vaccination.

Optic neuritis associated with MS

Optic Neuritis Treatment Trial

- 457 patients in three treatment groups 1) oral steroids (1mg / kg / day X 14 days), 2)IV steroids (250mg Q 6h X 3 days) followed by orals (as above for 11 days), 3) placebo
- Orals followed by short taper of 20 mg on day 15 and 10 mg on days 16 and 18
- Hospitalized while on IV methylprednisone
- Traditional treatment of oral steroids proved to be the least effective of the three. Actually increased recurrence rate. Very high dose orals not studied.

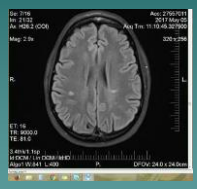
ONTT

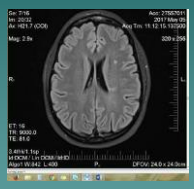
- IV hastens VA recovery by about 2 weeks but does not improve the end result. Can also give high dose orals instead: 1250 mg/ per day for three days
- Delays the onset of MS symptoms up to 2-3 years: no benefit at 5 years
- Plasma exchange helps about 50% of steroid non-responsive cases

ONTT 15-year F /U

- 294 patients seen 15 years out
- 15-year risk of developing MS was 50% (6% had known MS entering the trial)
- 72% if lesions on original MRI, 25% without
- VA 20/20 or better in 72%
- Factors indicating a lesser chance of developing MS include: 1) male gender, 2) optic disc swelling, 3) peripapillary hemorrhages and exudates, 4) no pain on eye movement, 5) NLP vision

MS lesions





Other demyelinating diseases with optic neuritis

- MOGAD
- NMO
- Combine for 10% of demyelinating optic neuritis

MOGAD

- Myelin Oligodendrocyte Glycoprotein Antibody Associated disease
- Optic nerve, brain, spinal column
- Discovered in 2007
- Average age 20-30, less of a female predilection
- Bilateral optic neuritis is more common, severe vision loss (CF is common)
- MOG-IgG antibody testing
- High dose steroids, optic neuritis responds very quickly

MOGAD

- Visible nerve swelling is more common than in MS induced optic neuritis
- Peripapillary hemorrhages are more common than in MS induced optic neuritis

NMO

- Neuromyelitis Optica Disorder
- "Devic's disease)
- Optic nerve and mostly spinal chord
- In addition to limb and muscle issues, hiccups and vomiting
- 80% women
- Any age, average 30-50
- Bilateral optic neuritis is common
- Steroids, others

Optic Nerve Head Drusen

- Increased prevalence in small nerves with small cups. Therefore, more common in Caucasians. Higher incidence in patients with RP (10%)
- Compression of axons leads to stasis of axoplasmic flow and hyaline is excreted then calcifies over time, leading to the formation of drusen
- Nerve appears elevated but no splinter hemes or exudates and the margins are distinct.
- Abnormal vessel branching

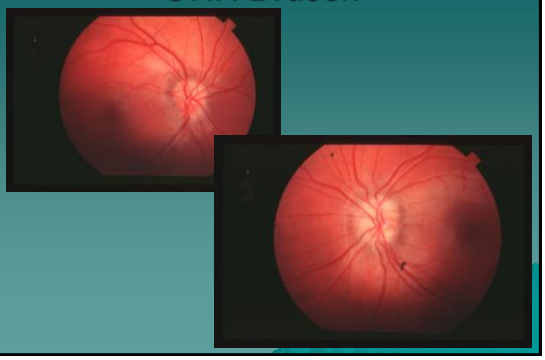
Optic Nerve Head Drusen

- Not always visible! Buried early in life but become visible with time.
- Can cause decreased vision and variable visual field defects. More loss with visible drusen (atrophy of NFL makes drusen more visible)
- Common and under diagnosed

Optic Nerve Drusen

- SVP/EVP not affected: APD and color vision loss rare but possible
- Change with time
- Use B-scan or OCT to detect buried drusen
- Also seen with CAT scan, MRI, IVFA, and FAF

ONH Drusen



ONH drusen detection with OCT

- Optic Disc Drusen Consortium Consensus……
- Always use EDI
- Blood vessels are more solid, cast a shadow, and can show as figure 8
- Drusen always prelaminar
- Drusen always hyporeflective
- Drusen often have a hyper-reflective border, especially superiorly

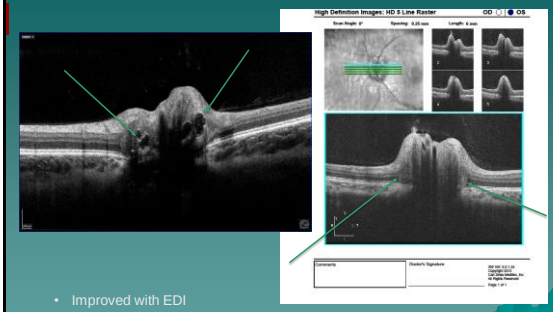
ONH drusen detection with OCT

- Drusen can conglomerate, and these areas can have some internal reflectivity from borders
- The old concept of a hypo-reflective fluid wedge at the edge of the nerve in true papilledema DOES NOT APPLY with SD-OCT. Was a time domain OCT artifact.

Peripapillary Hyper-reflective Ovoid Mass-like structures (PHOMS)

- "Fomms"
- Seen best with EDI
- Only seen with OCT, nothing else
- Circular innertube like structure around the disc above Bruch's membrane
- Herniated optic nerve fibers
- Seen in any condition that leads to nerve swelling or congestion
- ION, papilledema, disc drusen

ONH DRUSEN



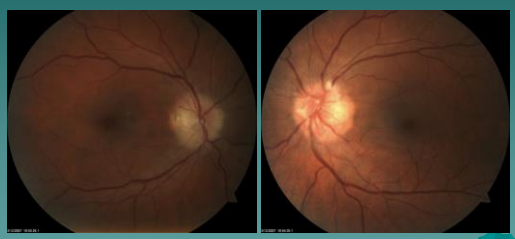
- Improved with EDI

PHOMS

SCHOOL OF OPTOMETRY

NFL loss with ONH drusen

Longstanding ONH drusen OU & new cat scratch disease papillitis OS



Diabetic Papillitis

- More common in young, type I diabetics but can also be seen in adults with type II
- Diffuse ONH edema that may be unilateral or bilateral
- Relatively mild vision loss
- No altitudinal defect on VF; various patterns of mild loss seen

Diabetic Papillitis

- Slow resolution of ONH edema but complete or nearly complete recovery of vision is the norm
- Like NAION, more prominent in nerves with small cups
- Is it real……..or just a variant of NAION?

Grave's disease

- Remember No SPECS…….
- Soft tissue edema
- Proptosis
- EOM involvement
- Corneal involvement from exposure
- Sight threatening complications
- Hyper (most common), hypo, or euthyroid.

Grave's disease

- The sight threatening complication is optic neuropathy from compression at the muscle cone. More common with little to no proptosis
- Orbital decompression or Tepezza infusion (possible issues with hearing loss / elevated blood sugar)
- Type II Grave's patients
- 75-80% of Grave's patients are smokers!

Papillophlebitis (optic disc vasculitis)

- An inflammatory variant of CRVO striking otherwise healthy, young adults (f 2x m)
- Disc edema out of proportion with retinal hemorrhaging
- Usually mild VA reduction to around the 20/30 level but can be worse

Papillophlebitis

- Vague prodrome of scintillating, colored lights with visual disturbances
- Enlarged blind spot on the visual field
- Dilated and tortuous veins
- Condition is self limiting over the course of several months and a complete recovery is the norm
- Separate entity? Systemic work-up? Are we looking for the wrong things? Antiphospholipid antibody syndrome (APA)

The end!