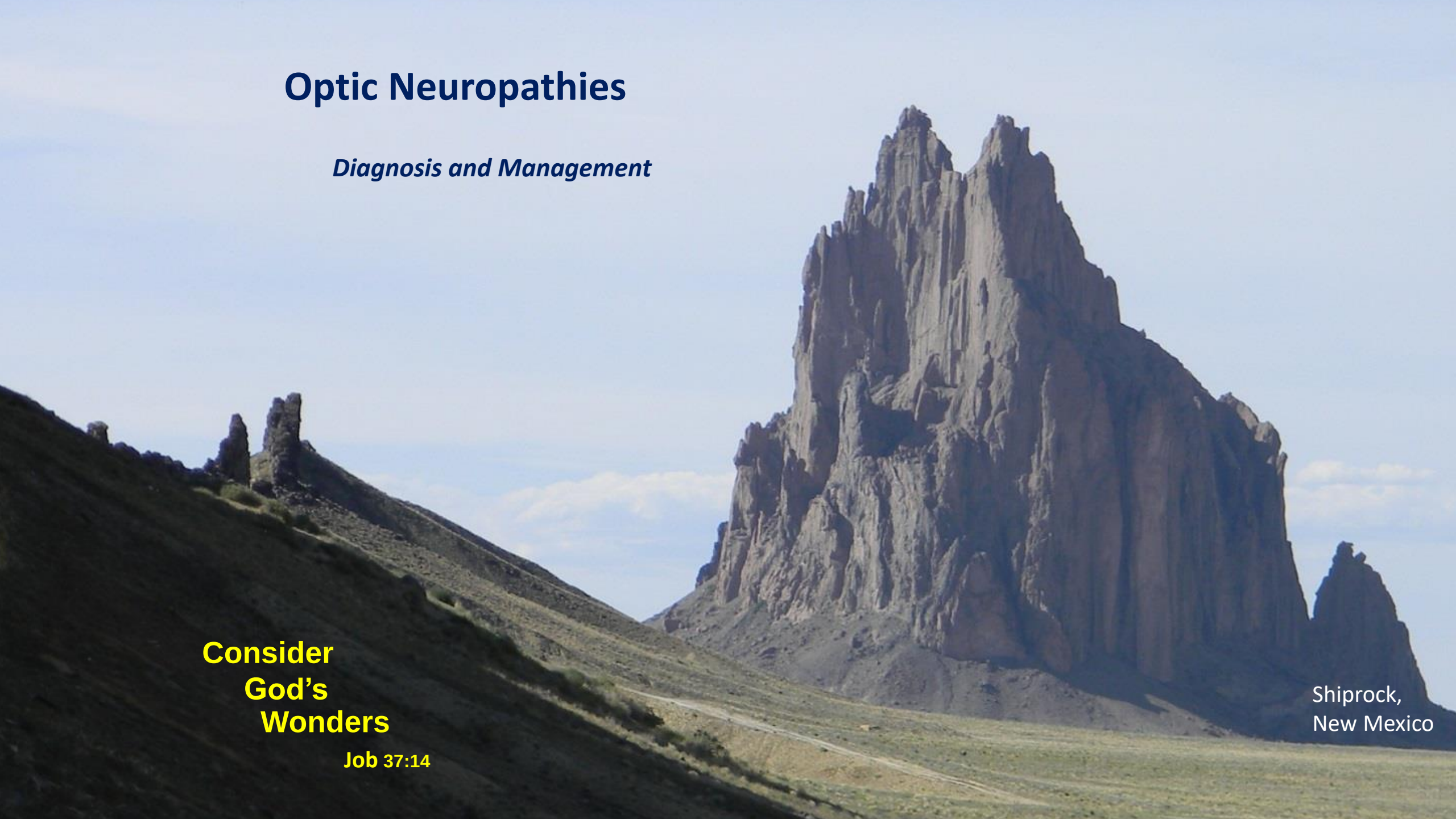
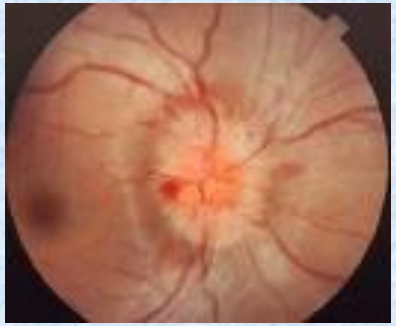
Optic Neuropathies

Diagnosis and Management



Optic Neuropathies are Difficult Diagnoses

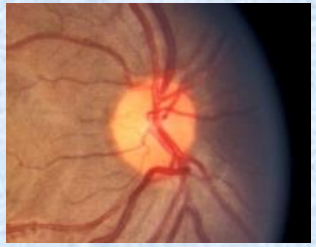
Even experts in Neuro-ophthalmology have trouble finding the causes of many cases.



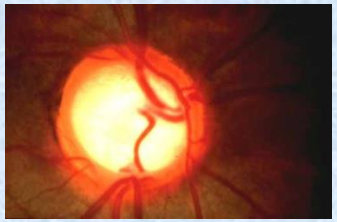
The case descriptions herein were developed for educational purposes and are for the most part composites , not necessarily of any particular patients.

The Disc Optic Neuropathies

1. No Change – appears normal

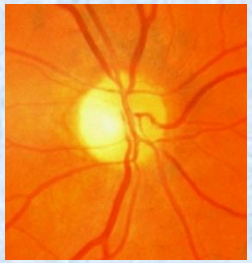


2. Cupping – Glaucoma



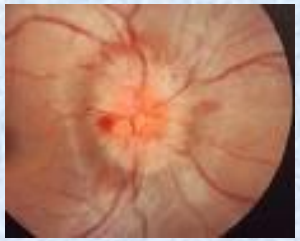
Usually not pallor of the remaining NR rim

3. Pallor – Atrophy



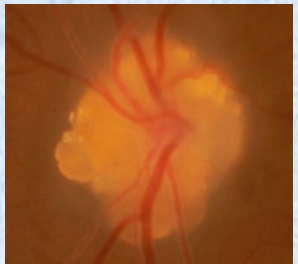
Suggests Chronic process or past insult

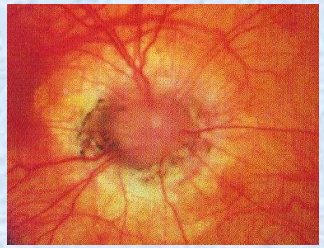
4. Elevation – Possible Edema



Elevation suggest Edema or Congenital Anomaly - clues for edema will be given

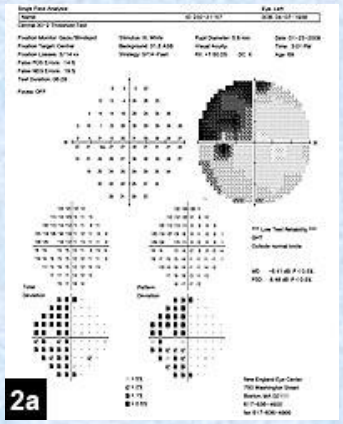
5. Unusual– e.g. drusen, dysplastic tumor, etc.



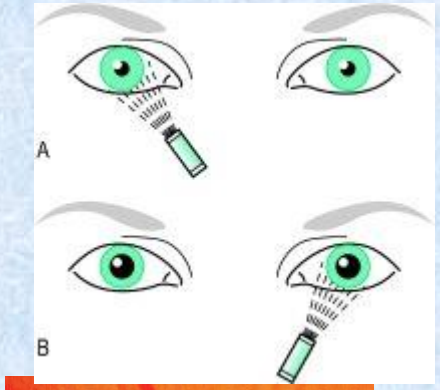


Symptoms and Signs of an Optic Neuropathy

1. Sudden or Gradual Loss of Vision or Visual Field, or Color Vision.



2. RAPD – Relative Afferent Pupil Defect



3. Disc Changes – Edema, Pallor, Hemorrhages

4. *Unexplained Visual Loss – “normal eye exam”*

Basic Differential Diagnosis

CINTAVO* (mnemonic)

C - *Congenital / Familial / Genetic*

I - *Inflammatory: Infectious / Allergic / Autoimmune*

N - *Neoplastic*

T - *Traumatic / Toxic*

A - *Aging: Degenerative*

V - *Vascular: Ischemia / Malformation / Hemorrhage*

O - *Other (OMNI-P): Obstruction / Compression*

Medication

Nutritional / Metabolic

Iatrogenic

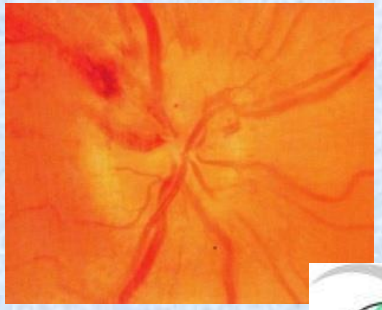
Pressure related: Blood, ICP, IOP

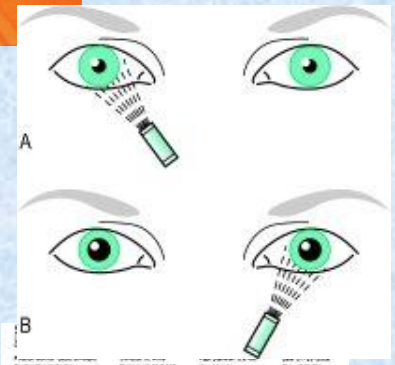
***Cintavo is a real word: Italian first-person singular, imperfect indicative of *cintare* - "to enclose or wrap up"**

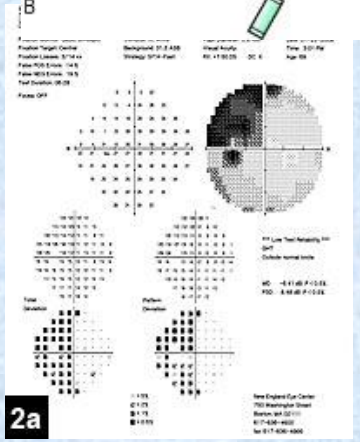
Optic Neuropathy?

Differential Diagnosis

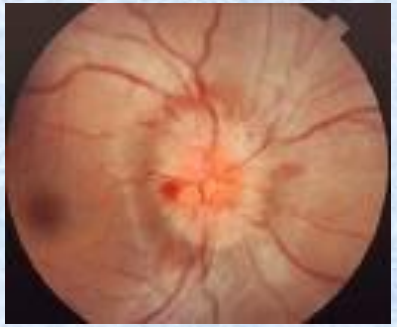
1. *Congenital Defect in Optic Nerve*
2. *Hereditary – e.g. Leber's Hereditary ON*
3. *High Intracranial Pressure*
4. *Inflammatory – Optic Neuritis*
5. *Neoplastic – Optic Nerve Tumor or Infiltration*
6. *Traumatic Neuropathy*
7. *Vascular – Ischemic Optic Neuropathy (ION)*
8. *Toxins / Medications*
9. *Compression – Tumor, TED, aneurysm*
10. *Nutritional Deficiency – e.g. B12, folate*
11. *Elevated Intraocular Pressure*







Disc Edema



High ICP

Ischemia – ION

Inflammation – Classic Optic Neuritis – or Atypical Optic Neuritis

Infiltrative – e.g. Leukemia, Lymphoma, Sarcoidosis

Hereditary – e.g. LHON

Compression – tumor, large muscles(Graves) or vessel (e.g. carotid a.)

Toxic - e.g. Methanol, Ethylene Glycol, Ethambutol

Ocular- disc edema is false localizing sign, e.g.

Venous stasis (BRVO CRVO), hypotony, posterior scleritis, uveitis (including: AMPPE, MEWDS)

OR

MAYBE NOT EDEMA, BUT SOMETHING THAT LOOKS LIKE IT

e.g. Anomalous Congenital Disc Elevation

or Abnormal Disc Vessels or growths

Approach to Patient with Suspected Optic Neuropathy

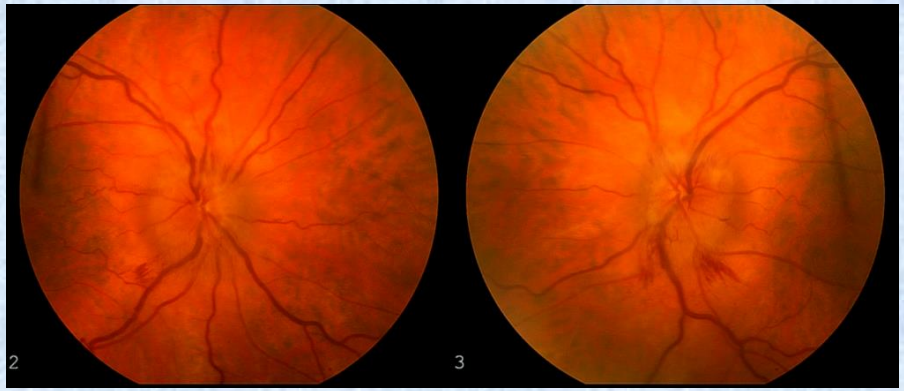
1. *Logical Analysis - Do Complete 8 Point Eye Exam*

2. Think about the more common things First:
    1. Papilledema
    2. AION
    3. Optic Neuritis (Classic)

Big 3

3. If the history / exam or the clinical course does not fit one of these problems then you must consider further problems and evaluation.

1. Papilledema



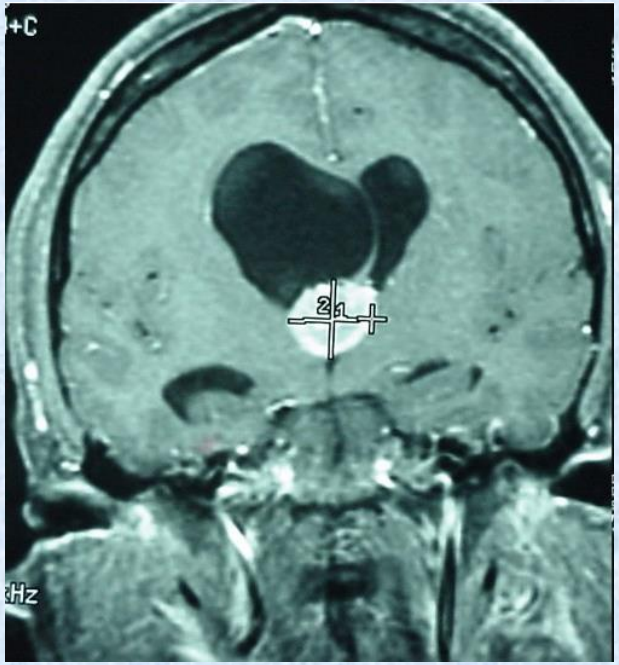
Optic Nerve Head Swelling *Secondary to*
Increased Intracranial Pressure

Symptoms

Headache
Transient Visual Loss
Pulsatile Tinnitus

Concern for Intracranial Problem

Colloidal Cyst → obstructive hydrocephalus



Typical Papilledema Presentation

- Symptoms:

  Headache – Chronic, Nausea/Vomitting

  Tinnitus

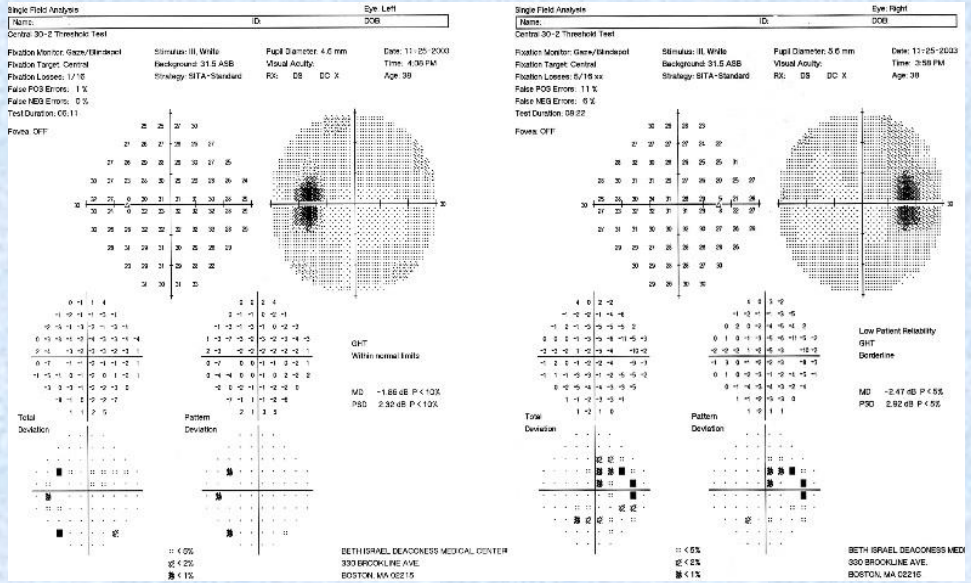
  Transient Visual Obscurations (seconds)

- Good vision early on:

  VA good

  VF: Usually normal or just enlarged Blind Spots

- Usually <u>Bilateral</u> Disc Edema*



Chronic Papilledema

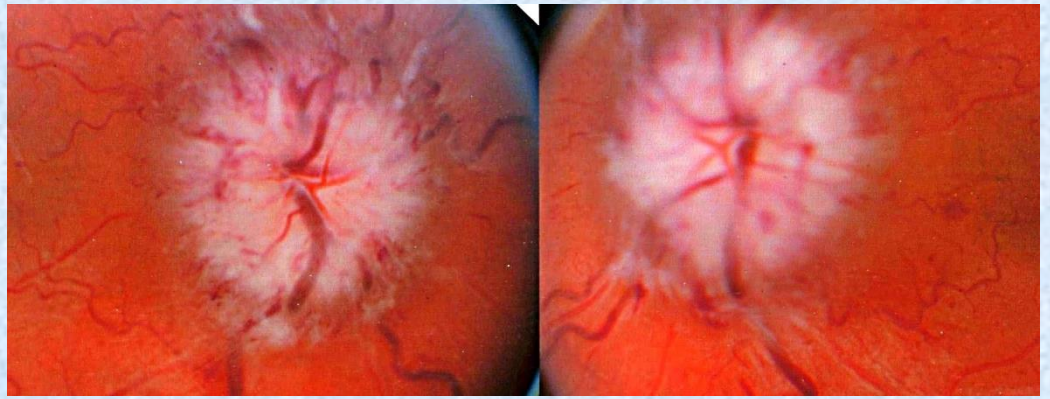
- Early Papilledema – no or little Visual Loss
- But, with continued High ICP → Chronic Papilledema →
  Disc atrophy and Visual deterioration

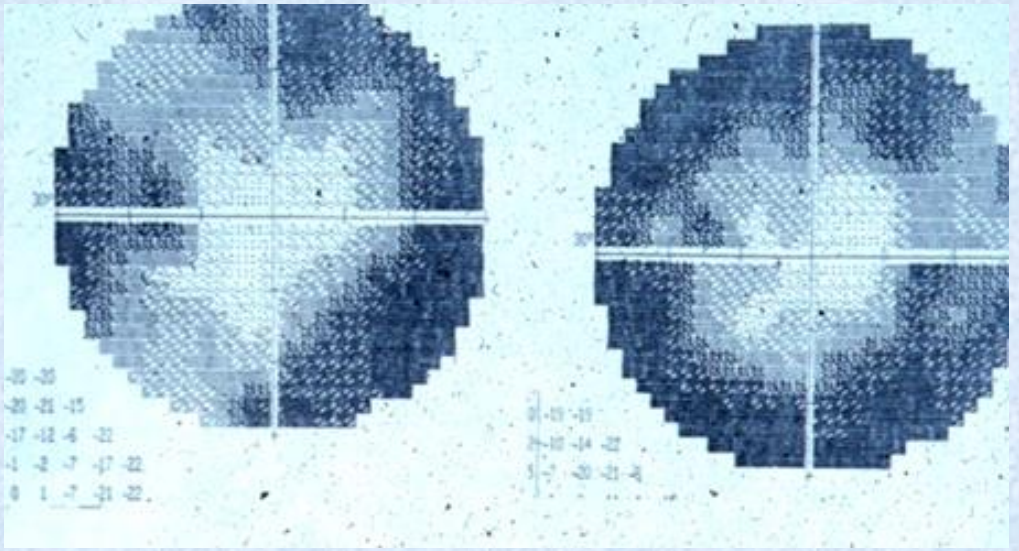
- Visual Loss can sometimes be
  reversed if the ICP can be lowered

Treatment:

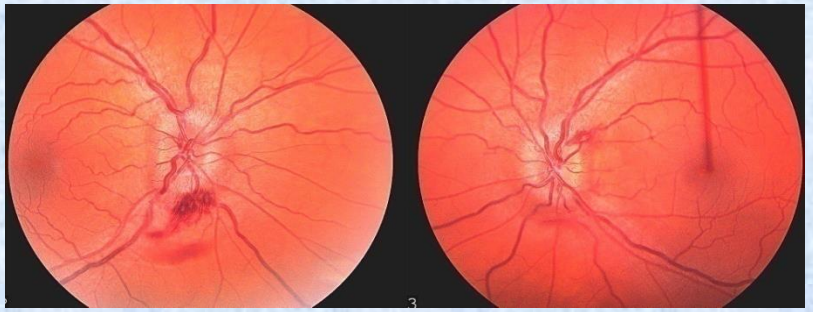
Treat underlying condition if possible
but if vision is deteriorating then

Consider Medical and Surgical Treatments





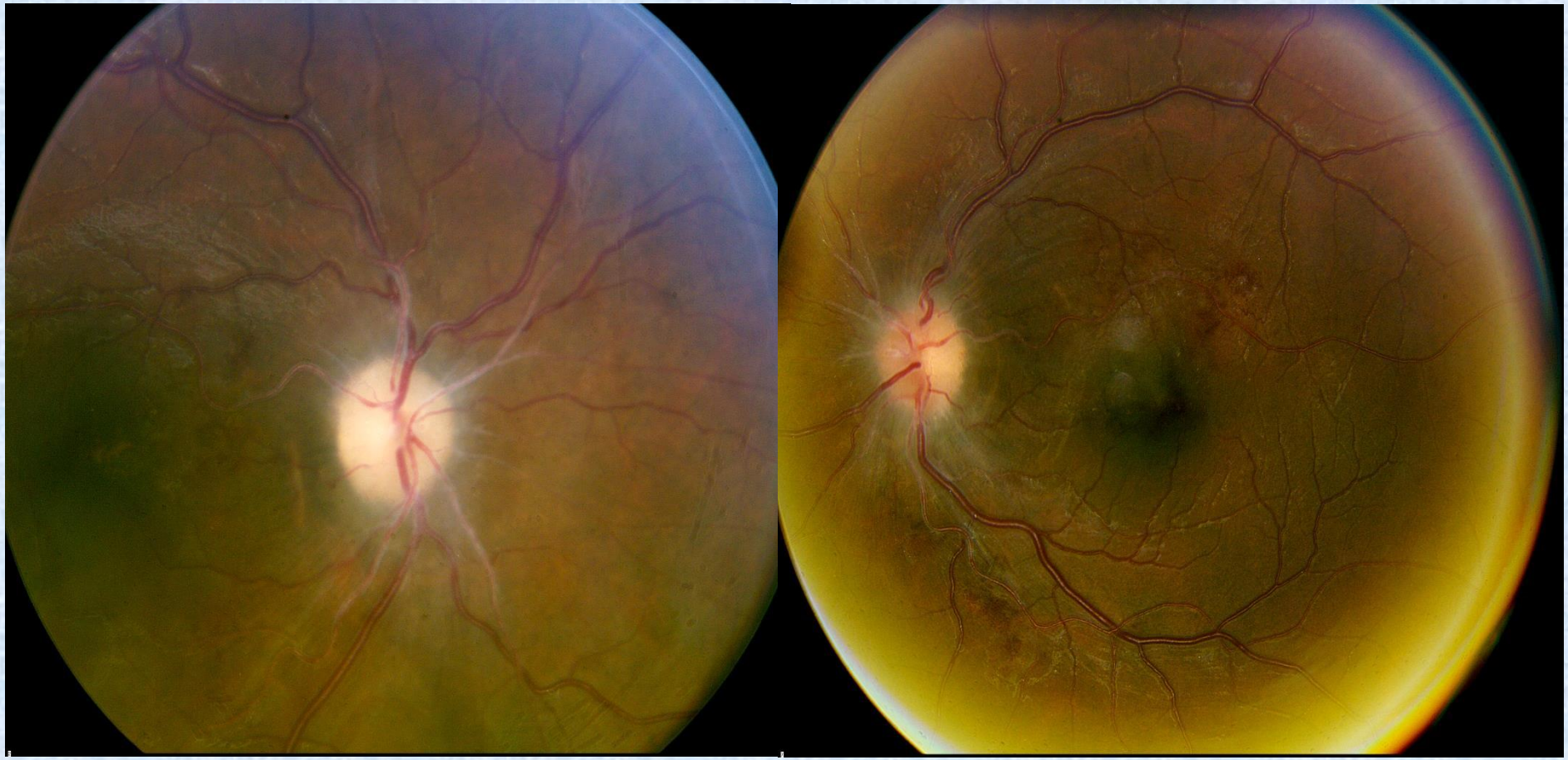
Acute Visual Loss in Papilledema



- With Visual Loss….
- Treat underlying condition if possible,

- ***BUT IF VISION IS GETTING WORSE THEN CONSIDER***
- Medical: Acetazolamide 500 mg PO 2x/d or 250 mg IV 4x/d
- Methyprednisolone IV 250 mg 4x/d or1.0 gram each day for 3 days
- Surgical: Lumbar Puncture (Drain)
- Optic Nerve Sheath Decompression
- or Shunting (LP or VP) Procedures

Optic Atrophy after Prolonged Severe Papilledema and Hypertension



Right **Left**

Increased Intracranial Pressure Differential Diagnosis

1. **Hypertension** – severe elevation
2. **Intracranial Tumor**, AVM, Carcinomatous Meningitis
3. **Medications** -Vitamin A, Accutane, Tetracyclines, Birth Control (BC) pills, Corticosteroid withdrawal, Growth Hormone Supplement, Thyroid supplementation, Lithium
4. Toxic: Ethylene Glycol, Lead (Pb)
5. Infection: **Meningitis,** Encephalitis; Lyme, HIV, post - Varicella, Malaria, Abscess
6. CNS Inflammation, Vasculitis, e.g. Lupus
7. **Trauma, Hematomas, Sub- Arachnoid hemorrhage**
8. Obstruction to Venous Drainage –***Venous Sinus Thrombosis*** *– hyper-coagulable states*, middle ear or mastoid infections
9. **Hydrocephalus**, Chiari Malformation, Craniosynostosis
10. Endocrine: Addisons, Hypoparathyroidism, Weight Gain
11. Other: Sleep Apnea, Anemia, Thyroid dysfunction
12. ***Idiopathic Intracranial Hypertension (IIH)***
    – **Pseudotumor Cerebri – Rule Out Diagnosis**

Evaluation of Increased Intracranial Pressure

1. Further History and Vital Signs
   - Medications, Medical/Surgical Problems, High BP

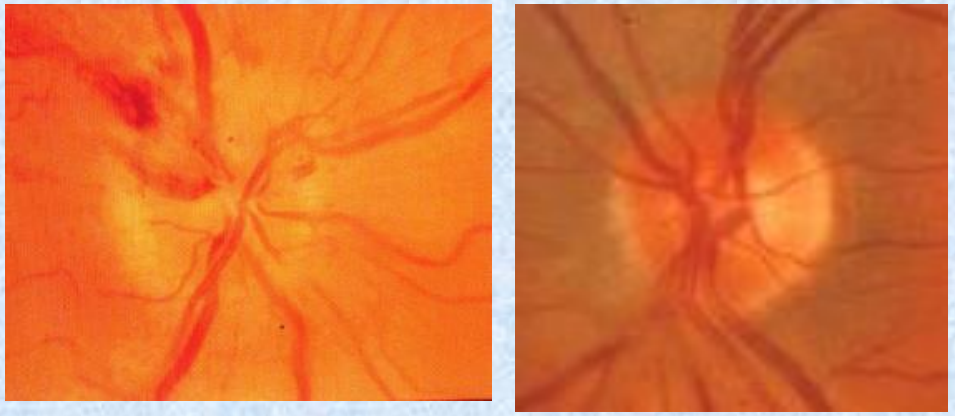
2. CT or MRI of Brain
   Might also consider MRV (MR Venography) for venous thrombosis

3. IF CT/ MRI is negative for Tumors or Malformations/obstructions:
   can consider Lumbar Puncture (LP)
   FOR: Opening Pressure
   and CSF Analysis (For RBC, WBC, Tumor cells, Glucose, Protein, Antibodies, Cytology)

4. If testing (Imaging and Lab for Blood and CSF are negative)
   then consider diagnosis of IIH / *Pseudotumor Cerebri*

2. AION (*Anterior* Ischemic Optic Neuropathy)

Ischemic Infarction of Optic Nerve Head

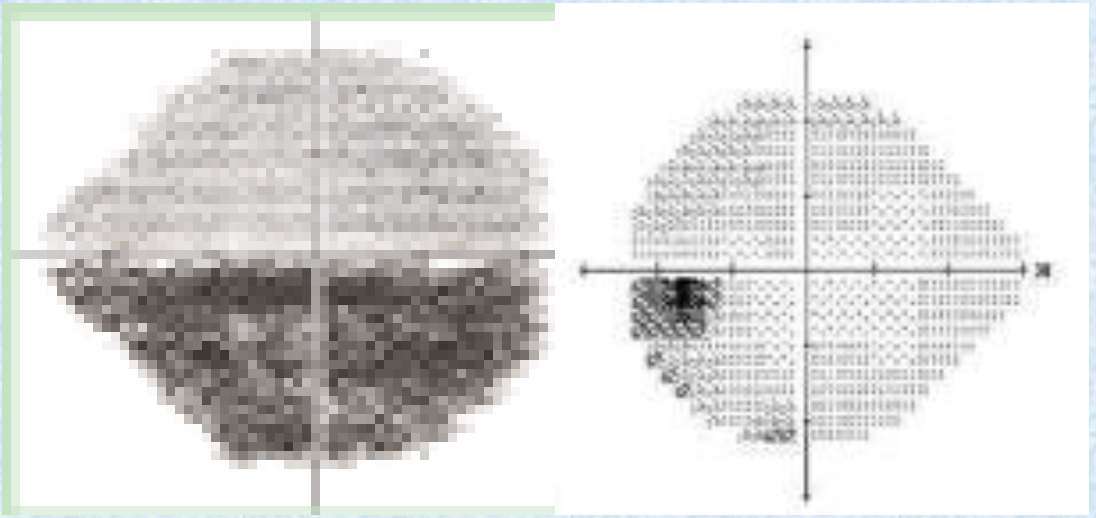


Signs and Symptoms:

Sudden Unilateral Visual Loss
VA and or VF

Usually Painless

VF loss – often respects horizontal midline,
frequently *Altitudinal* – most common *Inferior Altitudinal*



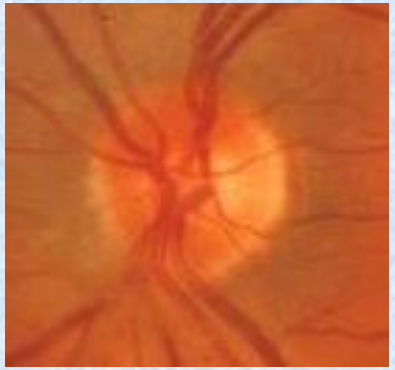
+ RAPD

Disc Edema

ION - Ischemic Optic Neuropathy

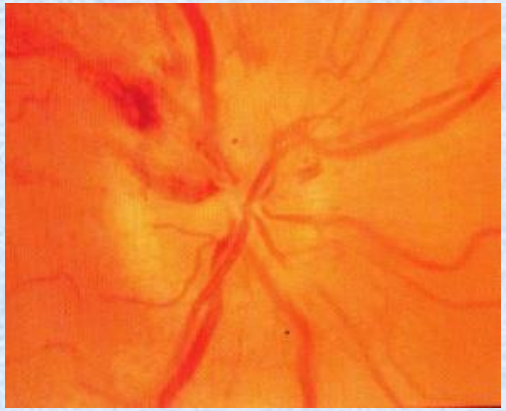
PION - posterior (no disc edema)

Need to differentiate from Retrobulbar optic neuritis



AION – anterior (disc edema)

- **AAION** - associated with Giant Cell Arteritis (GCA)
- **NAION (also NAAION)**– associated with other systemic conditions.



Need to differentiate from optic neuritis/ papillitis

Risk Factors for AION*

- Older Age

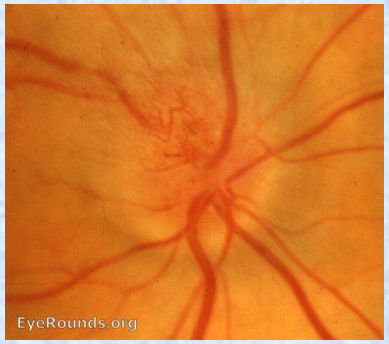
  AION most common optic neuropathy in pts > 50yo**
- Vasculitis - Giant Cell Arteritis (GCA) → AAION (Arteritic AION)

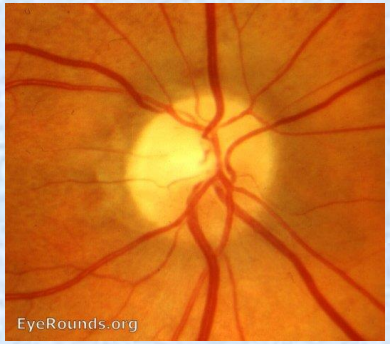
NAION

- Diabetes Mellitus, Hypertension, Hyperlipidemia
- Smoking
- "Disc at Risk" – small C/D – crowded disc →
- Sleep Apnea
- Nocturnal Hypotension
- Acute Hypotension – after - trauma, surgery
- Post Cataract Extraction
- Medications: Interferon, ***Amiodarone***, Viagra?

NAION

Non-Arteritic Anterior Ischemic Optic Neuropathy





- Often Sectoral Edema, should resolve in 6-8 weeks
  (If not resolve consider something else)
- Development of Sectoral pallor later on (2-3 mo).

- Visual Recovery is usually poor to modest
- 15% Fellow Eye involvement in 5 years – *work to decrease that risk*

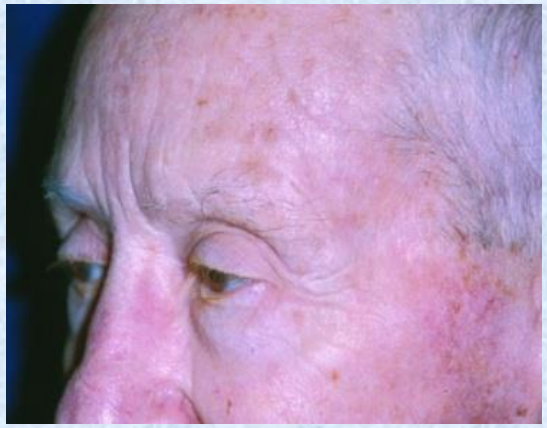
- Neuroimaging *not needed* in classic case of NAION

- Treatment:

  Corticosteroids - Not Proven Useful - except for cases of GCA (AAION)
  ASA qd – prevention of involvement other eye?
  Transvitreal Optic Disc Decompression, Intravitreal Avastin,
  Higher Dose Prednisone ?? ***No effective treatments shown***

- ***Referral to PCP or Cardiologist important to address medications, vascular risk factors and possible also arrange for a sleep study for Obstructive Sleep Apnea***

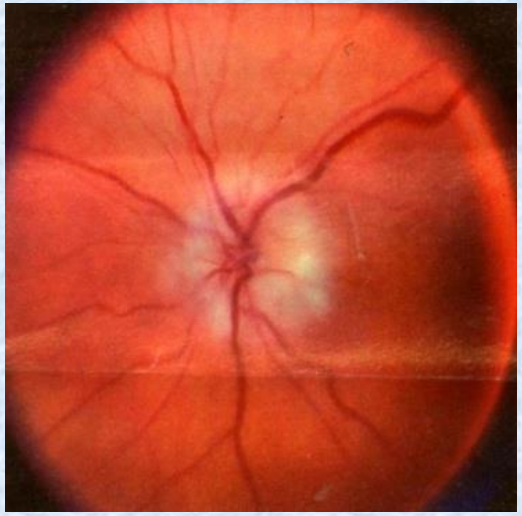
AAION – Arteritic AION



- *Mean Age 70 yo* ; 5-10% of patients with AION

- Classic Symptoms: Head/ Temporal Pain, Scalp Tenderness,
  Jaw Claudication, Anorexia, Malaise, Joint Pain,
  Symptoms of PMR

- Severe Visual Loss <20/200
- Chalky White Disc Edema
- AION is most common ocular manifestation of GCA,
  but other possibilities include: CRAO, Choroidal infarction, CN Palsy, etc.



- Diagnosis: Clinical Signs and Symptoms, Elevation of ESR and CRP, Temporal Artery Biopsy

- Treatment: Systemic Steroids: IV or PO
  Taper (1-2 months) and Long Term Treatment (2 years or more)

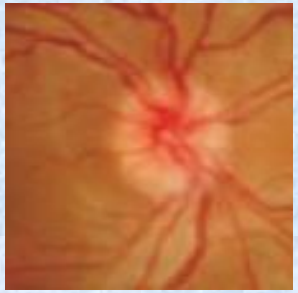
- *Risk of Fellow Eye Involvement: 80-95% if untreated*

Definitions

1. **Typical Optic Neuritis** – A Clinical Diagnosis with a classic presentation of painful sudden loss of vision in one eye suggestive of a demyelinating optic neuritis that will usually show a good visual recovery over weeks.

2. **Atypical Optic Neuritis** – Non-Classic presentation of optic neuritis with involvement of one or both eyes with poor visual recovery or progression of visual loss.

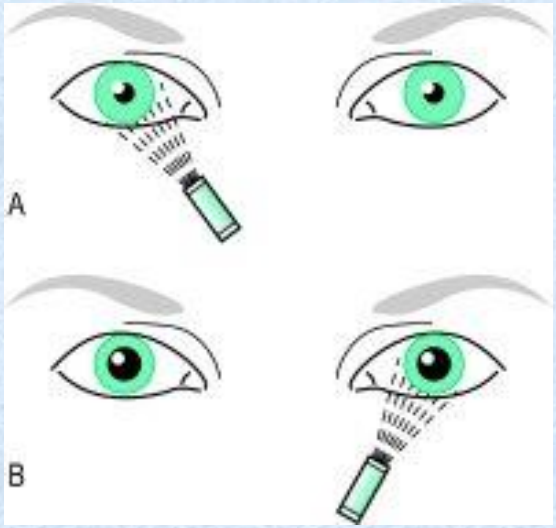
3. **Papillitis** – Optic Neuritis associated with visible edema of the optic disc on fundus exam

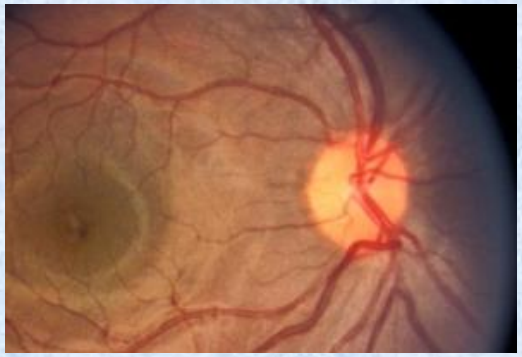


4. **Anterior Ischemic Optic Neuropathy (AION)**– Interruption of blood flow to the optic nerve resulting in sudden painless loss of vision in one eye and disc edema

3. Classic Optic Neuritis

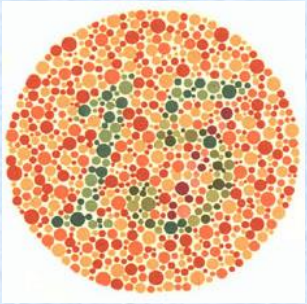
- Unilateral sudden loss of vision
  Women > Men
- Eye Pain, Pain on eye movement
- Age 20-50 years old (Younger)
- Usually marked decrease in visual acuity < 20/200
- + RAPD
- Disc swelling often absent (Retrobulbar)

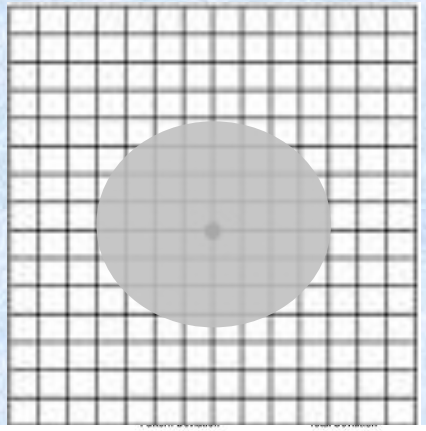




Classic Optic Neuritis

- **Visual Field loss:**
  central scotoma, altitudinal, arcuate, etc



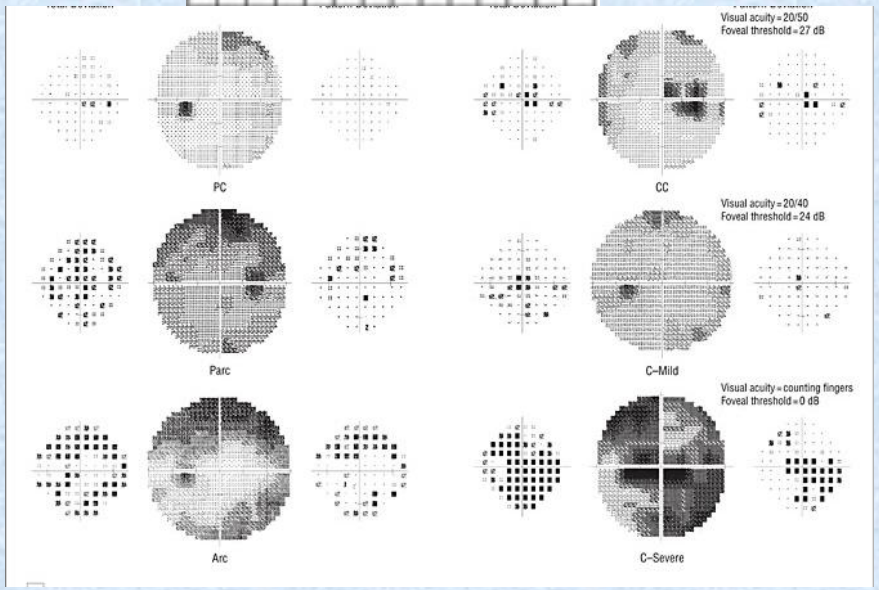


- **Color Vision Deficits**

- **Usually *good visual recovery* after 3-4 weeks- e.g. 20/20**

- **Usually no or little optic nerve pallor develops**

- **Steroids of ultimately little help**
  - **might affect rate of recovery**
    visual recovery is unaffected



ONTT – Optic Neuritis Treatment Trial

Neuroimaging? Yes, but not to make diagnosis of optic neuritis - but to look for white matter lesions suggestive of demyelination disease – like MS.

Possible Other Causes of Optic Nerve Inflammation

Usually will have more atypical presentation and course

Demyelinating: Neuromyelitis Optica = NMO

Autoimmune Optic Neuropathy

Systemic Autoimmune Disorders: Lupus, Bechets, Sjogrens syndrome

Viral, Post-Viral, Post-immunization

Retrobulbar **Papillitis**

Other infectious: Herpes: HSV, VZV, CMV, Syphilis, *Toxoplasmosis*, Cryptococcus,
Hepatitis A, B, and C, Bartonella / Cat Scratch*, Lyme, TB, Measles, Primary HIV, Typhus

Contiguous Inflammation :
- **Encephalitis, Meningitis (high ICP and inflammation)**
- **Orbit (orbital pseudotumor – e.g. optic perineuritis)**
- **Sinuses -Infectious (including fungal), Inflammation (Wegener's Granulomatosis)**

Sarcoidosis

CNS Vasculitis? – Primary or Secondary: Autoimmune Disease (e.g. Wegener's, SLE, GCA, etc.)
Toxic (Amphetamine, Cocaine) , Neoplastic, Infectious

Post-Partum

Chronic relapsing Inflammatory Optic Neuropathy (CRION)

Demyelinating Optic Neuritis

1. Typical Demyelinating Optic Neuritis
   Idiopathic or associated with Multiple Sclerosis

2. Neuromyelitis Optica - Spectrum Disorder: NMO-SD
   can be associated with other autoimmune disorders like SLE

   1. + Aquaporin - 4 antibody form
   2. negative AQP-4 form has more stringent clinical criteria –
      including 2 core clinical characteristics – including one from:
      a) optic neuritis, transverse myelitis or area postrema* syndrome

3. Myelin Oligodendrocyte Glycoprotein Antibody (MOG- IgG) - associated optic neuritis.

* The **area postrema** is a chemoreceptor zone involved in the central control of emesis. It is located at the floor of the fourth ventricle, in the dorsal medulla. The **area postrema syndrome** is defined as episode of otherwise unexplained hiccups or nausea and vomiting due to a lesion in this sensitive chemoreceptor region.

Factor	NAION	Optic Neuritis	Papilledema
Age			
Eye Pain			
Acute Visual Loss			
RAPD?			
Disc Edema			
VF defects			
C/D			
Visual Recovery			
Imaging Needed?			

Factor	NAION	Classic Optic Neuritis	Papilledema
Age	Older > 50	Younger <50	Any Age
Eye Pain	<10%	70-90%	No Eye Pain, but Headache
Acute Visual Loss	Yes	Yes	Usually Not
RAPD?	Yes	Yes	No
Disc Edema	100% Unilateral	~ 25% Unilateral	Usually Bilateral
VF defects	Usually Altitudinal but others possible	Many Possible Central, altitudinal, arcuate, etc	Early- Enlarged BS Chronic - arcuate, constriction, etc
C/D	Small (disc at risk)	No association	No association
Visual Recovery	Poor - Modest 33% of patients 2-3 lines	Usually good	Good if cause treated early
Imaging Needed?	*NO*	YES - MRI	YES* - CT or MRI

*What if patient's presentation or clinical course is **not** like any of the natural histories?*

- **Obtain Further History or Physical Findings thinking about diagnostic alternatives. Do automated VF testing if not already done.**

- **Consider Testing *based on your history and exam***
  - **Erythrocyte Sedimentation Rate (ESR, VS)**
  - **Neuro-Imaging – CT or MRI**

  - **Further Blood and Imaging Studies**
  - **Lumbar Puncture (Opening pressure, CSF analysis)**

Further Testing Options To Consider in Optic Neuropathies

- **CBC, C-Reactive Protein**
- **ANA, ANCA**
- **FTAbS, RPR, Bartonella Henselae Titres, Lyme Titres, HIV**
- **B12, Thiamine, Folate**
- **Testing for Sarcoidosis: ACE (Angiotensin converting enzyme level), Chest X-Ray, Gallium Scan**

- **Heavy metals Screening (As,Hg,Pb, Thallium) – urine or blood**
- **Tuberculous Testing: PPD, Quantiferon**
- **Blood for Leber's Mitochondrial DNA Mutation**

- **Further antibody testing for Vasculitis**

- **Lumbar Puncture for OPENING PRESSURE and CSF ANALYSIS**

  (CBC, *Protein, Glucose, Gram Stain and Cultures, Antibodies (RPR, Oligoclonal bands, etc.)**

Lumbar Puncture

Opening Pressure
in mm (or cm) H_2O

Normals

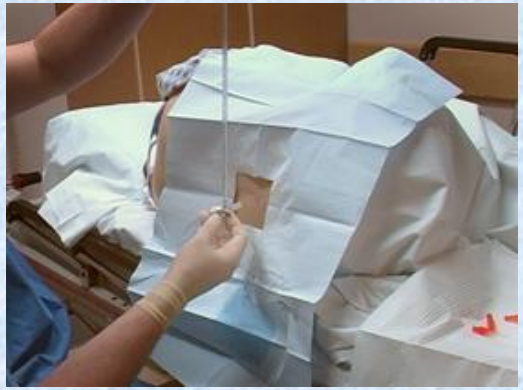
Standard Guideline: < 200 (<20)

AAFP: 10-100 (<8 yo) 60-200 (> 8 yo) <250 (obese)

N Engl J Med – 2010; 363:891

Reference range for cerebrospinal fluid opening pressure in children

11.5-28.0 cm H2O



Opening Pressure in Classic Lateral Decubitus Position, However …

Conclusions:

1) > 250 mm H2O – definitely elevated?
   Opening pressures can be falsely elevated
   Must take opening pressure in clinical context
   Is there obvious disc edema?

Lumbar Puncture

CSF Analysis

1. Cell Counts

Normal < 5 WBC per mm^3

WBC - elevated in infection (Pyogenic / Bacterial WBC >1000 - mainly PMNs)

"aseptic meningitis" Viral – (WBC <100 lymphocytosis), Atypical Bacterial (e.g. Mycobacterial), Fungal (e.g. Cryptococcus), Parasitic (e.g. Toxoplasmosis), Drugs (e.g. NSAIDs, Vaccines), Sarcoidosis, SLE, CNS Vasculitis, *VKH*

2. Protein

- elevated levels are ***sensitive*** for pathology, but not *specific*

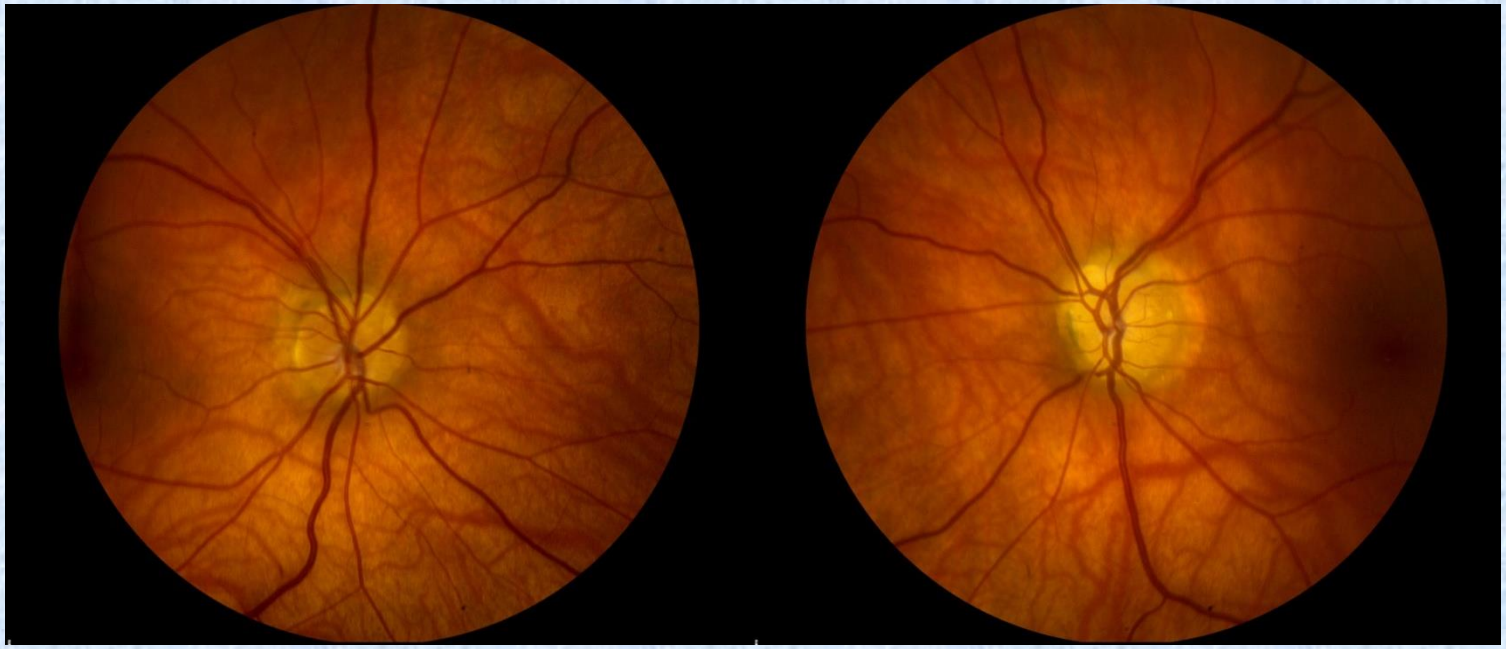
(infection, inflammatory conditions, hemorrhage, MS tumors (even spinal), malignancy). Normal range 15-60 mg/dL

3. Glucose - decreased in bacterial meningitis. Normal range = 50-80 mg/dL (2/3 BS)
4. Microbiology - Stains and Cultures - bacterial, acid fast, fungal, parasites
5. Cytology – looking for malignant cells
6. Serology – e.g. CSF VDRL

23 yo male referred for bilateral disc swelling

No headaches

VA: 20/25 OU, some non-specific VF loss in both eyes

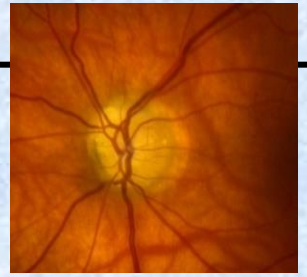


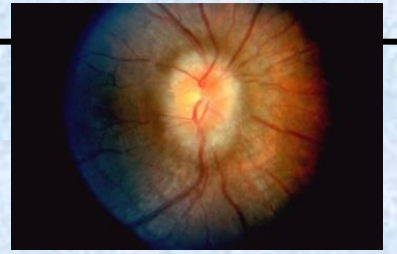
Congenitally Anomalous Discs - Drusen

No real edema

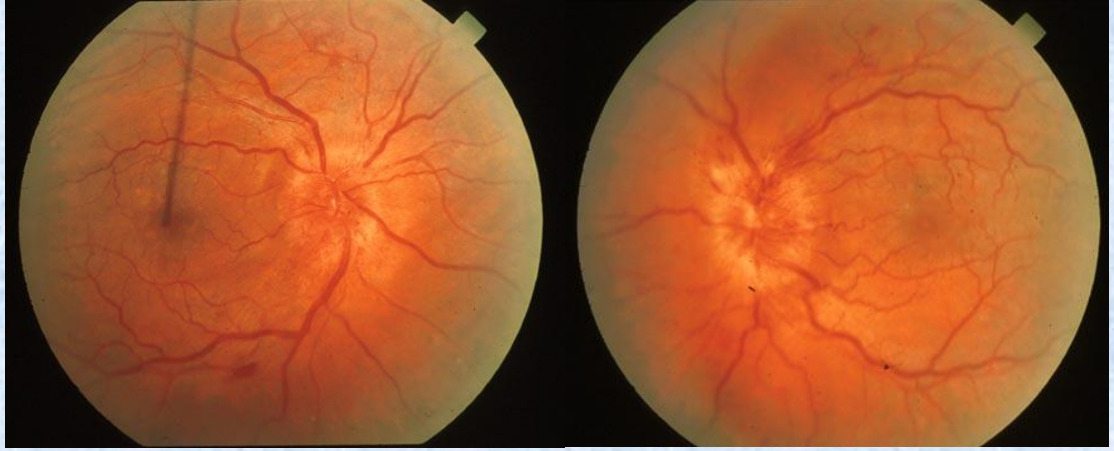
Differentiating between *Congenital* and *Acquired* Disc Elevation

Feature	Congenital	Acquired
Nerve Fiber Layer	Clear	Opacified
Large Disc Vessels	Anomalous	Normal
Small Disc Vessels	Normal	Telangietatic
NFL Hemorrhage	Rare	Frequent
Physiologic Cup	Small or absent	Normal
Drusen	Sometimes present	Absent





46 yo overweight woman with loss of vision in both eyes over last 3 weeks and headaches.



Papilledema, suspect high ICP

VA: 20/20 both eyes

VF: normal confrontational VFs

External, Motility, Pupil Exam Normal

Slit Lamp, IOP normal

Fundus Exam: Bilateral Disc edema – retina hemorrhage noted OD

Tentative Diagnosis:

Get Further History - negative

First Test: Check Vital Signs

BP very elevated 210/120

Malignant Hypertension

High Blood Pressure with Papilledema

65 yo man with sudden painless of vision on wakening one morning.

VA: 20/20, 20/200

VF →

+ Left RAPD

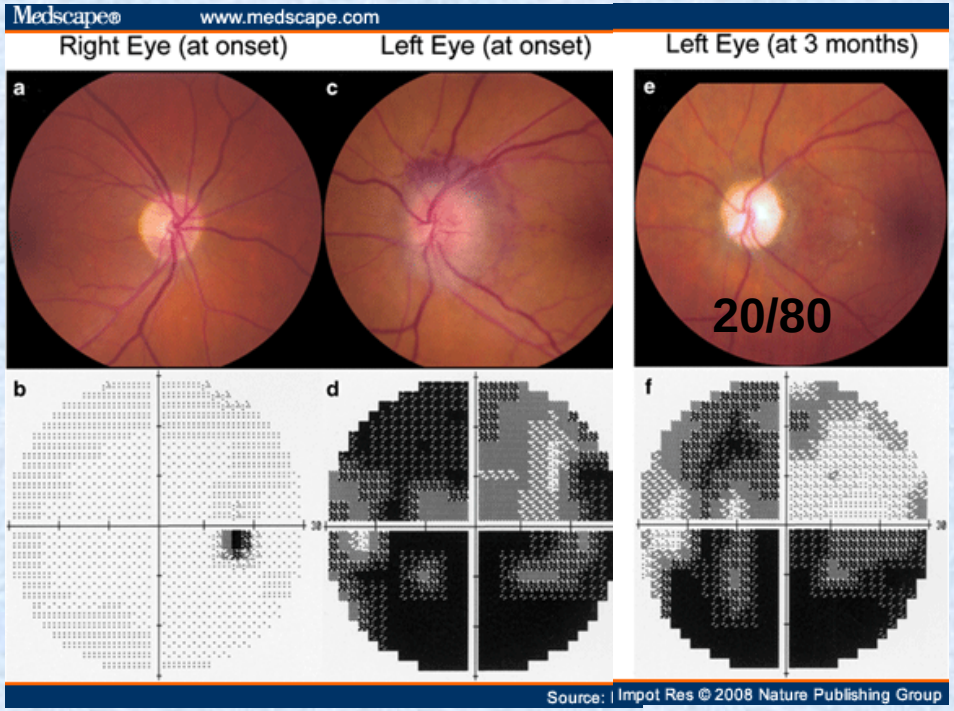
External, Motility, Pupils and Slit Lamp exam normal

Fundus: C/D 0.2 OD

Severe Disc edema OS

Tentative Diagnosis:

AION



medscape.com/.../584/197/ijir584197.fig1.

What do you do next?

Testing?

ESR <20 normal

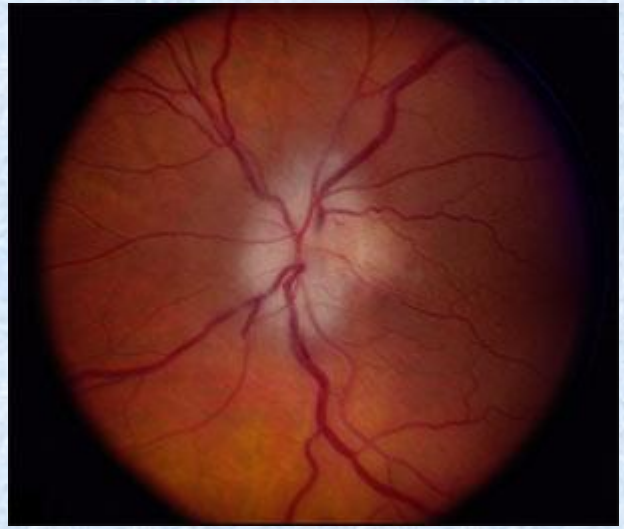
→ **NAION**

So no neuroimaging needed
Probably no steroids

Further History -what are you concerned about?

Giant Cell Arteritis (GCA)

78 yo woman, with sudden loss of vision in left eye, some headache and tenderness over scalp and temple.



http://kellogg.umich.edu/

VA: 20/20 OD , LP OS
VF: FTCF OD, Non-specific Loss OS
External, Motility and Slit Lamp all normal

Pupils: Strong Left RAPD
Fundus – OD C/D 0.2
OS - disc edema with early pallor already

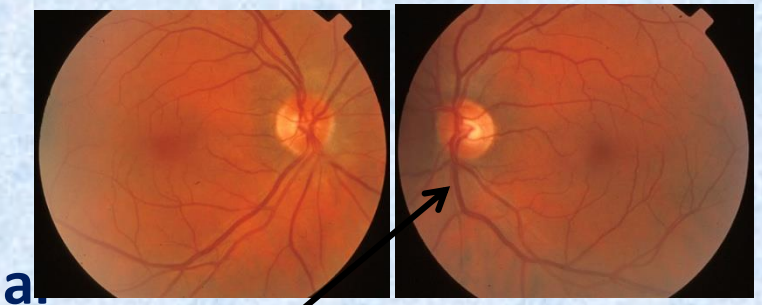
Diagnosis: AION – concern for ? **GCA / TA**

Giant Cell Arteritis Temporal Arteritis

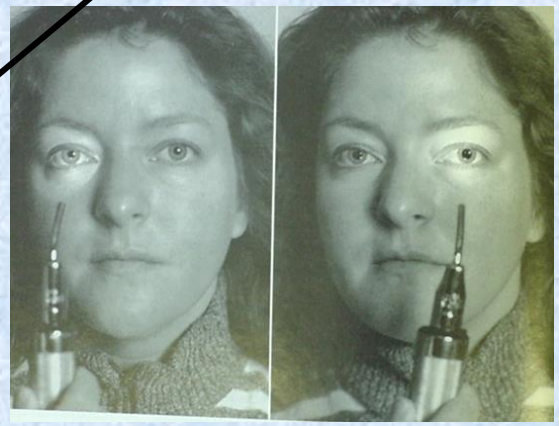
Management?

ESR, CRP, CBC, FBS
Admit to Hospital for High Dose Steroids
Consider Temporal Artery Biopsy

28 yo woman, sudden loss of vision in left eye,
some discomfort over eye and with movement.



VA: 20/20 OD , HM OS
VF: FTCF OD, Non-specific Loss OS
External, Motility and Slit Lamp all normal

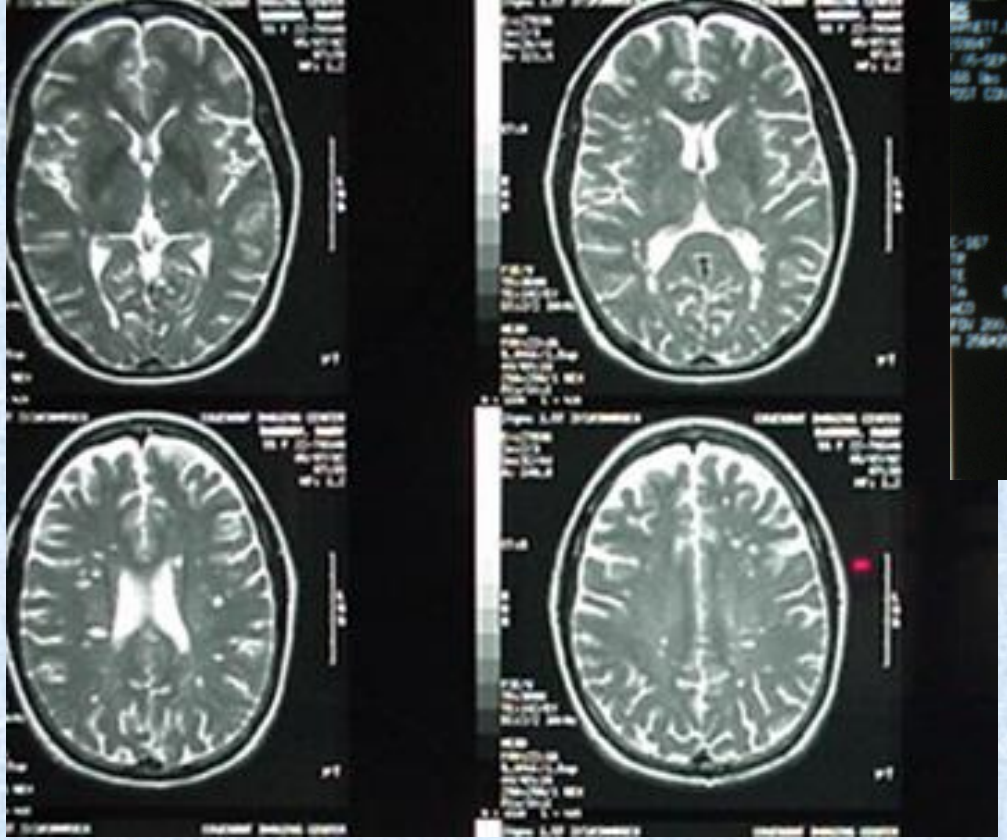


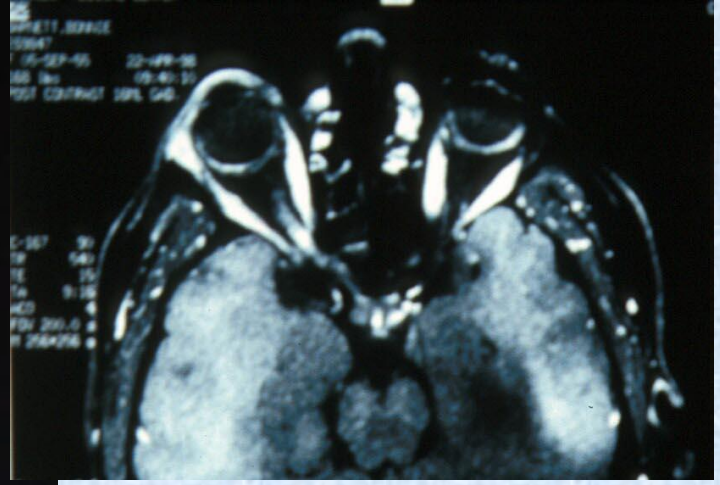
Pupils: Strong Left RAPD
Fundus – C/D 0.2 OD, 0.3 OS – no edema

Diagnosis:

Management? Classic Left Retrobulbar Optic Neuritis

MRI of Brain





Timely Consultation and admission with Neurology

White matter lesions noted in optic nerve and or brain

Should you give steroids??

Depends on patient - ONTT

ONTT

Optic Neuritis Treatment Trial

- <u>Some Major Conclusions</u>

1. Treatments with Corticosteroids
   a) may speed recovery of vision, ***BUT*** does not affect ultimate visual outcome in Classic Optic Neuritis
   b) may delay the onset of MS (by one year) in some patients

2. Development of Multiple Sclerosis

   Overall Risk - all patients with Classic Optic Neuritis

   38% at 10 Years

   MRI very helpful in predicting development of MS

3. Visual Outcome for most patients at 15 years follow-up was good

Archives of Ophthalmology 2003; 121: 944

ONTT
10 Year Follow-Up

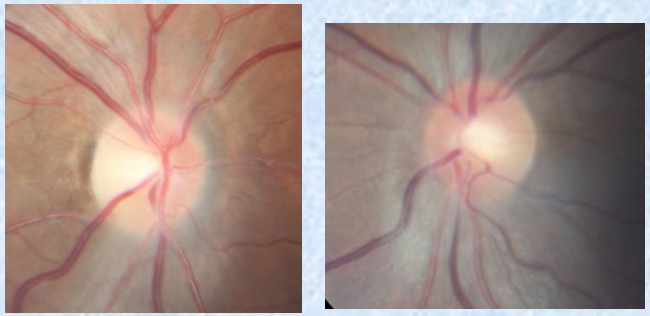
MRI=Baseline MRI

- 38% overall development of MS
- If no lesions on MRI then only 22%
- If one or more Lesions on MRI* then 56%

15 year data – No lesion 25%, 1-2: 65%, 3 or more – 78%

Recommendation – if has any lesion on MRI refer for Neurology evaluation

20 yo woman with sudden loss of vision and pain in right eye over 3 weeks, and is having some pain. Also with some paresthesias in arms and legs



VA: LP, 20/40
Pupils: 2+ Right RAPD
Remainder of Eye Exam normal
– minimal disc changes

Dx: Optic Neuritis OD
MRI of brain was read as negative
Admitted to Hospital for IV Corticosteroids

2 months later
– mild recovery of vision VA :HM and 20/20

Poor Recovery
Atypical Optic Neuritis

Consultation with Neurology

Diagnosis:

NMO = Neuromyelitis Optica

Neuromyelitis Optica (NMO)

Optic Neuritis +

Myelitis of the Spinal Cord

Associated with specific

NMO IgG autoantibody to water channel Aquaporin -4 (AQP4) in cell membranes of astrocytes

Can respond to IV Methylprednisolone , but if not

Consider:

Plasmapharesis / Exchange

Rituximab

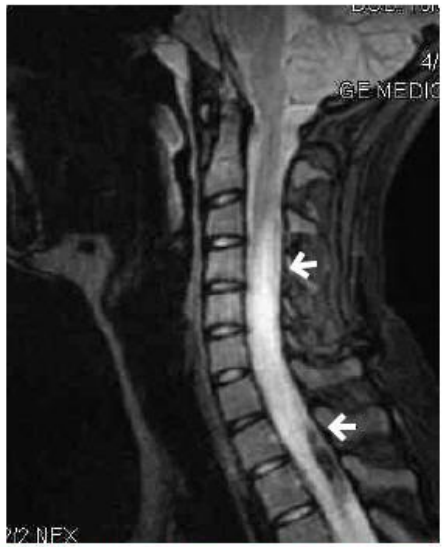


Figure 1. A longitudinally expansive (greater than three segments) lesion seen in the cervical (neck) spinal cord (between arrows).

Visual Loss and Weakness, Numbness (Often below a definite level of spinal cord), Loss of Bowel or Bladder Function

NMO Not the same as MS . They differ

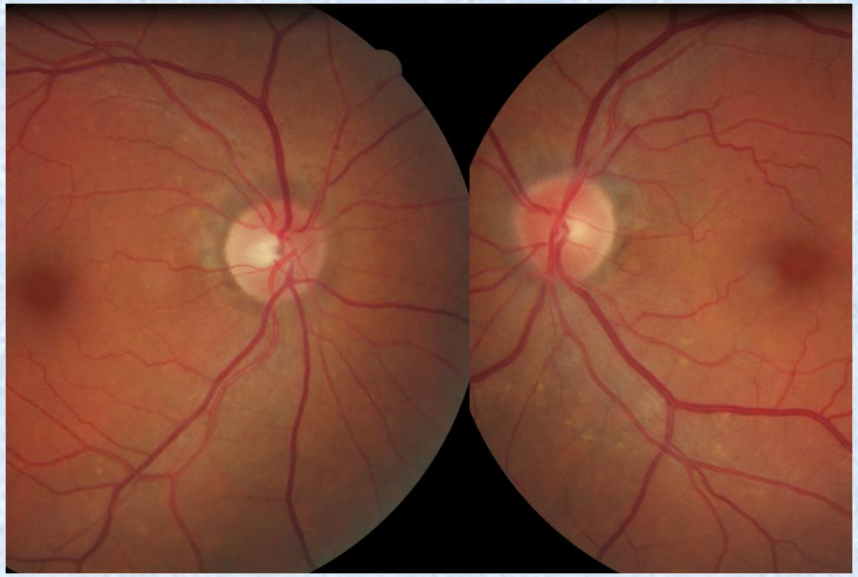
- immunologically (cellular vs. Ab)

- radiologically

- in treatment response

Suspect NMO in pt with optic neuritis with poorer visual recovery

68 yo man with sudden loss of vision OD noted after heart surgery
No headache



VA: NLP, 20/40
Pupils: 4+ Right RAPD
Remainder of Eye Exam normal

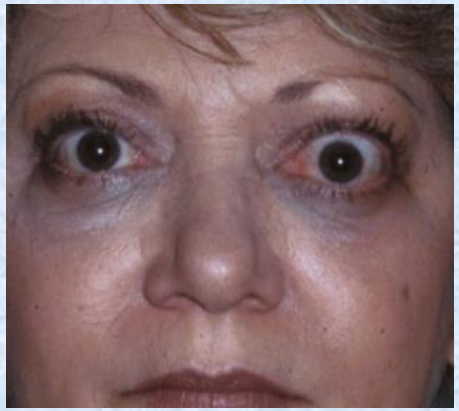
DDx: Retrobulbar Optic Neuritis
vs. Compression / Ischemia / ?

MRI of brain was negative

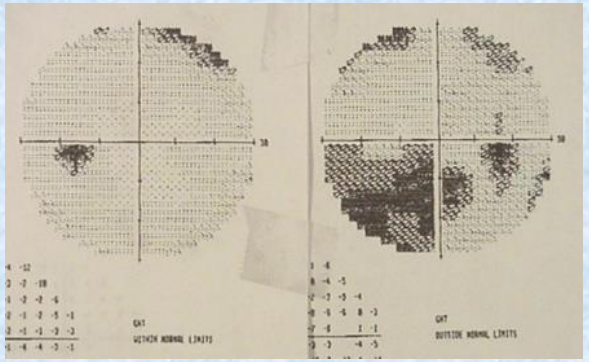
Diagnosis? **PION = posterior ischemic optic neuropathy**

Further Management? **Further History of GCA**
ESR, CRP, CBC

46 yo woman with loss of vision in right eye over 3 weeks, and is having some pain.



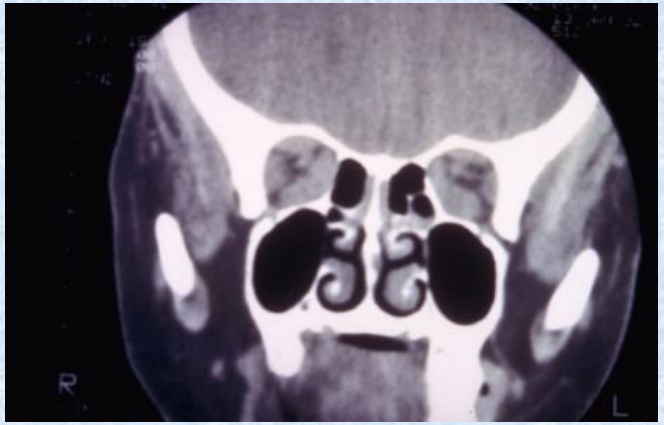
VA: 20/100 20/20
EOM: Full
Pupils: 2+ Right RAPD
SLE,IOP, Fundus – normal – no disc changes



ESR = 6 (normal)

Dx: Optic Neuritis OD
MRI of brain was read as negative
Opted not to treat but observe

CT!



F/U 2 weeks later – no improvement in symptoms
and now VA : 20/400 and 20/40

WHAT NOW
What do you notice about her?

Further Testing?

Compressive Optic Neuropathy
Graves Ophthalmopathy
Think about Orbital Disease

25 yo woman complains of headaches and occasional episodes of transient bilateral visual loss

- Exam:

20/25 OD and 20/20 OS

Confrontational VFs were normal

Pupils – PERRL –no RAPD. Eye exam otherwise normal except for bilateral disc elevation with NFL opacification and few splinter hemorrhages.

What do you suspect and what do you do next?

Papilledema

Further History/Exam – no: medications or toxins, trauma, or sleep apnea

- normal BP, overweight

MRI of brain – negative

LP: Opening pressure =340 mm,

CSF- no WBC, RBC, normal – protein + glucose

Pseudotumor Cerebri
(IIH= Idiopathic Intracranial Hypertension)
(not Benign)

Working Diagnosis?

Idiopathic Intracranial Hypertension

AKA: *Pseudotumor Cerebri, Benign (not) Intracranial Hypertension)*

Incidence:

1/100,000 overall, 2/100,000 women, 8-20/100,000 overweight women

Diagnosis:

Elevated ICP opening pressure (>200-250 mm H_2O)

You must rule out other causes before making firm diagnosis

(Negative History, Negative MRI (sometimes MRV too), Negative CSF analysis)

Treatment:

DEPENDS ON STATUS OF SYMPTOMS AND VISION

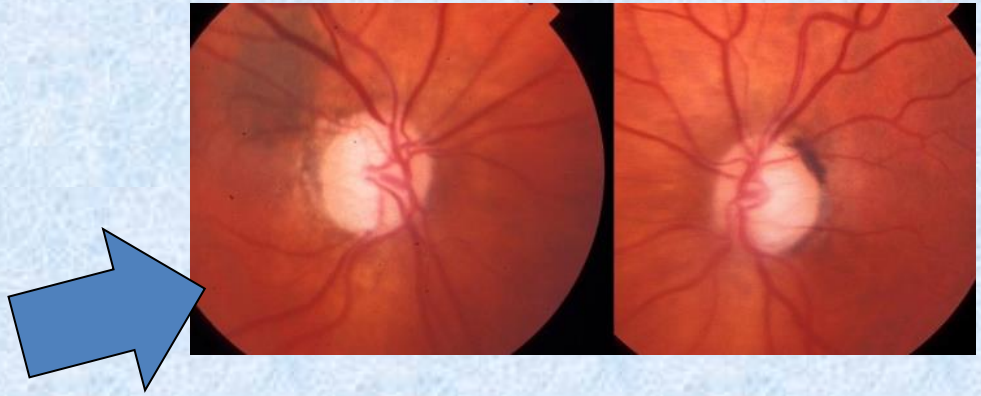
- If headaches are medically controlled and there is no significant visual loss:
  Observation (VF monitoring) and Weight Loss maybe all that is needed

- If there is significant headache or visual loss, then treatment needs to be more aggressive:
  Close VF monitoring, PO Acetazolamide, Serial LPs, IV Acetazolamide or Steroids
  Surgical – Lumbar Drain, ON Sheath Decompression or Neurosurgical Shunting procedures

35 yo woman with chronic visual loss over months and some headaches

- Exam:

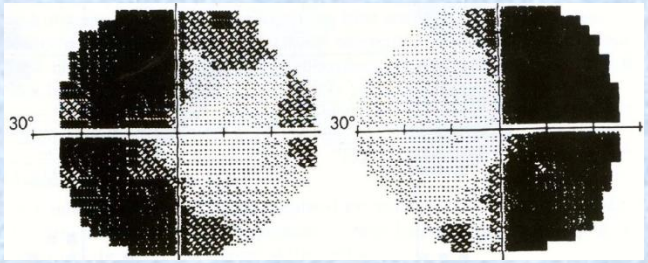
  20/70 OD and 20/50 OS
  Confrontational VFs were not normal
  IOP: 13,14 mmHg
  Pupils – PERRL –no clear RAPD
  Eye exam otherwise normal
  except for bilateral disc changes noted.



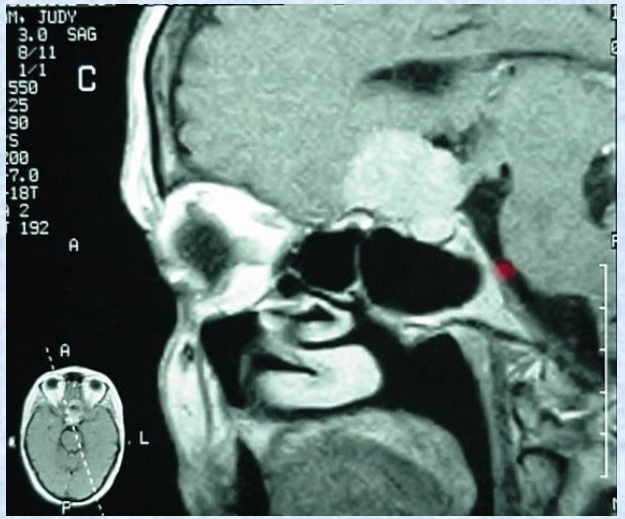
What do you suspect and what do you do next?
DDX: Glaucoma, Optic Atrophy (causes: compression, toxic, etc.)

Further History/Exam – no: family history of vision loss or glaucoma
Color Vision – 4/7 OD, 3/7 OS

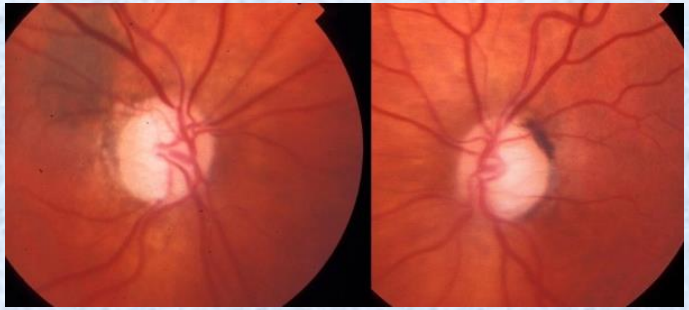
VF testing -



Optic Atrophy
Compressive Lesion



Low Tension Glaucoma versus Other causes of Optic Atrophy



Low (Normal) Tension Glaucoma (LTG, NTG) :

Glaucomatous Cupping with *corresponding VF loss*,

but repeatedly normal IOP

Q: When is apparent NTG not NTG?

or When do patients with NTG need further work-up?

NTG is fairly common, but your suspicion for something else should be elevated when:

- younger person with optic atrophy or cupping
- ***color vision loss (glaucoma does not have color vision loss early on)***
- Pallor of disc rim (pallor not usually seen in early glaucoma)
- VF loss out of proportion to the cupping present

42 yo man with poor vision and optic atrophy discovered on exam

- Exam:

  20/70 OD and 20/200 OS

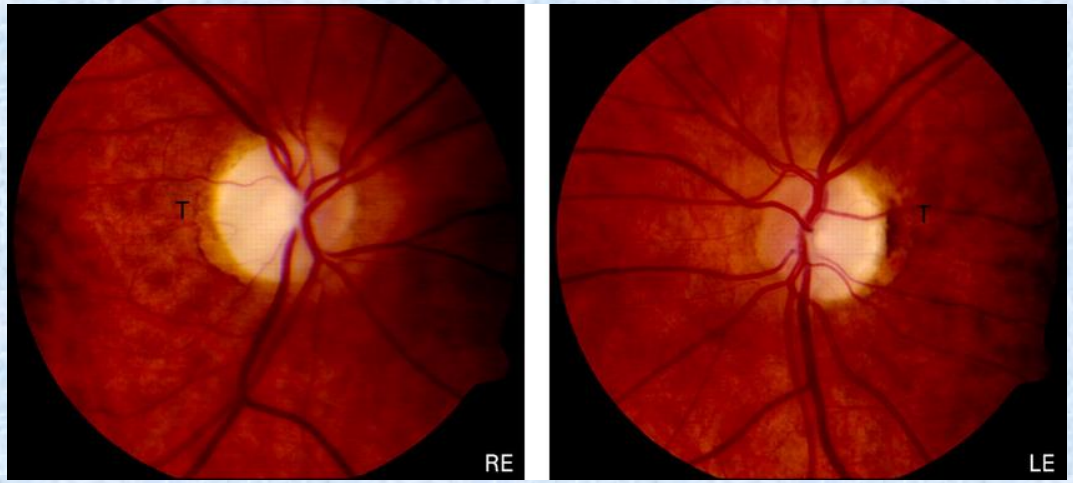
  Confrontational VFs showed some constriction

  IOP: 13,14 mmHg

  Pupils – PERRL – with mild left RAPD

  Remainder of Eye exam otherwise normal

  except for bilateral disc changes noted.



Bilateral Disc Pallor

What do you suspect and what do you do next?

Bilateral Optic Atrophy – etiology unknown

Further History including FHx
Visual Field testing
Neuroimaging?

Optic Atrophy / Disc Pallor

Seen with Damage to the Retina (NFL / Ganglion Cells), Optic nerve, Optic Chiasm or Optic Tract

Causes:

Ischemia - e.g. past AION or PION

Compression - e.g. Pituitary Tumor, Carotid artery, Hydrocephalus, Graves Ophthalmopathy

Chronic Papilledema - compression +/- ischemia – see high ICP list

High IOP - e.g. Glaucoma, Ischemic

(Loss of ganglion cell axons)

Inflammation - e.g. past Optic Neuritis, MS, Meningitis, Sarcoidosis, Autoimmune, Vasculitis, Infectious

Trauma – direct or indirect traumatic optic neuropathy

Toxic / Nutritional Deficit – e.g. Medications: Ethambutol, etc.
Methanol, Ethylene Glycol, Heavy Metals (Pb, Hg, As),CO, CCl_4
Vitamin Deficiencies (B_1,B_{12}, Folate, niacin)

Temporal Pallor

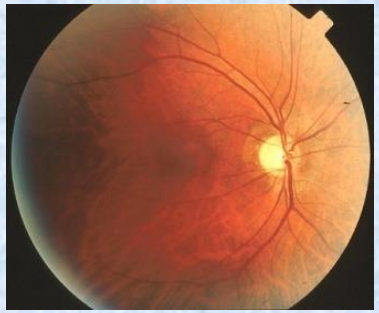
Congenital / Hereditary – e.g. **Isolated** : Autosomal Dominant Optic Atrophy (ADOA), Leber's (LHON)**
Non–isolated: Metabolic***, neurodegenerative diseases, Behr's Syndrome
Friedreich's and Spino- Cerebellar Ataxias
Associated Hearing Loss: Wolfram's Syndrome (DIDMOAD), Some ADOA

Retinal Damage - (False Ocular Localizing Sign) - CRAO, CRVO, Ischemic PDR, S/P PRP, Retinitis

The Diagnostic Yield of the Evaluation of Isolated Unexplained Optic Atrophy

form Univ. of Cincinnati and Univ. of Iowa (K. Golnik, A. Lee, R. Kardon, et. al.)

Ophthalmology 2005; 112: 757



1110 Charts reviewed - Exclusion Criteria included: children (<18 yo), other neurologic deficit (non-isolated), know ocular or systemic disorder for optic neuropathy, history suggestive of etiology: e.g. prior intracranial tumor, syphilis, GCA, toxin exposure, nutritional deficiency, family history

Leaving : 91 cases of unexplained Isolated Optic Atrophy

All underwent some form of neuro-imaging and Lab Testing* done in 51 of 91 cases

Important Results

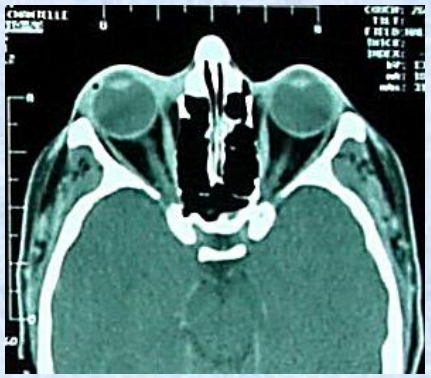
18 patients (20%) had a compressive lesion** – e.g. Meningioma, Pituitary adenoma, Craniopharyngioma

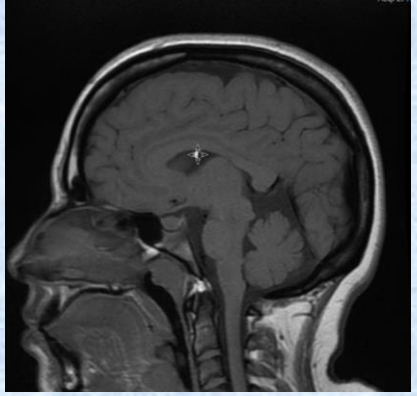
None of the patients had abnormal Lab testing* that could be linked to the Optic Atrophy

Conclusions

Many etiologies for optic atrophy can be determined by careful history, review of any records and past imaging studies, and a complete eye exam and visual fields. In cases that are truly "unexplained" and isolated a ***neuroimaging study is appropriate*** since 1 in 5 patients were found to have a significant compressive lesion. ***Screening lab studies are not warranted***, but should be ordered based on clinical presentation.

Disc Scenario	Visual Loss	More Likely Diagnoses
1. Bilateral Elevation/Edema	Little or none	Early Papilledema / High ICP Pseudo-papilledema (Anomalous discs)
2. Bilateral Edema	Significant	Simultaneous or Closely Sequential AION or Optic Neuritis Some Compressive and Toxic Optic Neuropathies, Meningitis Late - Severe Papilledema
3. Unilateral Disc Edema	Little or none	Papillophlebitis, Mild Diabetic Papillopathy
4. Unilateral Disc Edema	Significant	AION, Papillitis (Anterior Optic Neuritis) Compressive, Ocular (Hypotony, Uveitis, CRVO)
5. Bilateral Disc Pallor	Bilateral Significant	Past Severe Bilateral ON (AION, Optic Neuritis, Papilledema) Past or present Compression Congenital or Hereditary CNS/Metabolic Problem Past Severe: Glaucoma, CRAO, CRVO
6. Unilateral Disc Pallor	Unilateral Significant	Past Severe AION, Optic Neuritis or Compression Past Severe: Glaucoma, CRAO, CRVO
7. No Disc Changes	Significant Unilateral	Retrobulbar Optic Neuritis, PION, Early Compression, Traumatic ON
8. No Disc Changes	Significant Bilateral	Bilateral PION (Hypotensive or GCA) Early Chiasmal Process, Early Toxic Optic Neuropathy
9. Increased Cupping	Significant VF Loss	Glaucoma, Normal Tension Glaucoma or Mimic





Some clear Indications for Neuroimaging (CT, MRI brain or orbits)

Remember Imaging is not Necessary for every patient with diplopia, ophthalmoplegia, strabismus, nystagmus, visual loss (VA or VF), ptosis, disc edema / pallor, or headache.

Yet Consider for imaging for:

1. **Cranial Nerve Palsies** – non-isolated any age, or isolated in younger patients (<50 yo),…
2. **Ophthalmoplegia** – unilateral associated with orbital signs
3. **New Visual Field loss that respects the vertical midline**
4. **Bilateral Disc Edema** – when associated with headache or visual loss
5. **Optic Neuritis** – history of eye pain (movement) , sudden loss of vision, +RAPD , +/- disc edema
6. **Bilateral or Unilateral Disc Pallor – not previously explained**
7. Nystagmus – not explained by drugs, toxins, pre-existing infantile nystagmus, metabolic derangements
8. **Ptosis – when associated** with other neurologic or orbital signs or symptoms

Approach to Suspected Optic Neuropathy

1. Remember 3 most common conditions

    1) Papilledema, 2) NAION, and 3) Classic Optic Neuritis

2. If patient does not fit one of these conditions well:

    Consider DDX for optic neuropathies and ask further history and do more detailed exam as needed.

    Ocular Findings that can direct work-up: Signs of Uveitis, Bilateral Temporal Disc Pallor, etc.

    ***VF testing very useful** – e.g. specific patterns help direct diagnosis: hemianopic, centrocecal, etc.*

3. Testing

    a) First Consider: *Blood Pressure, ESR, Glucose Level*

    b) **Neuroimaging – especially for**

    - Typical or Atypical Optic Neuritis
    - Papilledema not explained by history/ exam (e.g. medications, BP)
    - Isolated Unexplained Optic Atrophy

    c) Other Testing

    1) Acute Optic Neuropathy:

    - LP: especially if suspect high ICP or CNS inflammatory condition
    - Other Testing: CBC, ANA, ACE, FTAbS, B12, etc. - *as clinically indicated*

    2) Optic Atrophy

    - *Screening Lab Testing not of much benefit in Unexplained Optic Atrophy*
    - *Lab Tests as indicated by History and Findings*

Treatment Options:

Treat the Underlying Condition if possible

Consider Use of Corticosteroids – if no clear diagnosis with other treatments
dependent on working diagnosis and risk factors (e.g. TB, DM, etc)

Other Options*: Plasma Exchange* – used in NMO Optic Neuritis (Archives 2012; 130:858)

Rituximab is a monoclonal antibody (CD20, from mouse tissue) that binds to a receptor on the surface of B cells. These cells are then destroyed and their levels in the circulation are decreased. It is approved for use in the treatment of lymphomas, leukemia, and autoimmune disorders.

Steroids and Optic Neuropathies

Responsive

- AAION (GCA)*
- Demyelinating Optic Neuritis**
- Some Atypical Optic Neuritis

  e.g. Sarcoidosis
  Wegener's
  Autoimmune Optic neuropathy
  Orbital Pseudotumor

- Compression Optic Neuropathy from Graves Disease

Unknown or Not Proven

- NAION***
- Toxic Optic Neuropathy
- Traumatic Optic Neuropathy
- Congenital / Familial (e.g. LHON)
- Compressive Optic Neuropathy**** (except Graves)
- Papilledema – though sometimes steroids can temporarily lower ICP and thus indirectly help optic neuropathy

Beware of Conditions that steroids can exacerbate: e.g. ***DIABETES****, Osteoporosis,TB, Syphilis, Herpetic, Fungal*

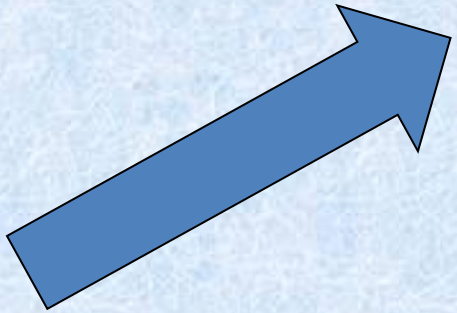
Typical Tapering Steroid Treatment

- Maybe first: IV – Methylprednisolone (Solumedrol)
  250 mg 4x/d or 1 gram once a day for 3 days

- Then Oral Prednisone Taper for at least 2 weeks:
- 1 mg/kg

- Example: 60 kg man
- 60 mg for 4 days then 40 mg for 4 days then 20 mg for 4 days and then 10 mg until patient follows up and then can decide whether to stop medication or continue at lower dose

Summary



1. Classic Optic Neuritis
2. NAION
3. Papilledema
(High ICP)

- *First Consider one of most common causes*

  (Does it fit the presentation/ Natural History?)

  and then manage appropriately

If the presentation or natural course do not fit one of the most common optic neuropathies, then consider further testing or referral

Thank You

Behold, **children** are a heritage *and* gift from the LORD

PSALM 127:3

The Freedman Family


The LORD is my light
and my salvation;
whom shall I fear?
Psalm 27:1

Appendix

Acute Optic Neuropathy

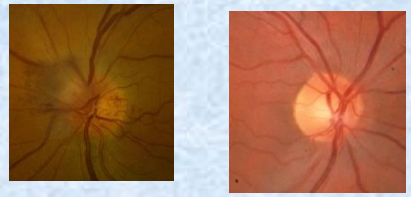
(As evidenced by unexplained VA loss, VF loss, RAPD, Disc Changes)

"Classic" Demyelinating Optic Neuritis:

Related to MS or NMO*, Idiopathic, ADEM**

Other Optic Neuritis (Often not classic course / "Atypical")

Post Viral or Immunization
Autoimmune (40-60 yo, responsive to steroids)
Contiguous Inflammation (Meninges, Orbit, Sinuses- e.g. Sphenoid Sinus)
CNS Vasculitis
Infectious: HSV, VZV, Toxoplasmosis, HIV, Bartonella, Cryptococcus, Hepatitis, Syphilis, TB
Other: Sarcoidosis, Optic Perineuritis (IOIS), IgG4-ROD, GBS (rare)



With **or Without**
Disc Swelling

Ischemic

Non-Arteritic Anterior Ischemic Optic Neuropathy - NAION
Arteritic Anterior Ischemic Optic Neuropathy – AAION (GCA)
Posterior Ischemic Optic Neuropathy - PION (peri-operative, arteritic, non-arteritic)
Post-op CE or PPV

Compressive

e.g. Pituitary Apoplexy, Thyroid Orbitopathy, Carotid Artery, Tumor …

Hereditary: LHON

Acute High ICP

Traumatic: Head (Forehead, Temple), Orbit, Globe

Paraneoplastic: Associated often with Small Cell Lung CA and CRMP-5 protein

Medications / Toxins: e.g. Ethambutol, Chemotherapy, Methanol, Ethylene Glycol

Radiation Optic Neuritis: can see months to years after treatment

Timing
Abrupt – ION, LHON

Subacute – optic neuritis

Insidious – compressive or metabolic

Character
Dark spot – optic neuropathy

Metamorphopsia - maculopathy

Unexplained Bilateral or Quickly Sequential Acute Visual Loss

Rapid loss of vision in both eyes simultaneously or sequentially with minimal ocular findings

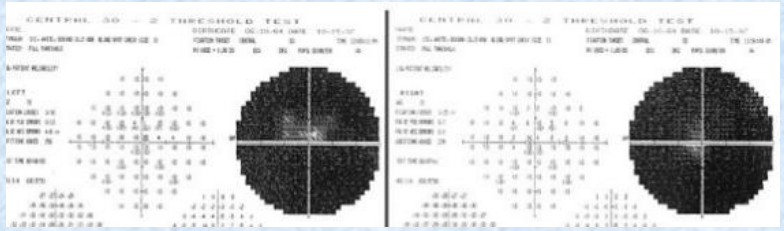
Vascular

Hypotension – e.g. PION after trauma, surgery, code

Severe Systemic Hypertension

Vertebrobasilar Insufficiency

Temporal Arteritis – e.g. PION



Retinal

Paraneoplastic: MARS and CARS*

Optic Nerve

LHON

Bilateral / Sequential Retrobulbar Optic Neuritis (e.g. Neuromyelitis Optica -NMO , MS not as likely)

Other Inflammatory – Post-infectious, Autoimmune, Infectious ON, Meningitis, Vasculitis, Sarcoidosis, GBS

Other Optic Neuropathy – Toxic (e.g. Methanol, Chemo), Nutritional, infiltrative

Paraneoplastic Optic Neuropathy* (e.g. small cell Lung CA)

PION – e.g. post-op, trauma, shock

CNS

Migraine

Compressive Lesion – e.g. rapidly expanding like pituitary apoplexy

Cortical Blindness – hypoxia, hypotension, PRES*,see more complete list under unexplained visual loss

Other

Sudden Refractive Changes: e.g. loss of accommodation, high Blood Glucose, etc.