NEUROPATHIES… OF THE OPTIC VARIETY

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OBJECTIVES

- Define abnormalities of the optic nerve
  - Very little on glaucoma
- Discuss diagnosis
- Review ancillary testing that may aid in diagnosis
- Differentials
- Cases

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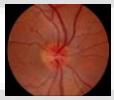
DEFINITIONS



- Optic Neuropathy – refers to any state that causes damage to the optic nerve
- Optic Atrophy – ONH pallor secondary to axonal death
- Papilledema – Swelling of the ONH secondary to increased intracranial pressure (ICP)
- Optic Neuritis – Inflammation of the optic nerve
  - Papillitis – Anterior inflammation (visible ONH swelling on ophthalmoscopy)
  - Retrobulbar – Posterior inflammation (No visible ONH swelling on ophthalmoscopy)
  - Neuroretinitis – Disc edema with significant macular edema (macular star)
- Pseudo disc edema - False appearance of swelling

Image: http://eyewiki.aao.org/Leber_Hereditary_Optic_Neuropathy

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OPTIC NEUROPATHIES

- Glaucoma
- Papilledema
  - PTC
- Optic Neuritis
- Ischemic
  - AION
    - AAION
    - NAION
  - PION
- Traumatic Optic Neuropathies
- Infiltrative Optic Neuropathies
- Compressive Optic Neuropathies
- Hereditary/Congenital Optic Neuropathies

Image: www.pbrnehealthchannel.com

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IS THIS GLAUCOMA?

Glaucoma

- Pink rim tissue
- Increased IOP
- Unless late stage:
  - Color normal
  - VA normal
- Sharpened rim edge that may be thinned or obliterated
- VF loss associated with focal RNFL loss
- Change in vision is generally slow

Non-Glaucoma

- Pale rim tissue
- Normal IOP
- Color, VA may be affected acutely
- Gentle rim sloping or intact rim 360 with pallor
- VF loss variable
- Sudden vision changes

Remember that it is possible to have glaucoma AND an additional optic neuropathy

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IS THERE A PROBLEM WITH THE MACULA?

Macular

- VA reduced
- Possible reduction in color (mild)
- Variable contrast sensitivity
- Metamorphopsia
- No APD (unless severe)
- May have a hyperopic shift with ME

Optic Neuropathy

- Highly variable VA
- Color vision defects
- Decreased contrast sensitivity
- Possible central or cecocentral relative scotomas
- APD common
- No change in RE

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THE PALE NERVE

- A nerve that is pale indicates there has been a problem in the anterior visual pathway (up to the LGN)
- A dead nerve cannot be a swollen nerve
  - A pale nerve probably WAS a swollen nerve
- A pale color alone does not make a diagnosis of optic atrophy.
  - Remember that slight temporal pallor can be normal

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PALLOR PATTERNS

- **Papillomacular bundles (ceco-central/central scotomas)**
  - Hereditary optic atrophies (*DOA, Leber's*)
  - acute demyelinating
  - compressive
  - toxic/nutritional
- **Arcuate bundles** (arcuate scotoma)
  - inferior bundles > glaucoma
  - superior bundles > ischemic optic neuropathy (AION/PION)
- **Polar regions** (altitudinal scotoma)
  - ischemic (AION/PION)
  - trauma
- **Temporal and nasal involvement**
  - chiasmal/optic tract lesions
  - local orbital compression

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PAPILLEDEMA

- Swelling of the ONH secondary to increased ICP
- Causes:
  - Intracranial neoplasm or mass
  - Infection
    - Encephalitis
    - Meningitis
  - Intracranial hemorrhage
  - Idiopathic (most commonly)

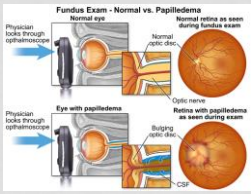

Image: http://www.medmovie.com/medlegal/2332pone02.html

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PAPILLEDEMA

Signs

- Enlarged blind spot
- ONH edema with:
  - Obscured vessels
  - RNFL hemes
  - Blurred margins
  - Disc hyperemia
- Paton's lines
- Possible ophthalmoplegia (CN6)
- Absent SVP
- Decreased c/d

Symptoms

- Often asymptomatic
- Headache
- Nausea
- TVO (lasting seconds)
- Diplopia
- Whooshing sounds
- Tinitus
- Dyschromatopsia
- Vision loss

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PAPILLEDEMA

- RNFL hemes
- Obscured vessels
- Blurred margins
- Disc hyperemia
- Paton's lines

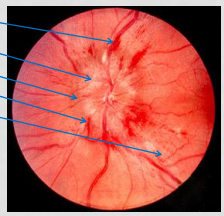

Image: http://en.wikipedia.org/wiki/Papilledema

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PAPILLEDEMA

- Workup:
  - Patients should be imaged to r/o intracranial mass and venous sinus thrombosis
    - MRI/MRV of brain and orbits with and without contrast
  - A normal MRI warrants lumbar puncture
    - Opening pressure
  - Check BP
  - Additional labs if LP is WNL:
    - CBC, ESR, CRP, ANCA, ACE, ANA

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PSEUDO DISC EDEMA

- These are usually normal variants
  - Tilted disc
  - ONH drusen
  - Hyperopic eyes
  - ONH hypoplasia (double ring sign)

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TILTED

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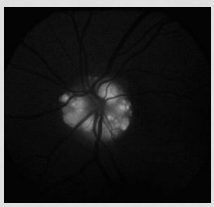
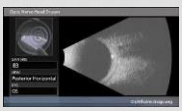
ONH DRUSEN





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HYPEROPIA

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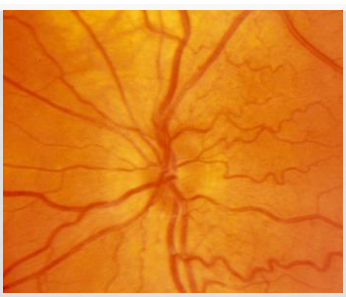
HYPOPLASIA



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PSEUDOTUMOR CEREBRI

- Most common cause of papilledema
- Seen classically in **F**at, **F**ertile, **F**emales (2:1)
- 5 criteria (Modified Dandy Criteria)
  1. S&S of increased ICP
  2. Increased CSP pressure
  3. Normal neuro findings (except 6th nerve pasly)
  4. Normal neuroimaging (no mass or thrombosis)
  5. No other identifiable reason for increased ICP

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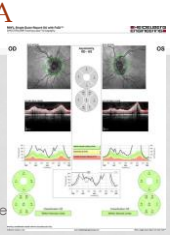
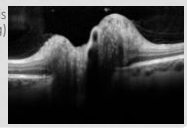
PAPILLEDEMA

- Treatment
  - Co-manage: Neurology is generally responsible for Tx of Papilledema
  - Take OCTs to monitor progress of ONH edema
  - In PTC, weight loss is often effective in reducing ICP
  - CAIs and Diuretics such as Diamox or Furosemide are often prescribed
  - Surgery may be indicated if no other treatment is effective (ON sheath decompression or shunting)
  - If another inflammatory etiology is identified, treatment of the underlying condition often relieves neuro symptoms.





Images: http://retinagallery.com/displayimage.php?album=809&pid=7021#top_display_media

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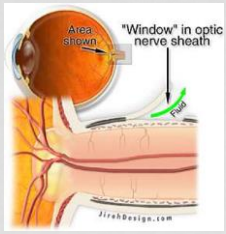
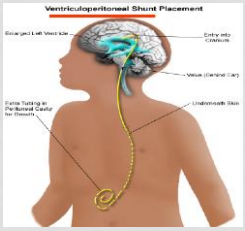
PAPILLEDEMA

- Surgical Treatment





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CASE 1

- 40 yo WF
- CC: Loss of VA in OD
- HPI: started 2 weeks ago. Dull retro-orbital ache. Color and contrast also seem to be decreased. Also lost vision 1 year ago in the left eye but resolved spontaneously
- PMHx: Migranes
- POHx: RCE OD
- Meds: Allegra-D®, Multivitamin

Case info and images courtesy of University of Iowa Ophthalmology and Visual Sciences

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CASE 1

- BCVA:
  - OD: 20/20
  - OS: 20/20
- Pupils:
  - OD: 1-2+ APD
- EOMS:
  - FROM OU with pain on adduction and abduction OD
  - Red target testing revealed red desaturation OD temporally and centrally, normal OS
- SLE: WNL OU

Case info and images courtesy of University of Iowa Ophthalmology and Visual Sciences

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CASE 1

- DFE: WNL except for trace temporal pallor OS. Small C/Ds

Case info and images courtesy of University of Iowa Ophthalmology and Visual Sciences

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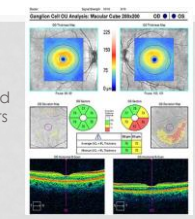
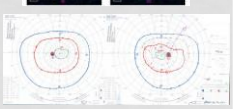
CASE 1

Additional Testing

- Goldmanm Perimetry
  - OD: Inconsistent answers and mild constriction of I2e and I1e isopters
  - OS: Full
- OCT ONH:
  - WNL
- Ganglion Cell Analysis + IPL
  - OD: Normal ganglion cell layer thickness
  - OS: Reduced ganglion cell layer thickness inferiorly





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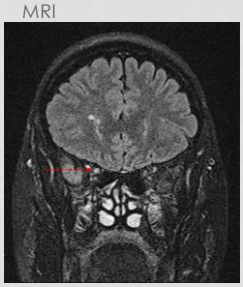
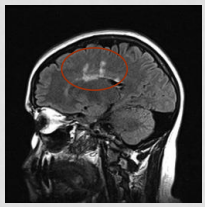
CASE 1

MRI





Case info and images courtesy of University of Iowa Ophthalmology and Visual Sciences

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CASE 1

- Diagnosis
  - Optic neuritis of the right eye with a presumed previous episode of optic neuritis in the left eye

Case info and images courtesy of University of Iowa Ophthalmology and Visual Sciences

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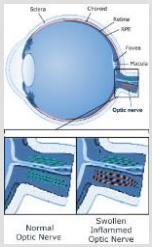
OPTIC NEURITIS

- Inflammation of the ONH
- Usually in younger pts (< 45 y.o.)
- Many have h/o previous episodes

- Causes:
  - Demyelination is the most common cause
  - Infectious
  - Autoimmune
  - Vasculitic



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OPTIC NEURITIS

SIGNS

- Acute decreased VA
  - 20/20 to NLP
- VF defect
  - Central/Paracentral
- ONH swelling (35%)
- Decreased CV and contrast sensitivity
- (+) APD
- Increased latency and decreased amplitude on VEP
- Altered depth perception

SYMPTOMS

- Pain on eye movement
- Dyschromatopsia
- VA loss
  - Days to weeks
- Phosphenes with eye movement or loud noises
- Decreased perception of brightness

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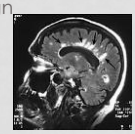
MULTIPLE SCLEROSIS

- 20% of MS diagnoses are made due to an episode of optic neuritis
- 50-60% of patients with MS will have an episode of optic neuritis (nearly 100% in post-mortem studies) Generally retrobulbar optic neuritis
- Loss of vision with pain on eye movement
- **"The doctor sees nothing, the patient sees nothing"**
- Symptoms worse with heat - Uhthoff's sign



http://emedicine.medscape.com/article/340254-overview

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MULTIPLE SCLEROSIS

- Systemic symptoms include: tingling, slurred speech, dizziness, tremor, weakness/numbness in one or more limbs
- 15-45 year olds
- Female predilection
- Decreased amplitude, increased latency on VEP
- MRI with FLAIR sequence
- Follow axonal loss with OCT

Image: www.eyesitetexas.com

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OPTIC NEURITIS TREATMENT TRIAL

- 1991 – 2006, 13 sites , 389 subjects
- Findings:
  - High dose IV methylprednisolone followed by a course of oral pred accelerated visual recovery by a few weeks.
    - However, this provided no long term benefit to vision
    - It provided a short term reduction in MS development but by 3 years, the effects had subsided
  - Oral pred alone did not improve visual outcome
    - Increased risk of new attacks
    - Placebo controls recovered vision in ~6-8 weeks and did better than the oral pred cohort
  - Brain MRI is an excellent predictor of early MS risk after optic neuritis
    - Pts with 1 or more lesions carry a 72% risk of MS development within 15 years
  - If a pt did not show brain lesions on MRI, factors that are associated with a low 5 year risk of MS
    - Lack of pain, optic disc edema, peripapillary hemes, retinal exudates, mild vision loss

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OTHER CAUSES OF OPTIC NEURITIS

- Infectious:
  - Syphilis (VDRL, FTA-ABS)
  - Cat-scratch disease (bartonella henselae)
  - Lyme Disease
  - TB
  - Herpes
- Inflammatory
  - Sarcoid (ACE)
  - SLE (ANA)
  - Papillophlebitis
- These etiology should be ruled out in atypical cases

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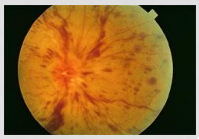
INFLAMMATORY

- Papillophlebitis (Big Blind Spot Syndrome)
  - Think CRVO in a healthy, young adult
  - Same considerations as a CRVO in an elderly pt
    - Increased area of capillary non-perfusion increases risk of neo
    - Watch IOP – neovascular glaucoma
    - Monitor at least monthly until resolution
    - If non-ischemic : Good prognosis



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CASE 2

- 69 year old white male
- CC: "Vision in my right eye seems to be blurry near my nose" Started 2 days ago
- PMHx: Hypertension x 22years. Controlled
- POHx: 2 years ago, suddenly lost vision in OS. Unsure of cause
- BCVA:
  - OD: 20/16
  - OS: 20/40
- Pupils: 1+ APD OS.
- EOMs, CVF: WNL
- IOP
  - OD: 16 mmHg
  - OS: 15 mmHg
- C/D; 0.1 OD,OS
- Anterior seg: WNL except for 1+ NS

Case presentation and images: Retinagallery.com

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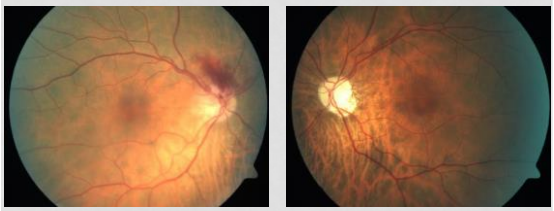
CASE 2



Case presentation and images: Retinagallery.com

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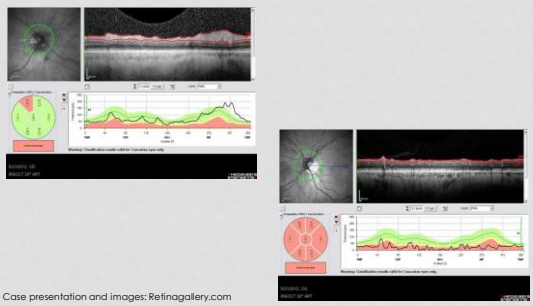
CASE 2



Case presentation and images: Retinagallery.com

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CASE 2

- Orders?
  - CBC with ESR and CRP
- BP: Ensure proper control
- Consider ASA

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ANTERIOR ISCHEMIC OPTIC NEUROPATHY

Arteritic

- Nearly always from Giant Cell Arteritis (GCA)
- Minority of AION cases
- Fellow eye is involved within 2 weeks (75%) without treatment (systemic steroids)
- Visual recovery may occur in affected eye with treatment
- ESR and CRP elevated

Non-Arteritic

- Many contributing factors but may be spontaneous
- Majority of AION cases
- 40% involvement of fellow eye
- Treat underlying association
- Consider daily aspirin

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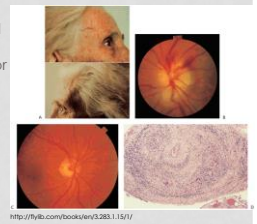
Arteritic Anterior Ischemic Optic Neuropathy

- Occurs in the setting of GCA.
- Disc may be swollen initially but often becomes cupped and pallid
- >55 years old but often older
- Look for APD, color vision, central or altitudinal VF defects.
- May have 6th nerve palsy
- Labs: CBC, ESR, CRP
- Must ask about:
  - Temporal pain
  - Jaw Claudication
  - Headaches
  - Fever
  - Fatigue
  - Weight loss
  - Transient vision loss
  - Polymyalgia rheumatica



http://flylib.com/books/en/3.283.1.15/1/

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AAION WORK UP

- Sensitivity of blood work
  - ESR 76% to 86%
  - CRP 97.5%
  - Both 99%
- Temporal artery biopsy is needed to confirm diagnosis
  - Pts are usually on steroids for a year or more
  - GCA pt population is not ideal for long term steroid use so correct diagnosis is often critical
  - Comanagement with PCP, neuro-ophthalmology/neurology

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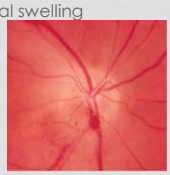
NAION

- Generally younger (40-60) with sectoral swelling (commonly)
- Flame shaped hemes
- VF defects (inferior altitudinal)
- Normal ESR
- "Disc at risk"
- May be spontaneous but occurs in association with hypercholesterolemia (70%), smoking (50%), HTN (40%),DM (30%),and ischemic heart disease (20%)
- Sleep apnea



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POSTERIOR AION

- Retrobulbar ischemia that does not result in ONH edema
- Rare
- Diagnosis of exclusion
- 3 types:
  - Arteritic: From GCA that affects other arteries than the posterior ciliary artery
  - Non-arteritic: Same considerations as NAAION
  - Perioperative: Due to prolonged systemic procedures (cardiac/spinal). Mechanisms include prolonged arterial hypotension (blood loss, prolonged anesthesia), anemia, periorbital edema and even direct ONH compression from prolonged period in prone position
    - VA loss is generally severe and permanent

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AAION VS NAION

	AAION	NAION
Age	>55	<55
Associations	GCA (may also cause CRAO)	Chol, HTN, DM, Ischemic heart disease, smoking
Systemic Symptoms	HA, scalp tenderness, jaw claudication, arthritis, weight loss	Usually none, consider meds, h/o sleep apnea
Ocular S&S	Vision loss, APD, color defect, swollen ONH (pale)	Vision loss, APD, color defect, swollen ONH (sectoral), more hemes
Testing	CBC, ESR, CRP (all elevated), TAB	CBC, ESR, CRP (normal)

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CASE 3

- 61 yo F, frail,100lbs
  - 12/09: admitted to hospital for SOB, started rifampin, ethambutol 1200mg, 2 to TB
  - 3/10: VA blurry, trouble reading
  - 4/10: VA CF OU
  - 5/10: MRI ordered, told mini-cva
  - 5/10: D/C ethambutol & rifampin

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CASE 3

7/5/10
- VA: 20/400 OU
- Pupils: reactive no APD
- CF: central scotoma
- IOP: 17mmHg
- Fundus: mild temp pallor
- MRI report: encephalomalacia postlateral R occipital lobe: old infarct

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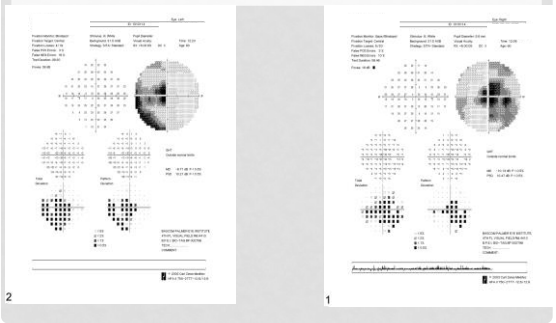
CASE 3



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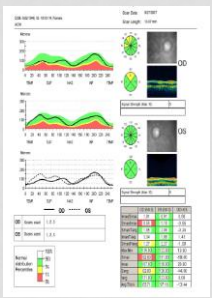
CASE 3



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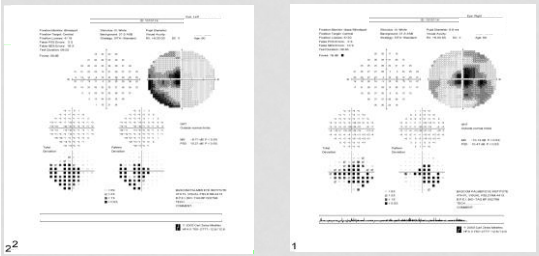
CASE 3

2 months later



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ETHAMBUTOL OPTIC NEUROPATHY

- Affects the optic nerve and spreads to the anterior chiasm
- Dose dependent
  - Increased risk if > 25 mg/kg/day
- Usually manifests within 2-4 months but possibly sooner
- Central/cecocentral scotomas in drug toxicities
  - Ethambutol may present with bitemporal scotoma
- Usually improves with d/c of drug but not always full recovery

Image: www.sciencephoto.com

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TOXIC OPTIC NEUROPATHY

- Most commonly from Ethambutol
  - Other toxic agents include:
    - Isoniazid
    - Chloramphenicol
    - Streptomycin
    - Lead
    - Arsenic
    - Chloroquine
    - Methanol/Ethanol
- Remember that an APD will only be present in unilateral/asymmetric cases. Toxic causes of optic neuropathy are often bilateral and symmetric

Image: www.glogster.com

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NUTRITIONAL OPTIC NEUROPATHY

- Often associated with alcohol or tobacco toxicity since abusers may be malnourished
- Mainly lack of B vitamins
  - B_1 (Thiamine)
  - B_2 (Riboflavin)
  - B_6 (Pyridoxine)
  - B_{12} (Cobalamin
  - Folic acid
- Treatment is supplementation of appropriate vit, although prolonged malnutrition may result in irreversible damage

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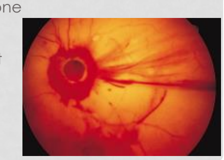
TRAUMATIC OPTIC NEUROPATHIES

- Can be from direct or indirect trauma
- Direct
  - Penetrating foreign body or bone fragmentation
- Indirect
  - Transmission of energy through the skull that results in damage of the canalicular portion of the optic nerve due to deformation of the sphenoid bone
  - Optic Nerve Avulsion – detachment of the ONH from the point of attachment with the globe. Usually due to deceleration injuries (auto accidents)



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INFILTRATIVE/COMPRESSIVE OPTIC NEUROPATHY

INFILTRATIVE

- Sarcoid
- Several malignancies
  - Lymphoma
  - Leukemia
    - Emergency in pediatric patient. Immediate radiation is needed to save vision
  - Carcinoma
  - Any metastasis

COMPRESSIVE

- Neoplasms
  - Intraorbital
  - Suprasellar (pituitary adenoma most commonly)
- TED
- Hematoma

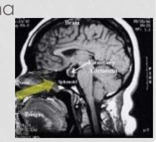

Image: http://www.brain-surgery.com/insensitive-pituitary-adenoma-dealing-with-radiation/

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HEREDITARY

- Dominant Optic Atrophy
  - Most common hereditary optic neuropathy
  - Avg age of onset = 4-6 years old
  - Wedge shaped pallor and excavation of the temporal disc
  - May have PPA, non-glaucomatous cupping, arterial attenuation and loss of foveal light reflex

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HEREDITARY

- Leber's Hereditary Optic Neuropathy
  - Mitochondrial DNA mutation
  - 10- 30 year old males (9:1 predilection)
  - Unilateral rapid, severe vision loss followed by vision loss in the fellow eye within a year (as soon as days to weeks)
  - CLASSIC TRIAD:
    - Peripapillary telangiectasia
    - Hyperemic disc with RNFL swelling
    - No leaking of the disc on FA
      - Distinguishes LHON from true disc edema
  - Prognosis is better if mutation is identified at point 14484

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CONGENITAL

- Morning Glory Syndrome
  - Unilateral large disc surrounded by an elevated ring of pigment with central glial tissue
  - May be a form of optic nerve coloboma
  - Females > Males (2:1)
  - Possible local serous retinal detachment
  - Usually severe vision loss

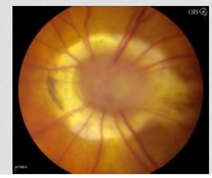

Image: http://retinagallery.com/displayimage.php?album=search&cat=0&pid=7505#top_display_media

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CONGENITAL

- ONH hypoplasia
  - May be unilateral (idiopathic etiology) or bilateral (associated with maternal DM, or drug use)
  - Classic "double ring" sign due to visualization of the scleral tissue
  - VA ranges from normal to NLP
  - Up to 50% have a constant tropia (generally eso)

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THANK YOU!!!

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