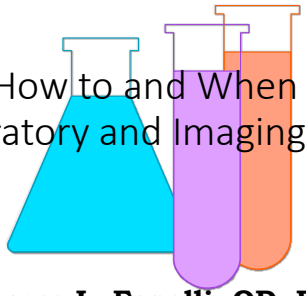
How to and When to: Laboratory and Imaging Studies



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Disclosures

- I have received honorarium and/or serve on he advisory or speakers bureau of:
- Allergan
- Alcon
- Heidelberg
- Review of Optometry
- CE in Italy

There are no conflicts of interests in this presentation

Goals of the Presentation

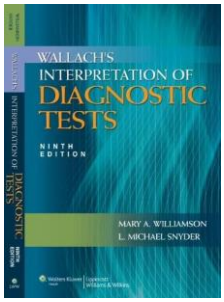
- One Goal, and One Goal Only:
- To give you one nugget of information that you can take home and actually use in your practice, maybe two.
  - Use that information to make you a better clinician

Course Outline

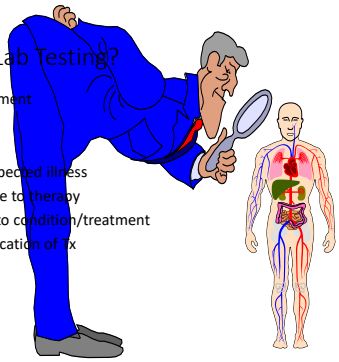
- Lab Studies for Anterior Segment Disease
  - Uveal tract
- Lab studies for Posterior Segment Disease
  - Retinal vascular
    - Arterial
    - Venular
  - Optic Nerve

Course Outline

- Review of indications for imaging
- Recommended imaging techniques



Why order Lab Testing?



- Objective measurement
- Helpful in DDx
- Dx confirmation
- Screening for unsuspected illness
- Monitor compliance to therapy
- Monitor response to condition/treatment
- Medico-legal justification of Rx

Why Order Testing???

Clinical Confirmation
confirmatory diagnosis
Adjunct to Thorough Examination
covering the bases

Co-Management vs. Direct Involvement
refer vs. orchestrate

Can I Order Lab/Image Test?

- Yes, most states allow ODs to order;
  - Diagnostic Laboratory test for eye related conditions
  - Radiological Imaging test for eye related conditions

What Are My Options?

- Hospital
- In-office
- Reference Laboratory
- Imaging Center
  - Hospital based
  - Private imaging center

Typical Laboratory Tests

- Complete Blood Count (CBC)
- Blood Chemistry/Profiles
- Urine Analysis
- Serology

Profile Examples

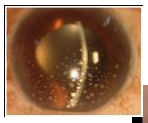
- Autoimmune Profile
  - Anti-ANA antibodies, ANA, Complement C3
- Lipid Profile (VAP Cholesterol)
  - Cholesterol, HDL, LDL,Triglycerides
- Thyroid Function Profile
  - Free Thyroxin index (FTI), T4, T3 Uptake, Thyroid Stimulating Hormone (TSH)

Imaging Tests Available

- Plain Film X-Ray
- Computed Tomography (CT)
- CT Angiography (CTA)
- Magnetic Resonance Imaging (MRI)
- Magnetic Resonance Angiography (MRA)
- Magnetic resonance Venography (MRV)
- Carotid Doppler Ultrasonography
- Temporal Artery Ultrasonography

Anterior Segment Indications for Laboratory Studies

- Typically for the evaluation of patients with chronic, recalcitrant and/or bilateral ocular inflammation
  - Uveitis
  - Episcleritis
- Graves Disease

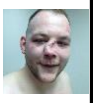


Uveitis

- BEFORE ordering lab tests or referring the patient out for secondary treatment:
  - Make sure the uveitis is being properly treated topically
  - Aggressive topical management:
    - Cycloplegia (atropine) BID-QID
    - Pred Forte (Dexamethasone) Q1-2H

Anterior Segment Inflammation

- Episcleritis
  - Often induced by exogenous sources
    - OSD, DES, environment, chronic allergies
      - Eliminate the etiology
    - ?? 25% of cases have underlying etiology
- Uveitis
  - Often induced by extraneous sources
  - ??? % systemic etiology
    - Infection—Zoster, bartonella
    - Autoimmune--rheumatoid, sarcoid, ankylosing spondylitis
    - Inflammatory—IBS, Crohn's



Ant Seg Inflammation

- Autoimmune Diseases
  - 20-50 y/o
  - Underlying inflammation suspected
    - In early stages of (unknown) disease, many patients will test negative
    - > 2/3 of patient will initially not be lab+
  - The chronicity of the ant seg inflammation is what threatens vision

International Uveitis Study Group

Ant Seg Autoimmune Dz

- These present a diagnostic challenge in clinic
- Thorough history is critical
- Rheum consult?
- Negative finding = idiopathic

Anterior Seg Inflammation

- Sarcoidosis
  - Inflammatory disease systemwide
  - 'granulomatous' uveitis
  - Pulmonary infiltration/granuloma
  - Elevated ESR and ACE
    - ACE is produced by endothelial cells and monocytes
    - ACE is elevated in 60-90% of active sarcoidosis
    - ACE can also be elevated in Histo/Toxo/TB

Anterior Seg Inflammation

- Rheumatoid/Lupus and JRA
  - Different demographics…autoimmune
  - Adult rheumatoid difficult to Dx early on
    - Weekend warrior? Getting old?
  - Rheumatoid Factors (RF)
    - Various antibodies + in 70-90% pts w Rheumatoid
  - ESR and CRP
    - A measure of current activity

Rheumatoid--Autoimmune

- ANA (anti nuclear antibodies)
  - Immune system attacking cell nuclei
  - When elevated, may indicate several autoimmune disorders
  - When low, less likely to have Lupus (SLE)

- HLA-B27
  - A genetic marker elevated in diseases that are seronegative spondyloarthropathies
    - Ankylosing Spondylitis
    - Psoriatic Arthritis
- Compliment System
  - Various proteins involved in mediating inflammation
  - When low, inflammation generally symptomatic

Don't forget Syphillis

- The great mimicker
- An infection associated with disseminated inflammation

Take Home Lab Pearls-Anterior

- For all uveitis patients:
- CBC with Diff
- ESR
- CRP
- RF
- ANA
- FTA-Abs
- VDRL or RPR

Take Home Lab Pearls-Anterior

- If Sarcoid or TB suspected, add:
  - ACE
  - CXR
- If younger and suspected AS or Reiter's, add:
  - HLA B27
  - PA and LAT lumbar plain films
- Infectious? Add:
  - Lyme?? (ELISA then Western Blot), toxo titers as warranted by history

Posterior Segment Indications

- Retinal inflammatory/infectious
  - Retinology handled
- Retinal Vascular
  - Hemorrhage
  - Arterial
  - Venular
  - Optic Nerve

Retinal Hemorrhage

- Associated with a variety of etiologies
  - Diabetes, HTN, atherosclerosis, Valsalva, infection, trauma, red cell etiologies, white cell etiologies etc etc etc

Complete Blood Count (CBC)

- WBC w/ Differential
- RBC Count
- Hematocrit
- Hemoglobin
- RBC Indices (MCV, MCH, MCHC)
- Peripheral Blood Smear
- Red Cell Distribution
- Reticulocyte Count
- Platelet Count

Table 1: Complete blood count (CBC) before treatment

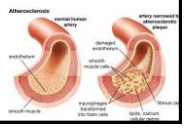
Parameters	Results	Reference values
Red blood cells count (10^{12}/l)	4.6	5–7.9
Packed cell volume %	27	30–45
Hemoglobin Conc. (g/dl)	8.7	12–19
White blood cells (10^{9}/l)	4.3	3–14.1
Neutrophils %	34	58–83
Lymphocytes %	48	8–24
Monocytes %	3	2–10
Eosinophilia %	2	0–3
Basophils %	Nil	0–1

CBC

- 70-80% of hematological diseases can be diagnosed by simple CBC
- Do you run labs on all retinal heme patients?????

Atherosclerosis Risk in Communities Study ARIC

- Initiated by the National Heart Blood and Lung Institute
  - Investigate factors that are involved with the development of atherosclerosis and the incidence of CHD, stroke and other cardiovascular diseases
  - Measure cardiovascular disease rates in communities over time
  - 15,792 initial participants



ARIC Stroke and Retinopathy

- Wong et al
- 1684 participants
- One arm of study compared MR findings with retinopathy in the context of STROKE
- retinopathy included:
  - microaneurysms, retinal hemorrhages, soft exudates, hard exudates, macular edema and optic disc swelling

ARIC Prelim Results

- The overall incidence of stroke was found to be related to:
  - 1: MR findings of white matter lesions
  - 2: presence of "retinopathy"

ARIC
Does Retinopathy relate to MR Lesions

- Findings:
  - No retinopathy:
    - 9.9% have MR lesions
    - 1 out of 10
  - With retinopathy:
    - 22.9% have MR lesions
    - 1 out of 4 !!!

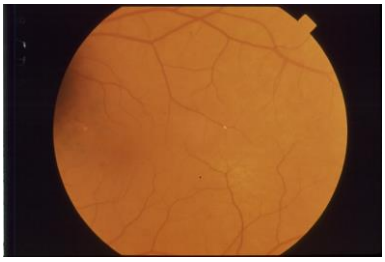
What about both together in a patient???

Atherosclerosis Risk in Communities

- Findings:
  - 5year cumulative incidence of stroke:
    - (-) white matter lesions and (-) retinopathy: 1.4%
    - (+) white matter lesions and (+) retinopathy: 20.0%
  - The study suggests that healthy people with white matter lesions detected by MRI may benefit from a retinal examination to assess their risk of stroke.

Retinal Arterial Indications

- Emboli

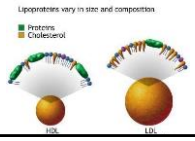


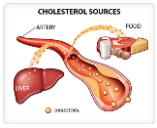
What About Cholesterol

- We know we have a problem in the USA
- Modify my Habits?????
- Just give me Lipitor

Lipoproteins

- 5 categories
  - HDL (high density lipoproteins)
  - LDL (low density lipoproteins)
  - Chylomicrons
  - VLDL (very low density lipoproteins)
  - IDL (intermediate density lipoproteins)



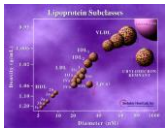


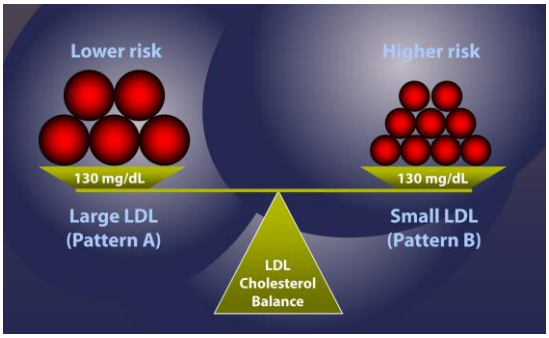
Low Density Lipoprotein

- One type of lipoprotein that transports cholesterol and triglycerides from liver to peripheral tissues
- Serum is water based; LDL's allow fats and cholesterol to circulate
- LDL particles vary in size and density
  - Subtype A
    - Larger, less dense
  - Subtype B
    - Smaller, more dense

LDL Subtypes A and B

- Subtype B is more likely to penetrate vascular endothelium
  - More highly associated with risk of CAD
- normal vascular endothelial gaps are about 26nm





Measurements of LDL

- Measurement of LDL is widely available and relatively inexpensive
- Not very well correlated with development of atherosclerosis
- Measurement of sub types of LDL are more correlated with cardiovascular disease

Accurately Assessing Risk

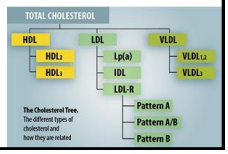
- 85% of lipid panels are same basic testing available for years 1970's
- Estimates LDL-C levels
- Recent data:
  - 1.3M US adults
  - Calculated LDL vs measured LDL
  - Friedewald is lower than direct LDL in high risk patients
    - Risk UNDERESTIMATED by 25-60%

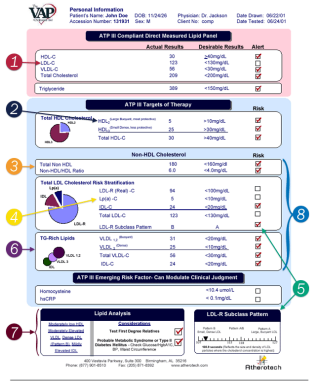
Friedewald Estimated vs Directly Measured LDL-C and Treatment Implications. J. Amer. College Cardiology. 62.8 732-739 August 2013 Martin, Blaha et al

THE VAP TEST FROM ATHEROTECH®

YOUR HEART PARTNER™

- Vertical Auto Profile
- Directly measures LDL
  - Friedewald Formula not accurate when triglycerides are elevated
- LDL Pattern B
- LDL Pattern A





Take Home Pearls

- Standard LDL calculations don't mirror the RISK of atherosclerosis
- New substrates: apoB, apoA1, and stratification of LDL types are being looked at as *predictors* of AS
- AS includes a whole host of ophthalmic conditions

When does ASCVD Begin?

- PDAYS Study
  - Pathobiological Determinants of Atherosclerosis in Youth Study
  - Lesions in the intimal lining of ALL the aortas and 50% of the Right Coronary Arteries are present by age 9

Homocysteine (AminoAcid)

- Elevated plasma levels of homocysteine is an established risk factor for ASCVD, Cerebrovascular disease, perpheral vascular occlusive disease
- Hcy levels are lower in premenopausal women than in men and post menopausal women
  - May be related to the increased incidence of ASCVD in postmenopausal women

Homocysteine and the Eye

- Include Hcy levels in work up of patients with:
  - ASCVD
  - emboli
  - TIA, TVB
  - retinal vascular disease,
  - neuro visual field defects,
  - vascular diplopia

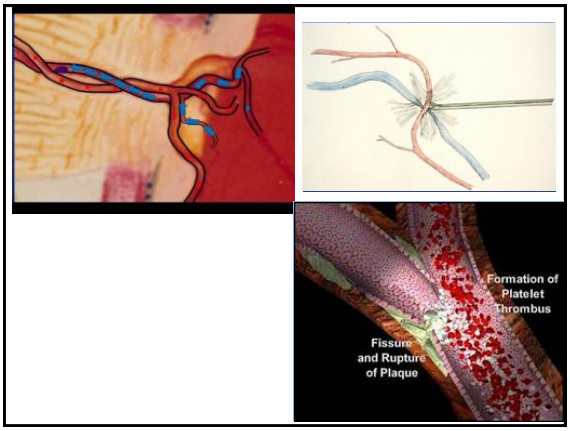
Retinal Vein Occlusions

Retinal Vein Occlusions: Etiology????

- What is the underlying problem?
  - THROMBUS
- Our goal, clinically, is to determine HOW that thrombus formed

Retinal Vein Occlusions

- Did the thrombus form because a thick walled artery compressed a thin walled venule?
  - Then ASCVD is the underlying problem
- What if there is no evidence of ASCVD causing a compressive etiology?
  - Clotting moves up the differential list



Clotting Considerations in RVO

- In the absence of clinical findings of ASCVD (no dyslipidemia, no diabetes, no HTN…)
- What can make the patient clot more readily?

Antiphospholipid Syndrome APS

- AKA: antiphospholipid antibody sydrome
- Autoimmune where by antibodies (anticardiolipin antibodies) are produced that ultimately increase coagulability
  - Arterial and venular thrombus formation
- 'younger' individuals
  - History of multiple miscarriages

Factor V Leiden

- Genetically inherited autosomal dominant
- Anticoagulant protein C cannot inactivate Factor V…..coagulation
  - Primarily venular thrombus formation
- Consideration in young patients <45 and Caucasians of European descent

Labs for Coagulability

- CBC
- Anticardiolipin Antibodies
  - ELISA
- Factor Leiden V
  - Lab to determine

Retinal Vascular Labs: Summary

- Considerations of which labs is predicated upon patient specific findings……ALWAYS!

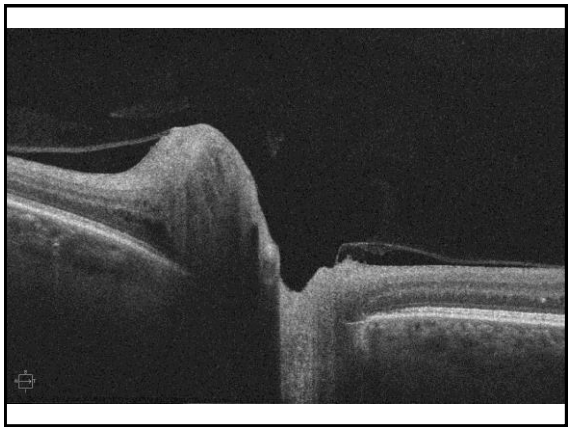
- CBC as baseline
- ASCVD etiology???
  - Lipids, stratified
  - Diabetes, HTN, obesity, smoking???
  - Homocysteine
  - CRP
- Extraneous coagulation
  - Antiphospholipid antibodies
  - Factor V Leiden

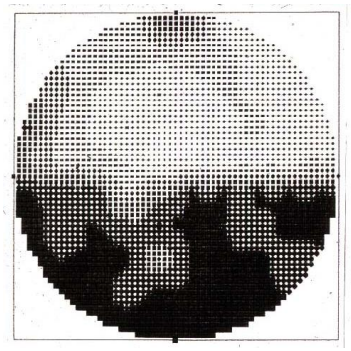
Optic Nerve Indications

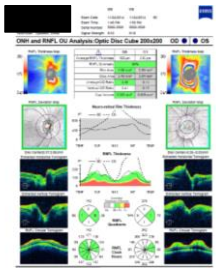
- NAION
- AAION

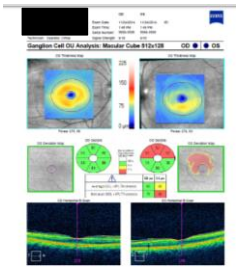
57 y/o Hispanic Woman

- c/o acute loss of vision OS
- BCVA:
  - 20/20 OD
  - 20/200 OS



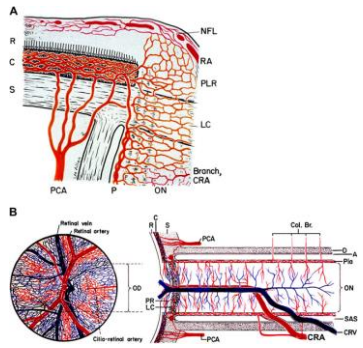






Nonarteritic Anterior Ischemic Optic Neuropathy (NAION)

- 2nd most common optic neuropathy
- Age > 50
- Caucasian predilection (based-on cup size)
- Rapid onset painless vision loss (+/- acuity)
- Afferent pupillary defect



Risk Factors for NAION

- Hypertension: 34-47%
  - *Only significant for young, age-matched NAION patients*
- Diabetes: 10-24%
  - *Statistically significant for all ages of NAION*
- Homocysteine (?)
- MI (?)
- Smoking (?)
- Stroke (?)
- CRP (?)
- Thrombophilic factors (lipoprotein (a), factor V Leiden) (?)
- *Iatrogenic factors (PDE-5 inhibitors) (?)*

Lee MS, et al.*Ophthalmology* 2011
INagy V, et al. *Graefes Arch Clinc Exp Ophthalmol* 2005
Arnold AC *J Neuro-Ophthalmol* 2003
Pianka et al. *Ophthalmology* 2000

Optic Disc - Acute

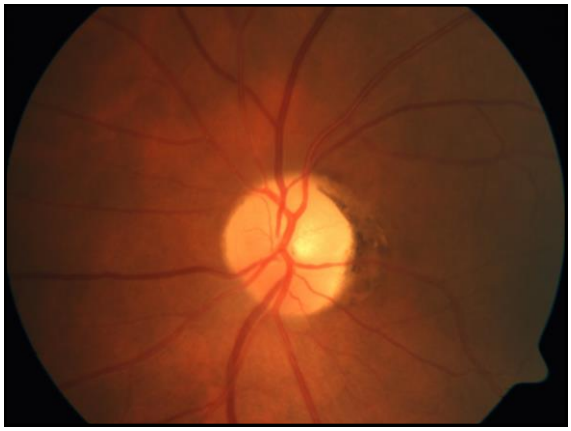
- Disc edema with mild-modest hemorrhage
  - Coexistent or preceding vision loss
- Prelaminar capillary telangiectasis
- Juxtapapillay arteriolar attenuation & sheathing
- *Small cup in same/fellow eye ("disc at risk")*

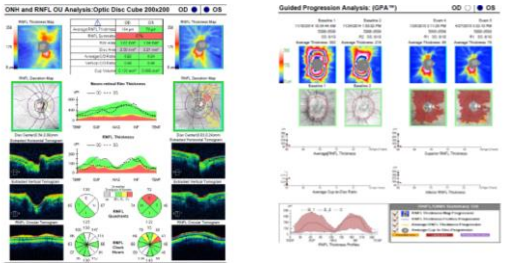
Optic Disc - Chronic

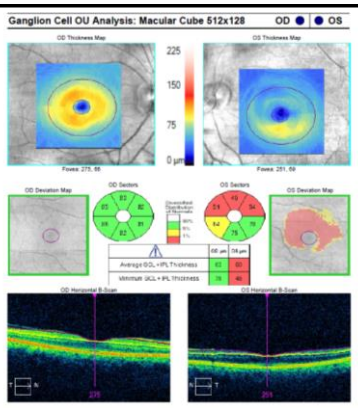
- Rapid optic atrophy
  - *< one month*

F/U x 6 months

- BVA:
  - 20/20 OD
  - 20/80 OS







Visual Recovery with NAION (IONDT results)

- Optic nerve sheath decompression
  - Improved: 32.6%
  - Worsened: 23.9%
- Followed
  - Improved: *42.7%*
  - Worsened: *12.4%*

IONDT Research Group *JAMA* 1995

Clinical Kernels: NAION

- Older age than optic neuritis
- Vasculopathic risk factors (notably diabetes)
- No pain!
- Some disc hemorrhage
- Altitudinal field / ganglion cell complex loss
- Approximately 40% spontaneous visual improvement (dyschromatopsia not as pronounced as in ON)
- PDE-5 inhibitors (?)

Arteritic AION/ GCA

- GCA is an arterial vascular disease
  - It affects arteries of medium size
  - Temporal artery as well as other distributions of the external carotid
- 2-10% of GCA patients develop a CRAO either at onset of other symptoms or at a later date

GCA/AION

- Sudden onset of vision loss
- Fatigue, malaise, claudication, neck pain, facial pain
- + APD
- Disc swelling/hemorrhage

- Older than NAION

GCA/AION

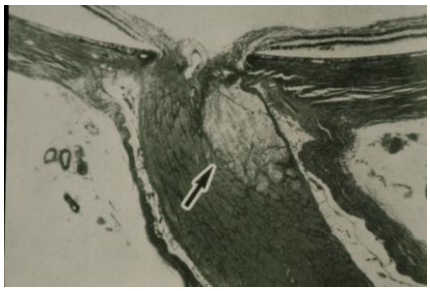
- Vision loss is severe, and other eye is at risk

- STAT Labs:
  - CBC w Diff
  - ESR
  - CRP

GCA/AION

- C Reactive Protein levels:
  - are a marker of vascular inflammation
  - if elevated, are a risk factor for cardiovascular disease
  - if elevated, are more sensitive in determining AAION than ESR

Inflammatory Disease - AION Discussion



Ischemic Optic Neuropathy

- **Hayreh et al**
  - **AJO March 1997**
    - **ascertained reliability, sensitivity and specificity of signs, symptoms and diagnostic tests for early diagnosis of GCA**
  - **Findings most strongly suggestive of GCA:**
    - **1: jaw claudication**
    - **2: C-reactive protein > 2.45mg/dl**
    - **3: neck pain**
    - **4: ESR > 47mm/hr**

Ischemic Optic Neuropathy

- **Hayreh et al, AJO March 1997**
- **Sensitivity of CRP: 100%**
- **Sensitivity of ESR: 90%**

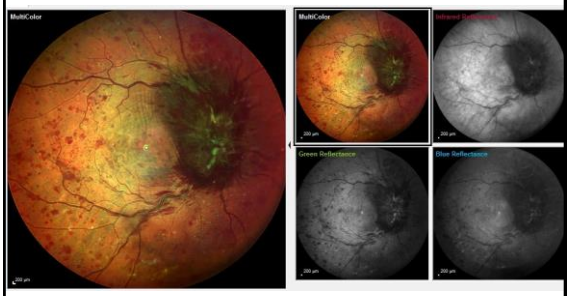
- **ESR + CRP gave best specificity (97%)**

Clinical Kernel: Arteritic-AION

- AKA: Giant Cell Arteritis
- Elevated CRP and ESR
- Patients need to be medicated with oral steroids (60-80 mg/day)
- Definitive diagnosis is via temporal artery biopsy
  - Biopsy must be made within 2-3 days of starting PO steroids
  - Temporal artery ultrasonography

Case

- 82 y/o new patient referred for evaluation of vision loss OD
- Difficult historian…onset of symptoms vague
- Recent cessation of HTN and cholesterol meds secondary to lethargy 'not feeling well
- CF OD
- + APD OD



Case

- ESR = 18
- CRP = 0.45
- BP in office 198/106

Case Not GCA!

Case Management

- HTN and Lipid control…D/C ASA

Case Management

Retinal Vascular/ON Summary

- Atherosclerosis remains a significant etiology for many retinal vasculopathies
- Venular Problem?
  - AS, clotting etiologies….history and demographics
- Non Glaucomatous Optic Neuropathies
  - Sudden vision loss, APD
  - History and demographics.

IMAGING
Part 2

Plain Film X-Ray

- Electromagnetic Radiation
- Exposure Film
- Advantages: Fast, Widely Available, Inexpensive
- Disadvantages: Limited Value, Radiation to the Eye and Body
- Indications: Fractures, Chest/Sinus Films, Foreign Body Localization
- Ordering: Series Requested, Tentative Dx, Views Requested

Plain Film X-Ray

- Fairly limited use in primary eye care
- Typically CXR and Lumbar PA and Lateral Views
  - Sarcoidosis
  - Reiter's
  - HLA-B27
  - Anklyosing Spondylitis

Computed Tomography

- Many advantages:
  - Readily accessible
  - Inexpensive
  - Good overall views
- Disadvantage:
  - Electromagnetic radiation
  - Does not image soft tissue well

Computed Tomography

- What it images well:
- Bone
- Air
- Fresh hemorrhage

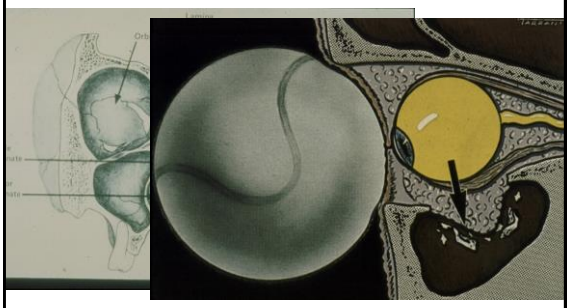
Computed Tomography (CT)

- Same Physics as Plain Film
- Computer Integrated & Image Formation
- Soft Tissue Differentiation
- Contrast Enhancment Usually Recommended
- Indications: Orbital Fx, Foreign Body, Intracranial Acute Hemorrhage (sub Arachnoid), Sinus
- Ordering: Same as Plain Film, w/ or w/o Contrast

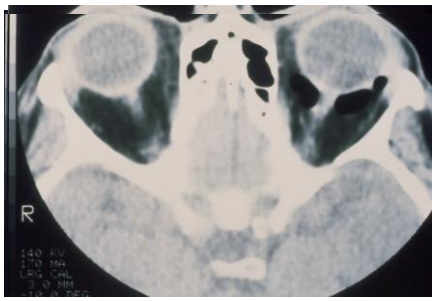
CT - Orbital Trauma (Subjective)

- 52 YOWF c/o Face vs. Ground in Bike Accident. She Denies Reduced VA or Diplopia. Her Cheek is Tender and c/o Retro-Orbital Pain when Sneezing.
- POHx: Unremarkable
- PMHx: Unremarkable
- Meds: None
- NKDA

CT - Orbital Trauma Discussion



CT - Orbital Trauma Image Results



CT Angiography

- Same physics as conventional CT
  - Electromagnetic radiation
- More software intensive than conventional CT
- Contrast material usually employed
- Quickly becoming as useful as conventional angiography
  - Sharp images
  - Low morbidity and mortality

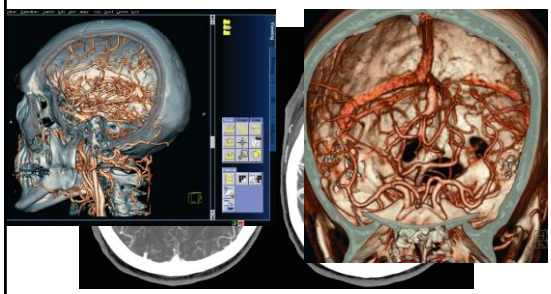
CT Angiography

- Clinical Uses:
  - Pulmonary emboli
  - Venous thrombosis
  - Aortic aneurysms and dissections
  - Carotid stenosis
  - Cerebral aneurysms
  - Cerebral tumor vascular supply
  - Coronary artery visualization

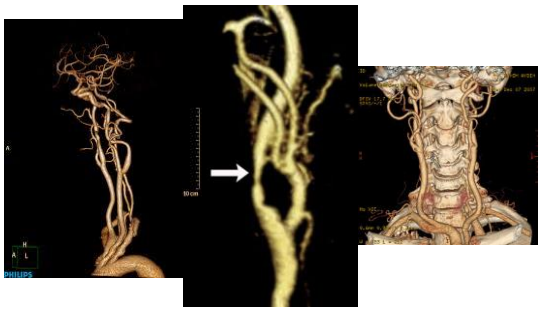
CT Angiography

- Contraindications/Complications
  - Contrast dye (iodine) related
  - Pregnancy
  - Extravasation at injection site
- Limitations:
  - Unable to visualize small vessels
  - Patient movement blurs images
  - Significant stenosis difficult to visualize

CT Angiography



CTA: Carotid Arteries

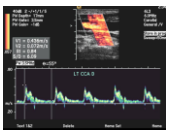


CTA: Carotid Arteries

- Digital Subtraction Angiography is considered the gold standard (Carotid Dz)
  - Risks associated with procedure
- CTA of Carotids
  - Slightly underestimates degree of stenosis
  - Less invasive, less risk
- CTA vs DSA:
  - Highly correlated

Carotid Artery Disease

- Ordering Protocol
  - Carotid Dopplers
    - Non invasive
    - 'Screener' for presence of likely disease
      - Quantifiable stenosis
  - CTA
    - Mildly invasive
    - Surgical Guidance



Magnetic Resonance Imaging (MRI)

- Atomic Orientation and Signal Production by Alternating High Levels of Magnetic Fields
- Superior for Soft Tissue Differentiation
- Gadolinium Contrast
- Special Techniques for Orbits (Fat Suppression/Surface Coils)
- Some Limitations
- Ordering: Indicate Area of Question w/ or w/o Contrast, r/o Diagnosis, Special Techniques

MRI-EOM Deficit Subjective

- Sunday page by local urgent care MD
- Has a 22 year old white female with complaints of "eyes not working together"
- MD says vision good, pupils look OK, but her eyes are doing something he has never seen before
- Sounds like decompensated phoria; OK to see patient Monday AM

EOM Pattern

MRI and Multiple Sclerosis

- Case just seen MRI needed to confirm clinical suspicion of pontine lesion
- How do we typically see patients in whom we suspect that MS may be at hand?

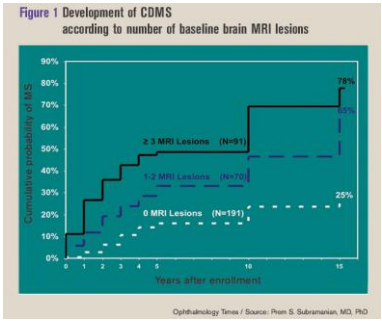
OK, ON and they're in you chair

- A 28 year old presents to you with classic findings of optic neuritis (+ APD, reduced acuity, decreased color vision, cecocentral scotoma). Do you image her with an MRI?
  - 1: Yes
  - 2: No

Obvious Next Question

- Why image a patient with classic findings of optic neuritis?
  - Incorrect answer:
    - To see if they have MS
  - Correct answer:
    - To assess their risk of developing MS

MRI and Optic Neuritis



Magnetic Resonance Angiography (MRA)

- Non-Invasive Angiogram
- Avoids Potential Complications of IV Angiogram
- Paramagnetic Contrast not Needed
- Generates 3-Dimensional Multi-Plane Scans
- Can Detect Aneurysms as Small as 3-4 mm
- Indications: TIA, OIS, CN Palsies, A-V Mal.

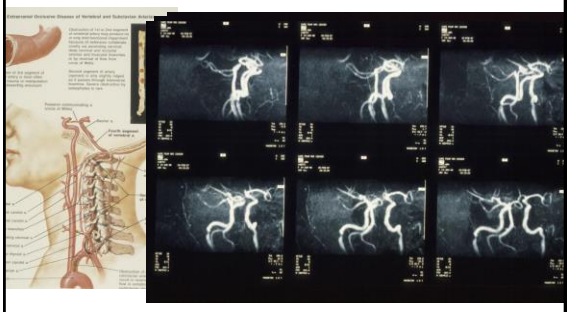
MRA - CN III Palsy (Subjective)

- 50 YOWM c/o Int. Horiz. Diplopia X 2 d. Pt. has Difficulty Verbalizing Specifics.
- POHx: Unremarkable
- PMHx: GI Ulcer
- FMHx: DM, HTN, CVA, Colon Ca
- Meds: Prilosec
- NKDA

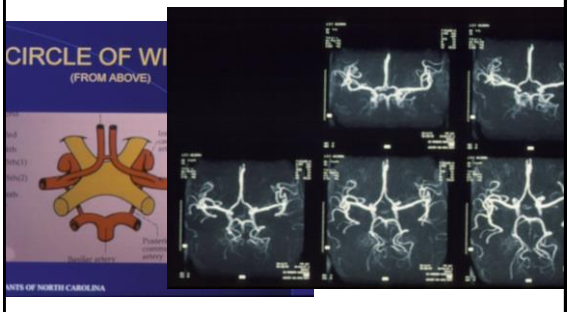
MRA - CN III Palsy (Objective)

- BVA: 20/25 OD, 20/25 OS
- Neuro: P 8mm/6mm Rd, -APD; CF FTFC, EOM Down & Out Deviation OD w/ 3 mm Ptosis
- SLE: Unremarkable
- TA: 16/14 mmHg
- DFE: Unremarkable
- BP: 185/95 LAS

MRA - CN III Palsy Discussion



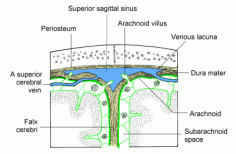
MRA - CN III Palsy Discussion

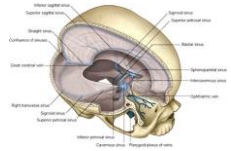


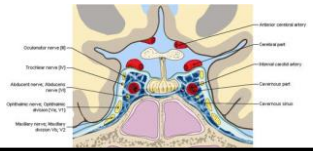
MR Venography MRV

- Useful in evaluating the dural venous sinuses
- Cerebral Venous Sinus imaging

Dural Venous Sinuses



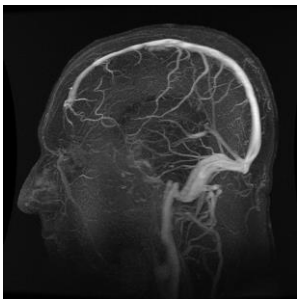


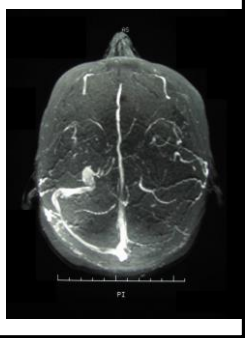


Dural Venous Sinuses

- An important component to evaluate for the patient with papilledema
  - The manifest disc swelling is a result of thrombosis in a dural venous sinus, preventing venous drainage from the head
    - Resultant increase in ICP

Magnetic Resonance Venography



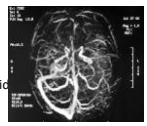


MRV Clinical Utilization

- + Papilledema
- Normal MRI
  - No space occupying mass
  - No shift/displacement of cerebral tissue
- Normal LP opening pressures*
  - *sometimes
  - Post partum
- Cerebral Venous Sinus Thrombosis

Cerebral Venous Thrombosis CVT

- Clinical picture resembles pseudotumor
  - Headache
  - Disc edema
- Cavernous sinus thrombosis
  - Cavernous sinus syndrome
- Considerations:
  - Hypercoaguable syndromes (anticardiolipin Ab's, Factor Leid
    trauma, pregnancy, dehydration, altitude sickness….
  - Mortality due to transtentorial herneation



Questions???

Thank You!