Retinal Findings with Systemic Disease

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Disclosure

- I have been on advisory boards/a consultant to/received honoraria from/ or been on speakers bureau list of the following:
  - Allergan, Alcon, Arctic Dx, Bausch & Lomb, Carl Zeiss Meditec, Freedom Meditech, Optos, Optovue, VSP, ZeaVision

These affiliations will have no affect on the content of this lecture

Course Objectives

- Discuss Ophthalmic tests for evaluating retina
- Discuss systemic conditions that affect retina, and how we factor into patient care
- Discuss findings associated with systemic diseases, both common and uncommon
- Know when to refer, and to whom

Another Objective

- To get you pumped up to think about and act on systemic disease issues for your patients…..

Getting pumped up…

Antioxidants

- Do you drink coffee?
  - Over 50% of Americans drink coffee
- Is this important?
  - Coffee is leading source (by far) for antioxidant intake in the US diet!!1
- Neither coffee nor caffeine intake were associated with early AMD per BDES
- Beware:
  - COFFEE and DOUGHNUT Maculopathy2

1. As reported by American Chemical Society 8/05
The Relationship of Coffee Consumption with Mortality  

- **2 Cohorts**
  - 41,736 men Hx Professionals FUp Study – 18 years
  - 86,214 women Nurse’s Hx Study - 24 years

- **Results**
  - After adjustment for age, smoking, other CVD and CA risk factors

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<td>&lt;1 cup / month</td>
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<td>1 c/m – 4 cups/w</td>
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<td>4-5 cups / day</td>
<td>0.80</td>
</tr>
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<td>&gt; 6 cups / day</td>
<td>0.74</td>
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</table>

P<0.001 for trend and independent of caffeine intake

Medical optometry: A different kind of “liability”

Bermuda version of psychiatric Dz

More Than Meets the Eye

- Macula off retinal detachment OD
- LP vision
- Systemic health: good?
- Meds: Valium, Oxycodone, Methadone, Elavil
- Tx: Vitrectomy and Scleral Buckle
- Post op: Corneal Abrasion and HM
- How did the abrasion happen???
- Bottle Top

Clinical exam

- **BIO best for clinical exam of peripheral retina**
- Condensing lens at slit lamp ideal for magnified posterior pole views
- Dynamic clinical exam
- Require examiner to document
- Some things best seen clinically, and unable to be seen with imaging devices
Optomap® Technology

- Virtual Point™ SLO Technology
- Dual Scanning Lasers
- 200 Degree Internal Angle of Retina
- High-resolution Digital Images in 1/4 of a Second
- No Pupil Dilation Required
- 2-3 Minute Procedure by Technician

Virtual Point™ Technology

- View the majority of the retina at one time (up to 200 degrees ≥82% of the fundus)
- Virtually place a scan point posterior to the iris plane
- Image the eye from the inside

Fluorescein Angiography

- Used for diagnosis in AMD, diabetic maculopathy, vascular occlusive disease, and many more conditions
  - Location
    - Subfoveal, Juxtafoveal, or Extrafoveal
  - Affecting vision?
  - Type of lesion, as in AMD
    - Classic, Occult, Mixed
  - Level of perfusion
    - Diabetics, Vascular Occlusive
  - Activity of lesion
    - Treatment options
  - NAFl given intravenously
  - First goes through Choroid
  - Most common side affects are yellowing of tears, urine and complexion

FA

- Why bother to discuss??
  - As more practices go to digital (both OD and MD), printouts will be more accessible
  - We will all be getting printouts of pt tests
  - Importance of recognizing pathology
  - Active part in patient education

Optical Coherence Tomography

- OCT provides a non-invasive, non-contact, quick, high resolution imaging of posterior segment
- Likened to an “Optical Biopsy”
- Objective, quantifiable, repeatable
- Based on technology similar to ultrasound, but uses light
- Resolution of 10microns with time domain and 5microns with spectral domain

Spectral Domain vs Time Domain

- Spectral Domain captures images 50x faster
- Uses Spectrometer vs single detector
  - So captures entire A scan simultaneously
- Resolution of 3-6micron vs 10 microns
- Therefore: faster + more information = higher resolution
A different side of OCT

- All of the instruments capture a tremendous amount of data
- Data usage is software dependent
- Sometimes Doctor has to “outsmart” the software to perform diagnostic tests…

Advanced Visualization: Slab

The Tissue Layer image allows you to isolate and visualize a layer of the retina. The thickness and placement of the layer are adjustable. This provides a virtual dissection of the retina by extracting the layer of interest.

Virtual Fluorescein Angiography

20/60 ‘Cataracts worse x 6 mos’

Advanced visualization

Surface tension/folds evident on en-face / c-scan

SDOCT Capabilities….
Healthy patient??...

- 32 yo male
- 2-3 month history of cough, dyspnea, chills, malaise
- Recently returned from International travel
- Lives in Midwest
- Health care professional
- No improvement with antibiotics and PO prednisone
- Abnormal chest x-ray
- Good vision
- Referred to Pulmonologist

SdOCT Capabilities.

Chest X-ray

- Calcified Granulomas
- Differentials?
  - TB
  - Sarcoid
  - Histoplasmosis
  - Lymphoma

Case continued

- CT ordered with contrast
- Labs ordered
  - CBC Normal
  - Normal Liver function
  - ESR 46 mm/hr
  - Negative TB skin test
  - ACE 44 U/L (7-46)
  - Histo Mycelial Ab Normal
  - Histo Anti H Ab 1:32

Histoplasmosis

- Treatment:
  - Sporanox (itraconazole) 200mg BID x 1 mo
  - 100mg BID x 2 mo
- Aside:
  - Value of prescription drug coverage!
  - Importance of good doctor patient relationship!!!
  - In case you were wondering, Histo has remained quiet, with no radiologic changes as of 4/06

Systemic Histoplasmosis

- Caused by Histoplasma capsulatum, a dimorphic fungus, that turns into a yeast at body temperature
- Endemic to Ohio, Mississippi, and Missouri River valleys
- Aerosolized fragments result in alveolar deposition
- Most infected people are asymptomatic
- Can involve CNS, liver, spleen, eyes, rheumatologic system, and hematologic system
Histoplasmosis cont.

- Symptoms can occur 3-14 days after exposure
- Approximately 250,000 infected annually
- Clinical manifestations in less than 5%
- About 90% with acute pulmonary histo are asymptomatic
- Enlarged hilar and mediastinal lymph nodes in 5-10% of patients
- Affects males 4:1
- Progressive disseminated histo mostly occurs in immunocompromised patients ex: AIDS

Good summary article: Trevino & Salvat: Preventing Reactivation of OHS. Optometry 1/06

Testing

- CBC generally normal
- Sputum cultures yield positive results in only 10-15% of acute pulmonary histo
- Complement fixing antibodies
  - Greater than 1:32 suggests active
  - Positive 5-15% of within 3 wks of fatal
- Immunoprecipitating antibodies
  - Anti-M detected in 50-80%, and remains elevated for years
  - Anti-H detected in 10-20% and becomes undetectable after 6mos. This antibody is most specific for active histo
- Imaging studies
  - Chest x-ray
  - CT scan
  - HLA-B7, HLA-DR2 and may be elevated more in people with CNVM

Treatment

- No treatment needed if asymptomatic
- Treatment if symptomatic, or progressive
- Treatments
  - Amphotericin B: drug of choice for overwhelming active histo, administered by IV
  - Itraconazole: Fungistatic, very active against Histo, minimal side affects
  - Liver functions must be monitored
  - Approximately 86% success when treating > 2mos
  - Ketoconazole: Fungistatic, well tolerated, does not cross blood/brain barrier

(P)OHS

- (Presumed) ocular histoplasmosis syndrome
- Not previously found post-enucleation in patients with typical POHS
- Has been found in eye of patients with known Histo
- Approx 1-10% pts. In endemic areas have ocular involvement, usually asymptomatic
- 10% will be bilateral

OHS

- Histo Spots
  - Atrophic yellowish white scars from previous multifocal or disseminated chorioretinitis
  - Can form streaks
- Peripapillary Atrophy
  - May represent atrophied granulomas that formed during active infective stage of
  - Neovascular membranes can form here, and involve macula

OHS

- Macular Involvement
  - CNVM tend to form in area of pre-existing histo spot
  - May be immune reaction against H. capsulatum
  - May be due to weakened Bruch’s membrane
  - 10% become bilateral at 5 yrs, and 20% at 10yrs
  - 81% with disciform macular scarring have pulmonary calcifications
Treating CNVM from Histo

- MPS
  - Argon laser to entire lesion effective if extrafoveal with 8% recurrence
  - Krypton laser if juxtafoveal with 23% recurrence
- Submacular Surgery (SST)
  - Benefit seen in surgical group if entering acuity worse than 20/100 (76% vs 50% same or better)
  - More recently shown beneficial with PPCNV1: different histopath
  - P0 experience no better with surg in any group2
- PDT
  - >50% remain equal or show improvement
  - No cases of severe vision loss as has been reported as has been with AMD patients
- Anti-VEGF Therapy

Central “Spot”

- 50yo female referred in with a “spot” in the center of her vision
  - Present for 1-2 wks
  - Referring OD noticed abnormality
  - VA 20/20 OU
  - Denies High stress or type “A” personality

Central Serous Choroidopathy

- Characterized by breakdown of the outer retinal barrier, with leakage of fluid through a defect in the RPE into the subretinal space, resulting in a neurosensory detachment
- Often times associated with high stress +/-
  - ED (Emotional Distress) may be related1
- FA or OCT must be done to rule out CNVM
- Other systemic associations
  - Use of corticosteroids* (Well documented in literature), pregnancy, increased adrenaline level, hemodialysis, collagen vascular disease, and hypertension
- Treatment?
  - Letter of diagnosis to PCP to make aware

Central Serous and Steroids

- How would you know about steroid use?
- What kinds of steroids
  - I have had cases of cream/ointment, oral
- Could hormones have same affect?
  - Patient on Androgel for “Low T”

ICSC

- Newer treatments proposed:
  - PDT
    - Success in multiple studies1
  - IVTA
    - May prevent leakage
  - Not study proven and counterintuitive
  - Anti-VEGF
  - Is it too easy to be successful with new treatments??

Case Study
- 44 yo native-american male
- Recent awareness of central blind spot
- 20/25 OU
- Diagnosis?
  - Solar Maculopathy
  - Systemic assoc???

Solar Maculopathy
- Bilateral yellowish spot in fovea with surrounding hyperpigmentation and OCT shows loss of cells at RPE layer
- Retinal phototoxicity vs photocoagulation
- Often happens in patients who use drugs or are on psychotropic meds
  - Sun gazing while "on drugs" or brief exposure with pharm. Dilated pupils
- No other systemic associations

Case Study cont.
- Take a closer look at the ONH
- What is this?
- No PEPS
- Idiopathic
- Warned of possibility of future CNVM

Case study
- 32yo female
- Good health
- 20/20 OU
- "retinal changes"

Angioid Streaks
- Diagnosis: Angioid Streaks
- Treatment: yearly exams, and home monitor with Amsler grid
- Note: proximity of Angioid streak to fovea
- Over 50% of Angioid streak patients have associated systemic disorders

Angioid Streaks
- Represent breaks in an abnormal Bruch's Membrane that may present spontaneously or as result of trauma
- Eventual RPE and choriocapillaris degeneration
- Generally radiate out from ONH, bilateral
- Color depends on fundus color and degree of RPE atrophy
  - Red: Lightly colored fundi, reflect underlying choroid
  - Brown: Darker pigmented fundi
  - Orange: Specific type of RPE mottling
Angioid Streaks: associated systemic conditions

- Pseudoxanthoma Elasticum
  - 80-90% have angioid streaks
  - Degeneration of collagen
  - Most common systemic
- Paget's Disease
  - 8-15% have angioid streaks
  - Metabolic bone disease
- Sickle Cell Disease
  - <5% have angioid streaks
- Ehlers-Danlos Syndrome
  - Skin fragility, joint hyperextensibility
- Diabetes
- Others: maybe coincidental
- PEPSI

Angioid Streaks

- Not problematic unless get CNVM
- If CNVM, standard is thermal laser, but >75% recur
- Monitor with Amsler grid

Case of Missing Labs

- RM is a 46 year old Caucasian male
- Referred for retinal changes, questionable macular edema
- Last physical 2-3 years prior
- "No systemic health problems", no medications
- Paramedic
- Note: Not a very healthy looking patient

“Healthy” Paramedic cont.

- Visual acuity: OD: 20/100 OS: 20/30
- Pupils, CVF, Amsler all normal
- Anterior segment: Normal, no iris changes
- Fundus exam:
  - Widespread microaneurysms, several cotton wool spots, vascular engorgement and crossings, dot and flame hemorrhages in post-pole and equatorially
  - Macular edema present OD, and possibly OS
- Fluorescein Angiogram ordered
  - Above changes noted, significant leakage in OD macula. Limited change to macula OS
- TX: Focal laser recommended
  - TX Cont: Letter sent to PCP telling of findings, recommend blood workup for DM and other vascular problems

Unhealthy Paramedic

- Vision after focal: OD: 20/70
- Retinal changes: worse
- Pt notes that has been to doctor, and now on meds for DM
- BP checked at visit and was 184/102

Paramedic

- 2 mos later he notes vision may be a little worse: OD: 20/200 OS: 20/40
- BS poorly controlled
- BP: 156/94
- We called CP for lab results…….
Case of Missing Labs

- MD office had no records of any lab work done!
- Pt self tested while on job, and treatment based on that
- Fairly non-compliant patient
- ? Compliant PCP
- Needs Endocrinologist consult...
- **This patient not only has diabetes, but also hypertension!**

Diabetes

- 2 types
  - Type 1 (previously insulin dependent)
    - Beta cell destruction leading to absolute insulin deficiency
    - Glucose stays in blood since can not enter insulin dependent tissues
  - Type 2 (previously non-insulin dependent)
    - Peripheral insulin resistance, maybe relative insulin deficiency or secretory defect
    - Treatment to decrease hepatic glucose production &/or decrease peripheral insulin resistance
    - May become insulin dependent

**Diabetes**

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**Testing**

- Should be more frequent if obese, family history, birth to large baby, hypertensive or dyslipidemia

**Diabetes**

- Most common retinal vascular disease
- Typical findings
  - MA, intraretinal hemorrhages, hard exudates, CWS, macular edema, IRMA, neovascularization, vascular changes...
- Non-proliferative diabetic retinopathy vs Proliferative retinopathy
- Macular edema

**Diabetic retinopathy**

- Will discuss later: NPDR, PDR and DME/CSME
NPDR

- **Mild**
  - At least 1 ma
- **Moderate**
  - Hemorrhages &/or ma’s (2A), CWs, or VB(< 6B) or IRMA (<8A)
- **Severe**
  - 4/2/1
  - 15% to PDR in 1 yr
- **Very Severe**
  - 2 or severe findings without neo.
  - 45% to PDR in 1 yr

1. As reported by ETDRS

Proliferative Diabetic Retinopathy

- **NVD or NVE**
- **High risk**
  - NVD >1/2 disk area
  - NVD and VH/PRH
  - NVE >1/2 disk area
  - VH/PRH
- **Untreated, can lead to VH or tractional RD**
- **Without tx, 50% blind in 5 years**
- **Current treatment: PRP when High Risk, may need vitrectomy**

Macular Edema

- **3 criteria**
  - Thickening <1/3DD from center of macula
  - Heme/exudate with thickening of adjacent retina <1/3dd from center of macula
  - Thickening >1dd size within 1dd center
- **Current treatment:** Grid/Focal laser
- **Investigational treatment:** IVTA

Diabetic Retinopathy Study

- **Randomized, prospective to evaluate PRP**
- **Primary outcome was severe vision loss defined as 5/200**
- **Demonstrated 50% decrease in SVL in PRP group**
- **Recommendation: PRP**
- **Complication: 11% lost 1 or more lines of acuity, and 5% had visual field loss**

Update on PRP

- **If CSME, must be treated before PRP, but, will PRP cause CSME?**
- **DRCR recently published:**
  - Compared 1 (1200-1600) vs 4 sitting (approx 300) PRP
  - Insufficient difference in thickness after tx: slightly more change in immediate f/u in 1 sitting, slight reversal by 8mo
  - Same vision at end with no correlation with VA and thickness

Early Treatment for Diabetic Retinopathy Study

- **Evaluated PRP and aspirin in pts with less than HR PDR OU, laser for DME**
- **Outcome was Moderate VL (doubling of visual angle)**
- **Results:**
  - >50% less MVL with laser for CSME
  - PRP for PDR, not needed earlier, but may be beneficial for Type 2
  - ASA 650mg did not alter retinopathy, VA or VH, or rates of vitrectomy
Diabetic Retinopathy Vitrectomy Study

- Is early vitrectomy beneficial?
- 20/40 was more common in early-vitrectomy group (1-6 mos.)
- Benefit seen in eyes with most severe disease
- In regards to VH, clear benefit to type 1, but not to type 2
- Today: 25g vitrectomy

Intravitreal Steroid for DME…The Next “Best Thing”

- NOT........
- Published paper shows that traditional focal laser better for CSME than 2 different doses of steroid injection
- At 2 yrs, focal more effective and less side affects than injection: in general
  - Just as convincing at 3yrs IVT stable vs laser gain!
- Subgroup:
  - Thicker OCT better with Laser
  - Worse VA than 20/200, better with 4mg steroid

Lucentis

- DRCR.net investigated Lucentis vs laser and/or steroid n= 691 people (~850 eyes).
- Grps (success is 20/20 or <250microns @ 1yr)
  - 1: sham injection + prompt laser treatment
  - 2: Lucentis + prompt laser (8/13)
  - 3: Lucentis + deferred laser treatment (≥24 weeks (9/13)
  - 4: IVK + prompt laser (3/4)
- Success: 32%, 64%, 52%, 56%
  - Lucentis gained 9 letters vs 3 in laser v 4 w steriod
  - Steroid better than laser for OCT, but not VA
  - Approx 30% Lucentis + 3 lines vs 15% w laser

A Really FAST Vitrectomy

- We will discuss:
  - UKPDS, DCT and DPP later
**Diabetes Control and Complications Trial & UK Prospective Diabetes Study**

- Pts randomized to conventional or intense control
- Showed slower progression for intense control group
- For those with no NPDR at start, if intense, then 76% less devel. of retinopathy
- If A1c down by 2%, PDR would decrease by 50%
- Decrease in A1C by 1 %:
  - 14% decrease in MI
  - 12% decrease in stroke
  - 37% decrease in microvascular dz
  - 21% decrease in any DM endpoint

DCCT reported relationship of A1C and avg. Glucose

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<th>Avg. Glucose (mg/dL)</th>
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<td>10.0</td>
<td>240</td>
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<tr>
<td>11.0</td>
<td>270</td>
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Control group in DCCT: 9-10%
Strict control group: 7%


10 years after DCCT

- 10 yrs later A1c was 8.07% vs 7.98% in the groups
- Prevalence of retinopathy progression or PDR less in intensive group after 10 yrs (24 vs 41% & 6.5 vs 19%)
- Other studies have confirmed retinopathy linked to initial BS control
- Similar effect seen in neuropathy and albuminuria
- Metabolic memory appears to last 10 years, but may wane at some time


**What We Need to Know**

- The Diabetes Prevention Program (DPP) showed that lifestyle modification of high-risk patients by 58% over 4 yrs.
- Walking
- Metformin
- Exercise was twice as effective as drug

**Hemoglobin A1c**

- Importance of A1c monitoring
- Critical to disease control and prevention of problems
- Does a patient know their last reading?
  - Good, bad, or worse response
- In office testing
  - www.a1chow.com

**Intravitreal Steroid**

**The Challenge for OD’s in Diabetes Care…**
Those Who Aren’t What We Call Them

Don’t Substitute a Part Of Any Person

For the Whole Person

You never know...
- Diagnosed with T2DM 2 wks ago
- Vision not good, Endo said due to BS fluctuation
- 20/50

Trivia: What do these 3 have in common
- JP Morgan, Alfred G Vanderbilt and Milton Hershey were all supposed to be on the Titanic
- If they were, we would never have known Krackel and Mr. Goodbar!

And today....

Trivia: What do these 3 have in common
- JP Morgan, Alfred G Vanderbilt and Milton Hershey were all supposed to be on the Titanic
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“Borderline Diabetic”
- 57yo female
- “Borderline diabetic” "(diet controlled)"
- Claritin D
- 20/60 OD 20/20 OS
- Last blood sugar: at last doctors visit
- BR: 186/94
- +APD
- Diagnosis?

Non-Arteritic Anterior Ischemic Optic Neuropathy
- Sent to PCP that day
- Blood sugar > 300 and started on 2 PO meds
- Started on HTN med
- Diet initiated
- Taken off Claritin D and put on Zyrtec
- No ocular treatment needed
- Will re-eval in 1 month
NAION

- Microvascular compromise
- Must rule out Arteritic disease with SED rate and CRP
- Further testing to include blood pressure, blood glucose, carotid, and CV work-up
- Altitudinal VF defect common
- May cause cupping of optic nerve
- 50% regain 20/60, but 40% <20/200
- Approx. 35% will develop on other eye
- No definitive ocular treatment

Arteritic ION

- True Emergency due to possibility of Temporal Arteritis
- Autoimmune process causing inflammation to vessel walls and pressure-perfusion imbalance
- Pts usually over 60yo
- Vision 20/60 to NLP
- Up to 75% become bilateral
- Some pts. will have retinal hemes (especially flame)

AION

- Prodromal symptoms in 75%
  - Jaw claudication, headaches, flashing or flickering, weight loss, malaise, scalp tenderness
- Systemic treatment with steroid should be initiated immediately, and may last 6mos
- Temporal artery biopsy is definitive

NAION vs AION

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<th>AION</th>
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<td>M</td>
<td>M</td>
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<tr>
<td>Female/60</td>
<td></td>
<td>F</td>
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<tr>
<td>Vision</td>
<td>Mild to Moderate loss +/- APD</td>
<td>Mod. to Dramatic +APD</td>
</tr>
<tr>
<td>Pupil</td>
<td></td>
<td>+/- APD</td>
</tr>
<tr>
<td>Treatment</td>
<td>Monitor</td>
<td>Address systemic</td>
</tr>
<tr>
<td>Optic Nerve</td>
<td>Sectoral to full edema</td>
<td>Full swelling and chalky</td>
</tr>
<tr>
<td>Prognosis</td>
<td>50% to 20/60</td>
<td>Poor</td>
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“Paramedic’s Friend”

- 65yo male
- Occupation: retired, but used to be field medic in military
- “My optometrist referred me because of my right eye, I am not sure what is wrong”
- “Good general health, my blood pressure runs low”
- My exam...

Hypertension??

- Vision: 20/400 OD
- Anterior Segment: normal
- Blood Pressure: 196/120
- What next...
- Sent to PCP directly from office
- Started on HTN meds
- Returned for laser 2 wks later
Hypertension

- 50-60 million Americans have systemic HTN (by today’s standards)
- Usually asymptomatic, but can lead to MI, PVD, CVA, renal disease, retinopathy
- Significant CVD risk at 140/90, and risk doubles with every increase of 20/10mmHg
- Risk factors include smoking, dyslipidemia, DM, age, family history, race, sedentary, obese, sodium...

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<th>Diastolic</th>
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<tr>
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<td>&lt;120</td>
<td>&lt;80</td>
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<tr>
<td>Pre-HTN</td>
<td>120-139</td>
<td>80-89</td>
</tr>
<tr>
<td>HTN</td>
<td>140-159</td>
<td>90-99</td>
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<tr>
<td>Stage 1</td>
<td>&gt;160</td>
<td>&gt;100</td>
</tr>
<tr>
<td>Malignant</td>
<td>&gt;120</td>
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- Refer to PCP in timely manner
- Goal of BP reduction to as low as tolerated
- Most patients will require 2 medications
- Lifestyle modification
  - 30 minutes of physical activity ≥4 days/ wk can lower SBP by up to 9mmHg
  - Weight loss of 10kg can lower SBP by 5-20mmHg

Branch and Central retinal vein occlusions

- Vein occlusions are second most common ocular vascular abnormality
- Arteriosclerosis is primary factor
- Increased venous and capillary pressure cause decreased blood flow
- Arterial thickening compresses vein
  - Endothelial cell loss, thrombus, or venous occlusion
- Most common systemic conditions:
  - HTN, hyperlipidemia, DM, smoking, obesity

Branch Retinal Vein Occlusion

- Major BRVO
  - 1st order temporal branch at ON or 1st order away from ON but involving macula
- Minor BRVO
  - Only macular branch
- Peripheral BRVO
  - No macular involvement

BRVO

- 50% develop collaterals with visual return in 6 mos
- NVD in 10% and NVE in 20-30%
- Acute signs should resolve by 6-12 mos
- May have macular RPE changes, even ERM

...What would you have done in 2008 and now in 2014?
**Current Treatment of Branch Retinal Vein Occlusion**

- Branch Vein Occlusion Study (BVOS)
  - 65% of eyes treated with grid laser photocoagulation gain 2 or more lines of visual acuity (3 yrs)
  - 37% of untreated eyes gain 2 or more lines of visual acuity (3 yrs)
  - Laser decreased NV by 50% but only 60% of treated eyes would have developed
  - **Therefore, grid laser photocoagulation is recommended for BRVO with macular edema**

**Central Retinal Vein Occlusion**

- Non-Ischemic
  - Rare APD, occasional CWS, moderate VA loss
  - 15% convert to ischemic at 4 mos, and 34% at 3 yrs
  - 50% VA <20/200
- Ischemic
  - Severe decreased VA
  - Marked APD
  - Tortuously and engorgement in all branches, numerous CWS, Severe ON edema
  - Iris NV in 50%
  - Monthly flu for 6 mos

**Previous Treatment of Central Retinal Vein Occlusion**

- Central Vein Occlusion Study (CVOS)
  - Grid laser photocoagulation reduces angiographic evidence of macular edema
  - Final median visual acuity in treated eyes was 20/200 (3 yrs)
  - Final median visual acuity in untreated eyes was 20/160 (3 yrs)
  - With or without treatment, approx. 33% Lose 3 lines of VA at 3 years
  - PRP did not prevent iris NV
  - **Therefore, grid laser photocoagulation is NOT recommended for CRVO, unless NV develops**

**So pt presents with VO & ME**

- First and foremost: Any ME from VO is no longer an "optometric" management: **There is proven benefit to Tx that are implemented earlier than before**
- Which treatment is best?
  - Not exactly up to us...But sort of...you choose!

**THESE are TODAY’S FDA approved options**

- **Anti-VEGF**
  - Bravo/cruise
  - For BRVO/CRVO
- **VEGF-trap**
  - Galileto/copernica
  - For CRVO

Retinal specialists preferred tx option & when they decide to tx may remain controversial ie regarding to what is standard of care. Yet, many employ AVT more frequently & start treating earlier than before.

**Investigative Treatments for Retinal Vein Occlusion**

- Treatments Investigated (CRVO):
  - Troxerutin
  - Hemodilution
  - Chorioretinal venous anastomosis
  - Radial optic neurotomy
  - tPA
  - Anti-VEGF compounds
  - Corticosteroids
- Treatments Investigated (BRVO):
  - AV sheathotomy
  - Corticosteroids
OD: “Diagnosed” at conference

Further progression/regression

Expanding our therapeutic options for CRVO/ME

- CRUISE (n=392): Safety/efficacy Ranibizumab (Lucentis) in pts with CRVO/ME over sham injections
  - Mean gain from baseline BCVA at 6M:
    - Sham injections: 0.8 letters
    - 0.3mg lucentis injection: 12.7 letters
    - 0.5mg lucentis injection: ~15 letters
    - 46-48% of pts in txed grp (using 0.3 mg - 0.5 mg respectively) gained >/= 15 letters at 6M
    - 17% of pts in sham arm had >/=15 letters improvement at 6M

CRUISE 2009 6M Phase 3 clinical results
www.roche.com

Expanding our therapeutic options for BRVO/ME

- BRAVO (N=397): Safety/efficacy Ranibizumab (Lucentis) in pts with ME 2° to BRVO over sham injections
  - Mean gain from baseline BCVA at 6M:
    - Sham injections: 7.3 letters
    - 0.3mg lucentis injection: ~17 letters
    - 0.5mg lucentis injection: ~18 letters
    - 55-61% of pts in txed grp (using 0.3 mg - 0.5 mg respectively) gained >/= 15 letters at 6M.
    - 29% of pts in sham arm had >/=15 letters improvement at 6M.

BRAVO 2009 6M Phase 3 clinical results
www.roche.com

Press Release
SCORE

Sept 2009 Arch Opt/NEI report

- CRUISE (n=271)
  - 3 yr data: pts receiving IVK were 5x more likely to experience visual gain of >/= 3 lines
  - pts 1ml IVK had fewer side effects than 4 ml IVK
- BRVO (n=411)
  - 3 yr data: 20–30% of ALL pts experienced VA gain > 3 line
  - pts in IVK group were more likely to develop complications

So, what do we do now???

- CRUISE: Lunecntis for CRVO
- BRAVO: Lucentis for BRVO
- SCORE for BRVO
- SCORE for CRVO
- Dex
- Galileo for BRVO
- Copernicus for CRVO
Latest Development in VO

- FDA has announced approval of Ozurdex (Dex) insert for treatment of ME from CRVO.
- WHAT’s NEXT?

Why studies are needed

“When you have a hammer, everything looks like a nail”
Jost Jonas, M.D.

Hemorrhage everywhere!

- 68 yo female
- Dramatic decrease in vision 1 wk prior due to Vitreous Heme
- Exam as seen after VH resolution
- Diagnosis and Treatment?

Macroaneurysm

- 1mo and 5 mo s/p focal laser
- VA returned to 20/20
- Blood Pressure at initial visit:
  - 186/98
- Hypertension is prime concern if macro-a seen, secondary concern of diabetes

RAM

- Most commonly in 6th or 7th decade of life
- Usually women, and only 10% bilateral
- Hypertension is prime systemic assoc. (2/3)
- Must also rule out cardiovascular disease, including increased cholesterol/lipid levels, and diabetes
- Communication to PCP

Dangers of Addiction

- 38 yo male
- Healthy
- No meds, but…
  - Viagra PRN
  - Frequent Alcohol
- 20/20 OD, 20/30 OS
- Ant Seg healthy
- Retina OS as seen
- Diagnosis?
Valsalva

- Not generally associated with systemic disease, but...
- More common in people with DM, HTN, and sickle cell
- Typical ocular findings:
  - Pre-retinal heme, subhyaloid heme
- Caused by sudden raise in intrathoracic pressure, which leads to increased intraocular venous pressure
- Causes break in macular capillary

“Drunken Pumpkin” Valsalva Maculopathy

- Common causes:
  - Vomit, cough, sneeze, constipation, exertion
  - Often seen with alcoholism, bulimia and GI problems
- Tend to resolve on own
- No long lasting damage
- What caused condition in this patient?

What do you think when you see this clinical image?

OD Macula  OS Macula

How about this Visual Field??

Pt. AM exam findings

- Pt AM is a 47yo female that has been on Plaquenil 200mg BID x 1 yr, weights approx 120lbs
- Being seen by request of her rheumatologist for screening for Plaquenil toxicity
- Vision corrects to 20/20 in both eyes
- Pupils and screening Matrix VF are normal
- Contrast is normal at 1.25% OU and color is normal
- MPOD is .31 OD and .38 OS
- IOP 18/17mmHg
- Schirmer is 0mm in both eyes w/ dry eye sx

Further findings: Cross Hair OCT: Worried yet??

No apparent Pt. degradation seen
This is the question

- When looking at the scans for this patient, can we tell if this is Plaquenil toxicity vs other macular abnormality?
- Is it likely to see such asymmetric changes due to Plaquenil?
- Cumulative dose is low, at only approximately 150,000mg (well below hypothesized “tipping point” of 1,000,000mg)
Bull's eye maculopathy
- Drug Toxicity
- Rarely seen due to less people on this drug
- More common in overweight people, or very thin people

Chloroquine Retinopathy
- First described in 1959
- Defined by acquired paracentral scotoma on VF with parafoveal RPE atrophy
- Dose related
- Exams every 1-2 years depending on dose
  - Hydroxychloroquine
    - Annually if on for >6 years, or >200g cumulative dose
    - 18 mos. if <6.5mg/kg
  - Chloroquine
    - Annually if <3.0 mg/kg

Chloroquine Maculopathy
- Much lower incidence in Hydroxychloroquine
  - But, both have the same therapeutic index
    - Higher incidence with Chloroquine may be due to 250mg pill size
- Testing should include fundus exam, Amsler grid, and red on white field (10-2)
- Multifocal ERG may be good screening exam to detect early (pre-clinical), reversible changes
  - mfERG changes in Hydroxychloroquine Therapy. Lai, T et al. AJO. November 2005

New Guidelines per AAO (the other one)
- Risk increases sharply to 1% at 5-7yrs or cumulative dose of 1000g (usual dose 400mg/d HCQ or 250mg/d CQ)
- New screening guidelines include baseline exam and then annually at 5yrs
  - Objective tests: mfERG or FAF or SDOCT
  - Subjective test: 10-2 **
  - Fundus exam still important, but findings are generally late stage

Importance of VF
- VF should be 10-2 and performed along with objective test
- Even though SDOCT is objective and more specific: 10% w early toxicity will show significant VF defect and “normal” OCT (in patients w 1000g cumulative)
- Compared VF to OCT profile and thickness….no GCC measurement

Marmor M, Melles R. Disparity betw VF and OCT w Hydroxychlorouine. Ophth. 6/14

Why is baseline so important
- 43yo female w Rx for Plaquenil
- Wants eyes checked before staring
- h/o autoimmune and neurologic disorders w multiple meds

Important notes:
- Recommendations screening for CQ and HCQ Retinop. Marmor et al. Ophthalmoology 2/11
- Marmor M, Melles R. Disparity betw VF and OCT w Hydroxychlorouine. Ophth. 6/14
Drug Induced Maculopathies
- Tamoxifen
- 1-6% incidence
- Related to total dose (10g) or daily dose
- Can happen very acutely
- Often improve after discontinue drug

62yo Female 20/20 OU
- 20/20 OU
- Anterior seg normal
- IOP, VF, pupils WNL
- No current meds
- ???What is this Drug induced visual change

Flomax (tamsulosin hydrochloride): primarily used for enlarged prostate
- Recent FDA reports of visual field changes

What about PO Fluoroquinolones?
- Previous reports of increased incidence of RD
- Compared (retrospectively) FQ, Macrolides and B-Lactam
- >92k FQ Rx’s to >38k pts, 107K Marcrolide Rx and 178k B-lactam Rx
- RD within 1yr: .03%, .02% & .03%
- Prophylactic Tx: .01%, .02%, & .02%
- Previous studies point to current use, and only 1 RD w current use in this cohort

Tamoxifen vs Evista
- STAR Trial: shows that Evista (approved for prevention and treatment of osteoporosis) may be as effective in Breast CA prevention as Tamoxifen in high risk post-menopausal women
- Evista was equally preventative with less side effects (Decrease CA by 50% in both groups)
- Evista had 38% less uterine ca and 29% fewer blood clots
- 20% reduced rate of cataracts and no retinal findings

Nevus
- Usually flat lesions of choroid, may have minimal elevation
- May develop drusen
- Estimated to be in 6-10% by Blue Mountain Eye Study
- Recent pub. stating 2.1%¹
- May be pigmented or amelanotic
- Observation for growth critical
- Ophthalmology Oct 2005 Singh et al
- Estimate conversion to melanoma to be 1/8845

Metastatic Disease

- Cancer is 2nd leading cause of death in US
- Choroidal met is most common ocular malignancy
- As high as 34% with choroidal met, have no previous dx of cancer
- Most common primary site is lung, followed by breast
- Despite rise in dermal melanoma, no rise in choroidal melanoma seen
- PET/CT scans most effective for detecting systemic met. BJO Sept. 2005

Metastatic Disease

- Most common sites of Choroidal Metastasis
  - Breast 39.7 – 65%
  - Lung 14-29.5%
  - GI 2.6-6.3%
  - Skin 2.0-4.5%
  - Prostate 1.3-3.6%
  - Kidney 9.4-0%
  - Unknown 4-18.3%
- Thorough systemic work-up needed in cases of ocular malignancies

Ocular Melanoma

- Early recognition of signs of small lesions likely to prove to be melanomas: symptoms, tumor margin touching disc, thickness > 2.0 mm, subretinal fluid, orange pigment

Percentage of Small Tumors that Grew

Easier Plaque Design Low Profile

**Choroidal Melanoma**
- 53yo caucasian female
- HTN and hypecholest.
- Referred by OD
- 20/20 OD  20/25 OS
- Suspicious lesion OD
- Sent for systemic w/u

**Post treatment**
- Systemic workup negative for metastasis or other ca
- Brachyplaque therapy
- Vision to 20/50 post tx
- CE and vision to 20/40
- Spread/mortality
  - Tumor configuration
  - Histology
    - Spindle
    - Mixed
    - Epithelioid

**Life Expectancy**
- High likelyhood of metastatic disease
  - 25% at 5 yr and 34% at 10yr
- If metastasize, poor prognosis
  - Death rate of:
    - 80% at 1 yr
    - 92% at 2 yrs
  - Approx. 1% survive 5 yrs
- Difficult to predict survival
- Not related to tumor size or treatment modality

**Routine exam finding**
- 54yo male in for routine exam
- 20/20 vision
- h/o Melanoma

**Drug induced retinopathy**
- Interferon treatment for 5 mos
  - Infusions 1/mo and injections 3/wk
- Typical onset 1-5 mos
- Often resolves w d/c Tx
- More common w HTN

**Quality of Life after Tx**
- Significant difference in vision for 1st year (plaque > enucleation), fading after 5 yrs
  - Most notably driving and peripheral vision
  - Patients treated with plaque had increased psychological distress following therapy
    - This faded after survival rates announced
    - Still distress in both groups

**COMS group. Devel. Of Metastatic Dz in COMS. Arch Ophth 12/05**
**Melia et al. Quality of Life: 5 yrs after Tx in COMS. Arch Ophth 2/06**
Familial Adenomatous Polyposis (FAP)
- Rare: 2.3-3.2/100,000
- Avg onset at 16yo
- Without Colectomy, colon cancer inevitable
- Autosomal dominant
- 75-80% have affected parent
- 78-88% have 4 or more fundus lesions

Retinal Consult
- 37 year old female
- Vision 20/20 OU
- No pain or pain with movements
- No APD
- Normal Anterior segment exam

Further History:
- Previous episodes of vision "Graying"
- Unable to take hot showers
- Electric like impulses through arms/back
- Numbness in fingers
- Clumsy walking
- Decreased contrast/color OS

Optic Neuritis
- What is the normal visual outcome?
- Will this recur?
- What is risk of MS?
- What is eye treatment?
- What is Systemic Treatment?
- What tests are needed?

ONTT, CHAMPS and ETOMS
- All 3 agree, and confirm likelyhood of progression to further demyelinization
- Recurrence of Optic Neuritis:
  - 28% at 5 yrs
  - 35% at 10 yrs
- Recurrence more frequent in those that eventually developed MS
- Single occurrence not associated with poor vision
- Multiple occurrence associated with worse vision, approx. 25% were 20/400 at 5 years
**Optic Neuritis and MS**

- 15-20% of MS present with ON
- 38-50% of MS will develop ON
- Most predictive factor in who will develop MS is presence of white matter abnormalities (demyelinating lesions) on brain MRI
- *Overall 10-year risk of MS 38%*
  - no baseline MRI lesions 22%
  - ≥ 1 baseline MRI lesions 56%*

**Treatment?**

- Oral steroids alone not affective
- At 3 years, MS risk for IV vs PO vs Placebo 17% vs 21% vs 26%
- IV methylprednisolone x 3 days followed by 11 days of oral pred.
- Treatment with IMA?
  - 12,000/yr with weekly/daily injections and side effects
  - Interferon Retinopathy
  - *NEW ORAL TX!!!*

**ON predictive factors**

- When no brain lesions were found, the following were not present in any cases of CDMS (clinically definite MS)
  - Severe disc swelling, painless, NLP, retinal exudates, disc or peripapillary hemorrhage

**OCT: Predictive value**

- RNFL thickness may be able to be predictive as to MS or level of vision loss
- RNFL thickness signif. reduced in MS eyes
- Disease free thickness>MS = fellow of ON > MS w ON
- Lower visual function with less RNFL
- Avg. RNFL thickness declined with increased neuro. impair. and disability

**Lattice Degeneration...**

- 30 year old male referred for evaluation of lattice degeneration and atrophic holes
- Very healthy athlete, no medications
- Exam findings:
  - VA: 20/20 OU
  - Anterior segment healthy
  - Peripheral retina: Lattice with holes
  - Posterior pole...

**Plaques**

- Several Hollenhorst Plaques
- Further questioning: No cardiovascular or carotid disease
- Treatment: Laser to lattice and holes
- Referral: To PCP for cardio and carotid work-up
- Pt lost to follow up
Hollenhorst Plaques

- Landmark article in AJO January 1973
- Carotid disease and heart disease about same incidence at time of plaque seen
- Patients 4x more likely to die of MI than CVA
- If embolus, mortality 54% over 7 years (2x that of age matched norms)
- Referral to PCP or internist

Artery Occlusion

- HH plaque along IF artery
- Acute finding due to retinal edema
- Central vision good
- Superior nasal scotoma
- Edema decreases with time

Artery Occlusion

- Rate reported by Will’s to be 1/10,000 with 1-2% bilateral
- 1/2-2/3 have HTN, and 25% DM, 25% CVD, 45% carotid artery dz
- Emboli see in approx. 20%
- 90% CRAO initial VA CF to LP if embolus
- Cell death may occur as quickly as 90 minutes (Hayreh)

Artery Occlusion

- Historically felt than 5% develop NV
- Duker et al 1991: 18.2% NVI, 15.2% NVG
- Hayreh: mean to NVI 5.5 weeks
- Can develop NVI without carotid disease
- Inner retinal cell death, but outer layers spared, and have high O₂ demand
- Treatment
  - PRP when NVI
  - Acute treatment
    - AC paracentesis, massage, carbogen,...
    - Acupuncture¹: marked visual improvement in 25%
    - TPA (EAGLE study in Europe)
    - Referral to PCP or internist for treatment of underlying systemic disease
- Article in Sept 06 AJO by S.S. Hayreh


Just last month

- 42yo healthy Caucasian female
- Work-in appt for “flashes in vision”
- 1 mo ago exam, completely normal exam
- Article in Sept 06 AJO by S.S. Hayreh
What is it??

Normal CBC, PT, PTT, ANA, SED, CRP, B12, A1c, Ferritin, VWF, factor 5, high LDL and Cholesterol, BP 118/84.

Last month

- 57yo male
- Routine exam
- No ocular or systemic “issues”

Just last month cont….

Is AMD strictly an ocular disease with no systemic associations?

- NO
- Several different theories and factors that point to AMD being systemically related
- “Systemic” treatments may be beneficial
- Nutrition modification is an easy way to treat systemically

AMD and Alzheimer’s Dz

- Both AMD and Alzheimers are related to:
  - Formation of drusen or lipofuscin
  - Both are linked to inflammation and Amyloid beta (Abeta) peptide accumulation
  - Both are linked to free-radicals and DNA damage
  - Studies suggest that micronutrient antioxidant therapy slows the progression of both.

What is about the most inflammatory thing we can do to our bodies?
CVD and AMD share many common risk factors

"sick eyes may occur in sick bodies related to smoking, obesity, inadequate nutrient intake, and other unhealthy behaviors".


Remember Pablo….Vision is important

- Can we allow our patients to see like this…regardless of ocular pathology?

Is this just pathology, or vision?

- Pathology…even systemic affects vision.
- Some easily modifyable factors that affect systemic health also affect vision!
- Smoking, no alcohol consumption and no physical activity
- Odds of VI were: 100% more for current smoker and same for no alcohol, 60% less if physically active,

Klein et al. Lifestyle and Vision. Ophth. 6/14

So now you are ready to “treat” systemic disease, but…..

- What is the most important thing we can do for our patients (in their “eyes”)
- CORRECT VISION!
  - That is why they come to us
    - Majority of vision impairment in diabetes is from lack of refraction
  - Practice the “Optometric Model”
  - Combining medical and optical “treatment”


Basic concepts

Lens care is medical care
- Treat optically to allow optimal benefit

UV protection

Vision Optimization

Trauma prevention

Thank You

jgerson@hotmail.com

Online Resources

- www.theretinaexchange.com
- www.retinalphysician.com
- www.pubmed.com
- www.optometricretinasociety.org
- www.optos.com