Review of Systems

Joseph J. Pizzimenti, OD, FAAO

pizzimen@uiwtx.edu

Financial Disclosures

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  - Review of Optometry
  - Optometric Management
- Paid Scientific Advisory Board Appointments
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  - EyePromise/Zeavision
- Consulting Fees
  - Zeiss
  - Maculogix
  - EyePromise/Zeavision

Financial Disclosure

- This course is based a column that I co-author in Review of Optometry, for which I receive an honorarium.
- I have no proprietary interest in any products.
Salute the Sponsors!

QUESTIONS?

Bob Marley
get up, stand up

For color slides:
pizzimen@uiwtx.edu
Course Goal

- To provide clinically useful information about caring for patients living with oculosystemic disease.

Pizzi’s 4 Pillars of Wellness

- Reach/maintain ideal weight
- Healthy Diet
- Supplementation
- Physical Activity

- The eye does not exist in isolation. It is an extension of the brain/CNS.
- The anatomy of the eye is structured to serve the functions of the retina.
- Primary reason for dilation is to detect systemic disease.
The eye is the only part of the body where neurological and vascular tissues can be viewed directly and simultaneously.

The Eye in Systemic Disease
- Inflammatory
- Infectious
- Vascular
- Endocrine
- Neurologic
- Collagen-vascular
- Neoplastic

The Eye in Systemic Disease
- Iris / Ciliary Body 15%
- Choroid 80%
- Sympathetic NS
- Retina 5%
- Auto-regulated

Ocular Blood Flow
- Iris / Ciliary Body 15%
Review of Systems Quiz

What is the most common cause of death in the United States?

A. Stroke.
B. Myocardial infarction.
C. Cancer.
D. Pneumonia.

Key Points

- Myocardial Infarction is the most common cause of death in USA.
- 610,000 per year
- Cardiac valve disease is most common cause of cardiac emboli to the eye.**
Hypertension

The Eye in Systemic Disease

How High is High??
Classification of blood pressure

<table>
<thead>
<tr>
<th>Category</th>
<th>Systolic</th>
<th>Diastolic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Optimal*</td>
<td>&lt;120</td>
<td>&lt;80</td>
</tr>
<tr>
<td>Normal</td>
<td>&lt;130</td>
<td>&lt;85</td>
</tr>
<tr>
<td>High-normal</td>
<td>130-139</td>
<td>85-89</td>
</tr>
<tr>
<td>Hypertension*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage 1</td>
<td>140-159</td>
<td>90-99</td>
</tr>
<tr>
<td>Stage 2</td>
<td>160-179</td>
<td>100-109</td>
</tr>
<tr>
<td>Stage 3</td>
<td>≥180</td>
<td>≥110</td>
</tr>
</tbody>
</table>

Grade 4 Hypertensive Retinopathy
Clinical Ophthalmoscopic findings

Grading of Hypertensive Retinopathy

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
<th>Diastolic BP Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Retinal vessels narrowed</td>
<td>&gt; 90 and &lt; 110</td>
</tr>
<tr>
<td>2</td>
<td>Nicking of retinal vessels</td>
<td>&gt; 90 and &lt;110</td>
</tr>
<tr>
<td>3</td>
<td>CWS, Hemes**, Lipid exudates</td>
<td>&gt; 110 – 115</td>
</tr>
<tr>
<td>4</td>
<td>Grade 3 + Optic disc swelling</td>
<td>&gt; 130</td>
</tr>
</tbody>
</table>

*Grades 3 and 4 increase risk of cerebral, heart and kidney problems.*
Elschnig Spots in Hypertensive Choroidopathy

Hypertension Quiz

- What is the most frequently encountered and primary manifestation of hypertensive retinopathy?
  a. dot-blot hemorrhages
  b. arteriole sclerosis
  c. exudative macular star
  d. optic nerve swelling
Hypertension Quiz

- What is the most frequently encountered and primary manifestation of hypertensive retinopathy?
  a. dot-blot hemorrhages
  b. arteriole sclerosis-widening/whitening of ALR
  c. exudative macular star
  d. optic nerve swelling
Atherosclerosis – Most common cause of thrombosis

- Diabetes
- Hypertension
- Hyperlipidemia
- Cigarette Smoking
- Alcohol consumption
- Obesity
- Genetics, Environmental (super-size), Psychological, Behavioral

Retinal Arterial Macroaneurysm

Classification of Hypertension

- Primary (“Essential”) Hypertension
  - Elevated BP without obvious “cause”
  - 90-95% of all cases
- Secondary Hypertension
  - Elevated BP with a specific cause
    - Kidney disease – both parenchymal and vascular
    - Coarctation of the Aorta
    - Endocrine – Adrenal
    - Neurologic
  - 5-10% of all cases

Risk Factors for Primary Hypertension

- Age (>55 for men; >65 for women)
- Excess dietary sodium
- Excess alcohol
- Cigarette Smoking
- Diabetes
- Hyperlipidemia
- Family history
- Obesity (BMI >30)
- Ethnicity
- Socioeconomic status
Hypertension and Ocular Disease

- Hypertension increases risk and progression of ocular disease in numerous situations:
  - More advanced DM retinopathy in HTNsive DM
  - Risk factor for retinal venous & arterial occlusion, embolism, macro-anureysm
  - MAY be risk factor for macular degeneration and open-angle glaucoma.

A-AION vs NA-AION

- Age: 65-75 vs 55-65
- Systemic symptoms/signs of GCA?
- Pain or HA?: 79% vs 10%
- Preceding amaurosis fugax?
- Degree of vision loss?: 20/400 or worse vs 20/60 or better
- Is the disc edema diffuse/sectoral?
- Pale vs hyperemic disc edema?
- Fellow eye "disc at risk"?
- Other signs of ocular ischemia?
Giant Cell Arteritis

GCA Diagnosis

- Need 3 of the following criteria (American College of Rheumatology for Classification of Giant Cell Arteritis)
  1. Age of onset ≥ 50
  2. New onset of localized HA (temporal)
  3. Temporal A. abnormality (tender or reduced pulsation)
  4. Elevated ESR (>50 mm/hr Westergren)
  5. + TA Biopsy

- 93.5% sensitivity, 91.2% specificity

Summary - Benefits of Lowering BP

<table>
<thead>
<tr>
<th>Condition</th>
<th>Average % Risk Reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke Incidence</td>
<td>35-40%</td>
</tr>
<tr>
<td>Heart Attack</td>
<td>20-25%</td>
</tr>
<tr>
<td>Congestive Heart Failure</td>
<td>50%</td>
</tr>
</tbody>
</table>

Treatments

- Step 1:
  - Lifestyle modifications
    - Diet and exercise
    - Limit alcohol and tobacco use
    - Reduce stress factors

- Step 2:
  - If lifestyle changes are not enough, drug therapy will be introduced

- Step 3:
  - If previous steps don’t work, drug dose or type will be changed or another drug is added

- Step 4:
  - More medications are added until blood pressure is controlled

Goals in Hypertension Therapy

- Lower blood pressure
- Facilitate regression of LV hypertrophy
- Reduce risk of coronary athero and myocardial infarct
- Mitigate renal damage
- Avoid stroke and CNS hemorrhage
- Prevent peripheral vascular and carotid athero

PROTECT THE EYES!!!
Carotid Artery Occlusive Disease

Hypoperfusion Retinopathy
and the
Ocular Ischemic Syndrome

**Dot and Blot hemes in mid-peripheral retina**

Carotid Artery Occlusive Disease

Carotid Occlusive Dx: Bruit
Carotid Doppler (Duplex)

Hypoperfusion Retinopathy

NVI and Cataract in Ocular Ischemic Syndrome

The Ocular Ischemic Syndrome (OIS)
Key Point

• Q: Bilateral involvement in patients with ocular ischemic syndrome may occur in up to approximately what percentage of cases?

• A: 20%

The Eye in Systemic Disease

Pathogenesis: Ocular Ischemic Syndrome

Non-invasive Carotid Doppler (Duplex) ultrasound**

• Atheromatous ulceration and stenosis at the bifurcation of the common carotid artery (90% occlusion has to be present)

Key Point

• The most common etiology of ocular ischemic syndrome is severe unilateral or bilateral atherosclerotic disease of which artery?

• Internal carotid

The Eye in Systemic Disease

Ophthalmic Signs of Carotid Occlusion: Ocular Ischemic Syndrome

• Dilated (but not tortuous) retinal veins
• Retinal Hemorrhages in mid-periphery (80%) of patients
• Cotton Wool Spots (5%)
• Neovascularization of the Disc (35%)
• Neovascularization of the Retina (8%)
• Rubeosis iridis/NVA (65%)
• Uveitis – mild anterior (20%)
• Emboli (retinal)
• Lower IOP - initially, then NVG
The Eye in Systemic Disease

OIS Work Up:

- Carotid artery evaluation (Carotid – Duplex Scanning) – ICA, ECA, CCA
- Color Trans-cranial Doppler (TCD) – ocular arteries
- Possible MRA (Magnetic Resonance Angiography)
- Computed Tomography (CT) Angiography
- Cardiology work up (Echocardiogram) – Transesophageal/Transthoracic
- HTN, DM, Lipid Panel, ESR, C-reactive protein

The Eye in Systemic Disease

Ocular Ischemic Syndrome

Treatment:

- Consider carotid surgery if warranted (Endarterectomy)
  - European Carotid Surgery Trial (ECST)
  - North American Symptomatic Carotid End. Trial (NASCET)
- Therapeutic approach – Aspirin (325 mg QD or BID), Plavix
- Control modifiable vascular risk factors (HTN, DM, dyslipidemia)
- Stop smoking
- Panretinal photocoagulation (PRP) if neovascularization

**Important Note:**
Leading cause of death in OIS = Ischemic heart disease
Second leading cause of death = Stroke
Causes of Embolism:

1. Cardiac Disease
   - Arrhythmias
   - Valvular Disease
   - Endocarditis
   - Ischemic lesions
   - Tumors

2. Carotid Disease

The Eye in Systemic Disease

55 yo AA male
BRAO OD

55 yo AA male OS

Central Retinal Artery Occlusion
What to do next? Any TIA or Retinal Ischemia/Emboli treated the same!

1/4 of patients with acute retinal ischemia (even if transient) had an acute brain infarction

10-15% of patients will have a disabling stroke within 3 months after a TIA, with half occurring within 48 hours after resolution of TIA.

Neurology’s SOC

- Neurologists consider an acute retinal artery obstruction a true medical emergency and classify it as a stroke.
  - the embolus goes to the eye rather than to the brain
- Patients with acute RAO need to be sent to nearest stroke center or hospital ER with a stroke center.
  - Neuroimaging to assess risk of a major cerebral stroke within the next few hours or days

Follow-up

- RTC at 1 month to check for neovascularization of disc/iris
- RTC at 3 months to check for neovascularization of disc/iris
- Neo of iris = 20% of patients at about 4 weeks
- Neo of disc = 3% of patients
- Extremely important to perform a complete medical work-up to stop the progression of the disease along with any systemic sequelae.

Conclusions

- Optometrists and their office staff should be aware of what constitutes an ocular/medical emergency involving the posterior pole.
- Stroke protocols should be followed in new CRAO/BRAO.
- Any neuro-ophthalmic sign in an older patient may be GCA!
**Inflammatory Disease**

**History**
- A 34 year-old black female presents symptoms of bilateral redness x 7 days
- Gradual onset, gradual worsening
- Mild pain, mild photophobia OU
- Ocular history positive for previous episodes OU

**Clinical Findings**
- Biomicroscopy
  - 2+ cells in AC OU
  - “Mutton fat” deposits on endothelium OU
  - Iris nodules OU
  - Areas of posterior synechia OU
- TAP: 9 mmHg OD/11 mmHg OS
- DFE
  - “Snowbanking”
  - Gray/white (old) vitreous “puff balls” inferior PP OU

**Anterior Seg Findings**
Posterior Seg “Puff-balls” and “Snowbanking”

What is your **ocular** diagnosis?

**Assessment**
- Bilateral anterior uveitis
  - Probably recurrent/chronic
- Granulomatous
  - Mutton-fat KPs
  - Iris nodules
- Prior posterior segment inflammation

**A Word About Uveitis**
**What is uveitis?**

- Defined as inflammation of the uveal tract.
- For decades, considered a single disease.
- Fact: Uveitis entails a multitude of diseases.
  - Some uvetic diseases are local, ocular immune.
  - Many are systemic diseases with ocular manifestations.

**Uveitis is an Immunological Process**

**Immune Privilege**

- The eye enjoys a special relationship with the immune system.
  - Ability to quench unwanted immune-mediated inflammation.
  - This ability is known as immune privilege.
  - Immune privilege enables ocular tissues to remain clear.
Common Etiologies of Anterior Uveitis

- In uveitis, immune privilege is overcome
- Idiopathic (post-viral syndrome)
- Human leukocyte antigen (HLA)-B27-positive or HLA-B27-associated
- Trauma or s/p intraocular surgery

HLA-B27

- HLA-B27 is present in 1.4-8\% of the general population.
- However, it is present in 50-60\% of patients with acute iritis.
- HLA-B27 diseases include:
  - Ankylosing spondylitis
  - Reiter syndrome
  - Inflammatory bowel disease
  - Psoriatic post-infectious arthritis

Review of Systems Quiz

- A granulomatous condition is characterized by an organized collection of:
  
  A. Macrophages.
  B. Eosinophils.
  C. Histamine.
  D. Tumor cells.
Find the Cells

- Dark adapt
- SL on max illum
- Low mag
- Optic section (long)
- Increase mag
- ID the cells
- Shorten to short optic section or conic beam
- Count the cells

Hypopyon

- A collection of leukocytes that settle in the inferior anterior chamber angle.

- Related to amount of fibrin which allows the WBCs to clump and settle.

- Highly suggestive of HLA-B27 disease, Behçet disease, or endophthalmitis.
**Hyphema**

- Can occur in eyes with a chronic uveitis (UGH)
- Due to neovascularization of iris/angle

**What is your plan?**

Ocular management?
Systemic testing?
Consultation?

**Actual Management**

- Treated anterior uveitis using conventional topical meds.
  - Steroid
  - Cycloplegic
- Ordered targeted systemic “uveitis” work-up
  - ACE will be elevated in up to 80% of patients with active S__________.
- Chest imaging

A granulomatous uveitis has an increased likelihood of being part of a s__________ disease process.
Corticosteroids

- Topical steroids are the mainstay to treat ocular inflammatory conditions
- Choosing which medication to use depends on the severity and location of the ocular inflammation

Bilateral Hilar Lymphadenopathy on Chest X-Ray in Pulmonary Sarcoid

Outcome

- Sarcoidosis
  - Patient was also placed on po Prednisone (short-term)
  - Good ocular response to medical therapy
- What imaging tests to order:
  - Chest X-ray
  - CT of chest and abdomen
Key Points: Sarcoidosis**

- A multi-system disease.
- Most often occurs between 20 and 40 years of age, with women being diagnosed more frequently than men.
- 10 to 17 times more common in African-Americans than in Caucasians.

QUESTIONS?

The Eye in Connective Tissue Disease

What is connective tissue?

“Cellular glue” that gives tissues their shape and helps them do their work. Cartilage and fat are examples.

There are over 200 disorders that impact connective tissue.
Connective Tissue Disorders
- Ankylosing Spondylitis
- Sjogren Syndrome
- Pseudoxanthoma Elasticum
- Ehlers Danlos Syndrome
- Paget’s Disease
- Marfan Syndrome
- Systemic Lupus Erythematosus

Angioid streaks are present in 85% of patients with PXE.
Differential Dx. of Angioid Streaks: PEPSI

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Key Clinical Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pseudoxanthoma</td>
<td>Redundant, “plucked chicken” skin, hypertension, weak peripheral pulses, gastrointestinal bleeding</td>
</tr>
<tr>
<td>Ehlers-Danlos syndrome</td>
<td>Blue sclera, joint hyperextensibility, fragile, elastic skin, excessive bruising</td>
</tr>
<tr>
<td>Paget’s disease</td>
<td>Extraskeletal calcification, bony erosion and abnormal formation, osteoarthritis, hearing loss, vertigo, tinnitus, slurred speech, difficulty swallowing</td>
</tr>
<tr>
<td>Sickle cell disease</td>
<td>Hemoglobin SS (most frequently), anemia, vaso-occlusive crises</td>
</tr>
<tr>
<td>Idiopathic</td>
<td></td>
</tr>
</tbody>
</table>

Angioid Streaks:

- Alterations/breaks of the Retinal Pigment Epithelium (RPE), Bruch’s Membrane and Choriocapillaris
- Patient is usually asymptomatic unless CNV develops
- Approximately 50% have associated systemic disease
- Decreased vision is secondary to CNVM or a streak through the fovea

Etiology:

- Pseudoxanthoma elasticum (85%)
- Ehlers Danlos syndrome
- Paget’s Disease
- Sickle Cell Anemia

Masqueraders of Angioid Streaks

High Myopia

- Lacquer Cracks

Trauma

- Choroidal Rupture
**Angioid Streaks**

**Management:** Angioid Streaks

- Observation if no CNVM
- Focal laser, PDT, Anti-VEGF if CNVM is present
- Management of underlying systemic disease

**Follow up:**

- Twice a year with a dilated fundus examination, OCT/OCTA
- Amsler Grid self-testing (~3 x week)

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**Epidemics and Other Major Public Health Challenges**

- Obesity/Excess Weight
- Smoking
- Age-related Eye Disease

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**The Pathology of Obesity**

- Skin: Yeast Infections, Gout
- Endocrine: Polycystic Ovarian Syndrome, Low Testosterone, High Estrogen
- Heart: Heart Attack, Stroke, CHF
- Pulmonary: Sleep Apnea
- GI: Gallstones, GERD
- Urinary: Incontinence
- Gyno: Abnormal Menses, Infertility
- Neuro: Depression, Memory Problems
- Cancer: Breast, Colon, Prostate, Bladder, Esophagus
- Post-Op: Pulmonary Embolism

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**Diabesity**

- M________________ S________ is characterized by central (abdominal) obesity, dyslipidemia, raised blood pressure, and insulin resistance.

- “Diabesity”
  - Up to 97% of type 2 caused by excessive weight
  - Obesity = Increased weight caused by excess accumulation of fat
  - “Over-fat” = normal BMI w/large waist
    - Visceral fat
* 3 or more are diagnostic of Metabolic Syndrome:

**Waist circumference:**
- Men — > 40 inches
- Women — > 35 inches

triglycerides ≥150 mg/dL

HDL cholesterol:
- Men — <40 mg/dL
- Women — <50 mg/dL

BP ≥130/85 mmHg

FPG ≥100 mg/dL

Obesity Trends* Among U.S. Adults
BRFSS, 1994

(*BMI ≥30, or ~ 30 lbs overweight for 5' 4" person)
“Diabetes Belt”

Age-Adjusted Prevalence of Diagnosed Diabetes Among U.S. Adults

2010

Statue of David returns to Italy after 3 years in the USA

“People are fed by the Food Industry, which pays no attention to health, and are treated by the health industry, which pays no attention to food.” - Wendell Berry

Medical Nutrition Therapy

ChooseMyPlate.gov
Food Matters
Optimal nutrition always starts with food.

Eat
Diets that “starve” are seldom sustainable.

Real Food
Not refined, synthetic, food-like products.

Not too much.
Portion size
Mostly plants.

A plant-intensive diet provides most essential nutrients.

QUESTIONS?
DM + Smoking = Blindness

Cigarette Smoking, Ocular & Vascular Disease

- Increased arteriolar stiffness (sclerosis)
- Increased Vascular Endothelial Growth Factor (VEGF)
- Development/worsening of DR
- Development/worsening of AMD

Arteriosclerosis with calcification of vessel wall

AMD + Smoking = Blindness
The AMD Epidemic

AMD: a sick eye in a sick body?

Is AMD a Systemic Disease?

Johanna Seddon, MD (Tufts U)

"Don’t smoke; follow a healthful diet rich in dark green leafy vegetables and low in fat; eat fish a few times a week; maintain a normal weight and waist size; exercise regularly; and control blood pressure and cholesterol."

"Anyone with signs of intermediate-level macular degeneration in both eyes or advanced macular degeneration in one eye should also take dietary supplements that contain lutein, zeaxanthin, vitamin C, vitamin E, and zinc."
Types of Hematologic Disorders

- Excess production of blood cells
- Impaired production of blood cells
- Destruction of blood cells
- Abnormal function of existing blood cells

Common Disorders

- Anemia
- Sickle cell hemoglobinopathy
- Hematologic malignancies

Anemia:
*A decrease in red blood cells and/or decrease in the level of hemoglobin.*

Prevalence of Anemia Worldwide
is more than 2 billion people
(World Health Organization)
Prevalence of Anemia:
approx 1 in 77 or 3.5 million people in USA (Mayo Clinic, CDC)

Anemia
- Microcytic- MCV<80fl
  - Iron Deficiency Anemia
- Macrocytic- MCV>100fl
  - Vitamin B12 Deficiency/Folate Deficiency
    - Pernicious Anemia**
  - Liver Disease
- Normocytic- MCV 80-100fl
  - Aplastic Anemia
  - Hemolytic Anemia
  - Anemia of Chronic disease

Vitamin Deficiency Anemia
- Folate and Vitamin B-12
- **Pernicious Anemia (megaloblastic)**
  ***lack intrinsic factor
  - needed to absorb vitamin B12 from GI*
  - Neurological deficits
Iron Deficiency Anemia

- Inadequate Fe+ intake
- Blood loss
  - recycled when blood cells die. If you lose blood, you lose iron
- Malabsorption

***most common cause of anemia***

- Chronic Diseases
  - Cancers, Collagen Vascular, Kidney

Anemia

- Symptoms
  - Fatigue
  - Dizziness
  - Headaches
  - Parathesia in fingers & toes

- Signs
  - Pallor of skin
  - Edema
  - Tachycardia

Anemic Retinopathy

- Retinal Findings:
  - hemorrhages, CWS
  - dilated & tortuous vessels, exudates
  - Roth spots
    - white-centered heme

Anemic Retinopathy

- DDX:
  - hypertensive and/or diabetic retinopathy

- Pathophysiology:
  - anoxia, venous stasis, angiospasm, increased capillary permeability, and thrombocytopenia
  - severity of the anemia/ increased blood viscosity

- Manifestation of systemic disease
Ocular Complications

Conjunctival pallor/jaundice or hemorrhage

Optic Nerve:
- Pallor
- Disc Swelling

Case: 44 yo BM

- CC: Floaters OD X 6 months / + frontal headaches
- PMHX: Positive Sickle Cell Trait** (most common)
  - Uncontrolled HTN X 15 years- h/o poor compliance with medications
- Blood pressure was 170/124 RAS
- BCVA: 20/20 OD, 20/20 OS.

Retinal Evaluation

OD: Fibrotic scaffolding with venous tortuosity and areas of NV

OS: Fibrotic scaffolding with venous tortuosity and hemorrhages

Case Report: 45 yo BF

- Annual wellness
- PMHX: stroke one-month ago/ Hypertension/ hypercholesterolemia
- Aneurysmal dilation of the ascending thoracic aorta, and + sickle cell trait.
- BCVA: 20/20 OD, 20/20 OS
- SLE: unremarkable
Retinal Evaluation

OD: Peripheral dot-hemorrhage

OS: (BRAO) with sea-fan neovascularization OS

Red-free and FA of OS

Ddx. of Peripheral NV

- Diabetic Retinopathy
- Familial exudative vitreoretinopathy (FEVR)
- Hyperviscosity syndromes
- Radiation retinopathy
- Sarcoidosis
- Ocular ischemic syndrome
- Sickle cell retinopathy
- Chronic myelogenous leukemia

Sickle Hemoglobinopathies

- The *most prevalent* genetic disorders in US
  - 10-14% of African-Americans/Mediterranean ancestry
- **Autosomal recessive**
- Pathophysiology
  - Sickle shape of RBC’s
    - Response to decrease $O_2$ tension
    - Hypoxia, acidosis, and ischemia
Sickling Crisis

Triggering Factors:
- Deoxygenation
- Dehydration
- Acidosis

polymerization

RBC Sickling

Hypoxia/ Acidosis/ Ischemia

Organ Damage/ Infection

Stasis

Sickle Hemoglobinopathies

- Morbidity and Mortality
  - Vaso-occlusive events + chronic hemolytic anemia => tissue damage
- Variants
  - Sickle cell anemia- Hb SS
  - SC disease- Hb SC
  - Sickle β-thalassemia
  - Sickle cell trait –A ** (Most prevalent variant)
  - 8-10% of the Black population
    - 35-40% HbS and 55-60% Hb A

Additional Testing for Sickle cell:
- CBC w/hematocrit
- Sickledex
  - Solubility test that detect the presence of Hemoglobin S
- Hemoglobin Electrophoresis
- DNA analysis

Ocular Complications

Focal iris atrophy in a patient with sickle cell disease
Ocular Complications of Sickle Cell

- Sickling → micro-vascular occlusion → ocular ischemia, infarction → neovascularization, and fibrovascularization
- Retinopathy
  - Increased severity in SC and ß-thal
  - Why???
    - May be due to higher blood viscosity…

Non-proliferative SC Ret

- Venous tortuosity (peripheral)
- Salmon Patch Hemorrhages
  - intra-retinal heme
- Black Sunbursts- RPE hyperplasia
- Dark without pressure
- Iridescent spots

Review of Systems Quiz

- Proliferative sickle cell retinopathy is characterized by ________________?
  a. Venous tortuosity of the peripheral vessels
  b. Salmon Patch Hemorrhages
  c. Black Sunbursts
  d. Sea-fan neovascularization
Review of Systems Quiz

- Proliferative sickle cell retinopathy is characterized by _______________?

  a. Venous tortuosity of the peripheral vessels
  b. Salmon Patch Hemorrhages
  c. Black Sunbursts
  d. Sea-fan neovascularization

Questions?

Proliferative Retinopathy

Five stages:

- **Stage 1.** Peripheral Arteriolar Occlusion
- **Stage 2.** Peripheral Arteriovenous Anastomoses
- **Stage 3.** Neovascular and Fibrous Proliferations- Sea Fan formation
  - Auto-infarct or spontaneously regress (20-60%)
- **Stage 4.** Vitreous Hemorrhage
- **Stage 5.** Retinal Detachment

Proliferative SCR. The peripheral retina (left) is completely nonperfused. The right side shows a partially perfused retina. The brighter areas are the junction where the NV is leaking.
Other Ocular Complications

- CRAO/BRAO
- Sickling maculopathy
  - Thin, atrophic macula
    - perform OCT
- Epiretinal membrane
- Optociliary shunt vessels
- Disc Signs
  - Segmentation of capillary vessels (rare)
  - **NOT** Neovascularization

**Treatment**

- Proliferative retinopathy:
  - Stages 1-2: follow-up in 3-6 months
  - Stage 3-5: Laser Photocoagulation or retinal surgery.
    - Peripheral circumferential retinal scattered photocoagulation (PCRP)
- New/future- anti-VEGF therapy
  - Study by Siqueria.........regression of retinal neovascularization with intravitreal Avastin® injection……..

**Take home message:**

*Marked sickle cell retinopathy* can occur in the presence or absence of systemic diseases

*Hypertension, Diabetes, Collagen Vascular Diseases, Sarcoidosis, Ocular Trauma*

**The Eye in Systemic Disease**

Leukemia – cancer that originates in the bone marrow – abnormal WBC’s
Leukemia

Proliferation of Immature WBC's

- Immune-compromised state
- Production of RBC's and platelets
- Hypertrophy of the bone marrow (bone pain)
- Organ infiltration
  1. Hepatomegaly
  2. Splenomegaly
  3. Renal insufficiency
  4. Hyperuricemia
  5. Arthralgia
  6. ↑ICP (meningeal infiltration)

Ocular involvement occurs in ~80% of cases

Ocular manifestations can be divided into three categories
  a. leukemic infiltrates
  b. secondary complications related to anemia, hyperviscosity
  c. opportunistic infections (CMV, fungal, etc.)

The ocular manifestations resolve after chemotherapy or radiation

Treatment of Leukemia
  - Chemotherapy
  - Radiation
  - Bone marrow transplantation
  - Biological therapy - Interferon

The Eye in Systemic Disease

Radiation Retinopathy

Radiation doses range from 11 – 35 Gy. Onset from 1-8 years
Case: 54 WF

- CC: non-specific ocular irritation
  OD>OS
- PMHX: frequent bruising of extremities for the last three months

Pertinent Findings

- Best-corrected VA: 20/20 OD, 20/20 OS.
- Pupils: Equal & round -APD
- EOM/CVF: Unremarkable
- SLE: Unremarkable

Review of Systems Quiz

- Enlarged lymph nodes are a clinical manifestation of _________________?
  a. Acute myelogenous leukemia-AML
  b. Sickle cell trait
  c. Iron deficient Anemia
  d. Pernicious Anemia
Hematological Malignancies

**Leukemia**
- Acute myelogenous leukemia-AML
- Chronic myelogenous leukemia-CML
- Acute lymphoblastic leukemia-ALL
- Chronic lymphocytic leukemia-CLL

**Lymphoma**
- Hodgkin Lymphoma
- Non-Hodgkin Lymphoma

Review of Systems Quiz

Enlarged lymph nodes are a clinical manifestation of __________________________?

a. Acute myelogenous leukemia-AML  
b. Sickle cell trait  
c. Iron deficient Anemia  
d. Pernicious Anemia

Leukemia

**Acute Leukemia**
- Rapid/progressive course that ends in death within months
- Without tx- avg survival rate is 4 months
- Immature leukocytes
- Enlarged lymph nodes, spleen
- Bone pain (bone marrow)
- CNS involvement

**Chronic**
- Non-specific symptoms/signs
- Weakness, weight loss, fever
- Unlike Acute- rarely causes pallor or bleeding
- Three phase:
  - Chronic phase- respond to treatment
  - Accelerated phase-difficult to control
  - Blast phase-transform into acute leukemia
Leukemia: Ocular Manifestations

- Petechial hemorrhages
- Neoplastic papillopathy- leukemia

Ocular Complications of Leukemia

- **Ocular Adnexa**
  - Lacrimal gland infiltration
  - EOM infiltration
  - Eyelid swelling (infiltration)
  - exopthalmos, chemosis, pain
- **Conjunctiva**
  - Infiltrates (leukemic plaques)
  - Subconjunctival hemorrhage
  - episcleritis
- **Cornea**
  - Peripheral ulcers with pannus

Leukemic Retinopathy

- Hemorrhages, exudates, CWS,
- Retinal vein tortuosity and dilation
- Retinal leukemia infiltrates
  - gray-white sheathing
- Peripheral retinal microaneurysms and retinal neovascularization
  - Sea fans
- Direct infiltration of the ONH, Papilledema

***Histopathological studies have shown the choroid to be the ocular structure most commonly involved by leukemia***

Leukemic Retinopathy

- Opportunistic Infections:
  - CMV
  - Toxoplasmosis
  - Herpes
  - Fungal
  - Bacterial
Management

- Leukemic retinopathy-usually is not treated directly
- Intraocular leukemic infiltrates-systemic chemotherapy or direct radiation therapy
- Anterior segment- radiation/ injection subconjunctival chemotherapeutic agents

Ocular S/E of Treatment

- Cytotoxic drugs
  - Cataracts, EOM palsy
  - Toxic optic neuropathy
- Bone Marrow transplantation with chemo
  - Graft-host diseases
    - Sjogren like illness- dry eye
    - Conjunctival keratinization
    - uveitis

Conclusion

- The eye does not exist in isolation, but is a mirror of systemic health.

Thank you for spending your precious time with me!

Joe