

Review of Systems

Live and Unplugged!

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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.



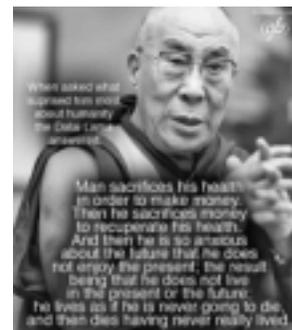
Course Goal

- To provide the participant with useful clinical information about caring for patients living with oculosystemic disease.

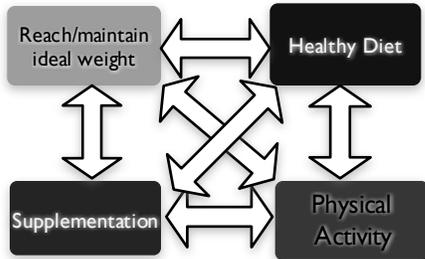


QUESTIONS

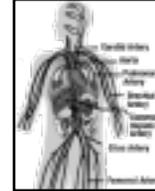
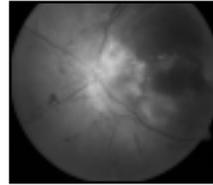
AND COMMENTS?



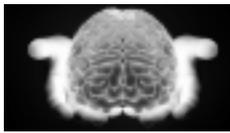
Pizzi's 4 Pillars of Wellness



- ❑ 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.

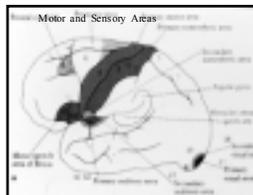
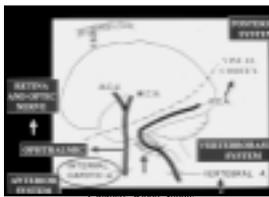


The Eye in Systemic Disease

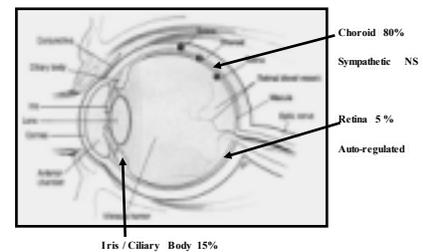
- Inflammatory
- Infectious
- Vascular
- Endocrine
- Neurologic
- Collagen-vascular
- Neoplastic



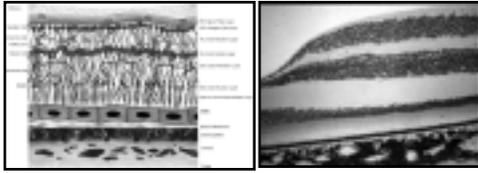
The Eye in Systemic Disease



Ocular Blood Flow



The Eye in Systemic Disease



Inner and Outer Blood Retinal Barriers Retina/RPE, Choroidal Pigmentation

Epidemics and Other Major Public Health Challenges



Public Health

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

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



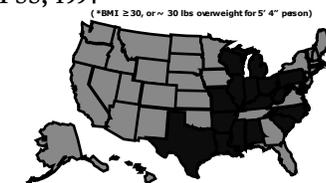
Diabetes

- Metabolic Syndrome is characterized by central (abdominal) obesity, dyslipidemia, raised blood pressure, and insulin resistance.
- “Diabetes”
 - Up to 97% of type2 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 \geq 150 mg/dL
- HDL cholesterol:
Men — <40 mg/dL
Women — <50 mg/dL
- BP \geq 130/85 mmHg
- FPG \geq 100 mg/dL

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

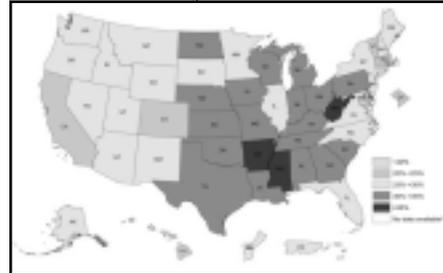


*BMI \geq 30, or ~ 30 lbs overweight for 5' 4" person)

Obesity Trends-2012



Obesity Trends-2014



“Diabetes Belt”

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

2010



“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



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
AND COMMENTS?



DM + Smoking = Blindness

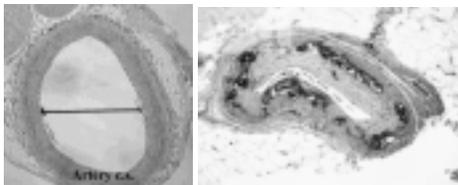


Cigarette Smoking, Ocular & Vascular Disease

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

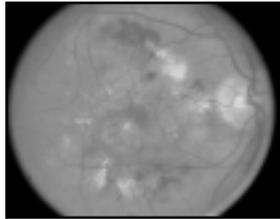


Arteriosclerosis with calcification of vessel wall

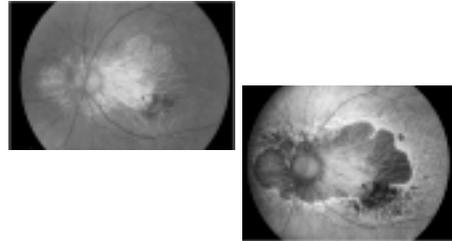


AMD + Smoking = Blindness

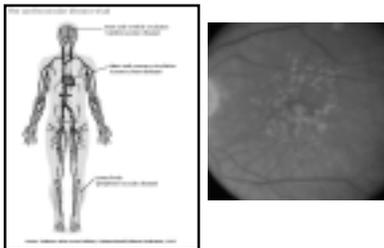
The AMD Epidemic



AMD: a sick eye in a sick body?



Is AMD a Systemic Disease?



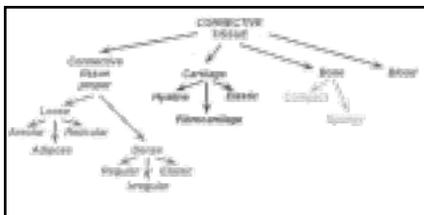
Johanna Seddon, MD (Tufts U)

" 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."

The Eye in Connective Tissue Disease



What is connective tissue?

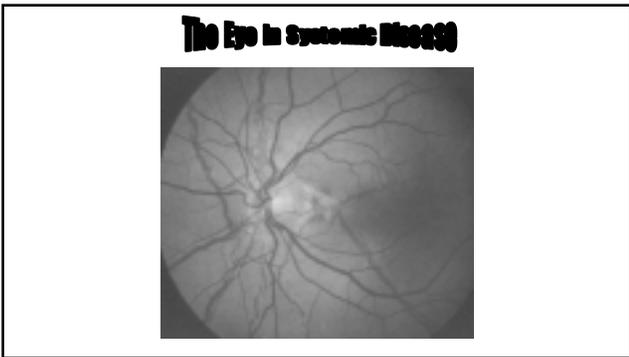
"Cellular glue" that gives tissues their shape and helps them do their work. Cartilage and fat are examples.

There are over 200 disorders that impact connective tissue.

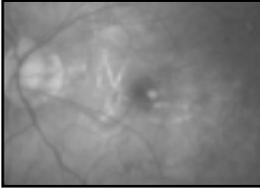
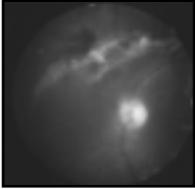


- Connective Tissue Disorders**
- Ankylosing Spondylitis
 - Sjogren Syndrome
 - Pseudoxanthoma Elasticum
 - Ehlers Danlos Syndrome
 - Paget's Disease
 - Marfan Syndrome
 - Systemic Lupus Erythematosus

Angioid streaks are present in 85% of patients with PXE.



Masqueraders of Angioid Streaks

High Myopia	Trauma
	
• Lacquer Cracks	• Choroidal Rupture

Differential Dx. of Angioid Streaks: PEPSI

Diagnosis Pseudocystoma	Key Clinical Features exudate, "plucked chicken" skin hypertension weak peripheral pulse gastrointestinal bleeding
Cherry-red spot syndrome	low vision joint hyperextensibility fragile, elastic skin excessive bruising
Page's disease	irregular calcification bony erosions and abnormal formation osteopenia hearing loss, vertigo, tinnitus slurred speech, difficulty swallowing
Sickle cell disease	hemoglobin SS (most frequently) anemia
Idiopathic	vascular disease common

The Eye in Systemic Disease

Angioid Streaks:

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

Etiology:

- Pseudoxanthoma elasticum (85%)
- Ehlers Danlos syndrome
- Page's Disease
- Sickle Cell Anemia

Angioid streaks

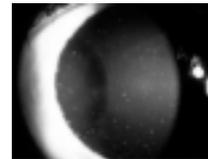
Management: Angioid Streaks

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

Follow up:

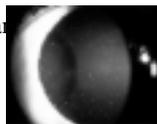
- Twice a year with a dilated fundus examination, OCT/OCTA
- Amsler Grid self-testing (~3 x week)

A Word About Uveitis



What is uveitis?

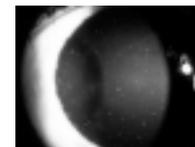
- Defined as inflammation of the uveal tract.
- For decades, considered a single disease.
- Fact: Uveitis entails a multitude of diseases.
 - Some uveitic diseases are local, ocular immune.
 - Many are systemic diseases with ocular manifestations.



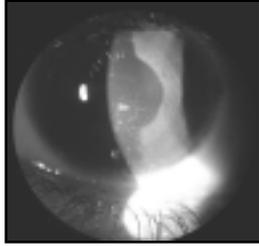
What is uveitis?

- Because the spectrum of pathogenesis ranges from autoimmunity to neoplasia to viruses, management requires an understanding of:

- Internal medicine
- Infectious diseases
- Rheumatology
- Immunology



Uveitis is an Immunological Process

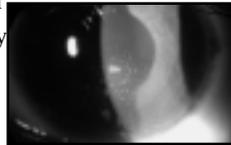


Immune Privilege

- 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.

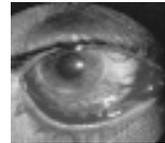
Common Etiologies of Anterior Uveitis

- 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



Hypopyon w/ HLA-B27

“A patient with recurrent, acute, unilateral, alternating anterior uveitis is nearly 80% likely to be HLA-B27 positive.”

Zamecki and Jabs
Am J Ophthal, 2010

Review of Systems Quiz

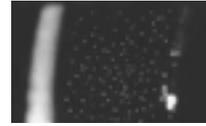
- A granulomatous condition is characterized by an organized collection of:
 - A. Macrophages.
 - B. Eosinophils.
 - C. Histamine.
 - D. Tumor cells.

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

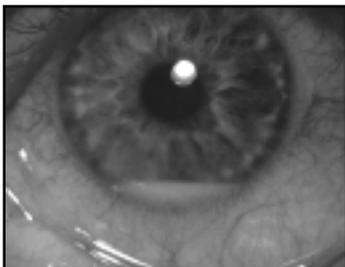


Hypopyon with 4+ cell and 3+ flare



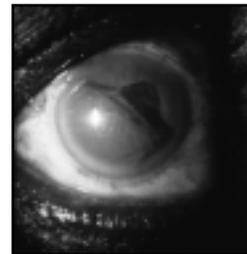
Hypopyon

- 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.

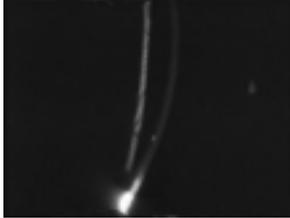


Hyphema

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



KPs and Iris Nodules



Serous/Exudative RD in Posterior Scleritis



Questions/Comments?



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.

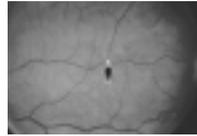
Review of Systems Quiz

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.



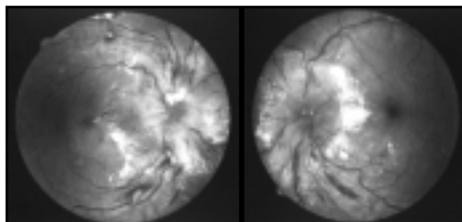
Hypertension



How High is High?? Classification of blood pressure

Category	Systolic		Diastolic
Optimal*	<120	and	<80
Normal	<130	and	<85
High-normal	130-139	or	85-89
Hypertension*			
Stage 1	140-159	or	90-99
Stage 2	160-179	or	100-109
Stage 3	≥180	or	≥110

The Eye in Systemic Disease



Grade 4 Hypertensive Retinopathy

The Eye in Systemic Disease

Clinical Ophthalmoscopic findings

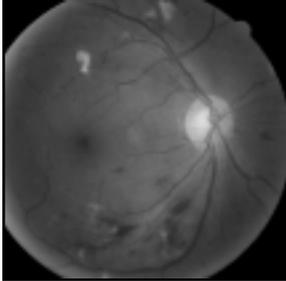
Grading of Hypertensive Retinopathy

Grade 1	Retinal vessels narrowed	> 90 and < 110 Diastolic BP
Grade 2	Nicking of retinal vessels	> 90 and < 110 Diastolic BP
Grade 3	CWS, Hemes, Lipid exudates	> 110 - 115 Diastolic BP
Grade 4	Grade 3 + Optic disc swelling	> 130 Diastolic BP

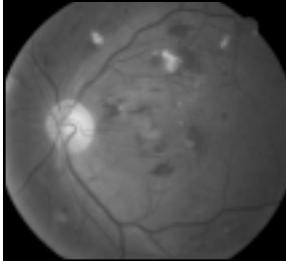
• Grades 3 and 4 = increase risk of cerebral, heart and kidney problems

The Eye in Systemic Disease

54 year old
 + Diabetes
 + HTN
 + Cholesterol

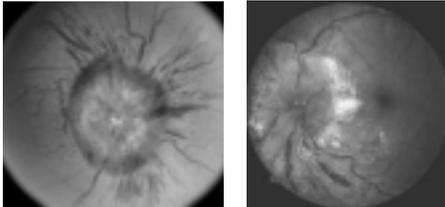


The Eye in Systemic Disease

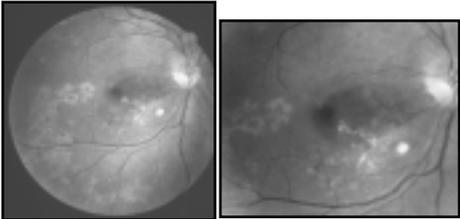


The Eye in Systemic Disease

Malignant Hypertension



Elschnig Spots in Hypertensive Choroidopathy



Hypertension Quiz

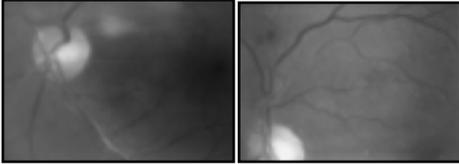
- What is the most frequently encountered and primary manifestation of hypertensive retinopathy?
 - a. dot-blot hemorrhages
 - b. arteriole sclerosis
 - c. exudative macular star
 - d. optic nerve swelling

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

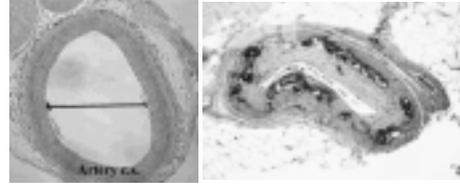
The Eye in Systemic Disease

Essential Hypertension – Long standing

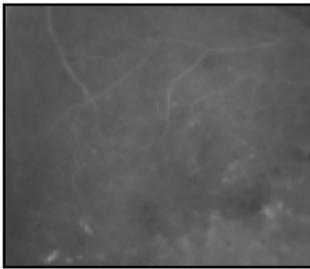


Arteriosclerosis Grade 2-3

Arteriosclerosis with calcification of vessel wall

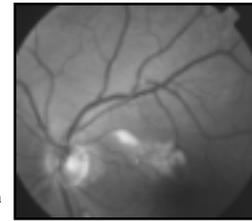


The Eye in Systemic Disease



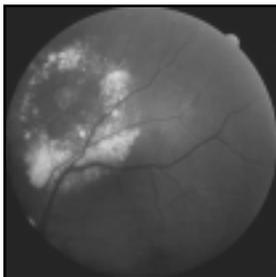
Atherosclerosis – Most common cause of thrombosis

- Diabetes
- Hypertension
- Hyperlipidemia
- Cigarette Smoking
- Alcohol consumption



Obesity → Genetics, Environmental (super-size), Psychological, Behavioral

Retinal Arterial Macroaneurysm



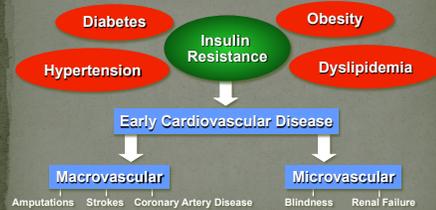
Classification of Hypertension

- 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

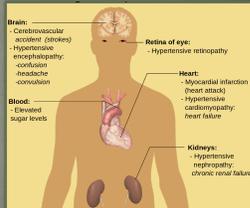
The Deadly Quartet



Wong TY, et al. *Am J Ophthalmol.* 2008; 141:448
 Opara JU, Levine JH. *South Med J.* 1997;90:1162-1168

Impact of Hypertension Morbidity/Mortality due to End-Organ Damage

- Cardiac: CHF, CHD, Sudden Death
- Cerebrovascular: Stroke, TIA
- Renal Tissue/Vascular: Renal Failure
- Vascular Disease: Peripheral and Aortic



Hypertension and Ocular Disease

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

Mitchell P, et al. *J Glaucoma.* 2004; 13:319
 Zau D, et al. *Ophthalmology.* 2016; 122:72

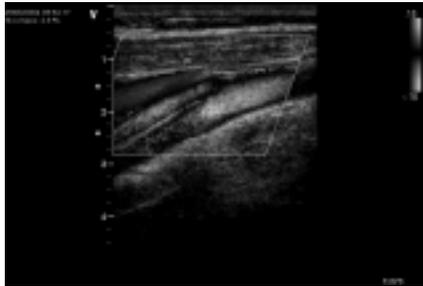
Summary – Benefits of Lowering BP

	Average % Risk Reduction
Stroke Incidence	35-40%
Heart Attack	20-25%
Congestive Heart Failure	50%

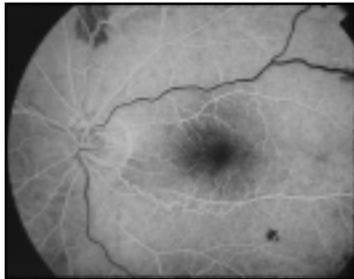
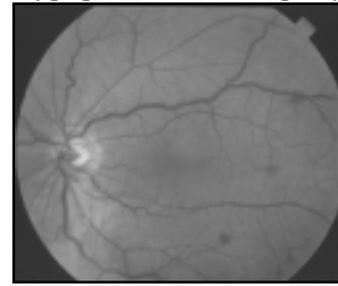
Treatments

- 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

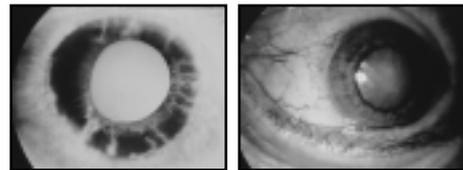
Carotid Doppler (Duplex)



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)



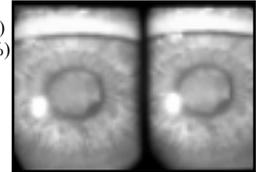
Key Point

- 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



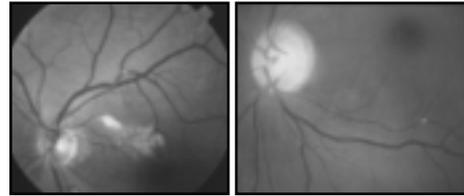
The Eye in Systemic Disease

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

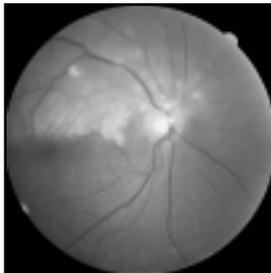
The Eye in Systemic Disease

Ocular Ischemic Syndrome



Cholesterol Plaques, disc pallor

The Eye in Systemic Disease



55 yo AA male
BRAO OD

The Eye in Systemic Disease



55 yo AA male OS

The Eye in Systemic Disease

Ocular Ischemic Syndrome

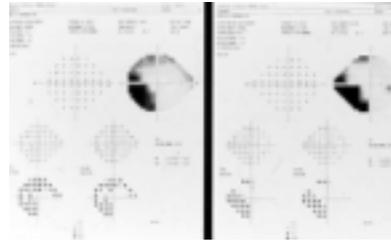
Treatment:

- 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:**

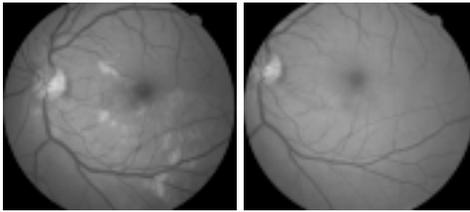
Leading cause of death in OIS = Ischemic heart disease
 Second leading cause of death = Stroke

The Eye in Systemic Disease



Occipital Lobe Infarct

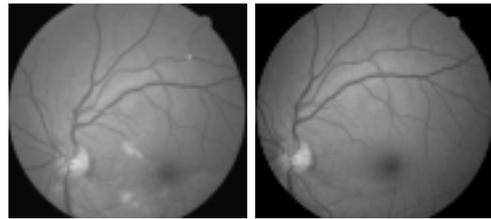
The Eye in Systemic Disease



Pre/post Endarterectomy

The Eye in Systemic Disease

Pre/post Endarterectomy



QUESTIONS AND COMMENTS?



Inflammatory Disease



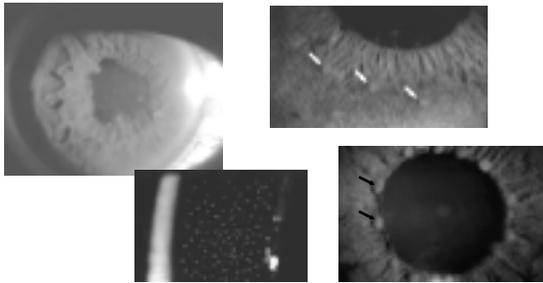
History

- 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

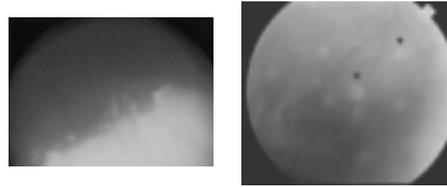
Clinical Findings

- 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

What is your plan?

- Ocular management?
- Systemic testing?
- Consultation?

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

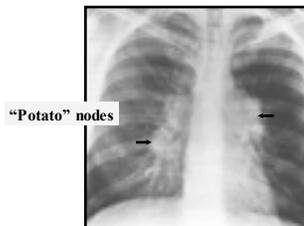
Actual Management

- 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

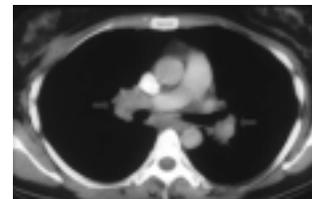
Corticosteroids

- 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



Bilateral Hilar Lymphadenopathy on CT Scan of Chest



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/Comments?



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

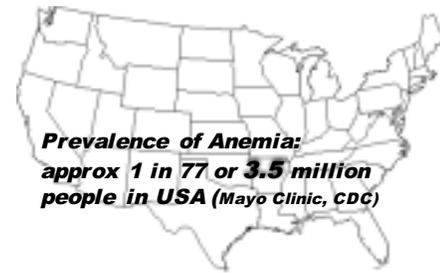
- Anemia
- Sickle cell hemoglobinopathy
- Hematologic malignancies

*Prevalence of Anemia Worldwide
affects more than 2 billion people
(World Health Organization)*



Anemia:

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



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

Folate aids in the production of red blood cells

Folate aids in the synthesis of DNA

Vitamin B12 Deficiency/Folate Deficiency

Pernicious Anemia**

Folate works with B12 and vitamin C to help the body digest and utilize proteins

Spinach, Broccoli, Lentils, Beans, Peas, Asparagus, Avocado, Orange, Grapefruit, Pineapple, Strawberry, Raisins, Raisin Bran, Raisins

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

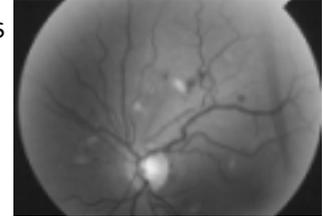


Brittle fingernails



Anemic Retinopathy

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



Anemic Retinopathy

- DDX:
 - hypertensive 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



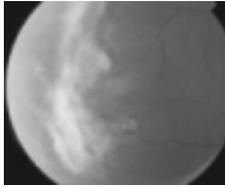
Questions/Comments?



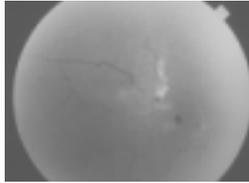
Case: 44 yo BM

- CC: Floaters OD X 6 months/ - flashes of light/ +frontal headaches
- PMHX: Positive Sickle Cell Trait
 - 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



OS: Fibrotic scaffolding with venous tortuosity and hemorrhages



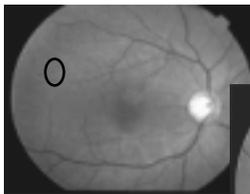
OD: Fibrotic scaffolding with venous tortuosity and areas of NV

Hemoglobin: HbA 60%, HbS 40%

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

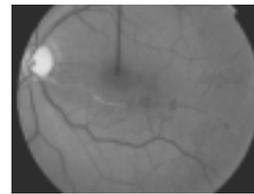


OD: Peripheral dot hemorrhage

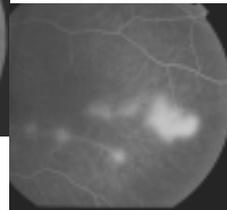


OS: (BRAO) with sea-fan neovascularization OS

Red-free and FA of OS



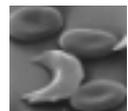
Hemoglobin: HbA 58.3%, HbS 38.1%



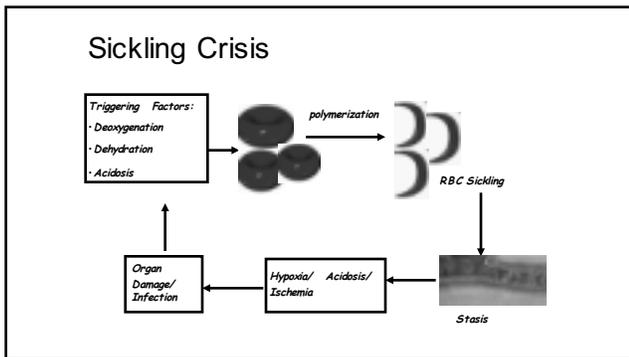
Ddx. Of Peripheral NV

- Familial exudative vitreoretinopathy
- Hyperviscosity syndromes
- Radiation retinopathy
- Sarcoidosis
- Ocular ischemic syndrome
- Sickle cell retinopathy
- Chronic myelogenous leukemia

Sickle Hemoglobinopathies

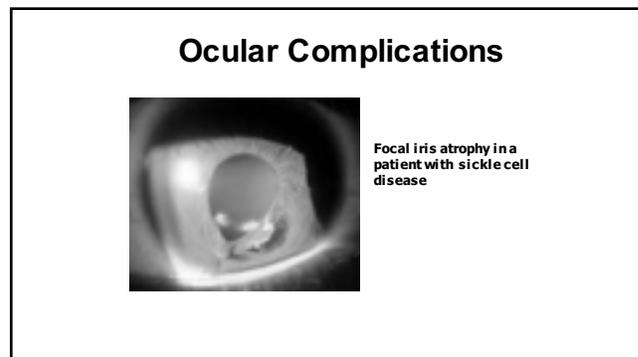


- The most prevalent genetic disorders in US
 - 10-14% of African-Americans/Mediterranean ancestry
- ****Autosomal recessive****
- Pathophysiology
 - Sickle shape of RBC's
 - Response to decrease O₂ tension
 - Hypoxia, acidosis, and ischemia



- ### 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 of sickle-cell dx.)
 - 8-10% of the Black population
 - 35-40% Hb S and 55-60% Hb A

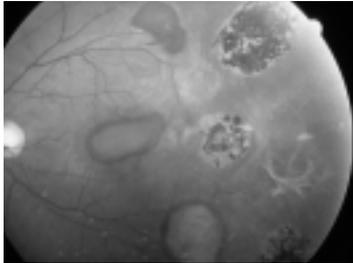
- ### Additional Testing for Sickle cell:
- CBC w/hematocrit
 - Sickledex
 - Solubility test that detect the presence of Hemoglobin S
 - Hemoglobin Electrophoresis
 - DNA analysis



- ### Ocular Complications of Sickle Cell
- Sickling → micro-vascular occlusion → ocular ischemia, infarction → neovascularization, and fibrovascularization
 - Retinopathy
 - Increased severity in SC and β-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 with-out pressure
 - Iridescent spots

Non-proliferative SC Ret



■ 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

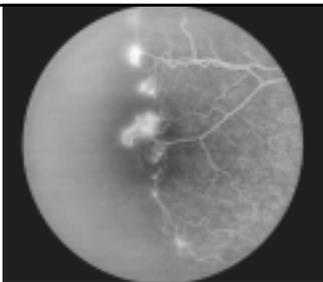
■ Proliferative sickle cell retinopathy is characterized by _____?

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

Proliferative Retinopathy

Five stages:

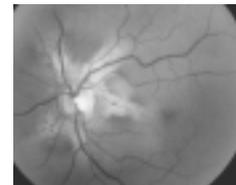
- **Stage 1.** Peripheral Arteriolar Occlusion
- **Stage 2.** Peripheral Arteriovenous Anastomoses
- **Stage 3.** Neovascular and Fibrous Proliferations-Sea Fan formation
 - Auto-infarct or spontaneously regress (20-60%)
- **Stage 4.** Vitreous Hemorrhage
- **Stage 5.** Retinal Detachment



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
- Epiretinal membrane
- Optociliary shunt vessels
- Disc Sign
 - Segmentation of capillary vessels (rare)
- **NOT** Neovascularization



ANGIOID STREAKS

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 Siqeria.....regression of retinal neovascularization with intravitreal Avastin® injection.....

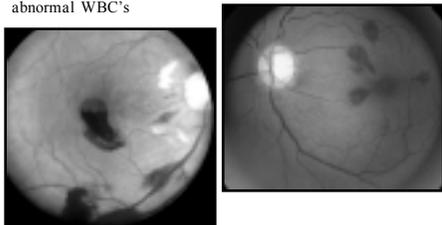
Take home message:

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

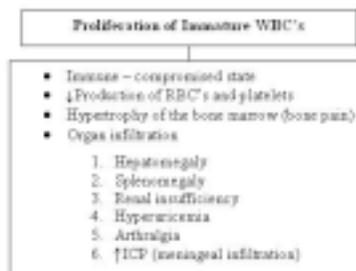
Hypertension, Diabetes, Collagen Vascular Diseases, Sarcoidosis, Ocular Trauma

The Eye in Systemic Disease

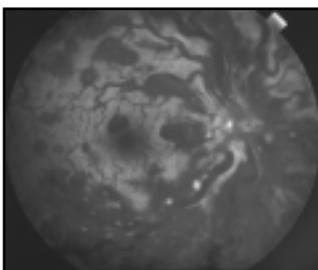
Leukemia – cancer that originates in the bone marrow – abnormal WBC's



Leukemia



The Eye in Systemic Disease



The Eye in Systemic Disease

Leukemia

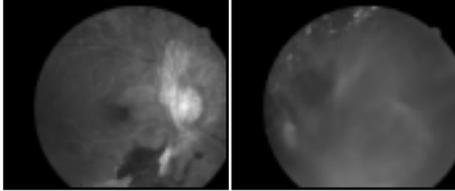
- Ocular involvement occurs in ~ **80%** of cases
- Ocular manifestations can be divided into three categories
 - a. leukemic infiltrates
 - b. secondary complications related to anemia, hyperviscosity
 - c. opportunistic infections (CMV, fungal, etc.)
- The ocular manifestations resolve after chemotherapy or radiation

Treatment of Leukemia

- Chemotherapy
- Radiation
- Bone marrow transplantation
- Biological therapy - Interferon

The Eye in Systemic Disease

Radiation Retinopathy



Radiation doses range from 11–35Gy. Onset from 1-8 years

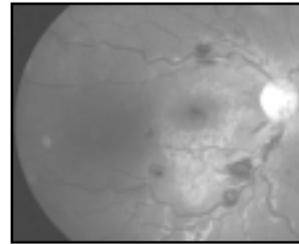
Case: 54 WF

- 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

Leukemic Retinopathy



WBC count of 112 (normal ranges: 4.5-11.5)

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

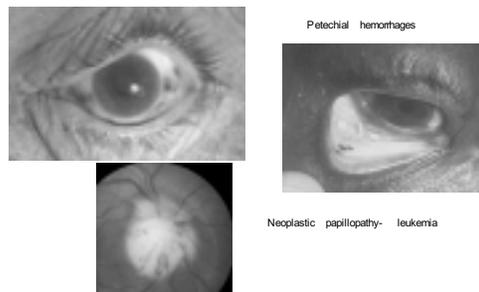
Leukemia

- Acute Leukemia
 - Rapid/progressive course that ends in death within months.....
 - w/out tx- avg survival rate is 4 months
 - Immature leukocytes
 - **Enlarged lymph nodes, spleen**
 - Bone pain (bone marrow)
 - CNS involvement

Leukemia

- 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



Ocular Complications of Leukemia

- Ocular Adnexa
 - Lacrimal gland infiltration
 - EOM infiltration
 - Eyelid swelling (infiltration)
 - ***exophthalmos, 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
Mickey and me!

Joe

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