

Review of Systems

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Financial Disclosure

- With respect to this course, I have no relevant financial relationships to declare.



QUESTIONS

AND ANSWERS



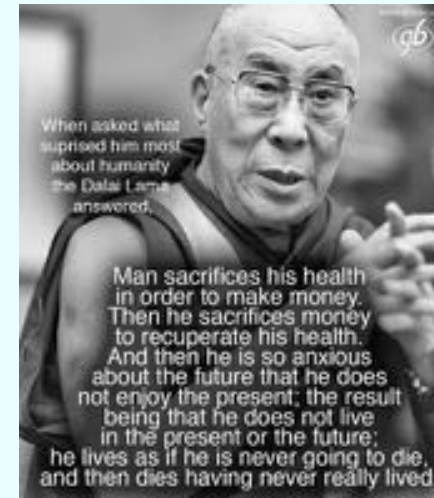
Course Goal

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

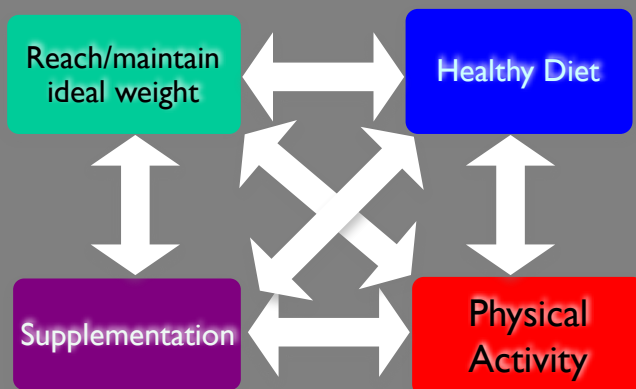


The Eye in Systemic Disease

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



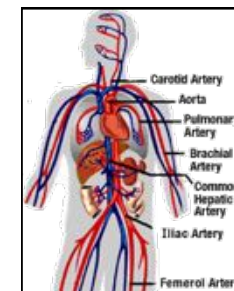
Pizzi's 4 Pillars of Wellness



❑ 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.

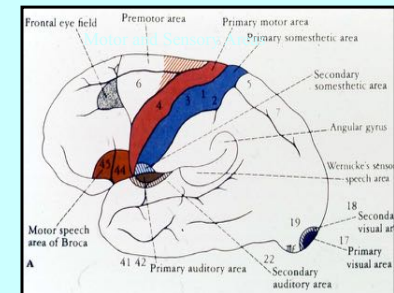
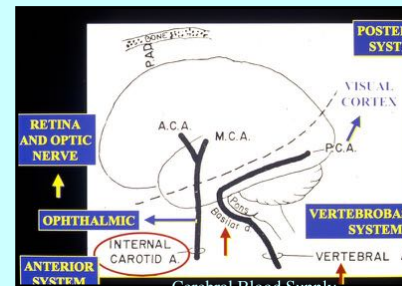
❑ Primary reason for dilation is to detect **systemic** disease.



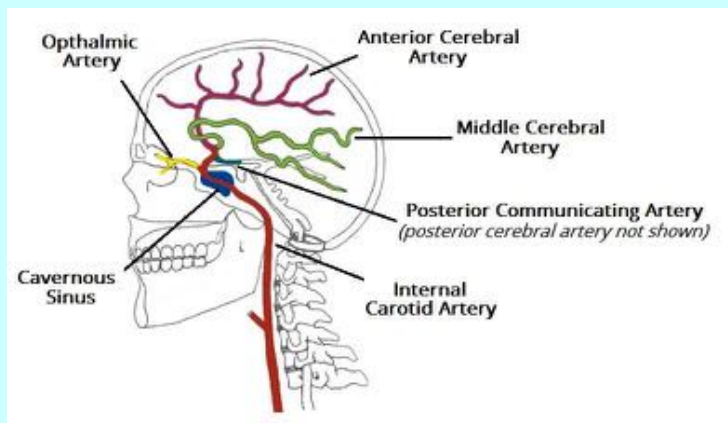
The eye is the only part of the body where neurological and vascular tissues can be directly and simultaneously viewed.



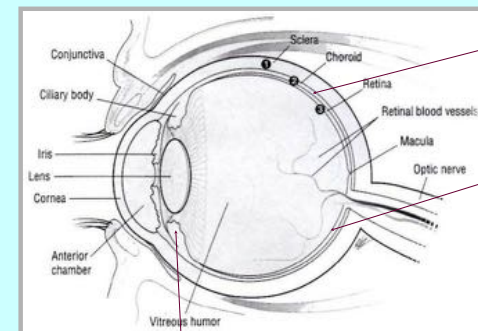
The Eye in Sytemic Disease



The Eye in Sytemic Disease



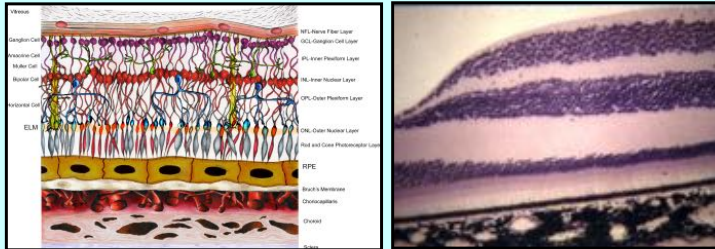
Ocular Blood Flow



Choroid 80%
Sympathetic NS
Retina 5 %
Auto-regulated

Iris / Ciliary Body 15%

The Eye in Systemic Disease



Inner and Outer Blood Retinal Barriers

Retina/RPE, Choroidal Pigmentation

Epidemics and Other Major Public Health Challenges



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

- 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 \geq 150 mg/dL



HDL cholesterol:

Men — <40 mg/dL

Women — <50 mg/dL



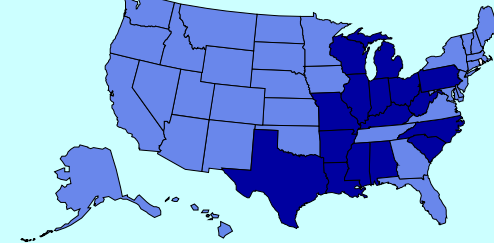
BP \geq 130/85 mmHg



FPG \geq 100 mg/dL

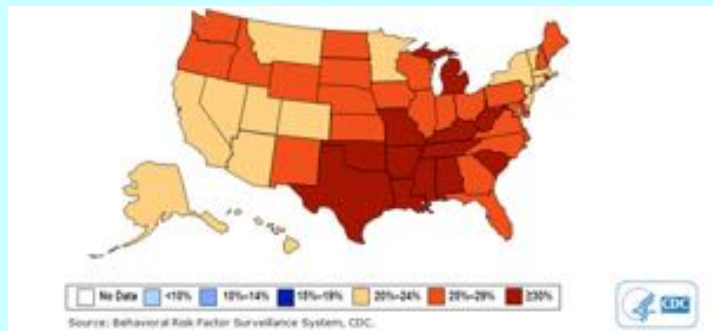
Obesity Trends* Among U.S. Adults BRFSS, 1994

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

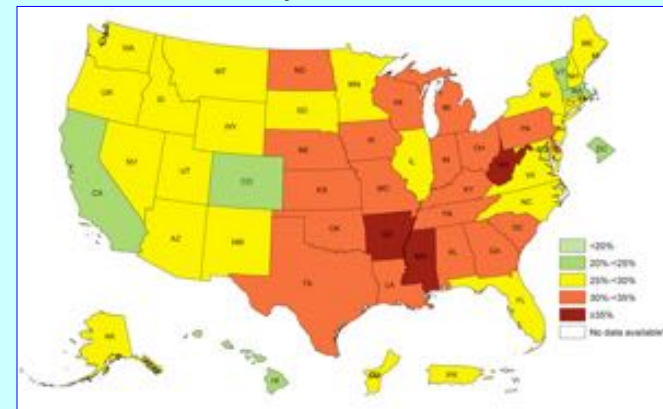


No Data <10% 10%–14% 15%–19% 20%–24% \geq 25%

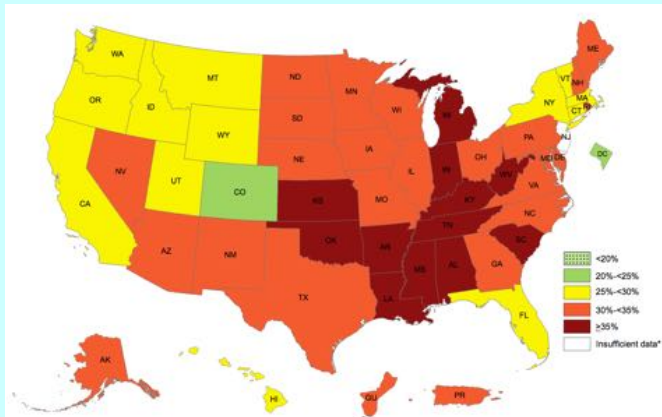
Obesity Trends-2012



Obesity Trends-2014



Obesity Trends-2019



Source: Behavioral Risk Factor Surveillance System

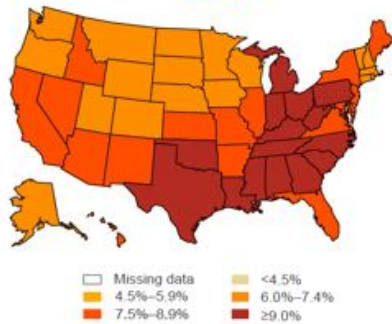


Statue of David
returns to Italy after
3 years in the USA

“Diabetes Belt”

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

2010



“Diabetes Belt”

Figure 2. Age-adjusted, county-level prevalence of diagnosed diabetes among adults aged ≥20 years, United States, 2013

2013 Diagnosed Diabetes Prevalence



Data source: United States Diabetes Surveillance System

"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

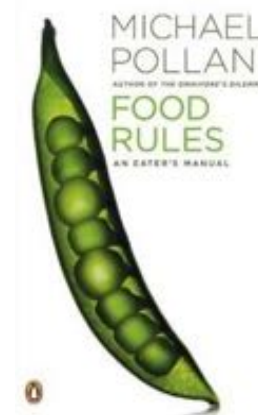
Not refined, synthetic, food-like products.

Not too much.

Portion size

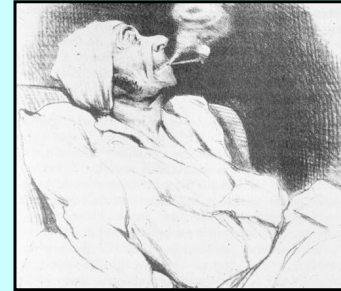
Mostly plants.

A plant-intensive diet provides
most essential nutrients.



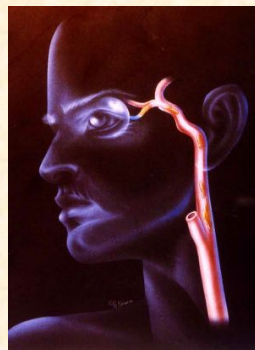


DM + Smoking = Blindness

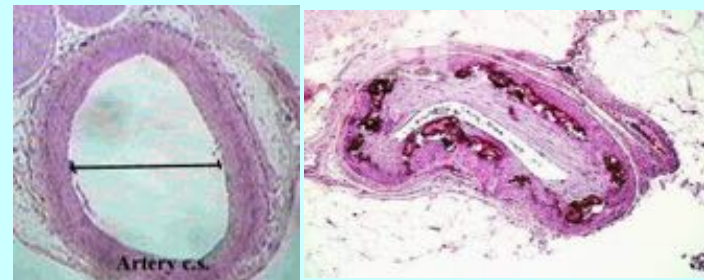


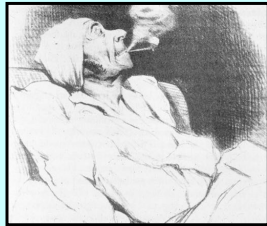
Cigarette Smoking, Ocular & Vascular Disease

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



Arteriosclerosis with calcification of vessel wall





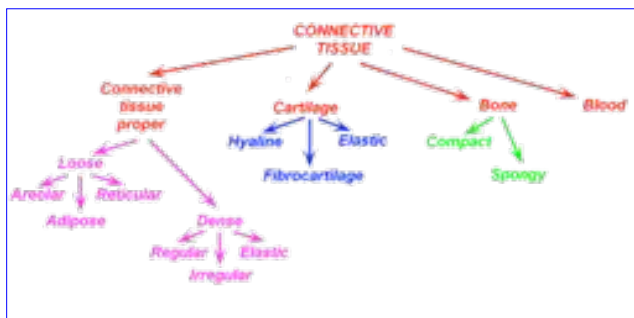
AMD + Smoking = Blindness

QUESTIONS

AND ANSWERS



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.

The Eye in Systemic Disease



The Eye in Systemic Disease



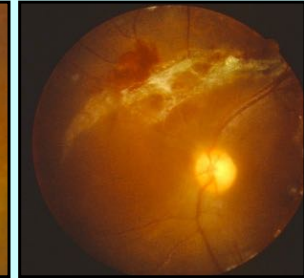
Masqueraders of Angioid Streaks

High Myopia



• Lacquer Cracks

Trauma



• Choroidal Rupture

Differential Dx. of Angioid Streaks: PEPSI

Diagnosis	Key Clinical Features
Pseudoxanthoma	redundant, "plucked chicken" skin hypertension weak peripheral pulses gastrointestinal bleeding
Ehlers-Danlos syndrome	blue sclera joint hyperextensibility fragile, elastic skin excessive bruising
Paget's disease	extraskelatal calcification bony erosion and abnormal formation osteoarthritis hearing loss, vertigo, tinnitus slurred speech, difficulty swallowing
Sickle cell disease	hemoglobin SS (most frequently) anemia
Idiopathic	vaso-occlusive crises

The Eye in Systemic Disease

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

Angioid Streaks

Management:

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

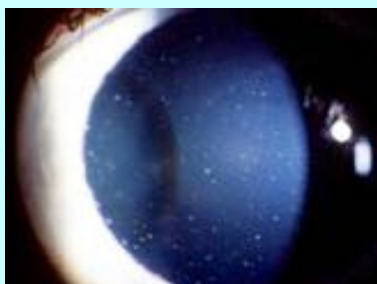
Follow up:

- Every 6 mon with dilated fundus examination, OCT/OCTA
- Amsler Grid self-testing (~3 x week)

Inflammatory Disease

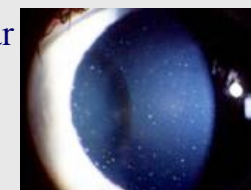


A Word About Uveitis



What is uveitis?

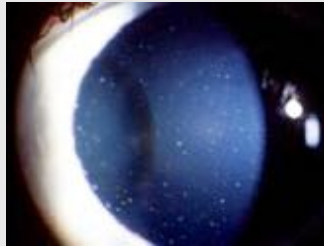
- Defined as inflammation of the uveal tract.
- For decades, considered a single disease.
- **Fact: Uveitis entails a multitude of diseases.**
 - Some uveitic diseases are local, ocular immune.
 - Many are systemic diseases with ocular manifestations.



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

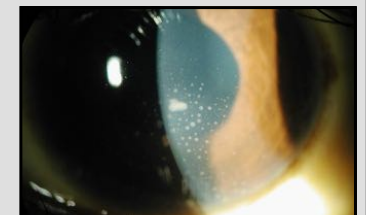


Immune Privilege

- The eye has 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 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

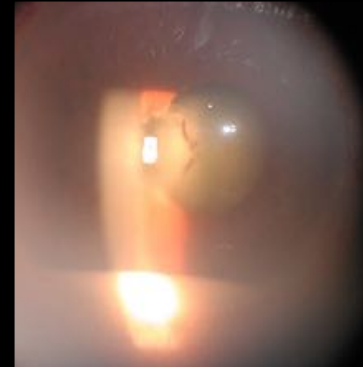
- A **granulomatous** condition is characterized by an organized collection of:
 - A. Macrophages.**
 - B. Eosinophils.
 - C. Histamine.
 - D. Tumor cells.

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



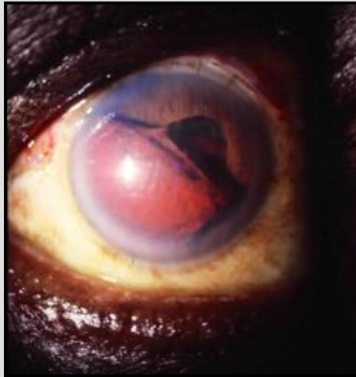
Hypopyon

- 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

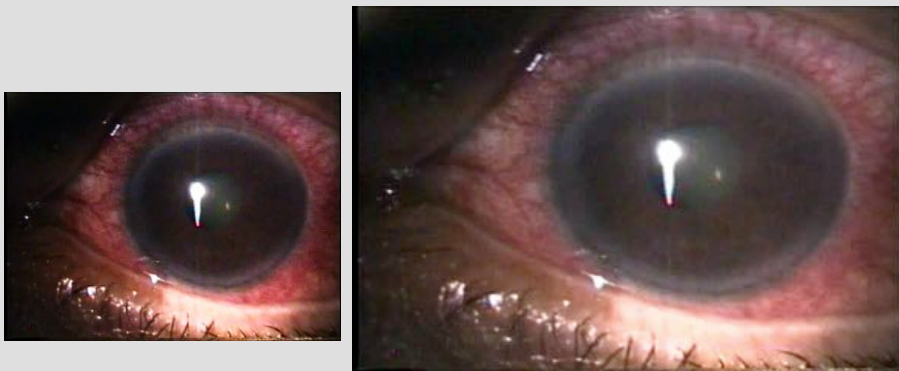
- Can occur in eyes with a chronic uveitis (UGH Syndrome)
- Can result from NVI/NVA



KPs and Iris Nodules



Serous/Exudative RD in Posterior Scleritis



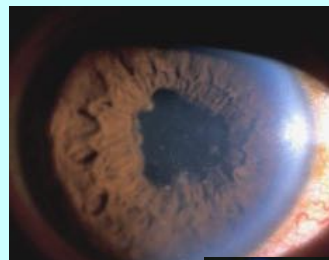
History

- 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

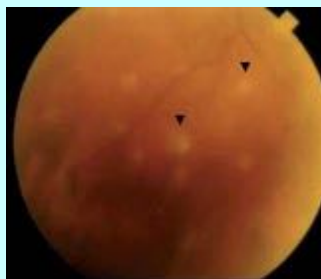
Clinical Findings

- 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.

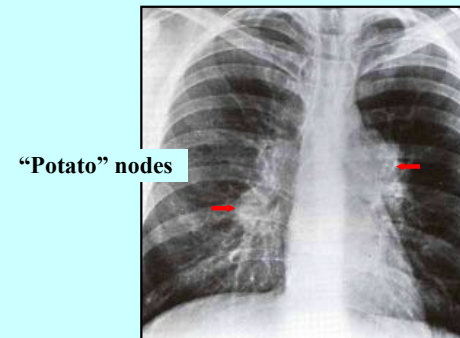
Actual Management

- Treated anterior uveitis using conventional topical meds.
 - Steroid
 - Cycloplegic (atropine)
- Ordered targeted systemic “uveitis” work-up
 - Serum lysozyme
 - 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 and Answers



Review of Systems Quiz

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

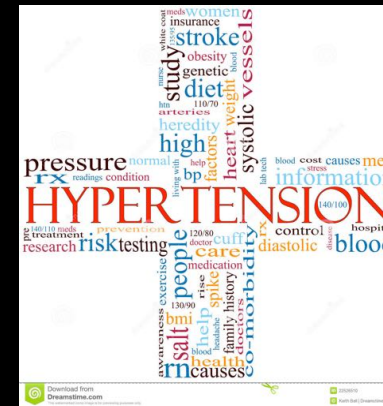
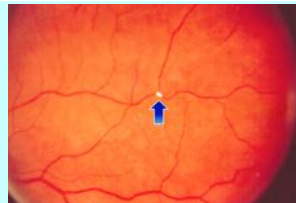
- A. Stroke.
- B. Myocardial infarction.
- C. Cancer.
- D. Pneumonia.

Review of Systems Quiz

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

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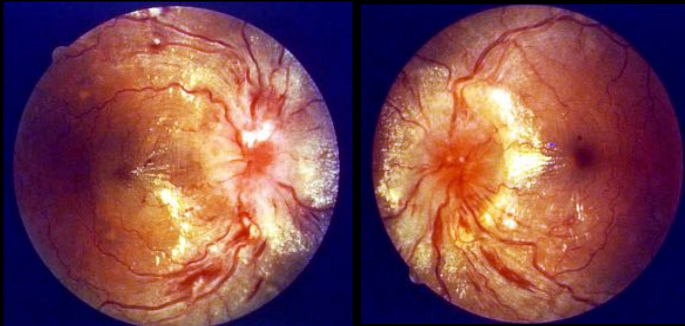
- Myocardial Infarction is the most common cause of death in USA.
- 610,000 per year
- Cardiac valve disease is most common cause of cardiac emboli to the eye.**



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

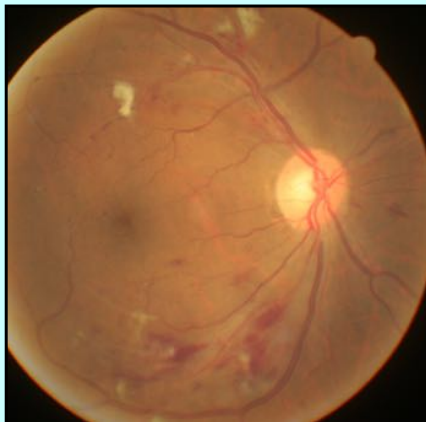
Grading of Hypertensive Retinopathy

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

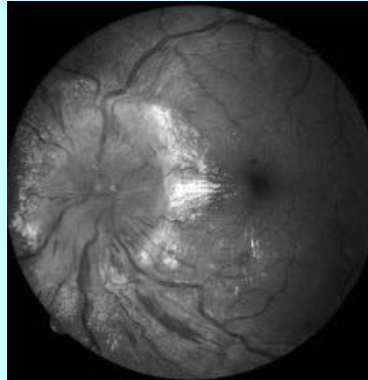
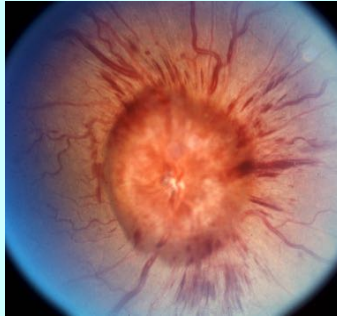


The Eye in Systemic Disease



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

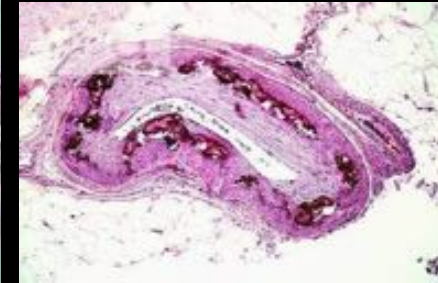
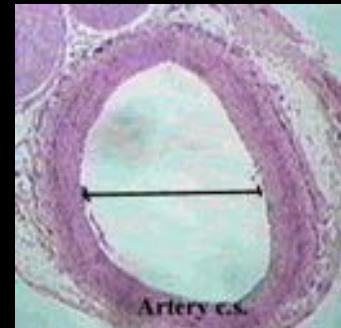
The Eye in Systemic Disease

Essential Hypertension – Long standing

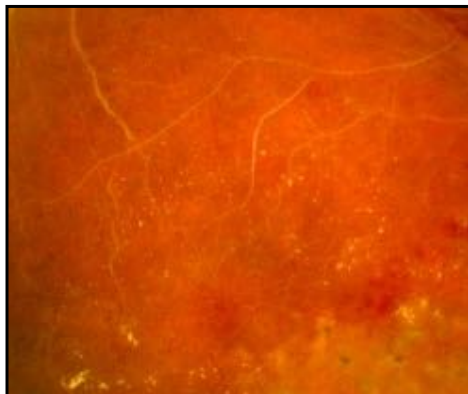


Arteriosclerosis Grade 2-3

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



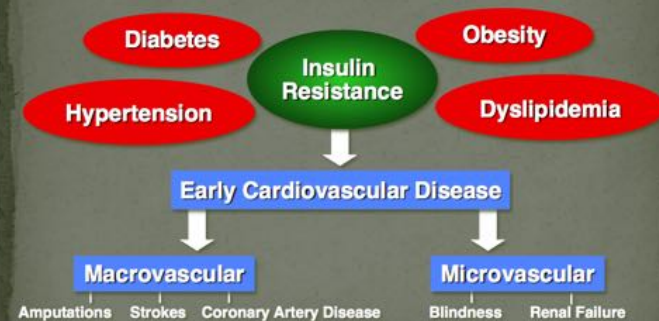
Classification of Hypertension

- 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

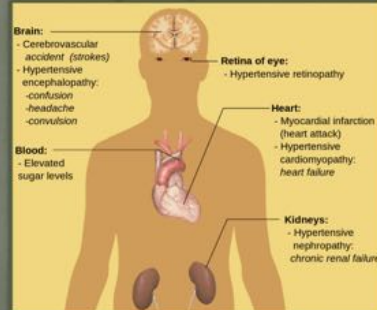
The Deadly Quartet



Wong TY, et al. *Am J Ophthalmol.* 2006; 141:446
 Opava 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 HTNsive 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*. 2015; 122:72

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!!!**

Summary – Benefits of Lowering BP

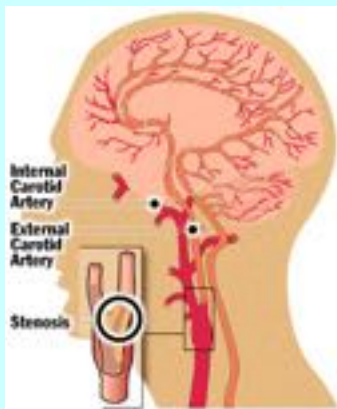
	Average % Risk Reduction
Stroke Incidence	35-40%
Heart Attack	20-25%
Congestive Heart Failure	50%

Questions & Answers



While nearly 1 million people visit Mackinac Island each year, the Island has less than 600 year-round residents.

Carotid Artery Occlusive Disease



Hypoperfusion Retinopathy

and the

Ocular Ischemic Syndrome

Carotid Artery Occlusive Disease

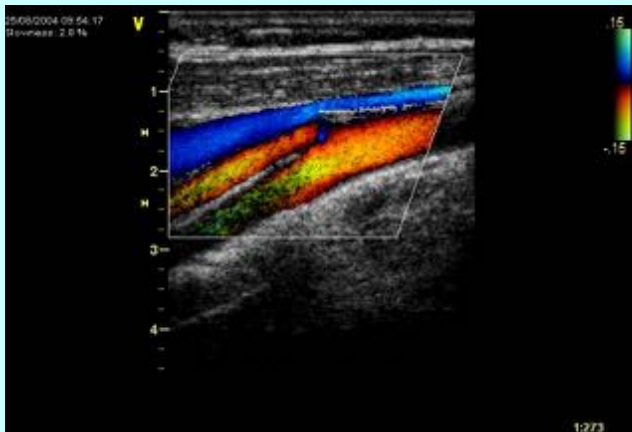


****Dot and Blot hemes in mid-peripheral retina**

Carotid Occlusive Dx: Bruit



Carotid Doppler (Duplex)



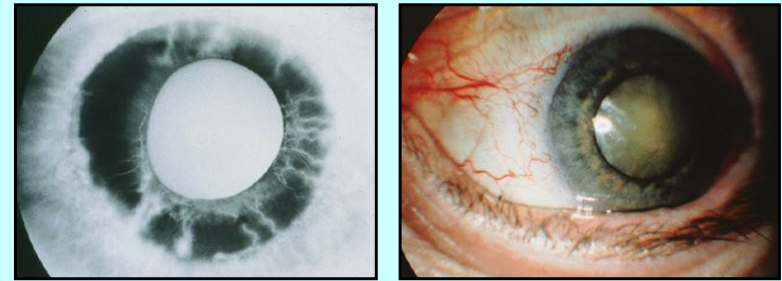
Hypoperfusion Retinopathy



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)



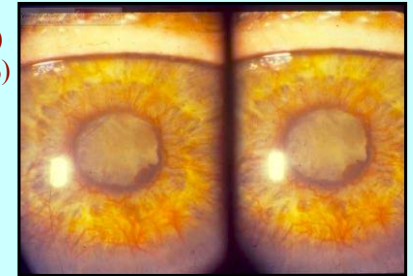
Key Point

- 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 Sytemic Disease

Ocular Ischemic Syndrome



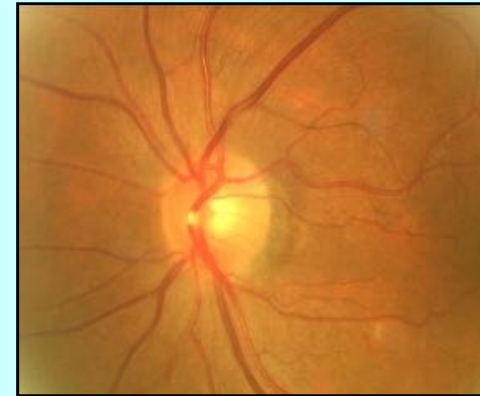
Cholesterol Plaques, disc pallor

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

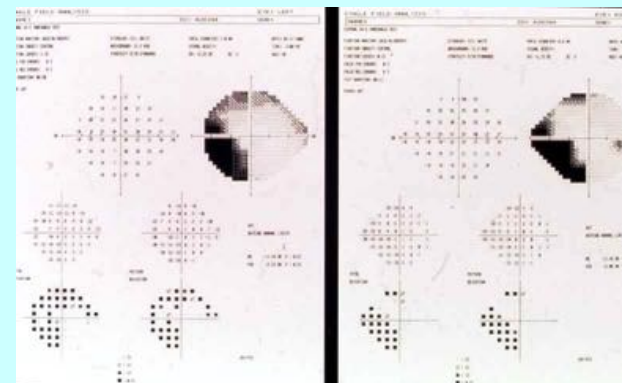
Treatment:

- 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:

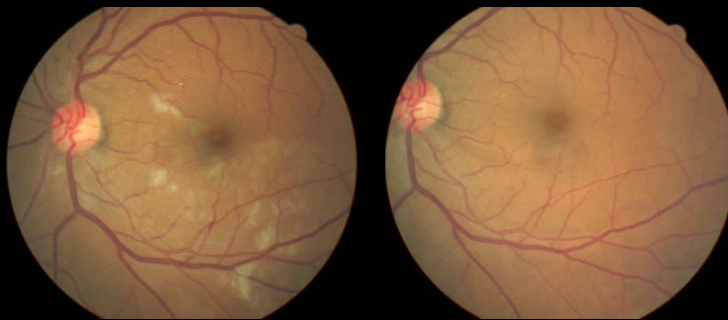
Leading cause of death in OIS = Ischemic heart disease
Second leading cause of death = Stroke

The Eye in Systemic Disease



Occipital Lobe Infarct

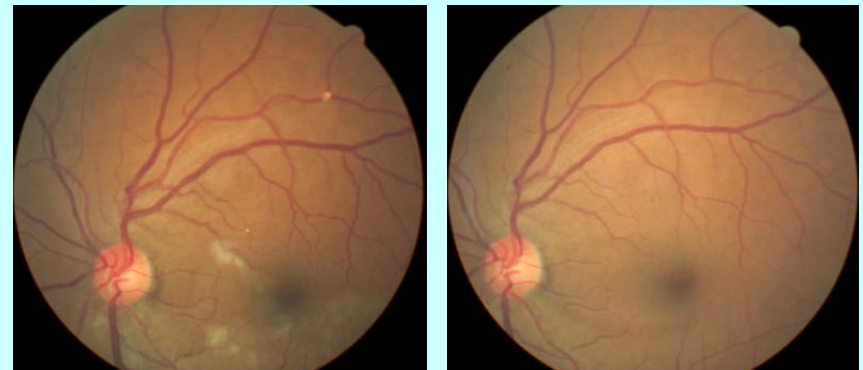
The Eye in Systemic Disease



Pre/post Endarterectomy

The Eye in Systemic Disease

Pre/post Endarterectomy



Causes of Embolism:

I Cardiac Disease

- Arrhythmias
- Valvular Disease
- Endocarditis
- Ischemic lesions
- Tumors



II Carotid Disease



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

Co-occurrence of Acute Retinal Artery Occlusion and Acute Ischemic Stroke: Diffusion-Weighted Magnetic Resonance Imaging Study

JUNWON LEE*, SEUNG WOO KIM*, SUNG CHUL LEE, OH WOONG KWON, YOUNG DAE KIM, AND SUK HO BYEON

Am J Ophthalmol 2014; 157: 1231-1238

¼ 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.



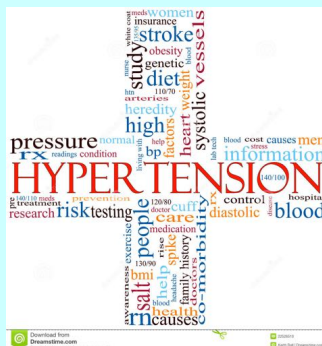
Neurology's STANDARD OF CARE

- Neurologists consider an acute retinal artery obstruction a true medical emergency and classify it as a stroke.
 - Embolus goes to the eye rather than to the brain
- Patients with acute RAO need to be sent to the nearest stroke center or hospital emergency room 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.

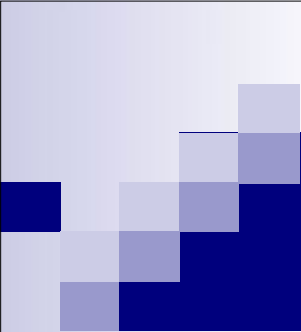
Questions and Answers



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