

# 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 we receive an honorarium.
- I have no proprietary interest in any products.



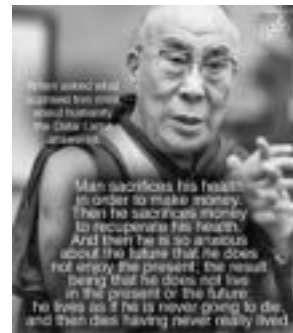
# Course Goal

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

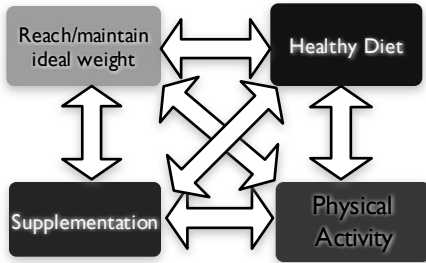


# QUESTIONS

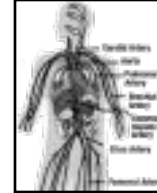
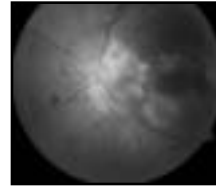
# AND COMMENTS?



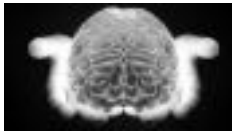
### Pizzi's 4 Pillars of Wellness



- ❑ 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.

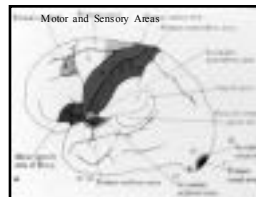


### The Eye in Systemic Disease

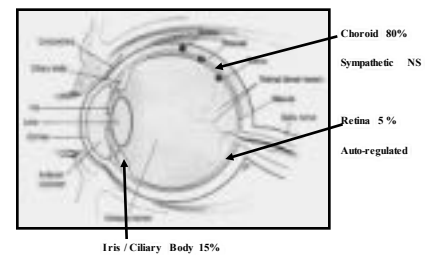
- Inflammatory
- Infectious
- Vascular
- Endocrine
- Neurologic
- Collagen-vascular
- Neoplastic



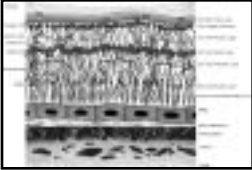
### The Eye in Systemic Disease



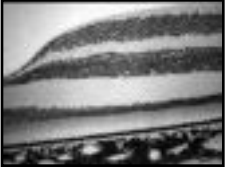
### Ocular Blood Flow



### The Eye in Systemic Disease




Inner and Outer Blood Retinal Barriers




Retina/RPE, Choroidal Pigmentation

## Neoplastic Disease



### "Nevoma"



## Follow or Co-manage?

### To Find Small Ocular Melanoma Using Helpful Hints Daily

- T= thickness (>2mm)
- F= subretinal fluid
- S= symptoms
- O= orange pigment
- M= margin touches disk


- No risk factors (<4%)
- 1 risk factor (36%)
- 3 risk factors (50%)
- 5 risk factors (70%)

**DOCUMENTED GROWTH - MEANS EVERYTHING**

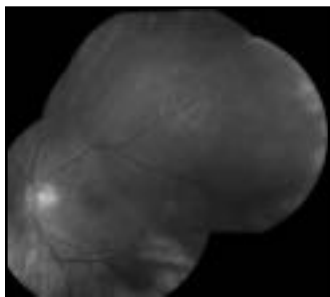
**Using Helpful Hints Daily= Ultrasound hollow, halo absent, drusen absent**

7/29/2016

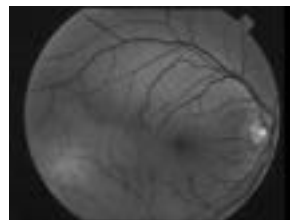
### OcularmelanomaCalculator.com



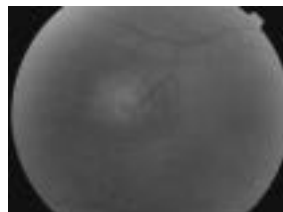




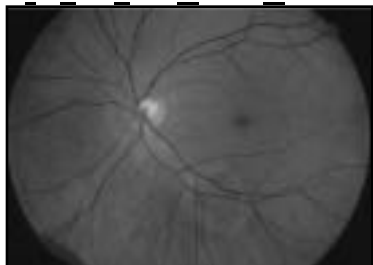
**Amelanotic Choroidal Melanoma**



**Choroidal Nevus?**



**To Find Small Ocular Melanoma**

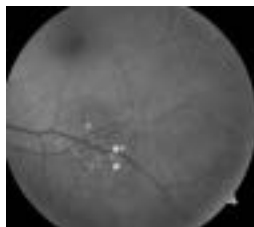


**NEVOMA**

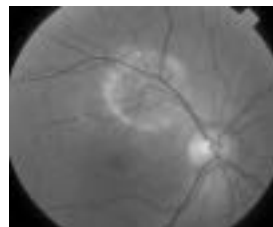
**Many patients with choroidal melanoma have no symptoms.**

Their tumors are found during a "routine" eye examination.

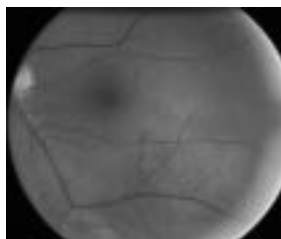
Nevus w/drusen



Halo Nevus



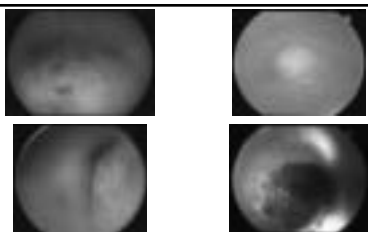
No drusen, no halo



Same eye



Primary choroidal melanomas



Questions and Comments?



### Treatment of Choroidal Melanoma

- Observation indicated in
  - elderly/infirm, lots of mets and very poor prognosis
  - small melanomas
- Enucleate, exenterate: large melanomas with secondary complications.

### Treatment of Choroidal Melanoma

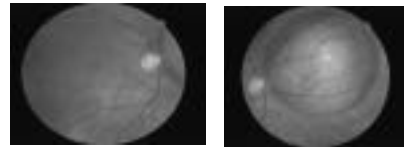
- Radiotherapy with plaque or external proton beam
- Transcleral resection
- Multiple treatment modalities:
  - Local resection + Plaque Rx + Photocoagulation

### Treatment Side Effects

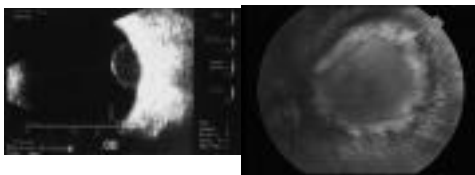
- Main side effect of focal ocular treatment is...
- Radiation retinopathy!
- NVD / NVE
- Exudative changes
- Macular edema
- Occurs several weeks to months after therapy



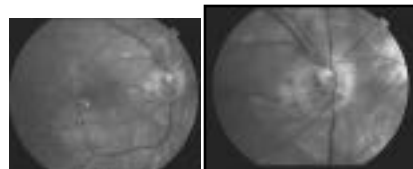
### Choroidal melanoma- pre-Radiotherapy



### Melanoma pre-Tx echography (left), post-radiotherapy (right)



### Radiation Retinopathy: exudate, NVD

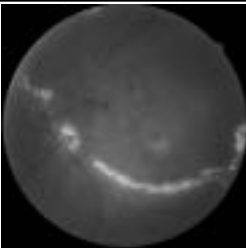


Acknowledgement: Shemol Reynolds, OD, FAAO

## Choroidal Melanoma pre-Tx




## S/P Radiotherapy

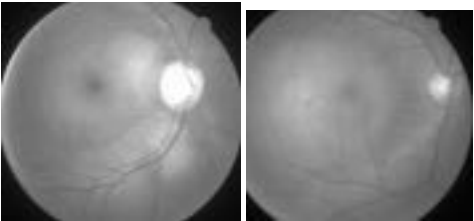


## Management of RR

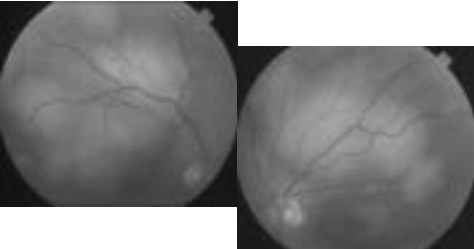
- Avastin/Lucentis/Eylea
- Laser
- Silicone oil at time of Brachytherapy
  - attenuates radiation dose, and may protect against radiation retinopathy



## Choroidal Metastasis



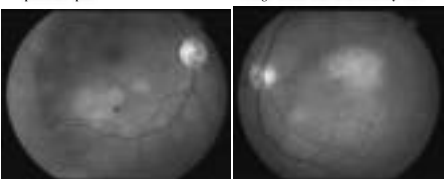
## Choroidal Metastasis



## METS

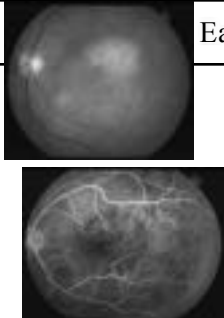
Multiple cream colored lesions in posterior pole

Large lesion with neurosensory RD





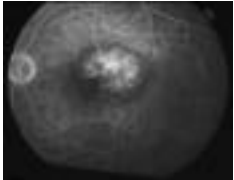
### Early IVFA OS




- Note blocking of the background hyperfluorescence in multiple areas including large central lesion

### Late IVFA

- Note late staining of large central lesion




### 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

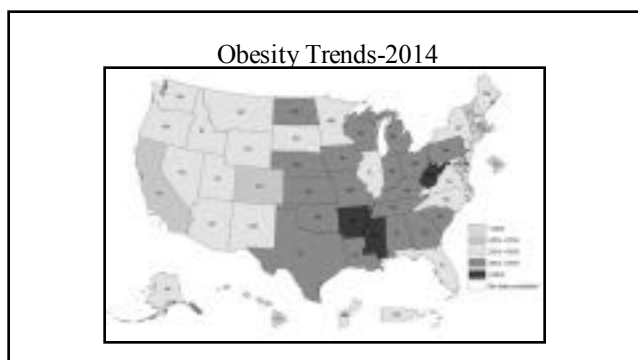
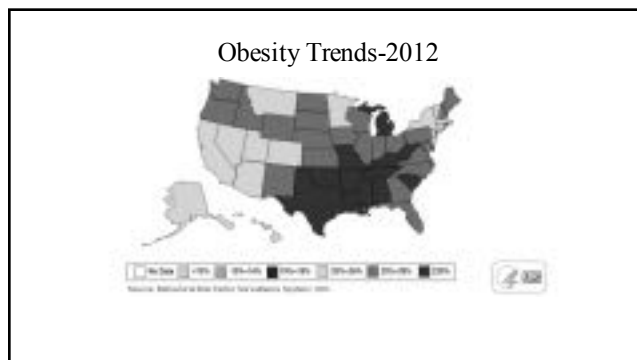
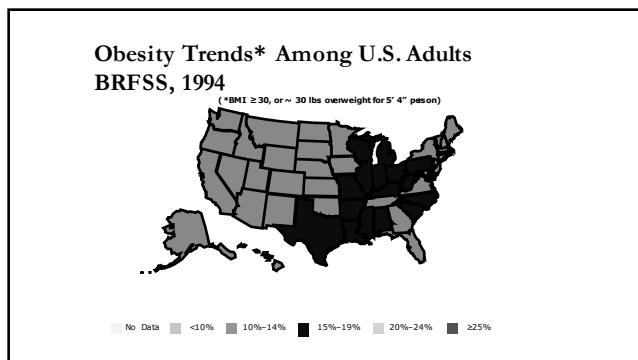


### Diabesity

- M\_\_\_\_\_ S\_\_\_\_\_ is characterized by central (abdominal) obesity, dyslipidemia, raised blood pressure, and insulin resistance.
- “Diabesity”
  - 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



QUESTIONS  
AND COMMENTS?



### 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

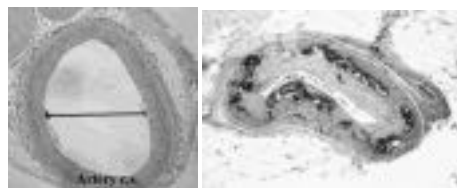


## Cigarette Smoking, Ocular & Vascular Disease

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



## Arteriosclerosis with calcification of vessel wall



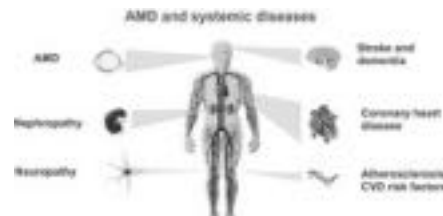


**AMD + Smoking = Blindness**

**Do age-related macular degeneration and cardiovascular disease share common antecedents?**

Age-related macular degeneration (AMD) and the various organ systems with which it has been associated. CVD, cardiovascular disease.

Kristin K. Snow & Johanna M. Seddon  
Ophthalmic Epidemiology Vol. 6, Iss. 2, 1999



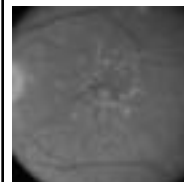
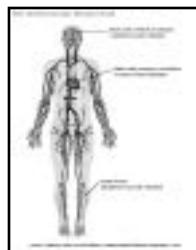
**Johanna Seddon, MD (Tufts U)**

" 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."

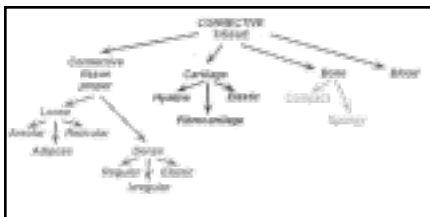


"Anyone with signs of intermediate-level macular degeneration in both eyes or advanced macular degeneration in one eye should also take dietary supplements that contain lutein, zeaxanthin, vitamin C, vitamin E, and zinc."

**Is AMD a Systemic Disease?**



**The Eye in Connective Tissue Disease**



**What is connective tissue?**

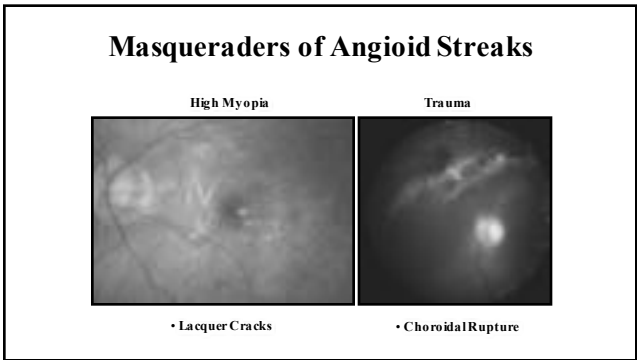
"Cellular glue" that gives tissues their shape and helps them do their work. Cartilage and fat are examples.

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

<b>Diagnosis</b>	<b>Key Clinical Features</b>
Pseudoxanthoma	whisker, "plucked chicken" skin hypertension weak peripheral pulses gastrointestinal bleeding
Chromocytoma syndrome	blue sclera joint hyperextensibility ligin, elastic skin excessive bruising
Page's disease	irregular calcification bone erosions and abnormal formation osteoporosis hearing loss, vertigo, tinnitus slurred speech, difficulty swallowing
Sickle cell disease	hemoglobin SS (most frequently) anemia
Marfan	vascular ectasia/aneurysm

### 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
- 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

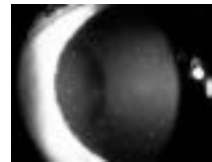
#### Follow up:

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

### Questions/Comments?



### 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



### What are HLAs?

- Human leukocyte antigens are proteins that help the body's immune system identify its own cells and distinguish between "self" and "nonself."
- HLA-B27 is found on cell surfaces. The HLA-B27 test determines the presence or absence of HLA-B27 protein on the surface of a person's white blood cells.
- People with HLA-B27 have an increased likelihood of developing autoimmune diseases.



### 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.

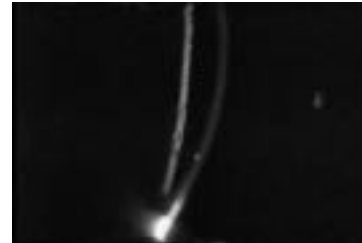


### HypHEMA

- 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 AND 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.

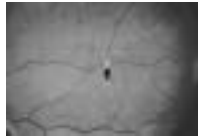
### Review of Systems Quiz

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

- A. Stroke.
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- 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

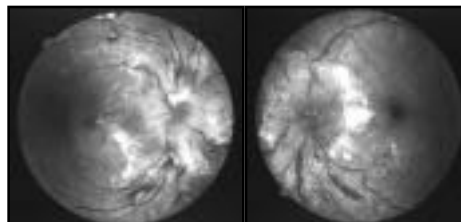
American College of Cardiology, 2017

**Categories of BP in Adults\***

BP Category	SBP		DBP
Normal	<120 mm Hg	and	<80 mm Hg
Elevated	120-129 mm Hg	and	<80 mm Hg
<b>Hypertension</b>			
Stage 1	130-139 mm Hg	or	80-89 mm Hg
Stage 2	≥140 mm Hg	or	≥90 mm Hg

\*Individuals with SBP and DBP in 2 categories should be assigned to the higher BP category.

**The Eye in Systemic Disease**



Grade 4 Hypertensive Retinopathy

**The Eye in Systemic Disease**

Clinical Ophthalmoscopic findings

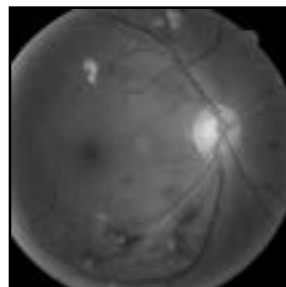
Grading of Hypertensive Retinopathy

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

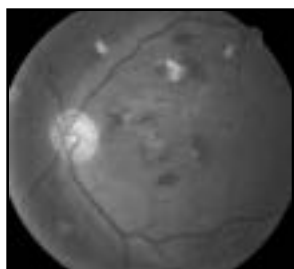
• Grades 3 and 4 = increase risk of cerebral, heart and kidney problems

**The Eye in Systemic Disease**

54 year old  
+ Diabetes  
+ HTN  
+ Cholesterol

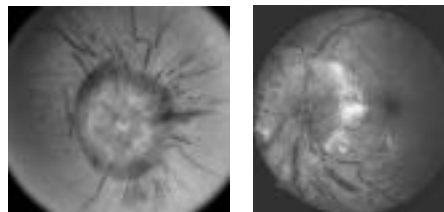


**The Eye in Systemic Disease**

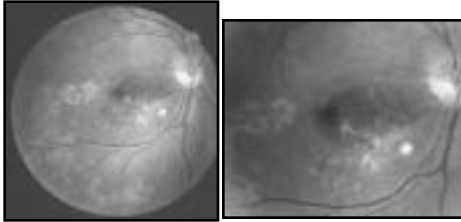


**The Eye in Systemic Disease**

Malignant Hypertension



Elschnig Spots in Hypertensive Choroidopathy



Hypertension Quiz

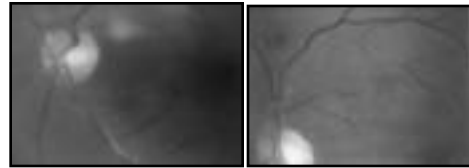
- What is the most frequently encountered and primary manifestation of hypertensive retinopathy?
  - a. dot-blot hemorrhages
  - b. arteriole sclerosis
  - c. exudative macular star
  - d. optic nerve swelling

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

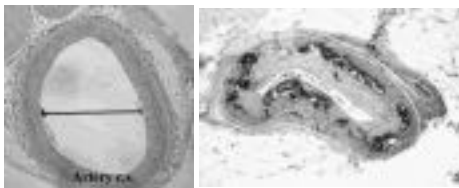
**The Eye in Systemic Disease**

Essential Hypertension – Long standing



Arteriosclerosis Grade 2-3

Arteriosclerosis with calcification of vessel wall

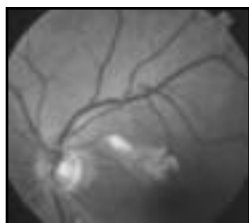


**The Eye in Systemic Disease**



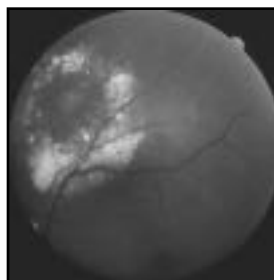
### Atherosclerosis – Most common cause of thrombosis

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



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

### Retinal Arterial Macroaneurysm



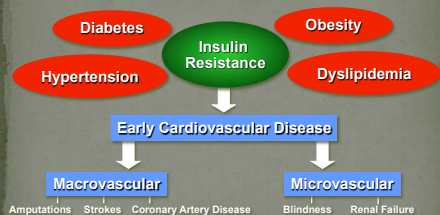
### Classification of Hypertension

- 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

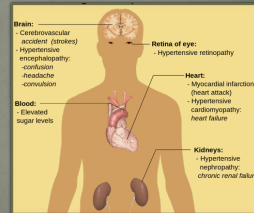
### The Deadly Quartet



Wong TY, et al. *Am J Ophthalmol*. 2006; 141:446  
 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 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;13:919  
Zou D, et al. Ophthalmology. 2015;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 initiated
- 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!!!**

### Questions and Comments?

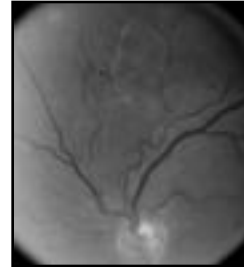


### Carotid Artery Occlusive Disease



**Hypoperfusion Retinopathy  
and the  
Ocular Ischemic Syndrome**

**Carotid Artery Occlusive Disease**

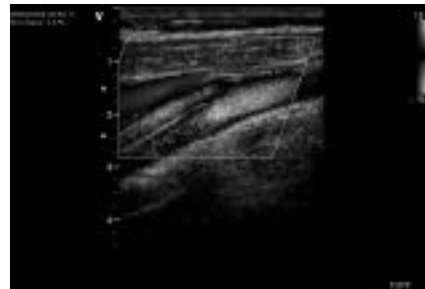


\*\*Dot and Blot hemes in mid-peripheral retina

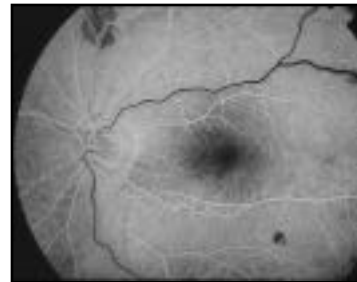
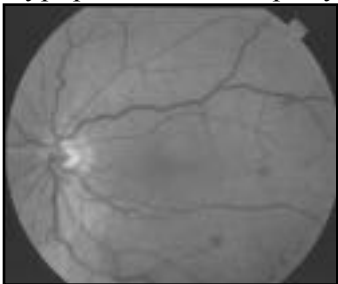
**Carotid Occlusive Dx: Bruit**



**Carotid Doppler (Duplex)**

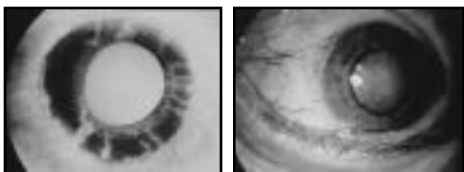


**Hypoperfusion Retinopathy  
Hypoperfusion Retinopathy**





### 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)



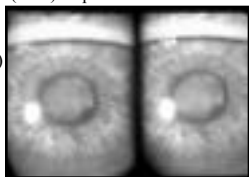
### Key Point

- 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



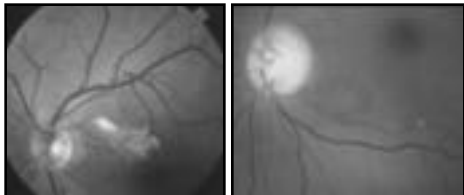
### The Eye in Systemic Disease

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

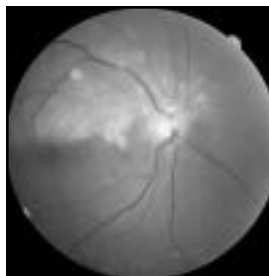
### The Eye in Systemic Disease

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:**

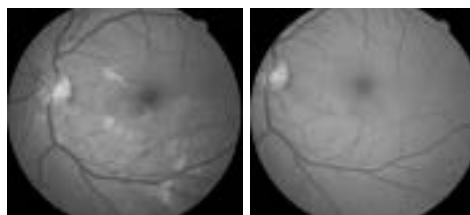
Leading cause of death in OIS = Ischemic heart disease  
Second leading cause of death = Stroke

### The Eye in Systemic Disease



Occipital Lobe Infarct

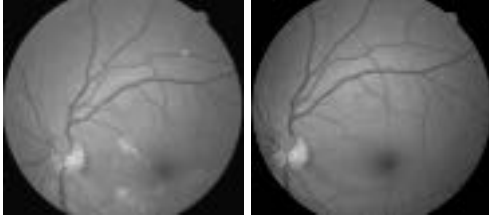
### The Eye in Systemic Disease



Pre/post Endarterectomy

## The Eye in Systemic Disease

Pre/post Endarterectomy



## QUESTIONS AND COMMENTS?



### 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*