

Slide 1

2025
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San Antonio

Course # 110

Oculosystemic Diseases
and the Drugs that Treat Them

Joe Pizzimenti, OD

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Slide 2

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San Antonio

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Disclosure statements:
No financial relationships to disclose

All relevant relationships have been mitigated.

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Slide 3

OCULOSYSTEMIC
DISEASES

And the Drugs That Treat Them

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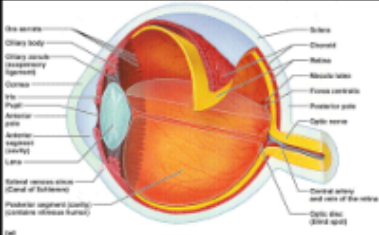
Slide 4

Disclosures

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

optometricretinasociety.org

Check out our E-newsletter



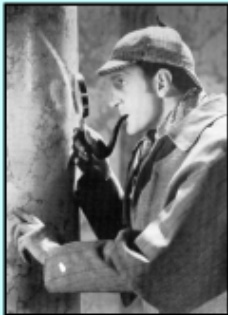
The diagram illustrates the internal anatomy of the human eye. Labels on the left side include: Iris, ciliary body, ciliary muscle (responsible for accommodation), Cornea, H₂O, Pupil, Aqueous humor, Anterior chamber, Posterior chamber (containing vitreous humor), and Retinal pigment epithelium. Labels on the right side include: Sclera, Choroid, Retina, Muscularis, Fovea centralis, Posterior pole, Optic nerve, Central artery and vein of the retina, and Optic disc (blind spot).

Questions?



The Eye In Systemic Disease

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

A black and white photograph of a man wearing a hard hat and safety glasses, looking intently at a large, textured surface, possibly a piece of machinery or a wall.

4 Pillars of Wellness

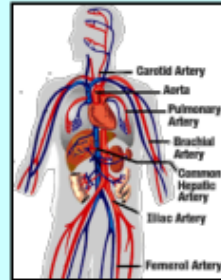
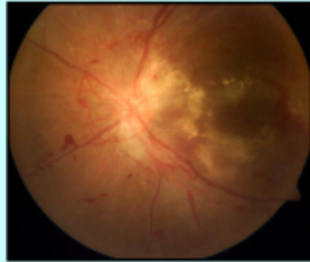
The diagram illustrates the four pillars of wellness as interconnected components. It features four colored boxes arranged in a square: a teal box at the top-left labeled 'Reach/maintain ideal weight', a blue box at the top-right labeled 'Healthy Diet', a purple box at the bottom-left labeled 'Supplementation', and a red box at the bottom-right labeled 'Physical Activity'. Every box is connected to every other box by a white double-headed arrow, indicating that all four pillars are interdependent and influence each other.

Slide 9

→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.



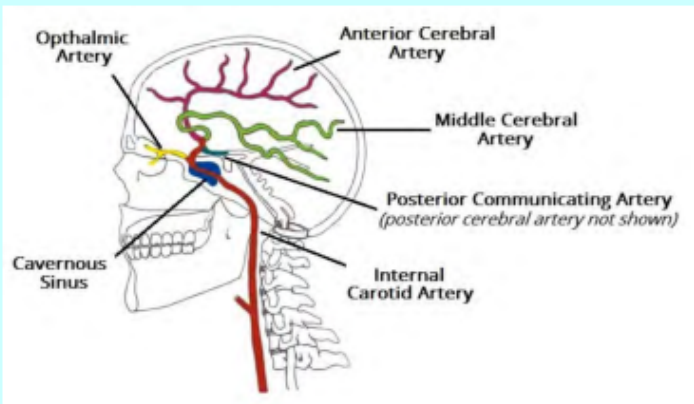
Slide 10

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



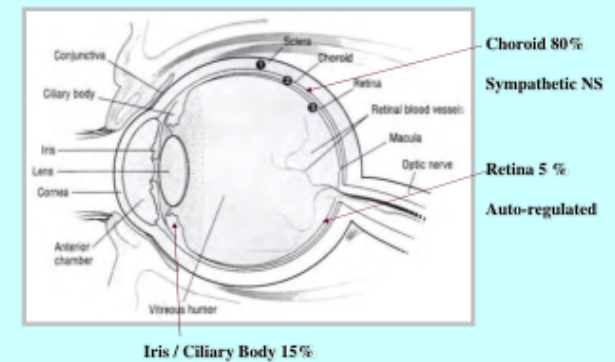
Slide 11

The Eye in Sytemic Disease

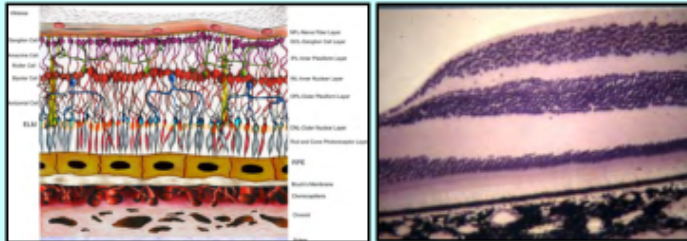


Slide 12

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



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 type 2 caused by excessive weight
 - Obesity = Increased weight caused by excess accumulation of fat.
 - “Over-fat” = normal BMI w/large waist
 - Visceral fat

*** 3 or more are diagnostic of Metabolic Syndrome:**



**** Waist circumference:**

Men — > 40 inches

Women — > 35 inches



triglycerides ≥ 150 mg/dL



HDL cholesterol:

Men — <40 mg/dL

Women — <50 mg/dL



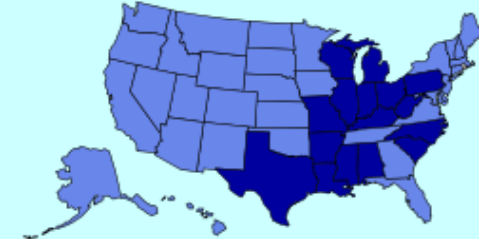
BP $\geq 130/85$ mmHg



FPG ≥ 100 mg/dL

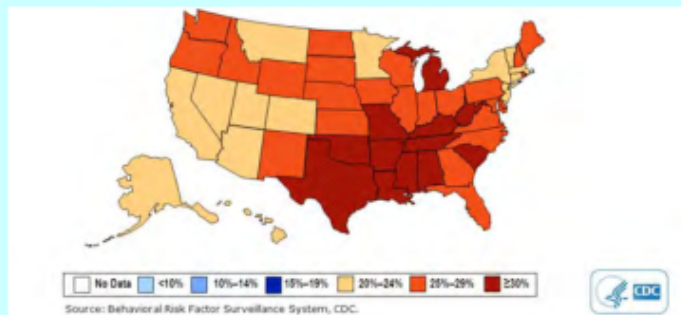
Obesity Trends* Among U.S. Adults
BRFSS, 1994

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

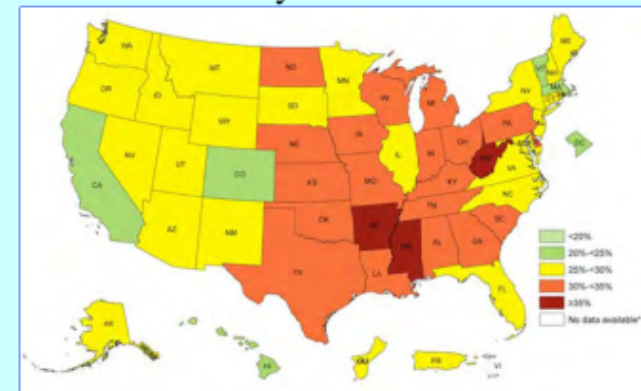


No Data <10% 10%–14% 15%–19% 20%–24% $\geq 25\%$

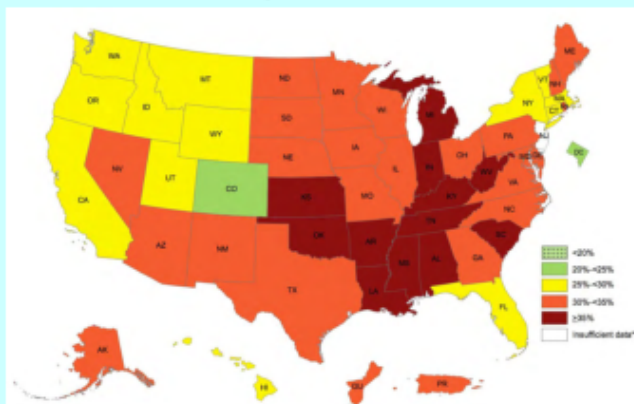
Obesity Trends-2012



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”

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



Data source: United States Diabetes Surveillance System.

QUESTIONS

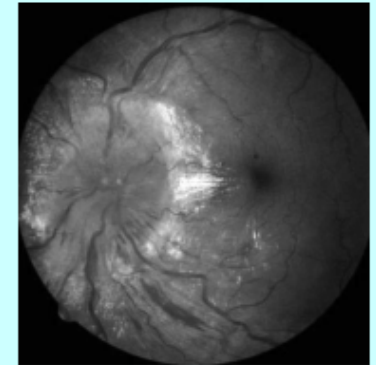
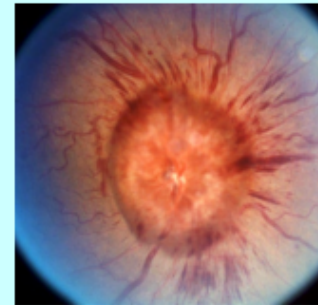
AND ANSWERS





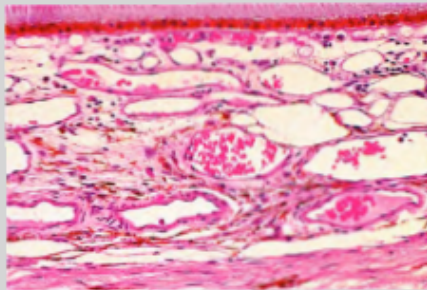
The Eye in Systemic Disease

Malignant Hypertension



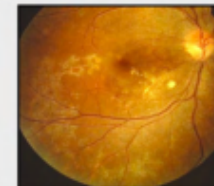
Choroid Microstructure

- Choriocapillaris
- Sattler's layer
- Haller's layer
- Supra - choroid

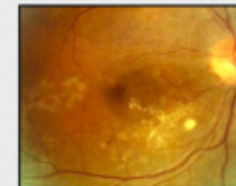


Hypertensive Choroidopathy

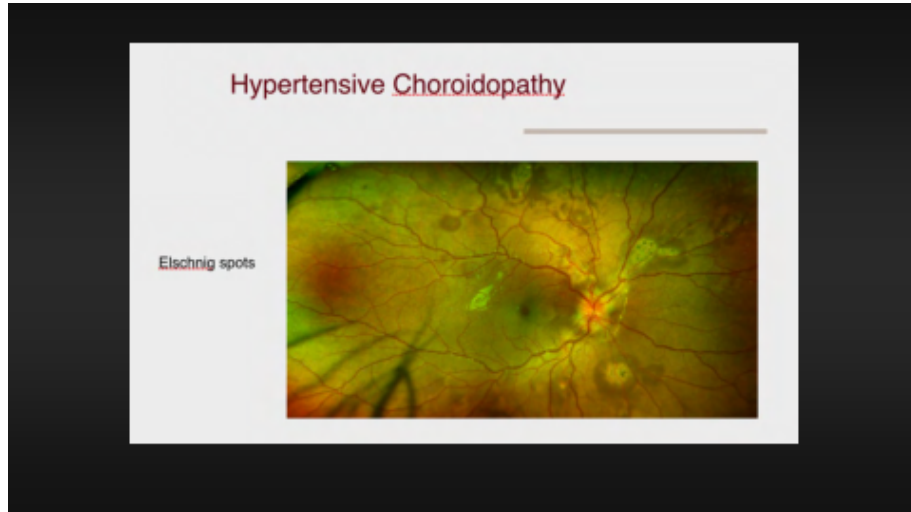
Elschnig spots



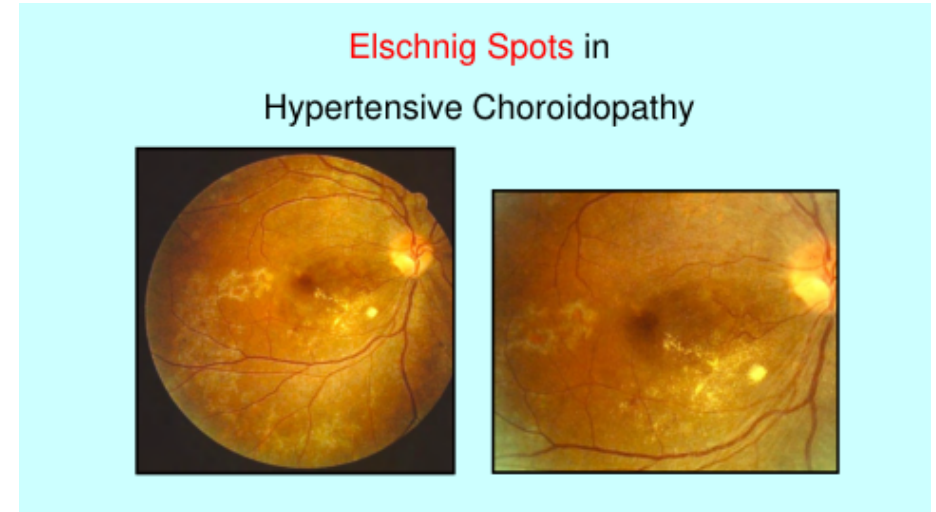
Siegrist streaks



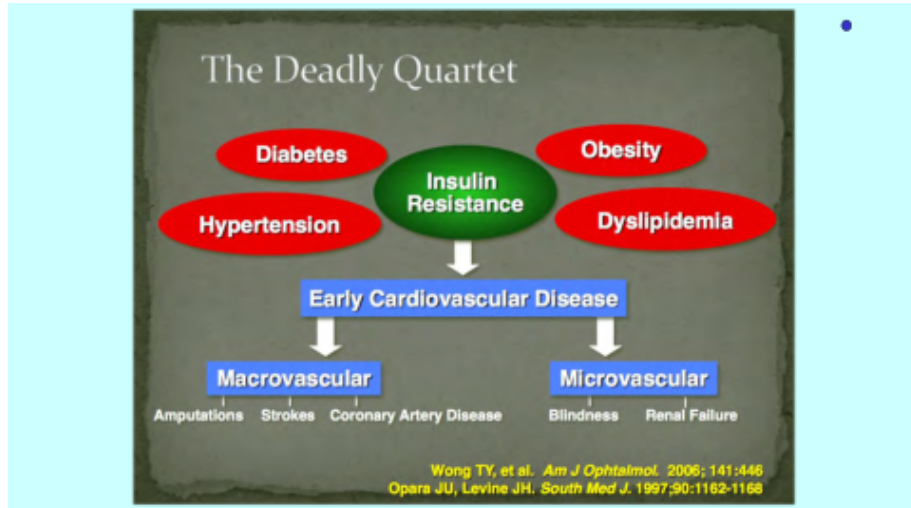
Slide 29



Slide 30



Slide 31



Slide 32

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

The slide lists four steps for treatment. The background of the slide is light blue.

Goals in Hypertension Therapy

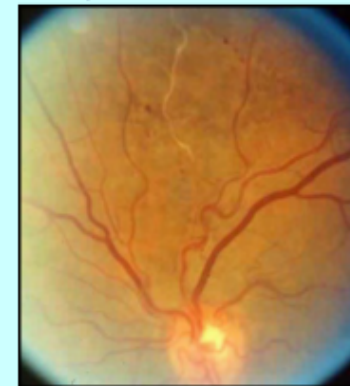
- Lower blood pressure
- Facilitate regression of LV hypertrophy
- Reduce risk of coronary athero and myocardial infarct
- Mitigate renal damage
- Avoid stroke and CNS hemorrhage
- Prevent peripheral vascular and carotid athero
- **PROTECT THE EYES!!!**

Summary – Benefits of Lowering BP

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

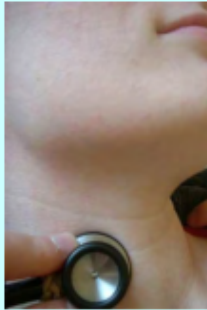
Hypoperfusion Retinopathy and the Ocular Ischemic Syndrome

Carotid Artery Occlusive Disease

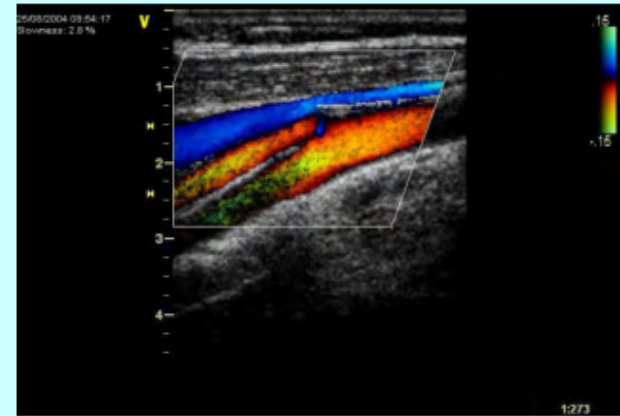


****Dot and Blot hemes in mid-peripheral retina**

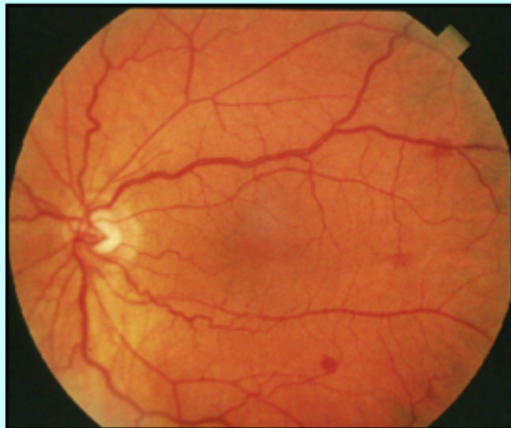
Carotid Occlusive Dx: Bruit



Carotid Doppler (Duplex)



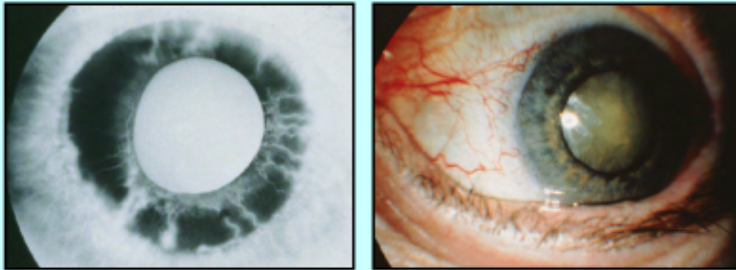
Mid-peripheral Hemes in Hypoperfusion Retinopathy



Hypoperfusion Retinopathy—same eye



NVI and Cataract in Ocular Ischemic Syndrome



The Ocular Ischemic Syndrome (OIS)

Key Point ▲

- Bilateral involvement in patients with ocular ischemic syndrome may occur in up to ~20% of all cases?

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 the Internal Carotid A.

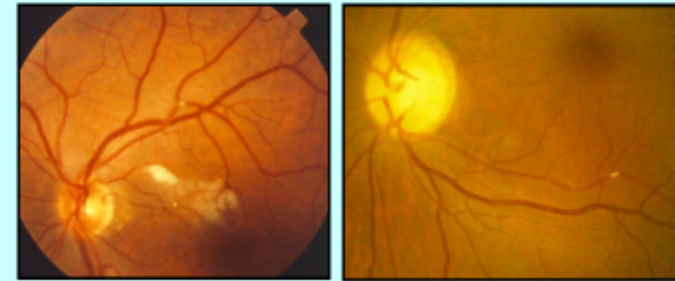
The Eye in Systemic Disease

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

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

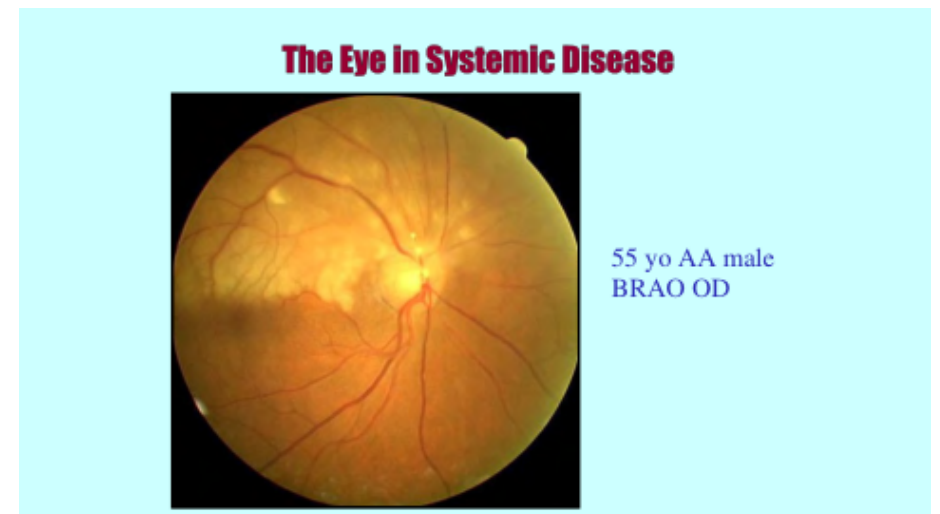
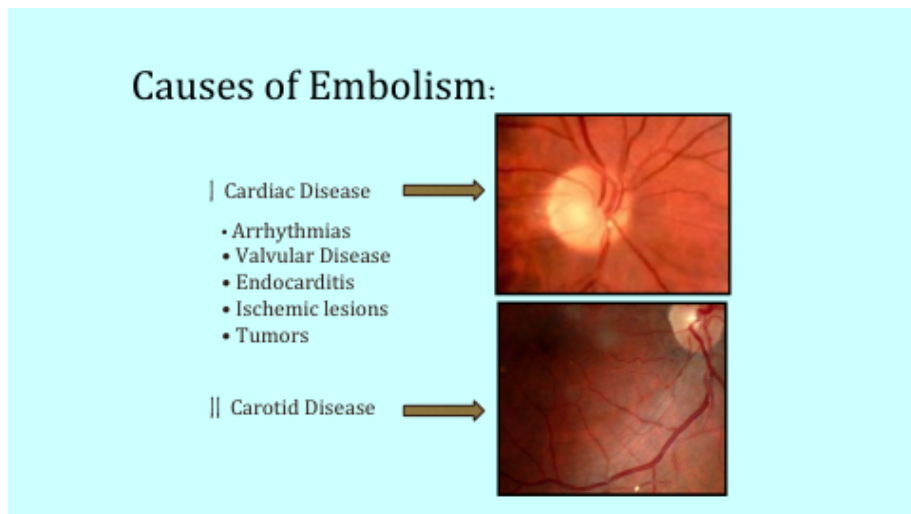
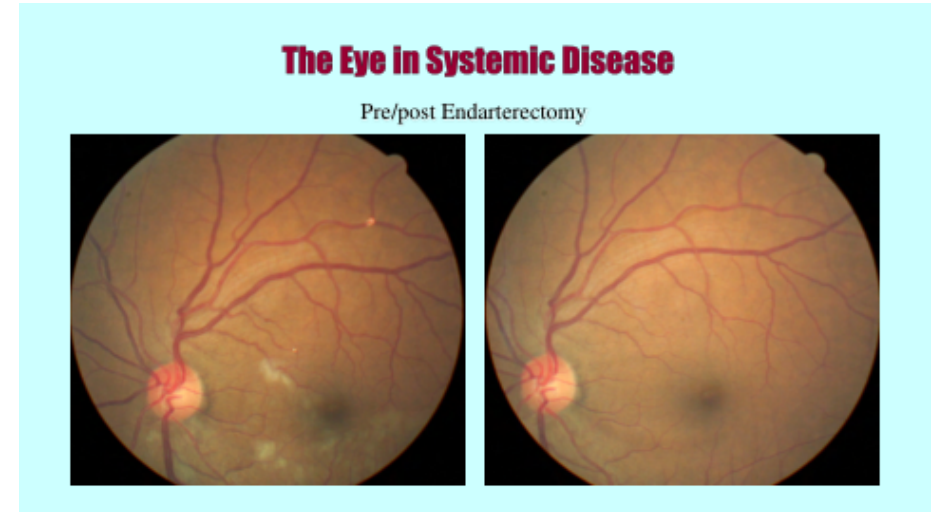
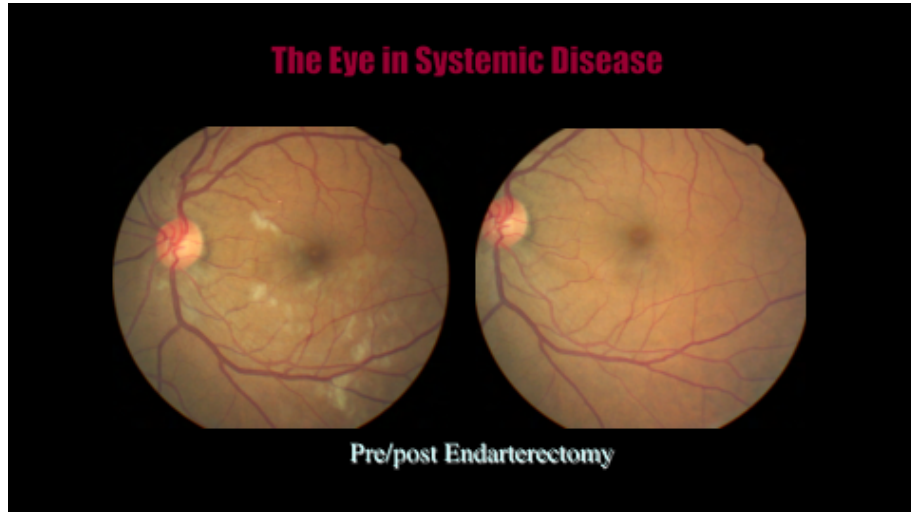
****Important Note:**

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

The Eye in Systemic Disease



Occipital Lobe Infarct



HCQ TOXICITY

Perform DFE annually.

What additional testing/work-up is appropriate?

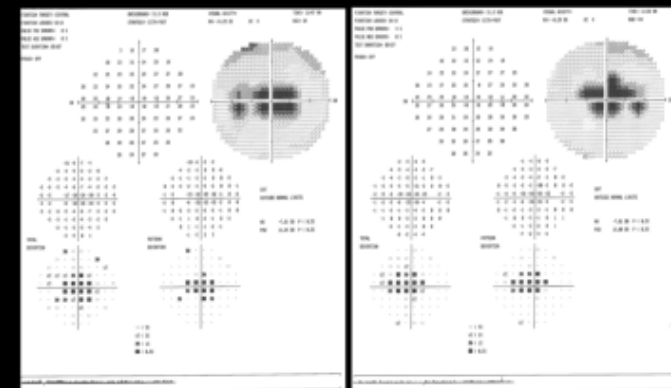
Case

- 65 Year old Asian Female
- Comes in with complaints of blurred and dimmed vision
- PMH: Rheumatoid Arthritis x 15 years
- OcHx: S/P CE and IOL OU

Ophthalmic Exam

- VA:
 - OD: 20/60 OS: 20/70
- IOP
 - OD: 14 OS: 13
- SLE:
 - OD: PCIOL OS: PCIOL
- DFE:

Patient Case: VY 65 y/o Asian Female Central Threshold Perimetry: Why 30-2?

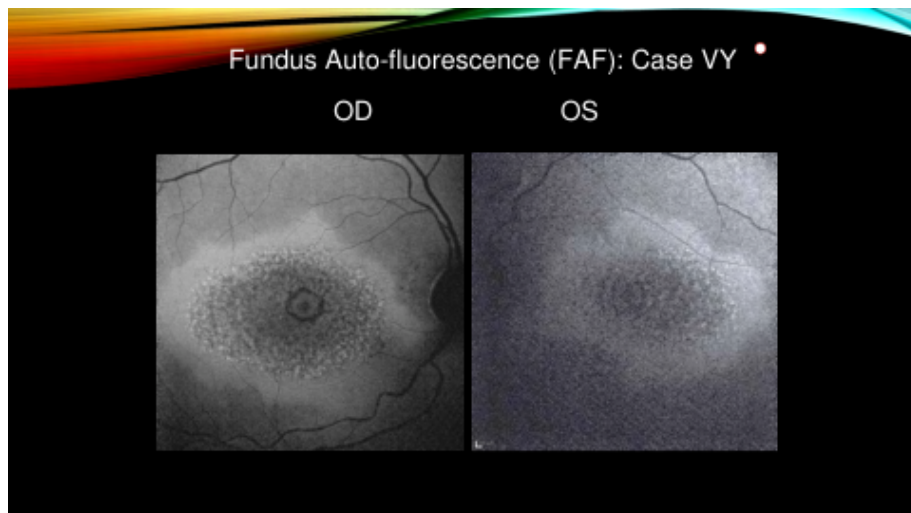
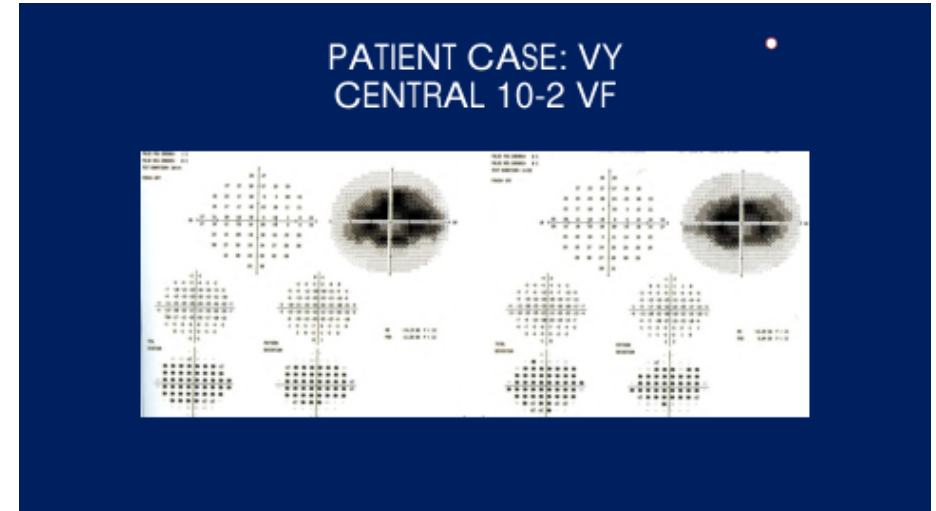


AMERICAN ACADEMY
OF OPHTHALMOLOGY
The Eye Doctors' Association

Pericentral Retinopathy and Racial Differences in Hydroxychloroquine Toxicity

Ronald B. Melles, MD,¹ Michael F. Marmor, MD²

Melles RB, Marmor MF. Pericentral retinopathy and racial differences in hydroxychloroquine toxicity. *Ophthalmology* 2015; 122: 110–116.



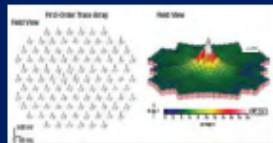
Imaging Technologies: FAF

What is autofluorescence in the retina?

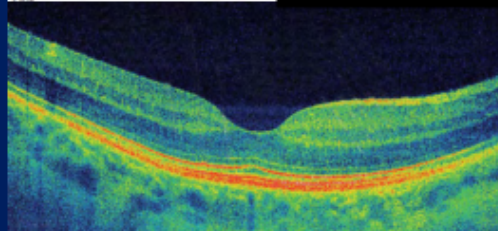
- It is the fluorescence of the **lipofuscin** molecule within the RPE cell layer that fluoresces with a certain wavelength.

19 years
64 years

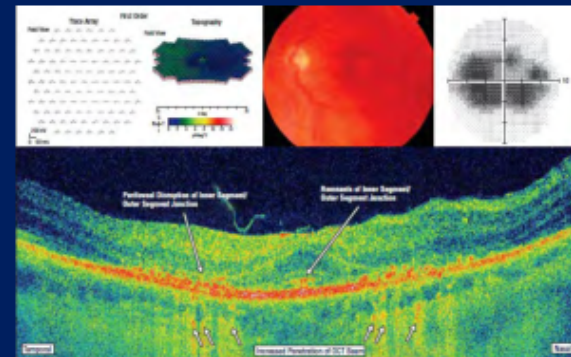
ANOTHER PATIENT ON PLAQUENIL



400 MG/DAY X 5 YRS
NO TOXICITY

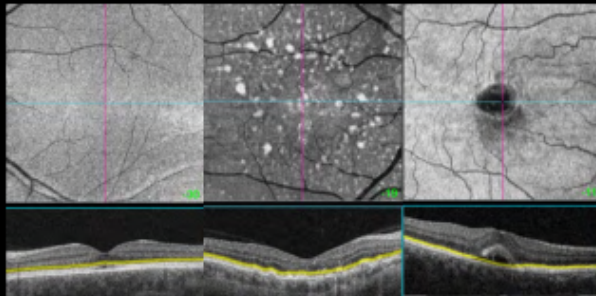


PLAQUENIL TOXICITY- MFERG



PLAQUENIL TOXICITY

- By the time “flying saucer” or “bullseye” is detected, significant toxic damage has occurred.
- May progress even if drug is stopped.
- Ganglion cell analysis and en face OCT may offer early detection.



What is the recommended maximum HCQ dose ?

- Calculate **Max Dose** in mg/day
- $2.3 \times \text{weight (in lbs.)} = \text{Max dose}$
- At recommended dose, risk of toxicity is < 1% after 5 years, < 2% after 10 yrs.
- Risk rises to almost 20% after 20 years. **
 - Our patient VY (~110-120 lbs) was taking 400 mg/d for 20 yrs
- Risk for HCQ maculopathy depends on **daily dose**, **duration of use**

American Academy of Ophthalmology Statement

Recommendations on Screening for Chloroquine and Hydroxychloroquine Retinopathy (2016 Revision)

Michael F. Marmor, MD,¹ Ulrich Kellner, MD,² Timothy Y.Y. Lai, MD, FRCOphth,³ Ronald B. Meller, MD,⁴ William F. Mieler, MD,⁵ for the American Academy of Ophthalmology

Background: The American Academy of Ophthalmology recommendations on screening for chloroquine (CQ) and hydroxychloroquine (HCQ) retinopathy are revised in light of new information about the prevalence of toxicity, risk factors, fundus distribution, and effectiveness of screening tools.

Pattern of Retinopathy: Although the locus of toxic damage is parafoveal in many eyes, Asian patients often show an extramacular pattern of damage.

Dose: We recommend a maximum daily HCQ use of ≤ 5.0 mg/kg real weight, which correlates better with risk than ideal weight. There are no similar demographic data for CQ, but dose comparisons in older literature suggest using ≤ 2.3 mg/kg real weight.

Risk of Toxicity: The risk of toxicity is dependent on daily dose and duration of use. At recommended doses, the risk of toxicity up to 5 years is under 1% and up to 10 years is under 2%, but it rises to almost 20% after 20 years. However, even after 20 years, a patient without toxicity has only a 4% risk of converting in the subsequent year.

HCQ SCREENING FREQUENCY

- **Baseline:** DFE within 1 year of starting HCQ
- **Visual field and SD-OCT** if macular abnormalities are present at baseline
- **Annual screening:** Begin after 5 years of use
 - Sooner in presence of "major risk factors"

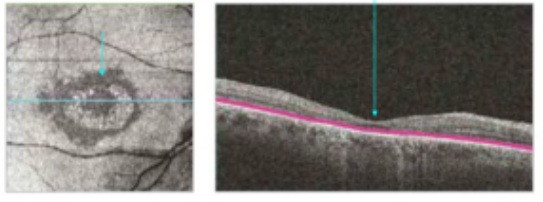
American Academy of Ophthalmology Statement

Recommendations on Screening for Chloroquine and Hydroxychloroquine Retinopathy (2016 Revision)

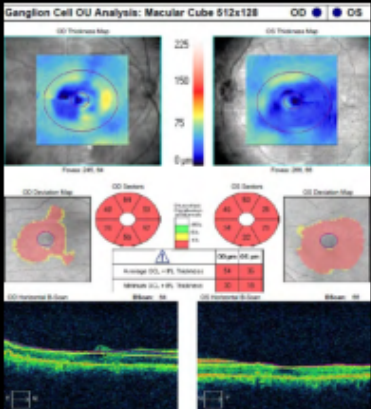
Michael F. Marmor, MD,¹ Ulrich Kellner, MD,² Timothy Y.Y. Lai, MD, FRCOphth,³ Ronald B. Meller, MD,⁴ William F. Mieler, MD,⁵ for the American Academy of Ophthalmology

PLAQUENIL MACULOPATHY WITH CLASSIC BULL'S EYE DUE TO ANNULAR FOVEAL ATROPHY

En Face IS/OS-Ellipsoid View



GCL + IPL loss in HCQ maculopathy



Expanded spectral domain-OCT findings in the early detection of hydroxychloroquine retinopathy and changes following drug cessation

David R. Lally, Jeffrey S. Heier, Caroline Beaulieu, Andrea J. Miller, Steven Miller, George P. Smith, Christopher B. Bressler, Michael J. Giblin, John S. Heier, John S. Heier, and Jay S. Heier

International Journal of Retina and Vitreous 2016; 3: 10

doi:10.1007/s10792-016-9388-8 | © The Author(s) 2016

Received: 1 April 2016 | Accepted: 27 June 2016 | Published: 10 July 2016

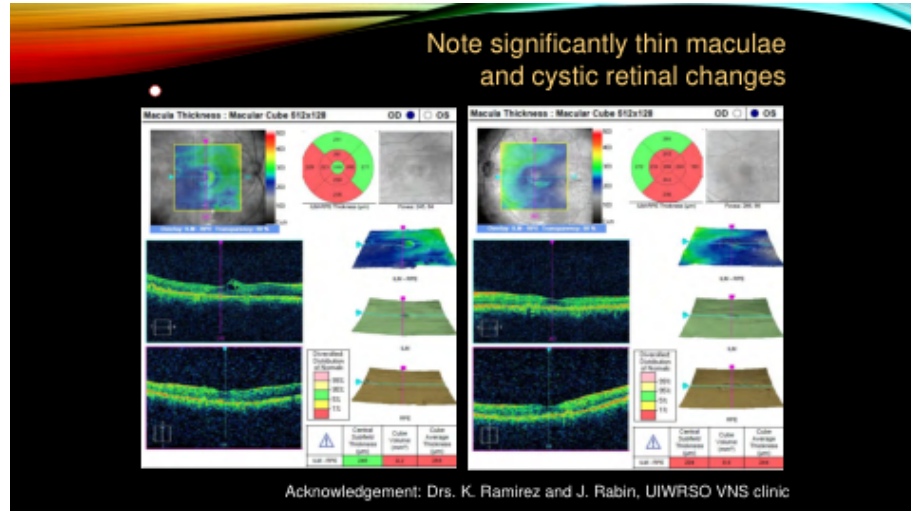
The Journal of Rheumatology
Volume 45, No. 10

Hydroxychloroquine Ocular Toxicity: Lessons Learned

© 2016 by American College of Rheumatology

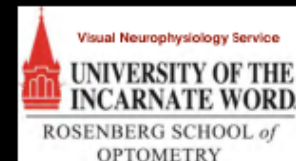
0893-7463/16/4510-1445-1454
http://dx.doi.org/10.1093/rheumatology/kew022

Acknowledgement: Drs. K. Ramirez and J. Rabin, UIWRSO VNS clinic



FROM THE AUTHORS

- “(Real) weight-based dosage and **early screening** (DFE, central fields, OCT, FAF, mfERG) are essential to prevent HCQ toxicity,
- particularly with certain **risk factors**: small stature, high total dosage, diminished renal function, concomitant tamoxifen use, and/or existing retinal/macular disease.
- **Interprofessional collaboration** to optimize patient outcomes.”

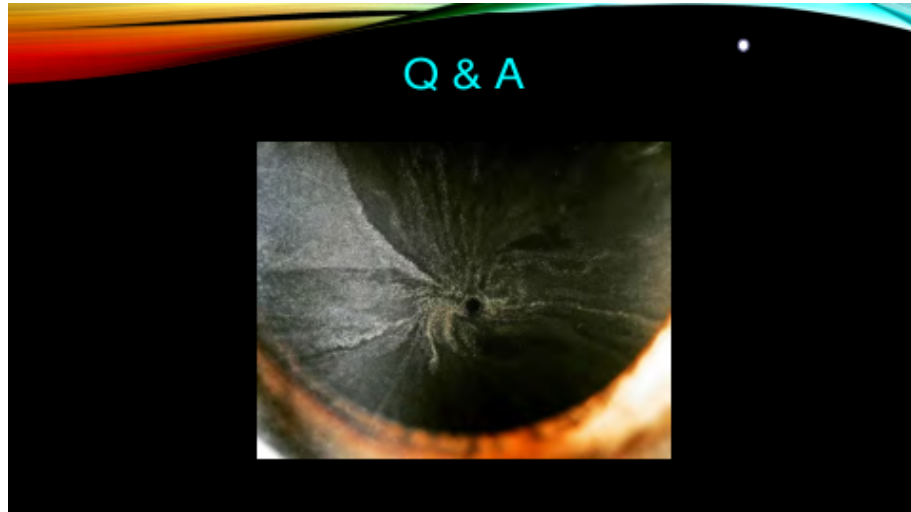


Plaquenil Maculopathy

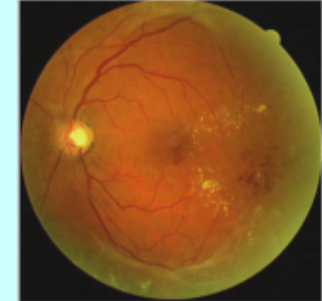
- Testing for patients on Plaquenil
 - DFE
 - VF 10-2 W/W (add 24-2 or 30-2 in Asians)
 - SD or SS-OCT: raster and cube scans
 - FAF
 - mfERG
- Increase frequency of monitoring (2+ visits per year) w/degree of pathophysiology.

Summary and Case Outcome

- MMI and other diagnostics are essential in evaluation of patients using CQ or HCQ on a chronic basis.
- Co-management team includes:
 - Optometry
 - **Rheumatology**
 - Other therapies: methotrexate, TNF inhibitors (our patient VY was switched to this drug class)



32 yo WM



- 5 ft 8 in tall, 265 lbs
- “sees red” OD
- Type 2 DM x 3 yrs
- Recent Dx. Obstructive Sleep Apnea (OSA)

What is Sleep Apnea?

- Apnea is defined as complete cessation of breathing for more than 10 seconds.
- SAS is characterized by repeated apneas or periods of shallow breathing during sleep.

Epidemiology

- OSA is most common in overweight or obese men.
- It occurs in approximately 22-24 percent of men and 9-17 percent of women.
- African Americans have a 2.5 times higher risk.

Epidemiology

- OSA occurs in 34 percent of NFL linemen

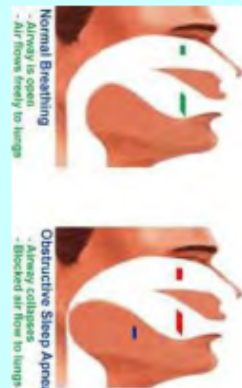


Types of Sleep Apnea

- Central sleep apnea (CSA)
 - caused by the loss of **ventilatory effort** controlled by the CNS
 - brain is not properly telling the body when to breathe
 - < 1%
- Obstructive sleep apnea (OSA)
 - caused by upper airway obstruction or collapse
 - ~85%
- Mixed sleep apnea (MSA)
 - ~15%
- The mechanisms underlying these different types of sleep apnea are likely to overlap.*

Obstructive Sleep Apnea

- An average of **at least 10** apneic and hypopneic episodes per sleep hour.
- Leads to excessive daytime drowsiness because of marked fragmentation of sleep.



Why should we care?

- Reported ophthalmic findings in patients with SAS include:
 - Floppy eyelid syndrome
 - Glaucoma
 - Keratoconus
 - HR, DR, RVO
 - Central serous chorioretinopathy (CSC)
 - Optic disc edema (IIH and non-IIH)
 - Non-arteritic anterior ischemic optic neuropathy

Who develops SAS/OSA?

- SAS can occur at any age.
- **Risk factors** include excess weight and obesity, male sex, **physical inactivity**, upper airway abnormalities (i.e. small airway or enlarged tonsils), alcohol use, loud snoring, family history, allergies, and wide neck girth.



Obesity and SAS



An obese young woman with the short, thick neck as typically seen in SAS.

Ocular Complications of OSA

- Changes in eyelid tissue
 - Floppy eyelid syndrome (FES)
- Changes in cornea
 - K-conus
- Changes in the optic nerve
 - The glaucomas
 - Open angle (OAG)
 - IOP-independent GLC (NTG) *
 - Non-arteritic anterior ischemic optic neuropathy (NAION)
 - Optic Disc Edema (IIH and non-IIH)
- **Changes in retina: DR, HR, RVO, CSC***





Floppy Eyelid Syndrome (FES)

- History: obesity, type 2 DM → suspect OSA
- Treatment/Management
 - CPAP
 - Lubricate
 - Anti-inflamm
 - Antimicrobial
 - Protect eye
 - Bandage CL
 - AMT
 - Combo Therapy



40 y/o BF
+FES, OSA, IIH

Diagnosis/Management of FES

Diagnosis

- Vital dye staining
- Abnormally lax upper lid on eversion

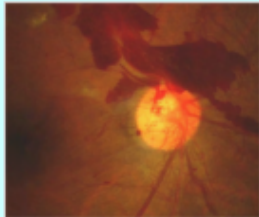
Treatment

- Goal: To protect ocular surface during sleep
 - Topical lubricants
 - Topical antibiotics for mild corneal/conj abnormalities
 - Educate patient to refrain from sleeping face-down
- Eyelid tightening procedure
 - Horizontal lid shortening

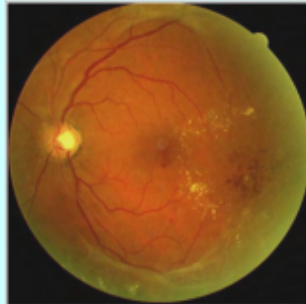
Questions and Answers?



32 yo WM

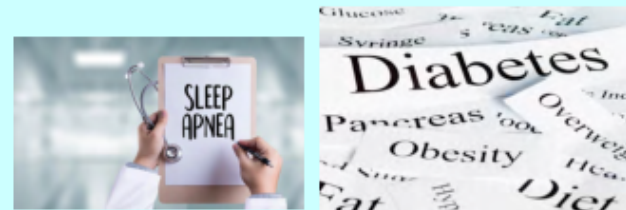


- 5 ft 8 in tall, 265 lbs
- “sees red” OD
- Type 2 DM x 3 yrs
- Recent Dx. Obstructive Sleep Apnea (OSA)



SAS and Type 2 DM

- The ADA recommends that all type 2 patients be screened for OSA, and vice versa.*



SAS and Type 2 DM

The most highly associated systemic complication of **obesity** is type 2 DM.

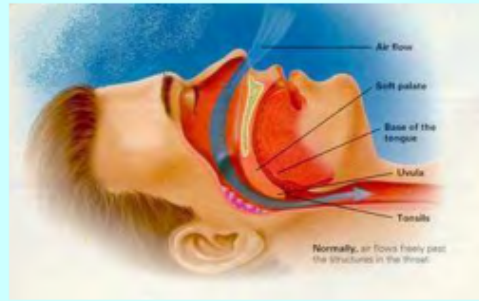
A1C Target Levels



Early Diagnosis is Essential!

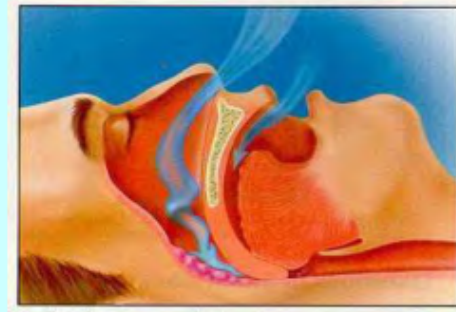
- OSA and retinal vascular disease have a high cost burden on the healthcare system.
- OSA creates systemic changes and hypoxic conditions that may incite or exacerbate retinal vascular diseases.
- Retinal changes may be the first clinical manifestation of otherwise undiagnosed OSA, so it is important to refer patients with new-onset retinal vascular disease for appropriate sleep testing.

Normal Air Flow



Air flows freely past structures in throat

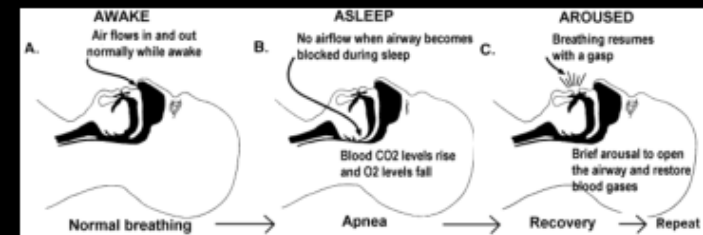
Blocked Air Flow



Upper airway collapse

OSA and Weight

- OSA is a sleep disorder that affects an estimated 22% of men and 17% of women globally ^[1].
- ~75% of individuals with a BMI greater than 40 kg/m² have OSA and that 58% of moderate-to-severe OSA cases are attributable to a BMI greater than or equal to 25 ^[2,3].
- The prevalence of OSA has increased by as much as 55% in certain age groups in the last two decades alone ^[4].



Impaired Blood Flow in OSA

Does your patient have OSA?

- Snoring marked by frequent **changes in loudness and frequency** (as opposed to quiet and steady) is highly suggestive.
- Excessive daytime sleepiness/tiredness or **fatigue**, especially when not active.
- Episodes during sleep when **breathing stops**.
- Periods of **loud snoring followed by silence** or a total absence of breathing, lasting from a few seconds up to a minute or longer.

Risk Factors for OSA

- Obesity/excess weight
- Male sex
- Upper airway abnormalities
- Alcohol use
- Snoring
- **Neck girth of more than 17 inches in men or 16 inches in women.**

Signs and Symptoms

- Loud snoring
- Feeling fatigued in the morning
- Falling asleep during the day
- **Memory loss**
- **Poor judgment**
- **Personality changes**

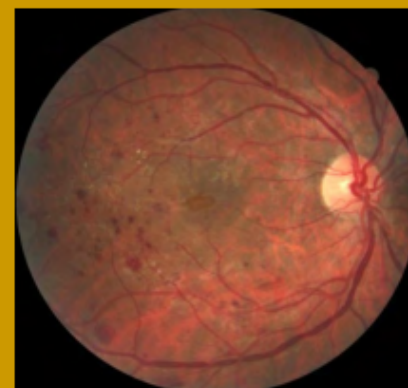
Why are there ocular vascular complications?

- The primary drivers of the ocular complications of OSA are **intermittent hypoxia, sympathetic system activation, oxidative stress, and adverse effects of endothelin 1** ^[14].
- Retinal vascular disease has a high economic burden on healthcare systems.
- Diabetic retinopathy alone cost the US health system **\$4.5 billion** in 2020 ^[15].

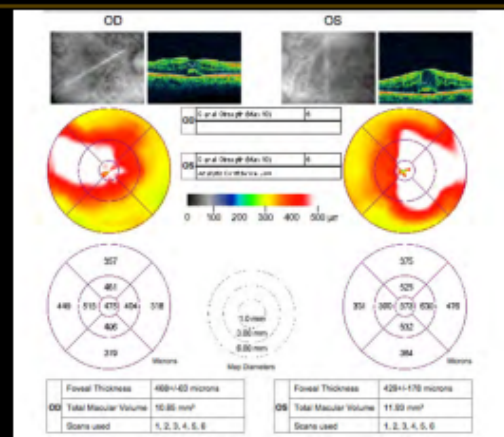
Case: 55 YO HM

5 ft 10 in, 295 lbs
 Central blur OD/OS
 Type 2 DM x 3 yrs
 +OSA, +HTN, +Dyslipidemia

OD: 20/100



OS: 20/200

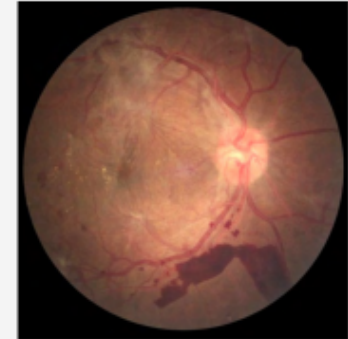


QUESTION:

WHICH FACTORS MOST INFLUENCE
THE ONSET, PROGRESSION AND
VISUAL OUTCOME OF DIABETIC
RETINOPATHY?

Systemic Conditions that May Exacerbate DR

- Dyslipidemia
- Hypertension
- Carotid occlusive dx
- Kidney disease
- Sleep apnea
- Anemia
- Obesity
- Vasculitis
- Neuropathy
- Nephropathy
- Vitamin D deficiency

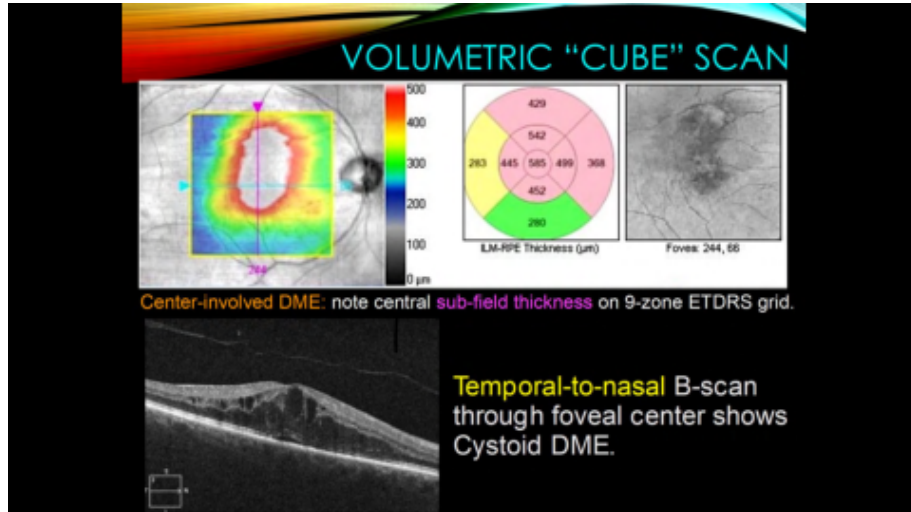


OSA and DM

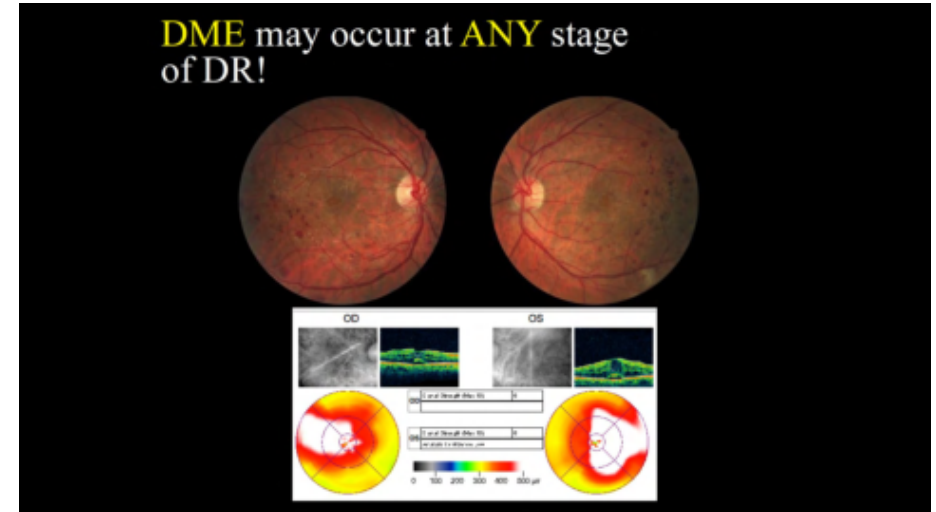
- The relationship between OSA and diabetes is bidirectional.
- Just as OSA may increase risk of developing diabetes, diabetes is a risk factor for developing OSA.
- During REM sleep, an increased apnea–hypopnea index (AHI) – the number of apneic and hypoxic events per sleep hour – is linked with DR, even when controlling for other risk factors ^[21].

OCT has forever changed
the classification and
management of DR, and
especially DME.

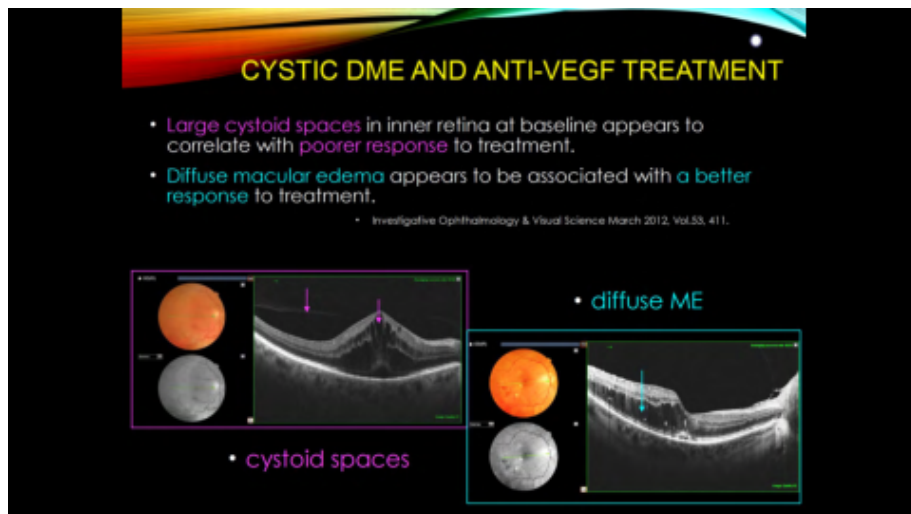
Slide 117



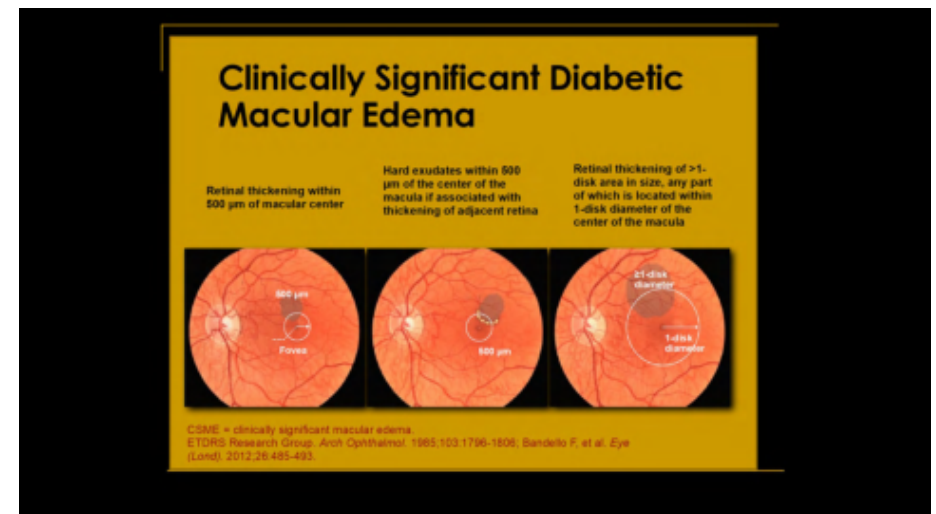
Slide 118



Slide 119



Slide 120



Clinically Significant Diabetic Macular Edema

OLD CRITERIA

Retinal thickening within 500 µm

Hard exudates of >1 disc diameter, any part located within 500 µm of the center of the macula

Retinal thickening of >1 disc diameter

1-disc diameter

500 µm

CSME = clinically significant macular edema
ETDRS Research Group. Arch Ophthalmol. 1985;103:1796-1808; Bandello F, et al. Eye (Lond). 2012;26:485-493.

DME Classification & Management: Center Involved or Not?

- Randomized clinical trials of anti-VEGF agents used the presence of DME in **OCT central subfield**.
- Older ETDRS definition of "clinically significant macular edema" modified in era of OCT.

central subfield

015p 2044 2652

IS THE TREATMENT WORKING?

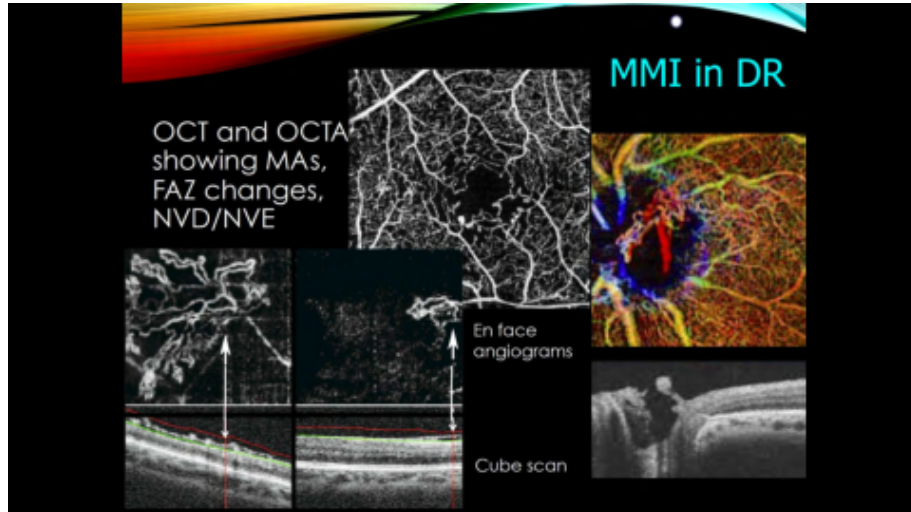
1st Visit

Previous Visit

Current Visit

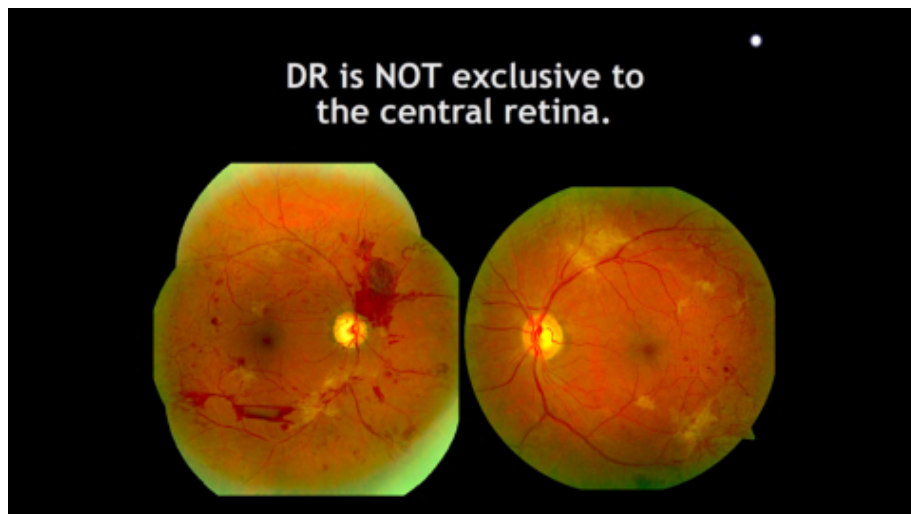
What is multimodal imaging (MMI)?

- MMI is the use of multiple technological systems to acquire images.
- These may include hybrid devices that can simultaneously perform more than one imaging modality.
- MMI does not replace, but rather it augments, traditional examination methods, such as DFE.

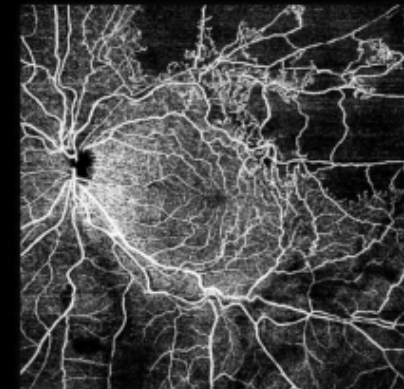


What is the purpose of MMI?

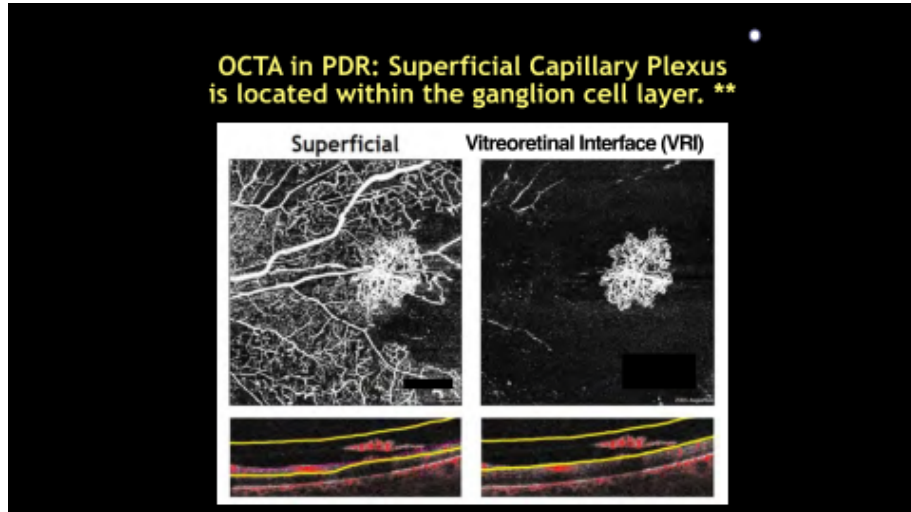
- Images acquired by MMI complement one another for the purpose of **diagnosis, prognostication, management, and monitoring of disease.**
- Common imaging modalities include:
 - color/multicolor fundus imaging
 - near-infrared reflectance (NIR)
 - fundus autofluorescence (FAF)
 - OCT and OCTA



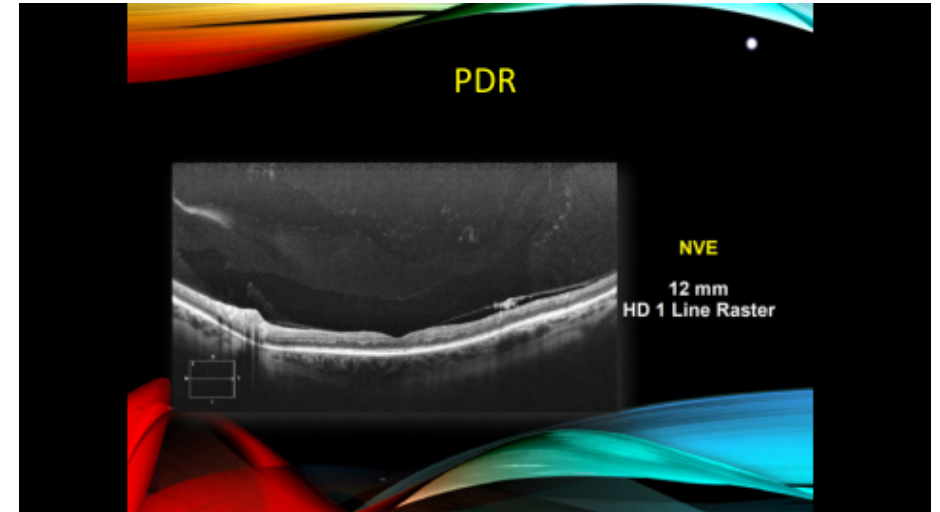
OCTA Beyond the Posterior Pole



Slide 129



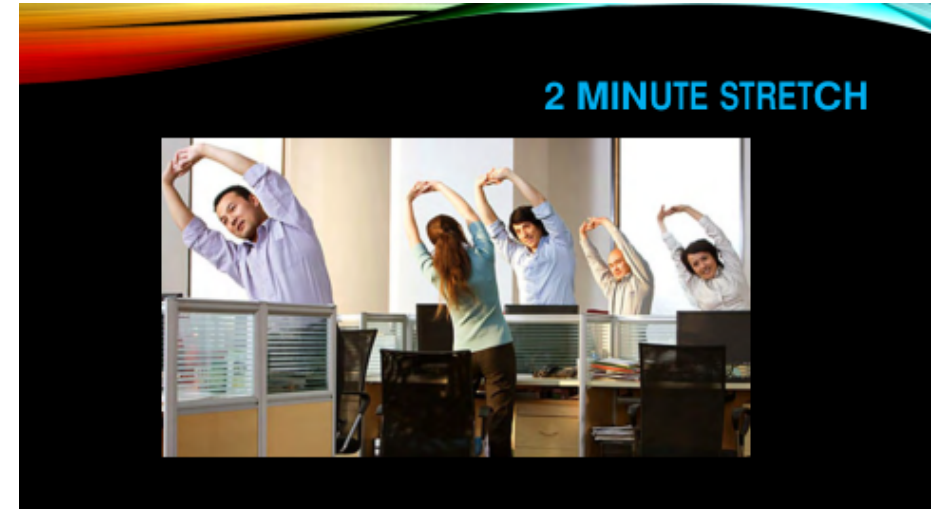
Slide 130



Slide 131



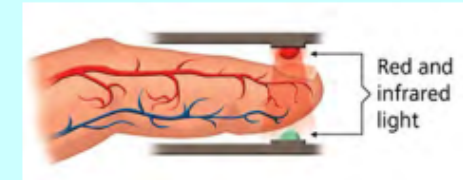
Slide 132



OSA: Making the Diagnosis

- Polysomnography
 - Eye movement observations (REM)
 - Electroencephalogram (arousals from sleep)
 - Chest wall monitors (respiratory movements)
 - Electrocardiogram (heart activity)
 - Electromyogram (limb movements)
 - Oximetry (measure oxygen saturation)

Pulse Oximetry



Pulse Oximetry

- Small beams of red/IR light pass through the blood in the finger.
- Measures changes of light absorption in oxygenated or deoxygenated blood.
- The pulse oximeter measures **oxygen saturation** levels along with heartrate.



Diagnostic Parameters

- Respiratory disturbance index (RDI)
 - # of obstructive breathing events (apneas) per hour
 - Used to diagnose and grade the severity of OSA

The Apnea-Hypoapnea Index

- **Apneas** are strongly associated w/reduced blood oxygen levels.
 - can decrease by up to 4%
- **Respiratory effort-related arousal (RERA)**
 - This is a breathing disorder characterized by obstructive upper airway (air)flow reduction...
 - ...that does not meet the criteria of an apnea or hypopnea

The Apnea-Hypoapnea Index

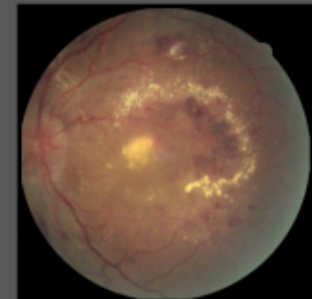
- **Hypoapneas** are events in which there is a decrease, *but not a total cessation*, of breathing during sleep.
- To calculate AHI
 - Simply add the total number of events (apneas, RERAs, and hypoapneas)
 - Divide this by the total number of hours slept during the study.

AHI: lower is better

$$\frac{\text{Apneas} + \text{Hypoapneas} + \text{RERAs}}{\text{Hours Slept}}$$

Sleep Apnea and DR/DME

- **DME**
 - ✓ Higher prevalence
 - ✓ Recurrence rate higher
 - ✓ Unresponsive to Anti-VEGF
- **PDR**
 - ✓ Higher prevalence
 - ✓ Worsening
- **Improvement of DME, PDR w/CPAP**

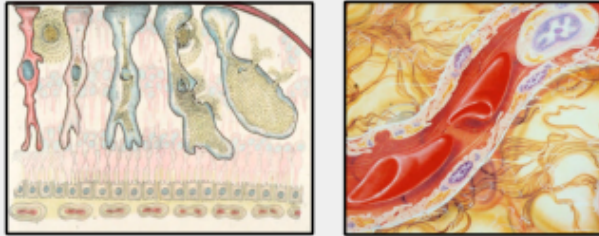


West, S. D., et al. "The prevalence of retinopathy in men with Type 2 diabetes and obstructive sleep apnea." *Diabetic Medicine* 27.4 (2010): 423-430.

Important Note: Diabetes is Inflammation

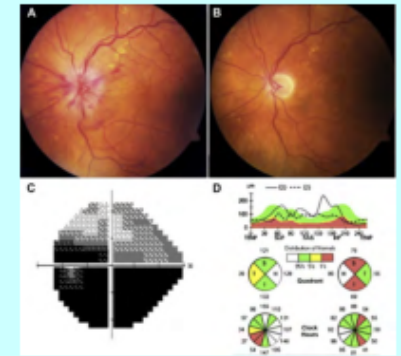
Leukocytes, once inside the retinal tissue, then secrete a variety of inflammatory substances such as TNF and VEGF

These released mediators then increase vascular permeability and stimulate more mediators to enhance the inflammatory reaction



Non-arteritic Anterior Ischemic Optic Neuropathy (NAION)

- Cause
 - Ischemic vascular disease
- Diagnosis
 - Rule out arteritic!
- Treatment/management
 - Systemic



SAS/DM/HTN

NA-AION



Hyperemic disc swelling

GCA

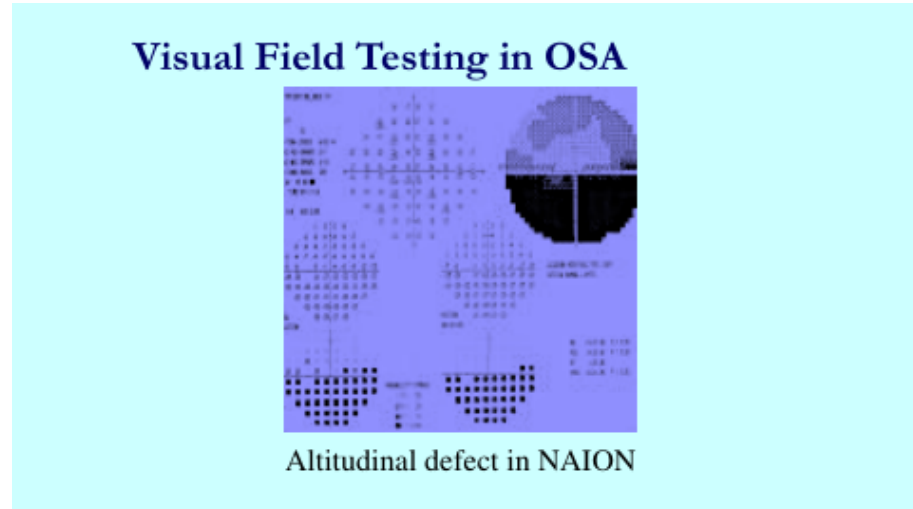
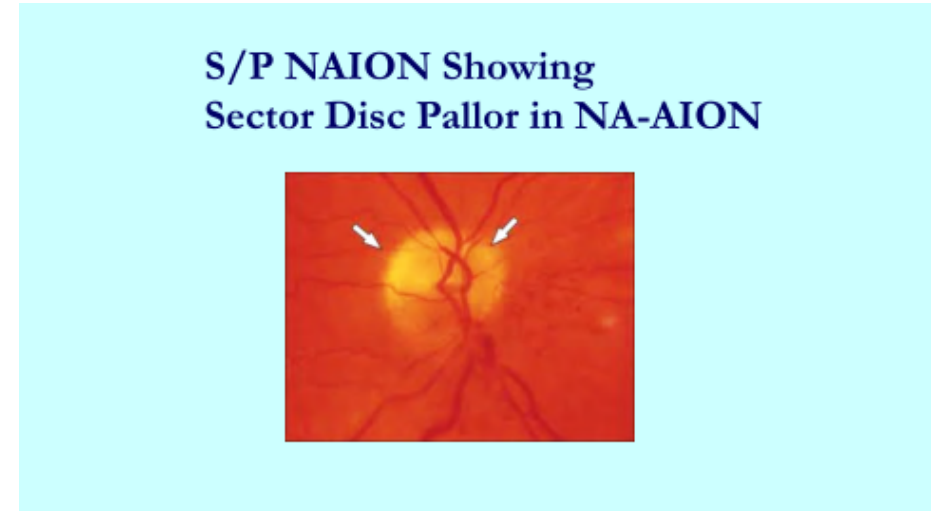
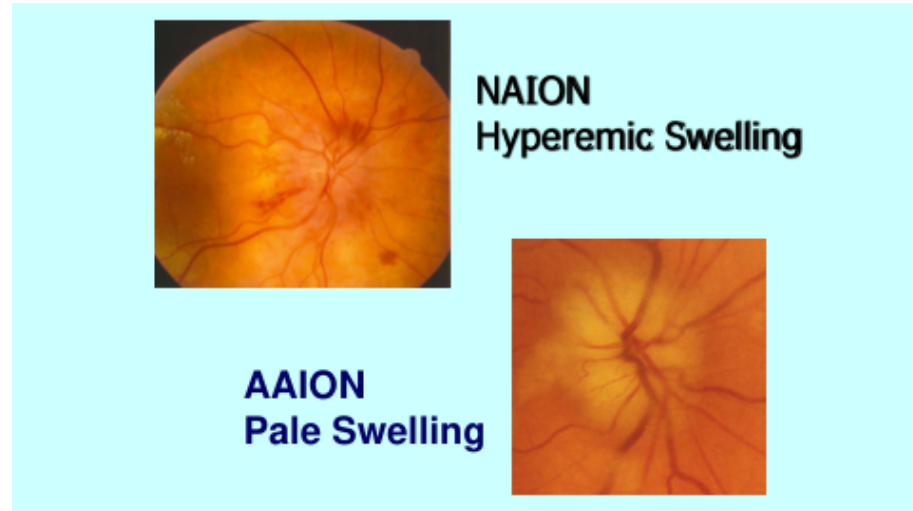
A-AION



Pale disc swelling

NAION Pathophysiology

- Alteration of the blood supply to the optic nerve head
 - Ischemic process affecting the SPCAs
 - As the ischemic episode evolves, disc swelling (edema) compromises circulation, leading to further neuronal damage.
- Common etiologies of NAION include CV Dx, DM, arteriolar sclerosis, OSA.*

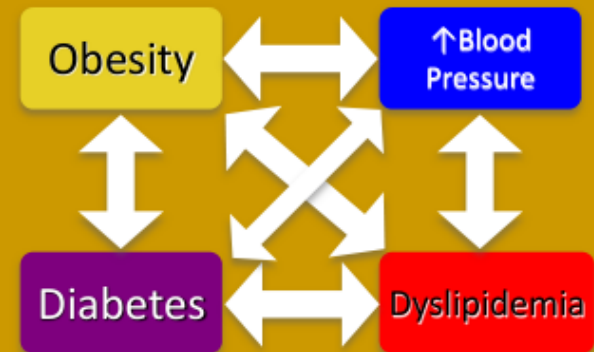


- SAS and Systemic Disease**
- **Systemic arterial hypertension** - present in ~50% of OSA cases.
 - Congestive heart failure
 - Pulmonary hypertension
 - Stroke
 - OSA is an independent Risk Factor*
 - **Metabolic syndrome**
 - Type 2 diabetes mellitus

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

Metabolic Syndrome

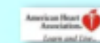


The Pathology of Obesity

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

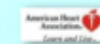


* 3 or more are diagnostic of Metabolic Syndrome:

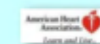


**** Waist circumference:**

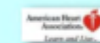
Men — > 40 inches
Women — > 35 inches



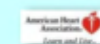
triglycerides $\square$ 150 mg/dL



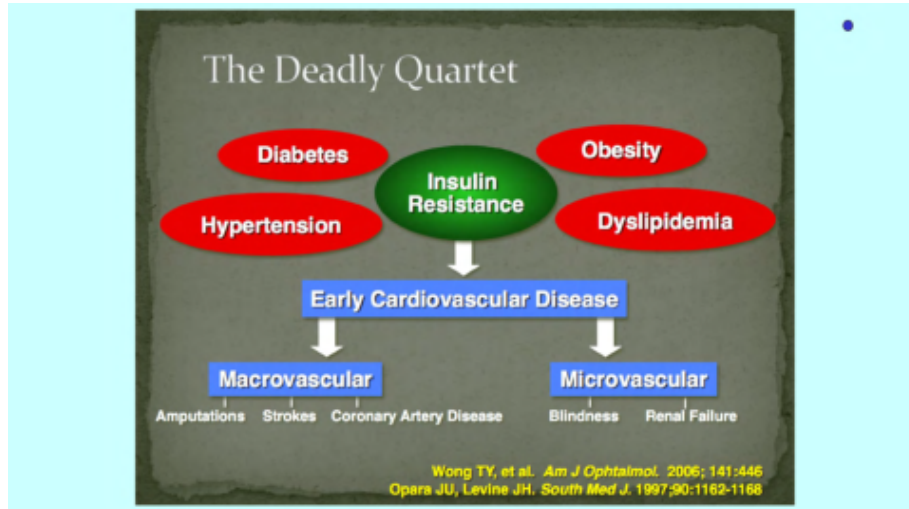
HDL cholesterol:
Men — <40 mg/dL
Women — <50 mg/dL



BP $\square$ 130/85 mmHg

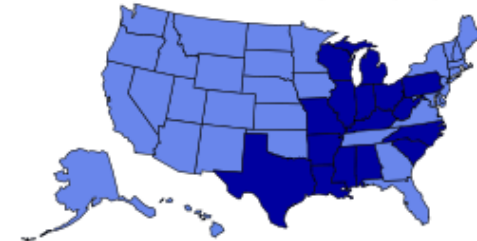


FPG $\square$ 100 mg/dL



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

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



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

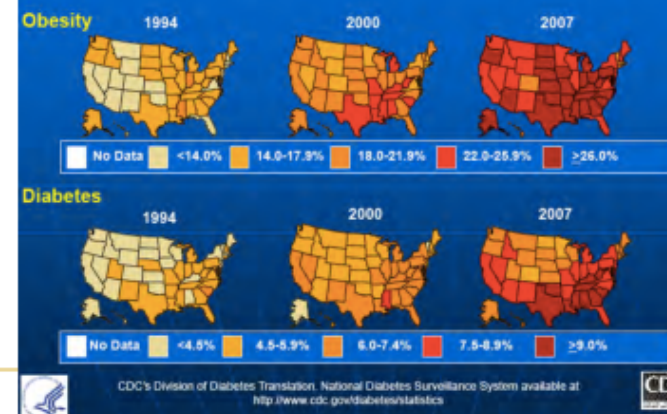
Obesity trends-2012

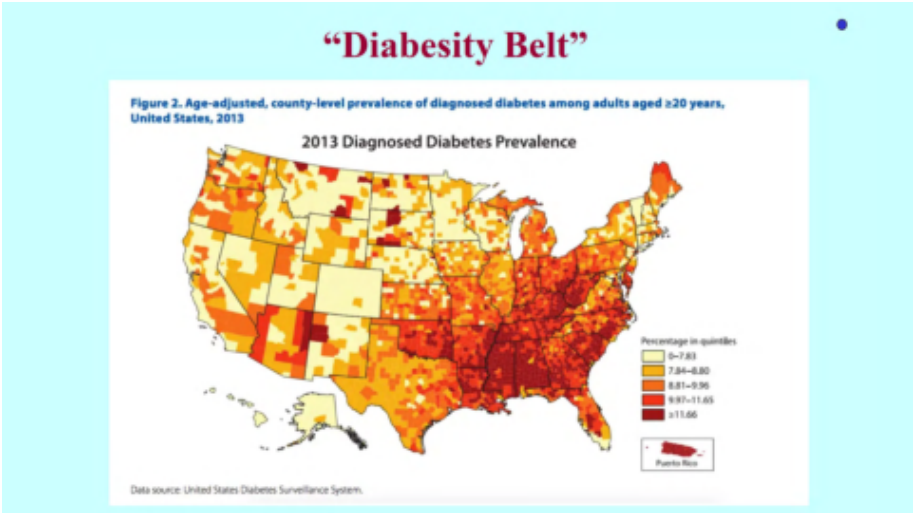
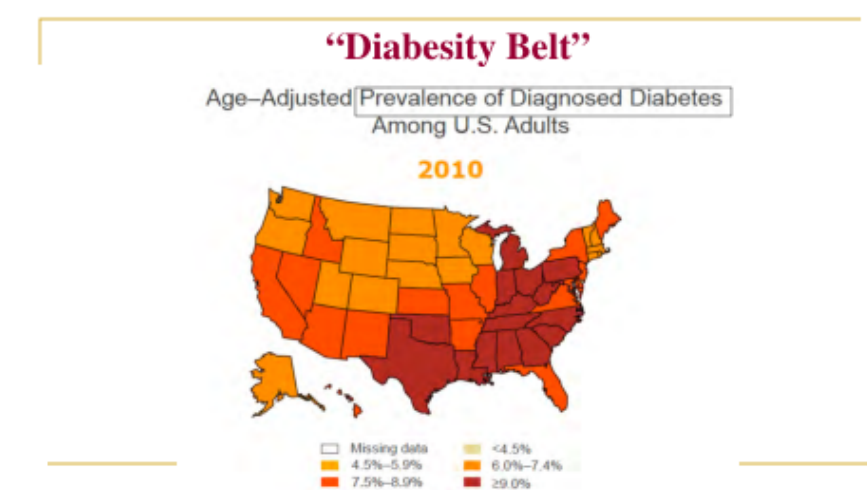
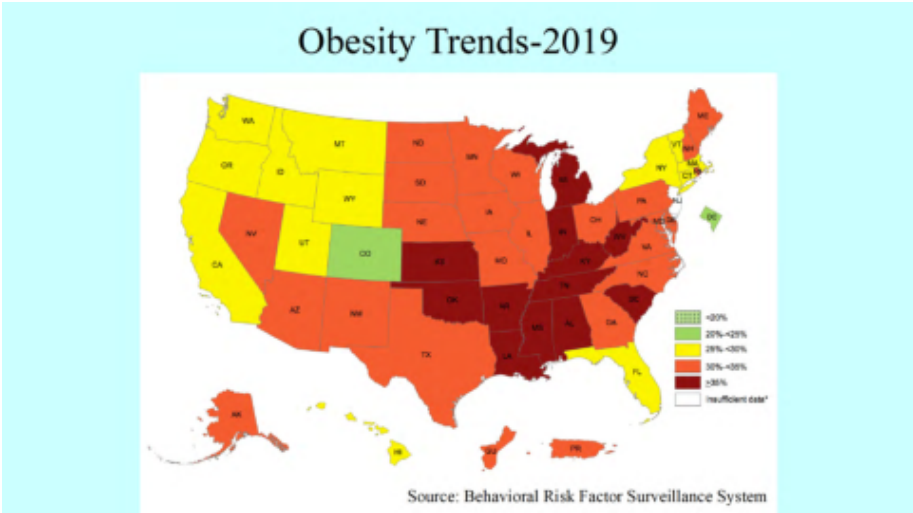


No Data <10% 10%–14% 15%–19% 20%–24% 25%–29% ≥30%

Source: Behavioral Risk Factor Surveillance System, CDC.

Age-adjusted Percentage of U.S. Adults Who Were Obese or Who Had Diagnosed Diabetes





QUESTIONS and ANSWERS



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

Obesity and Body Mass Index (BMI)

- World Health Organization (WHO) Classification
 - For adults, Grade 1 (simply called overweight) is a BMI of 25-29.9 kg/m².
 - Grade 2 (commonly called obesity) is a BMI of 30-39.9 kg/m².
 - Grade 3 (commonly called severe obesity) is a BMI greater than or equal to 40 kg/m².

Medical Nutrition Therapy



Systemic Complications of OSA

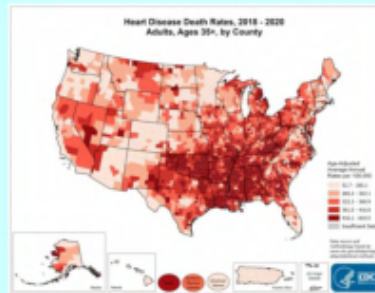
- HTN
- Type 2 DM
- Depression
- Accidents (traffic, workplace)
- Congestive Heart Failure
- Myocardial infarction
- Coronary Artery Disease
- Atrial Fibrillation
- Cognitive issues
- OSA is an independent RF for stroke.*



Key Points

- ▲ **Myocardial Infarction** is the most common cause of death in USA.

- 697,000 per year
- **Cardiac valve disease** is the most common cause of cardiac emboli to the eye.**



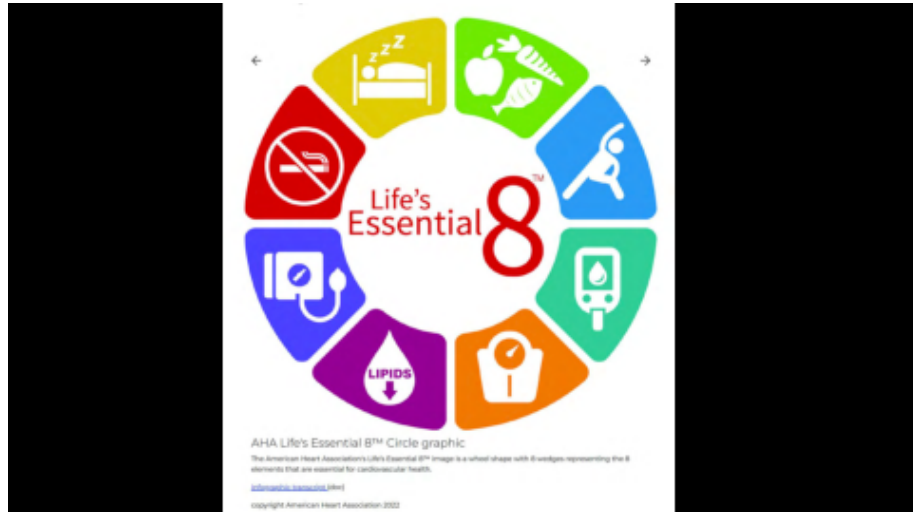
Warning Signs | Volunteer | Donate

Newsroom

Categories: [Advisories & Comments](#), [Heart News](#), [Program News](#), [Stroke News](#), [Diversity/Health Equity](#) | Published: June 29, 2022

American Heart Association adds sleep to cardiovascular health checklist

American Heart Association Presidential Advisory



Management of OSA

- Weight loss
 - Start with 5%
- Continuous positive airway pressure (CPAP)
 - Blows air into nostrils
- BiPAP therapy
- Oral appliances
 - Tongue retained devices
 - Bring lower jaw forward
- Uvulopalatopharyngoplasty (UPPP)
 - Surgical removal of anatomic obstructions

CPAP Therapy



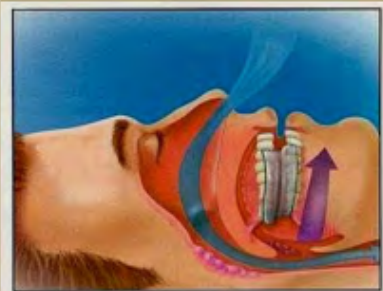
www.heart.org/health-topics/lifes-essential-8

BiPAP Therapy



- Main difference is that BiPAPs have 2 pressure settings: a prescribed pressure for inhalation (ipap), and a lower pressure for exhalation (epap).
- Dual settings allow the patient to get more air in and out of their lungs, making it easier to breathe during sleep.

Tongue Retaining Device



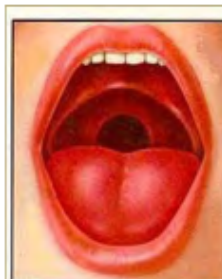
With oral devices, throat structures move out of your air passage, allowing air to flow freely through your throat.

Oral Appliances



The OA fits like a sports mouth guard or an orthodontic retainer. It supports the jaw in a forward position to help maintain an open upper airway.

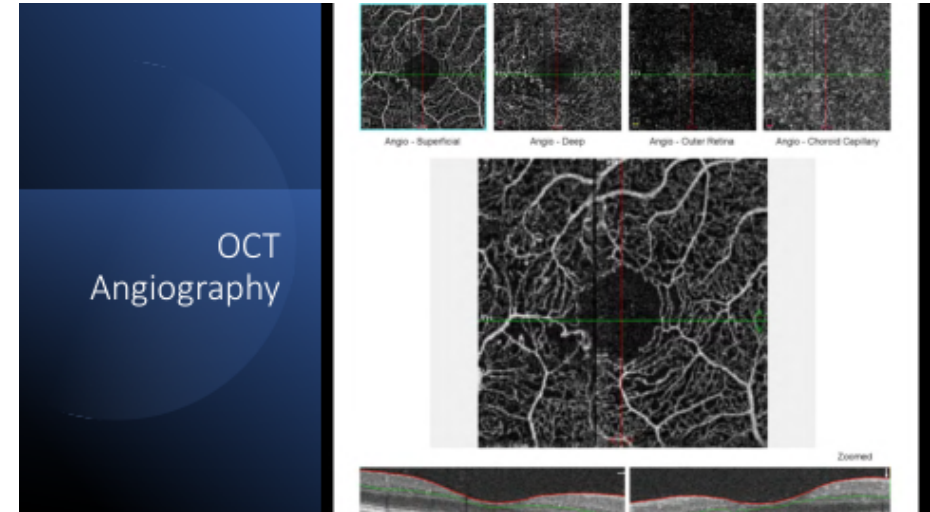
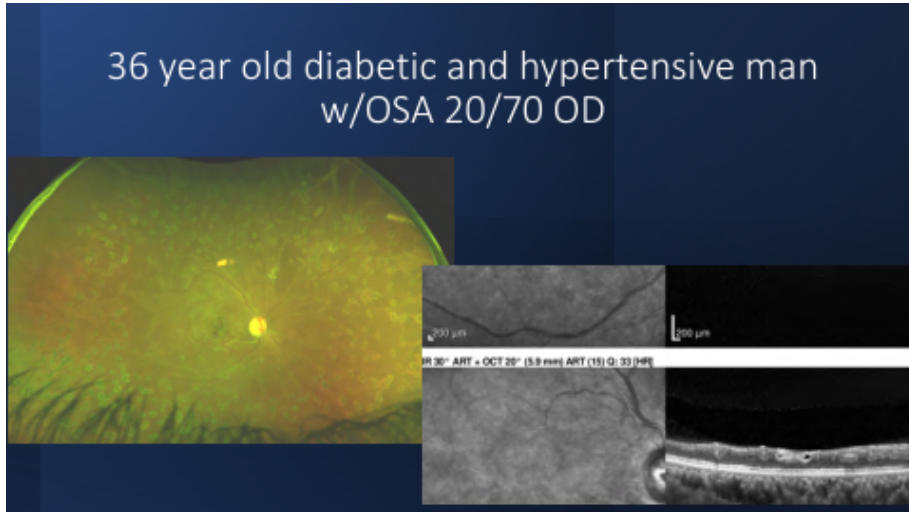
UPPP Surgery



During UPPP, your uvula and other tissue from the back of your mouth are removed.

Treatment and Management of SAS

- Patients in whom non-invasive therapy (e.g. CPAP, BiPAP, OAs) fails may be offered surgical options.
 - Patient should be made aware of the success rates for each surgical procedure.
 - Inform them that they might require more than one procedure, some fairly extensive.
 - Refer patients only to centers that have personnel experienced in these special surgical techniques



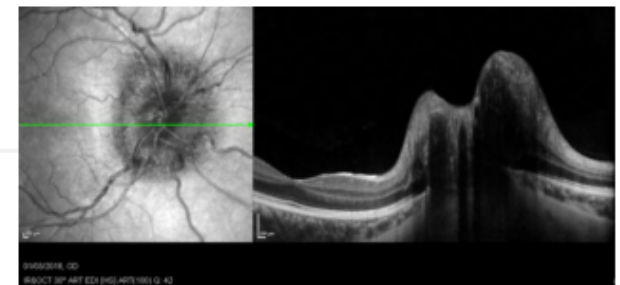
Treatment

- Proper treatment of OSA with continuous positive airway pressure (CPAP) therapy has been shown to improve visual sensitivity as well as RNFL thickness [16,17].
- It is essential to recognize the link between these disorders and OSA not only for the preservation of visual function...
- ...but also for proper treatment of OSA, and thus mitigation of the variety of morbidity and mortality because of uncontrolled, undiagnosed OSA.

Questions and Answers

IIH + OSA

AUDIENCE



Thank you!

Joe

pizzimen@uiwtx.edu



Co-manage Uveal Melanoma with:

Retina/Ocular Oncology
PCP
General Oncology

Genetic Testing on Small Melanoma (Shields, 2015)

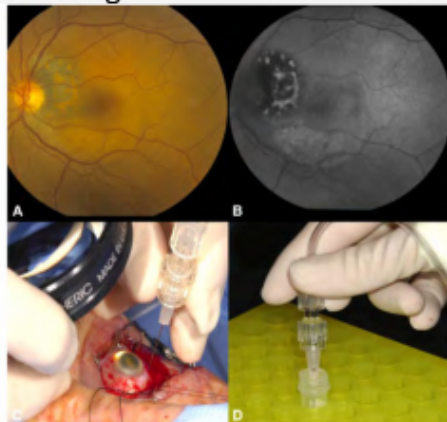
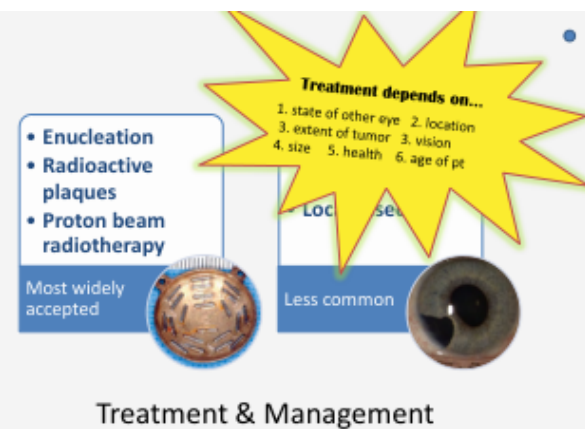


Figure 2. Present techniques of uveal melanoma management. A, Early detection of tiny choroidal melanoma using risk factors of subretinal fluid, orange pigment (B) confined to fovea and macula, orange pigment, and tumor reaching the optic disc. C, Tumor para-fovea fine needle aspiration biopsy and DNA storage in preservation for genetic testing.





Collaborative Ocular Melanoma Study

- Organized and funded in 1985 to address issues related to management of choroidal melanoma.
- Main Outcome: overall survival of patient following treatment
- > 4000 patients. 65% pts eligible

<u>Small</u> melanomas	< 2.5 mm in height
<u>Medium</u> melanomas	2.5 – 10.0 mm
<u>Large</u> melanomas	> 10.0 mm

Secondary outcomes: metastasis-free survival,
years of useful vision.

Brachytherapy for Uveal Melanoma

- Plaque left in place for 4 days to provide 8,000 centigray of radiation to entire tumor.
- The remainder of the body receives a small amount of radiation, about the equivalent of a chest x-ray.



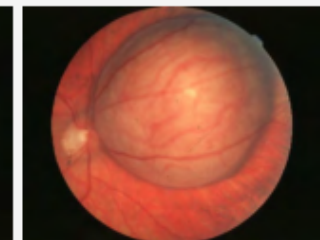
Treatment Side Effects

- Main side effect of focal ocular treatment is...
- **Radiation retinopathy!**



- NVD / NVE
- Exudative changes
- Macular edema
- Occurs several weeks to months after therapy

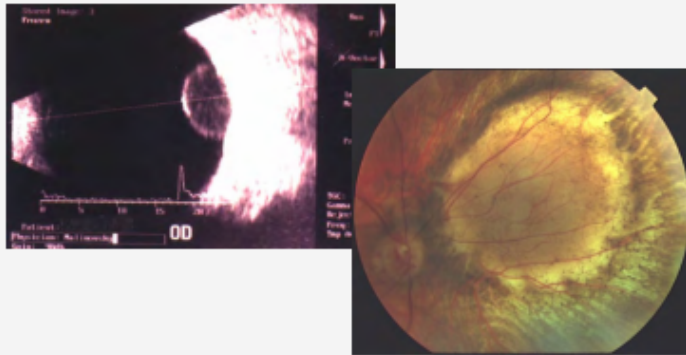
Choroidal melanoma- pre-Radiotherapy



Acknowledgement: Brad Sutton, OD

Slide 189

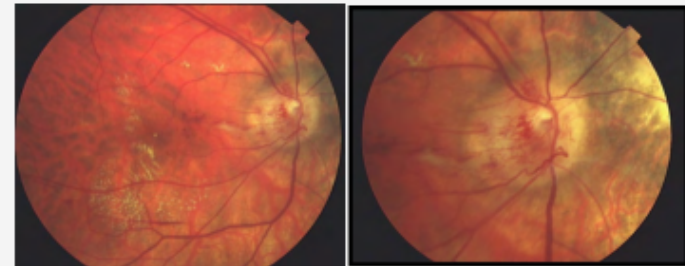
Melanoma pre-Tx echography (left),
post-radiotherapy (right)



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Radiation Retinopathy:
exudate, NVD

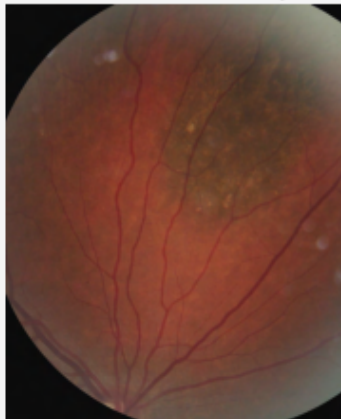
Acknowledgement: Brad Sutton, OD



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Choroidal Melanoma Pre-Tx

Acknowledgement: Sherrol Reynolds, OD, FAAO



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S/P Radiotherapy

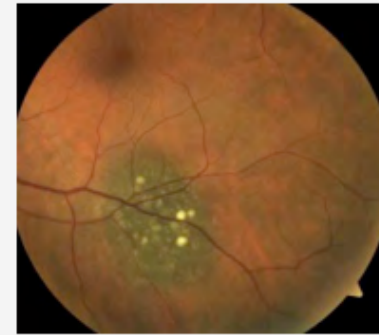


Management of RR

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



Questions and Answers



Melanoma Metastasis

Risk factors for metastasis from the choroid:

- Thickness > 2 mm
- Symptoms – Flashes, floaters, loss of vision
- Proximity to the optic nerve
- Documented growth



Shields CJ Shields JA. Risk factors for metastasis of small choroidal melanocytic Lesions. Ophthalmology 1995

METASTASIS

BOX 48.1 Sites for Metastatic Uveal Melanoma

- Liver 93%
- Lungs 24%
- Bone 16%
- Skin 11%
- Lymph nodes 10%
- Brain 5%
- Fellow eye 0%

Multiple sites involved in about half the cases.
In an atypical case consider a second primary tumor.

Ocular Melanoma Quiz

- What is the 10-year mortality rate for patients diagnosed with a uveal melanoma?
- a. 1 %
- b. 7%
- c. 9%
- d. 50%

Ocular Melanoma Quiz

- What is the 10-year mortality rate for patients diagnosed with a uveal melanoma?
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Conclusion

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

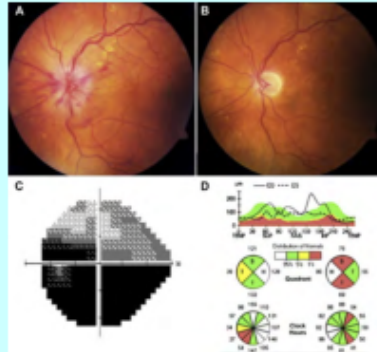


Thank you for spending your precious time with me!

- Joe

Non-arteritic Anterior Ischemic Optic Neuropathy (NAION)

- Cause
 - Ischemic vascular disease
- Diagnosis
 - Rule out arteritic!
- Treatment/management
 - Systemic



SAS/DM/HTN

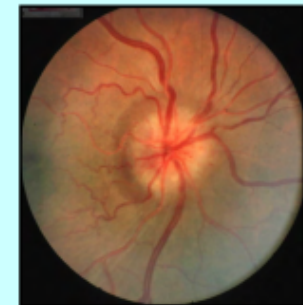
GCA

NA-AION

A-AION



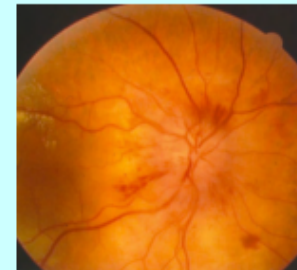
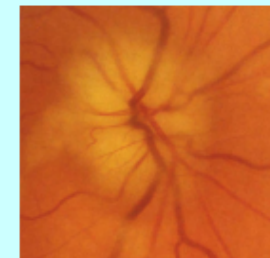
Hyperemic disc swelling



Pale disc swelling

NAION Pathophysiology

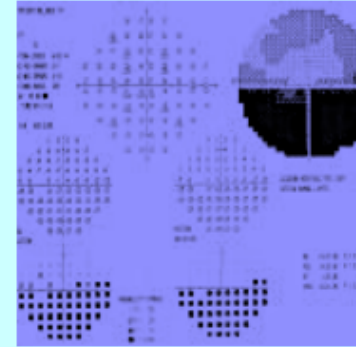
- Alteration of the blood supply to the optic nerve head
 - Ischemic process affecting the SPCAs
 - As the ischemic episode evolves, disc swelling (edema) compromises circulation, leading to further neuronal damage.
- Common etiologies of NAION include CV Dx, DM, arteriolar sclerosis, OSA.*

NAION
Hyperemic SwellingAAION
Pale Swelling

S/P NAION Showing Sector Disc Pallor in NA-AION



Visual Field Testing in OSA



Altitudinal defect in NAION

Keratoconus

- Diagnosis is clinical
 - Traditional and special diagnostic testing
- The FES has been linked with both
OSA and keratoconus in several studies.*
- Obesity and KC
- Treatment/management of KC

SAS and the Eye

- Marfan's Syndrome-related Complications (facial anomalies)
 - Ectopia lentis
 - decentered crystalline lens, secondary to disruption of surrounding zonular fibers
- Patients with ectopia lentis are at an increased risk for retinal detachment

SAS and Systemic Disease

- Half of all patients living with essential hypertension also have OSA.
- Likewise, half of patients who have OSA also have essential hypertension.
- Therefore, OSA appears to be a contributing factor in the development of essential hypertension.

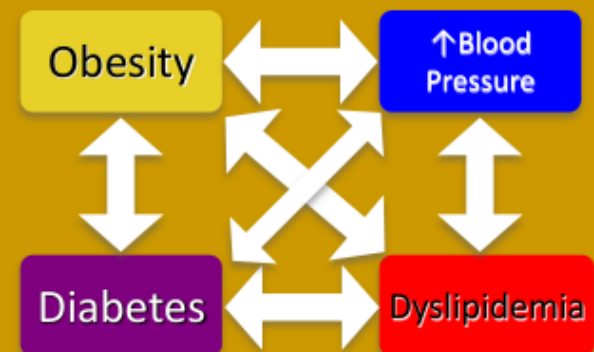
SAS and Systemic Disease

- **Systemic arterial hypertension** - present in ~50% of OSA cases.
- Congestive heart failure
- Pulmonary hypertension
- Stroke
 - OSA is an independent Risk Factor*
- **Metabolic syndrome**
- Type 2 diabetes mellitus

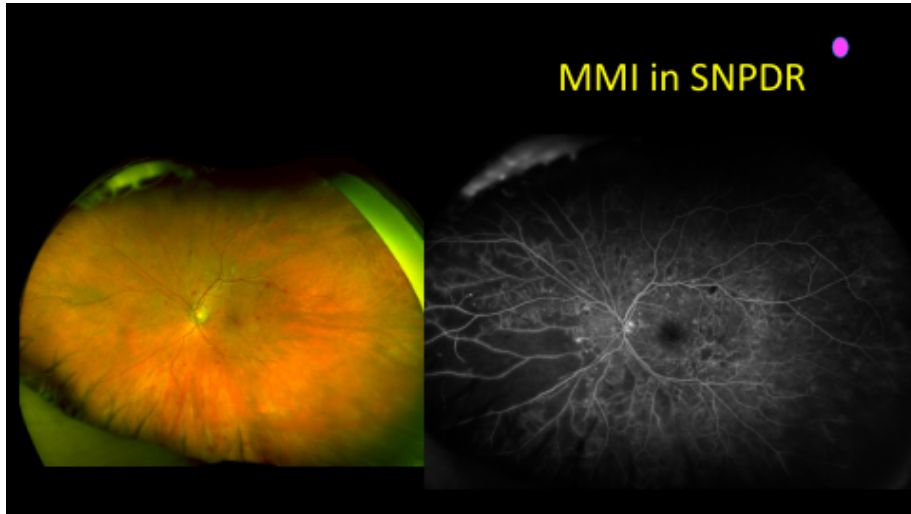
Diabesity

- M_____ S_____ is characterized by central (abdominal) obesity, dyslipidemia, raised blood pressure, and insulin resistance.
- *“Diabesity”*
 - Up to 97% of type 2 caused by excessive weight
 - Obesity = Increased weight caused by excess accumulation of fat.
 - “Over-fat” = normal BMI w/large waist
 - Visceral fat

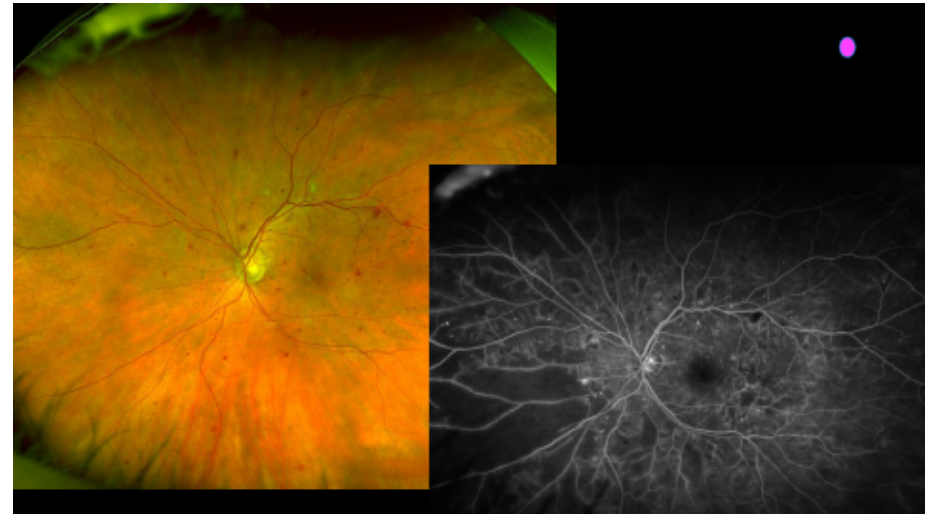
Metabolic Syndrome



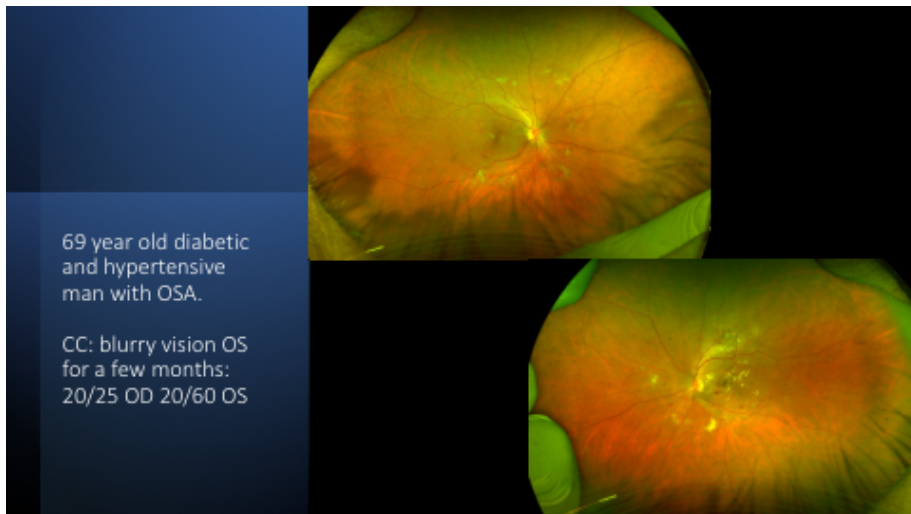
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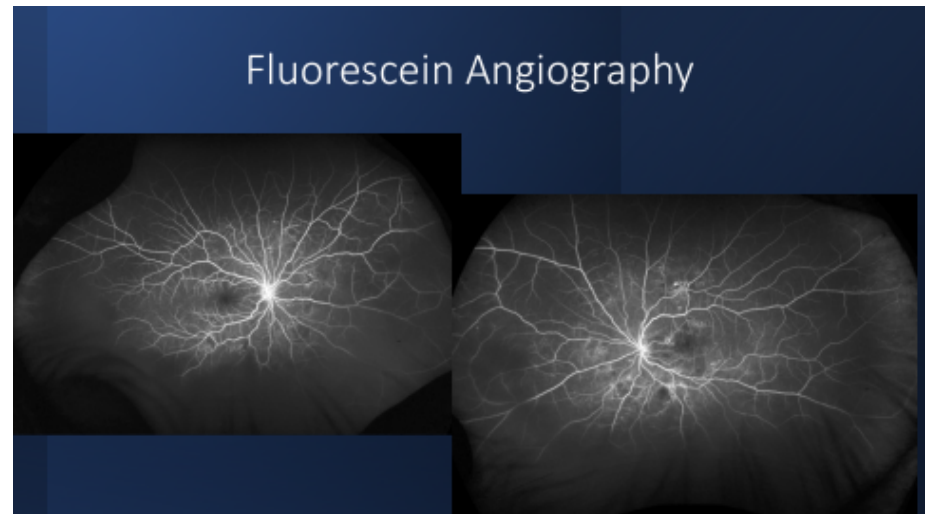
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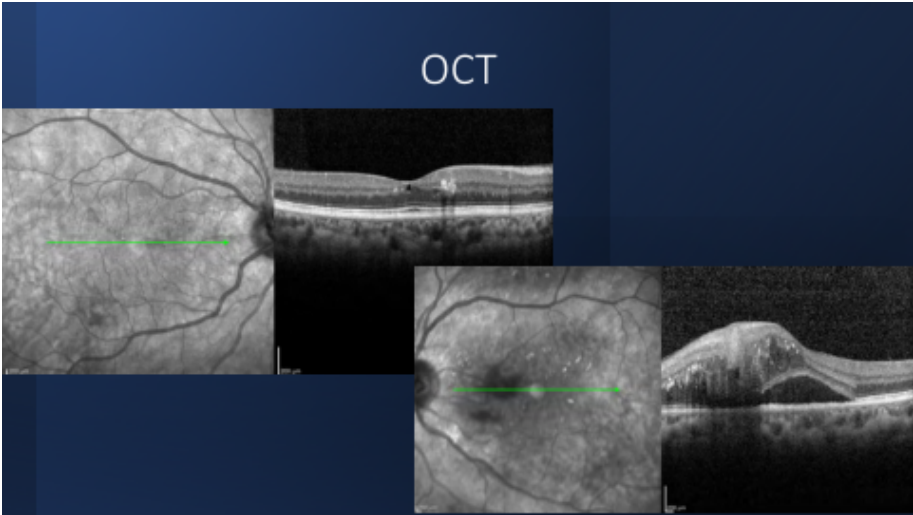
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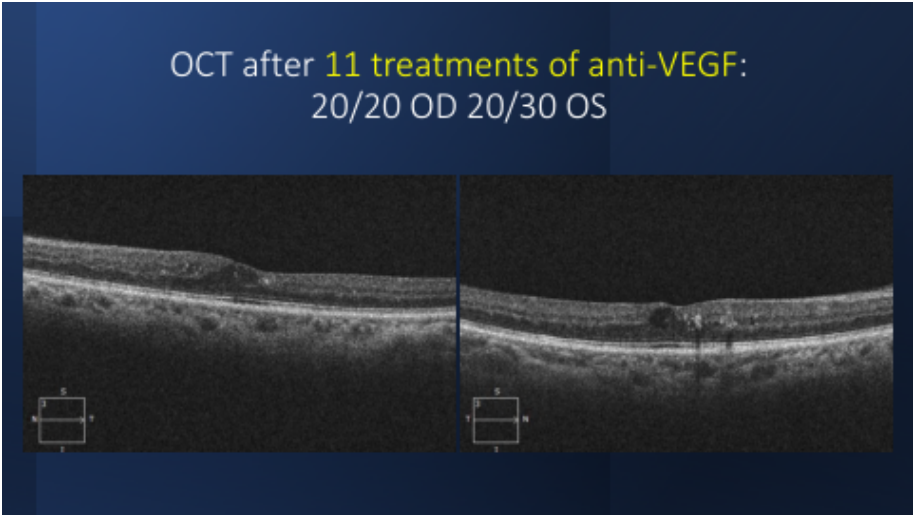
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Slide 217



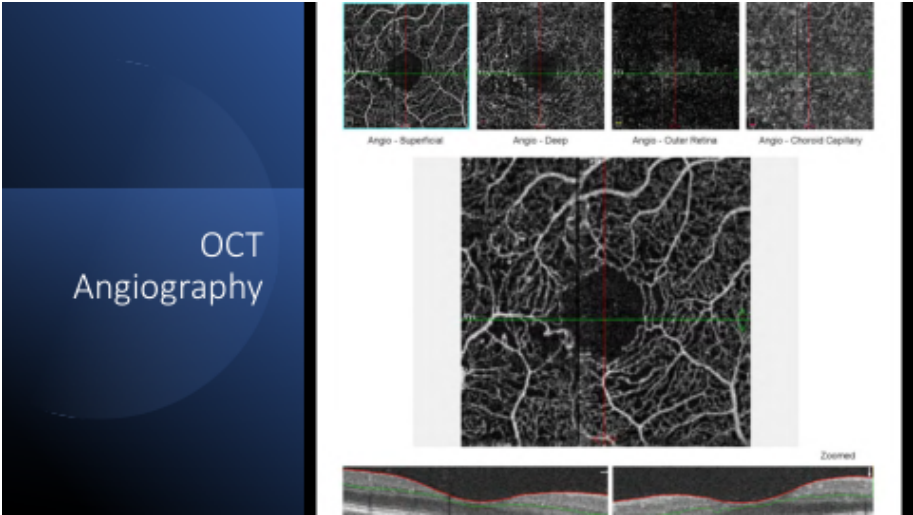
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Slide 220



Now what?

- ODs should refer patients with these ocular findings for a sleep study, particularly if patient fits the OSA demographic profile or complains of sleep disturbances.
- Similarly, sleep medicine specialists should recommend that all their patients have a thorough ocular health examination.
- More cross-referrals support better outcomes for our patients.



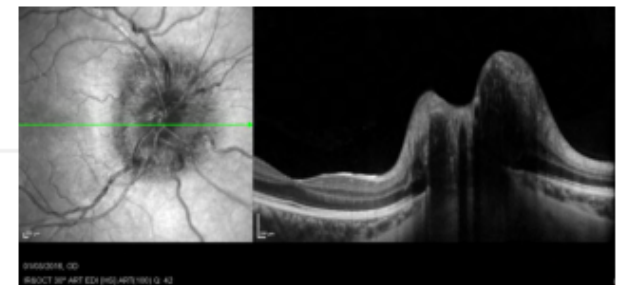
Treatment

- Proper treatment of OSA with continuous positive airway pressure (CPAP) therapy has been shown to improve visual sensitivity as well as RNFL thickness ^[16,17].
- It is essential to recognize the link between these disorders and OSA not only for the preservation of visual function...
- ...but also for proper treatment of OSA, and thus mitigation of the variety of morbidity and mortality because of uncontrolled, undiagnosed OSA.

Questions and Answers

IHH + OSA

AUDIENCE



Thank you!

Joe

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