



Ocular Manifestations of Systemic Disease

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Diseases and Surgery of the Retina, Macula & Vitreous

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Objectives

1. To describe the ocular signs and symptoms associated with selected systemic diseases and their serious ocular sequelae.
2. To review the important features of diabetic retinopathy and the current screening guidelines
3. To be familiar with the important ocular features of hypertension, thyroid disease, sarcoidosis and inflammatory conditions, malignancy and acquired immunodeficiency syndrome.

Introduction

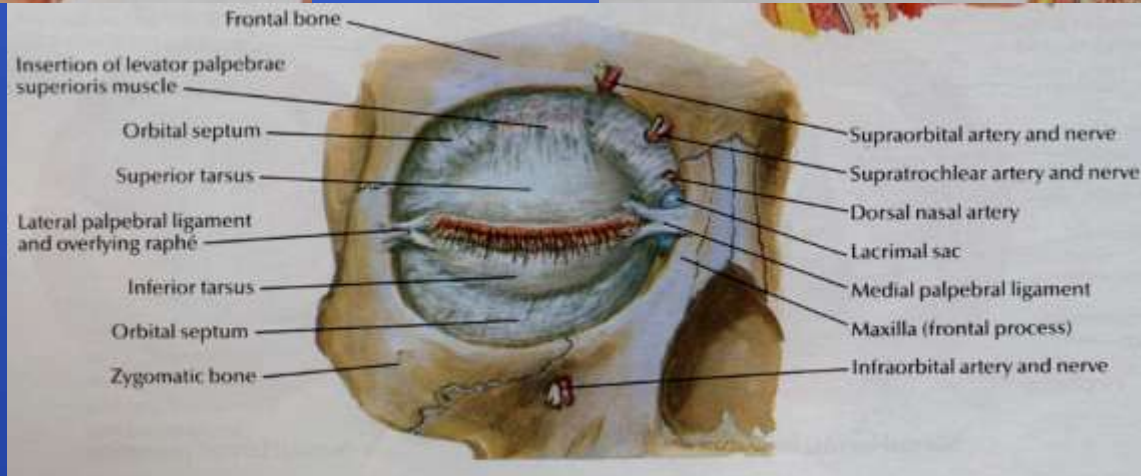
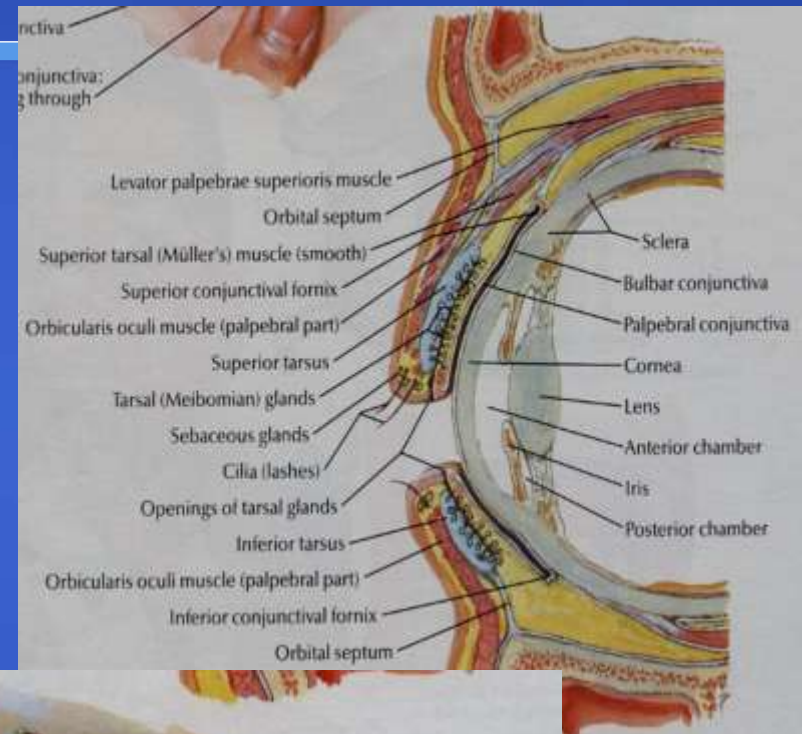
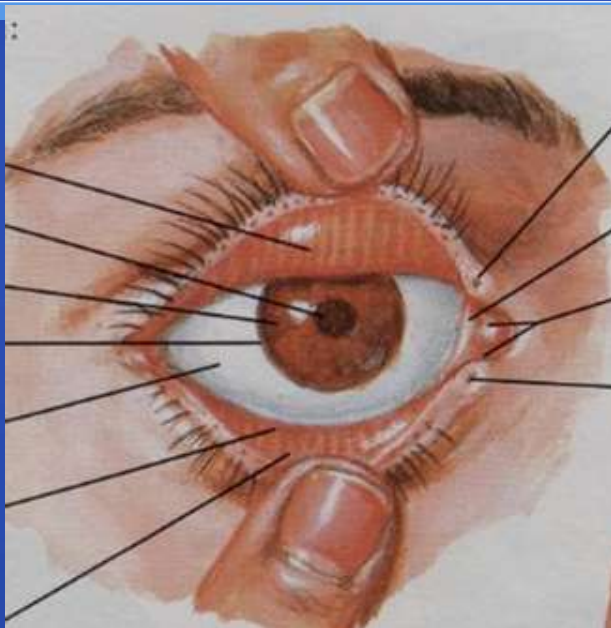
- “The eyes are the window to the soul.”
--English proverb
- Numerous systemic diseases have ocular manifestations
- Occasionally, the eye findings may be the first indication of underlying systemic disease leading to diagnosis

Differential Diagnosis

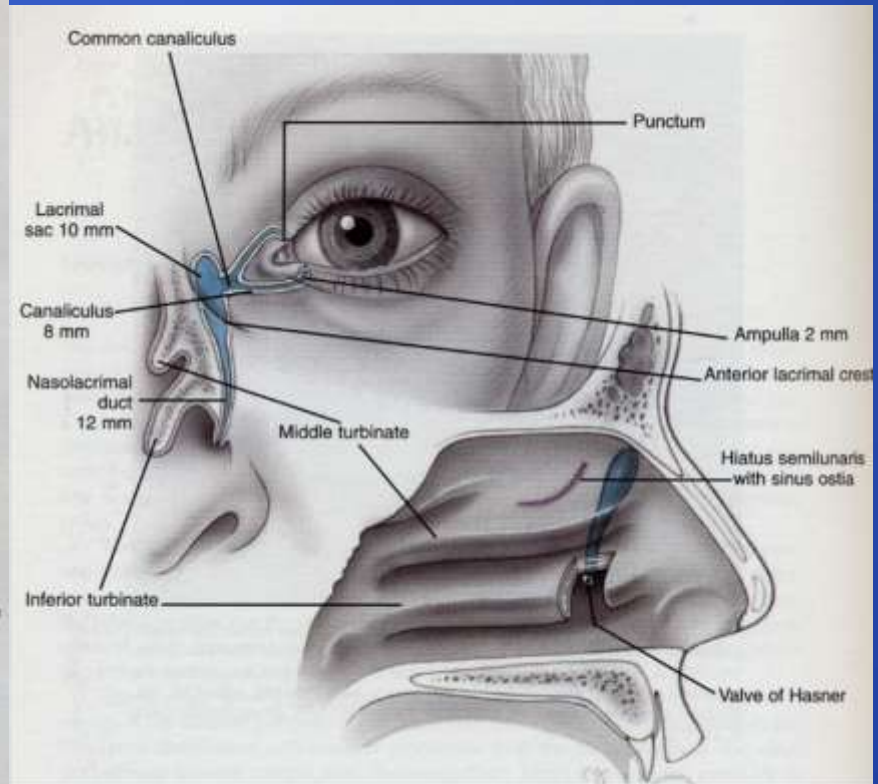
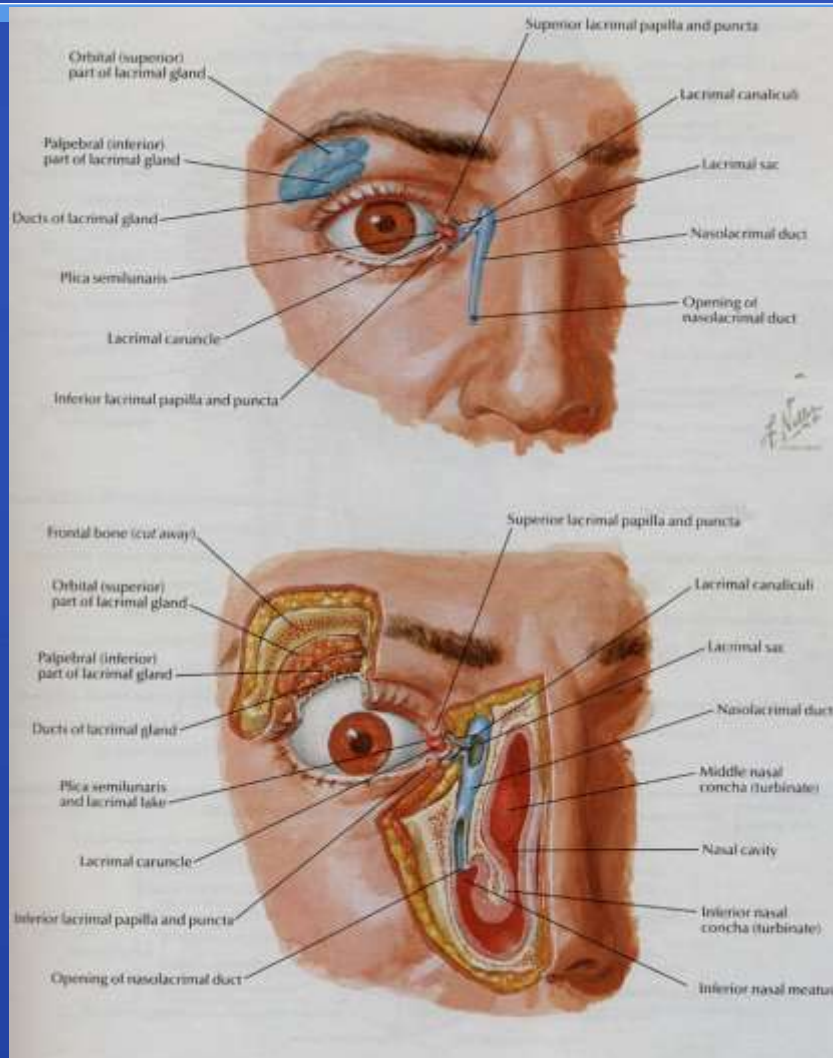
- Congenital
- Vascular
- Traumatic
- Neoplastic
- Autoimmune
- Idiopathic
- Infectious
- Metabolic/Endocrine
- Drugs/Toxins

Ocular Anatomy

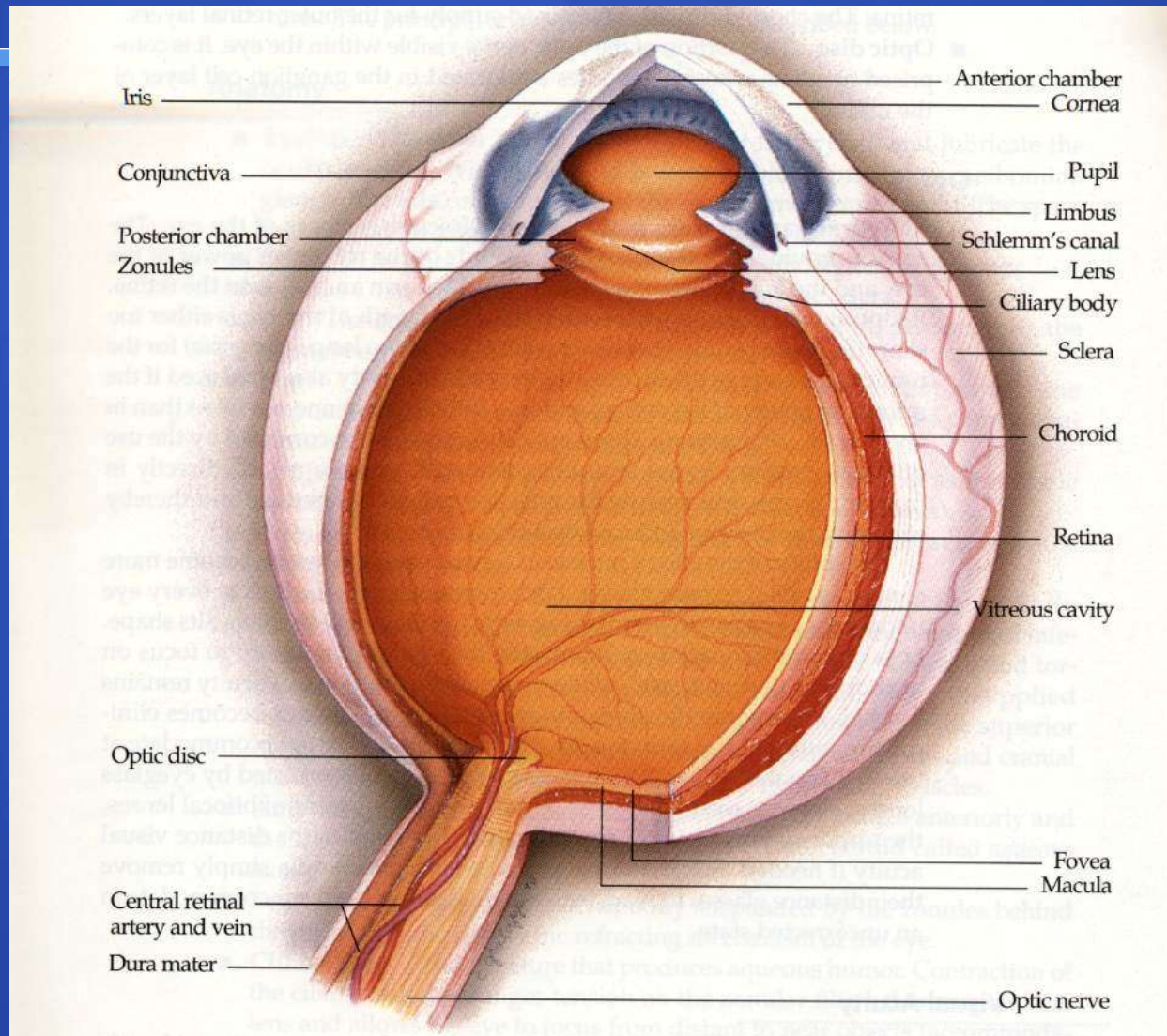
Anatomy: Periocular soft tissues



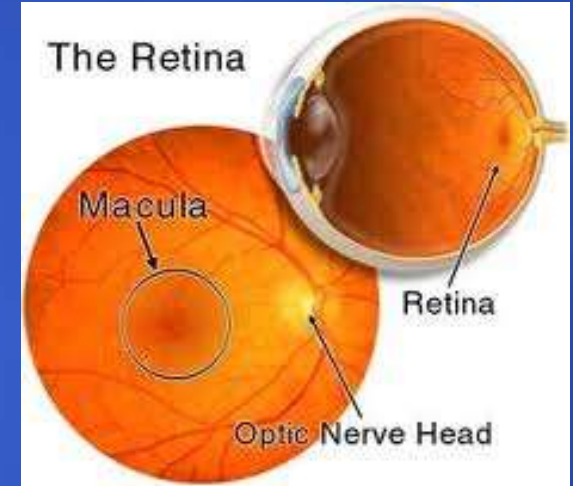
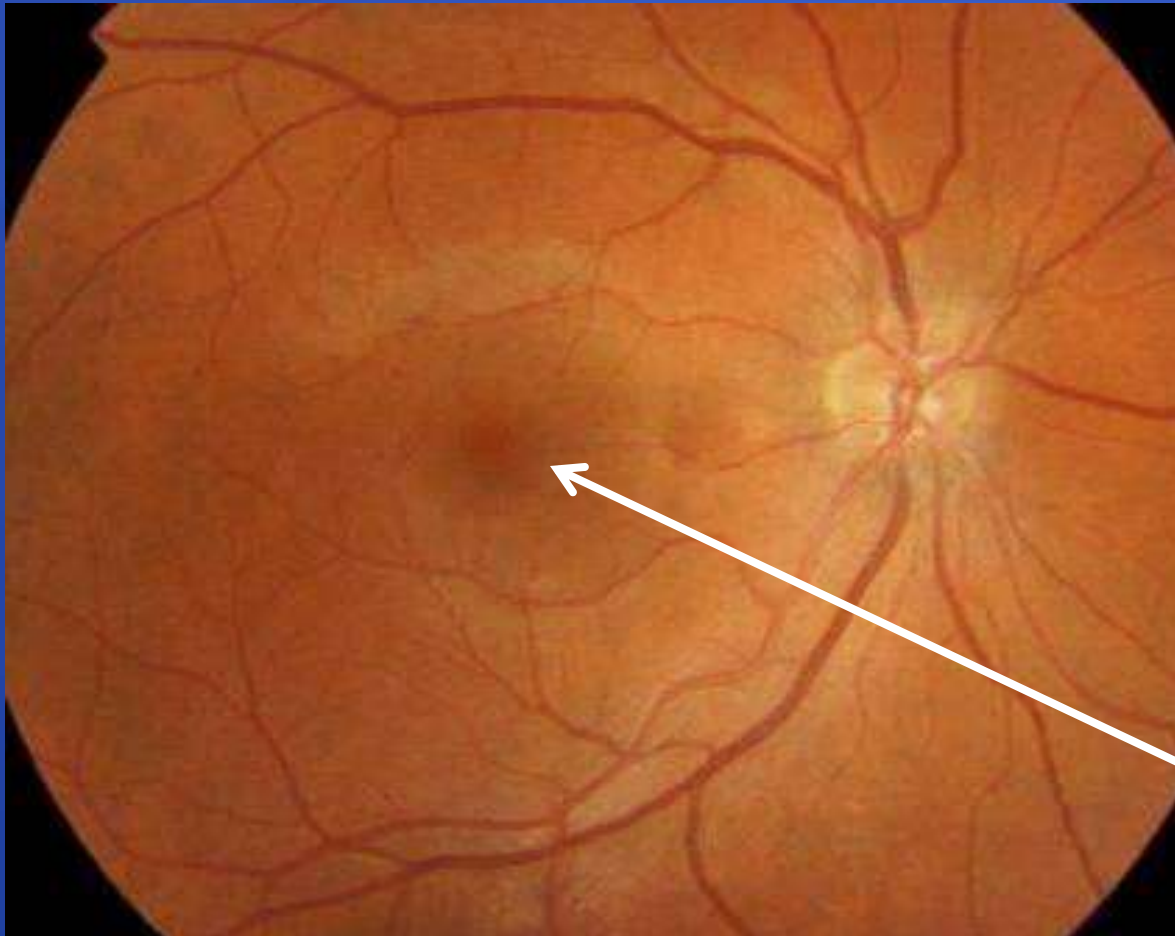
Anatomy: Lacrimal System



Anatomy: The Globe



Anatomy: The Retina



The macula = central vision

Examination



- Vision
- External
- Pupils
 - Relative Afferent pupillary defect (RAPD)
- Motility
- Exam of Anterior Segment (Slit Lamp)
- Dilated Ophthalmoscopy
- Visual Fields

Hypertension

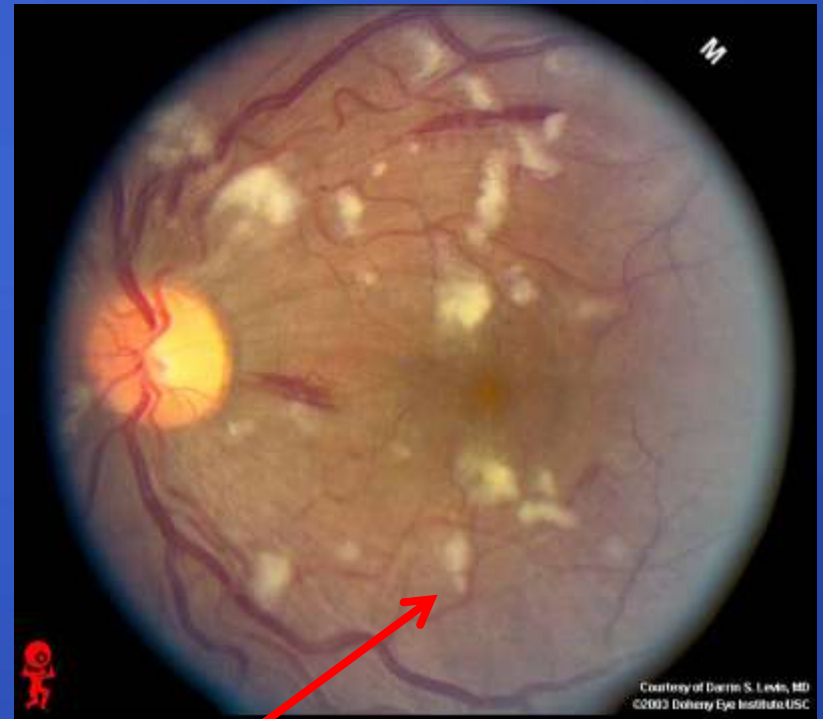
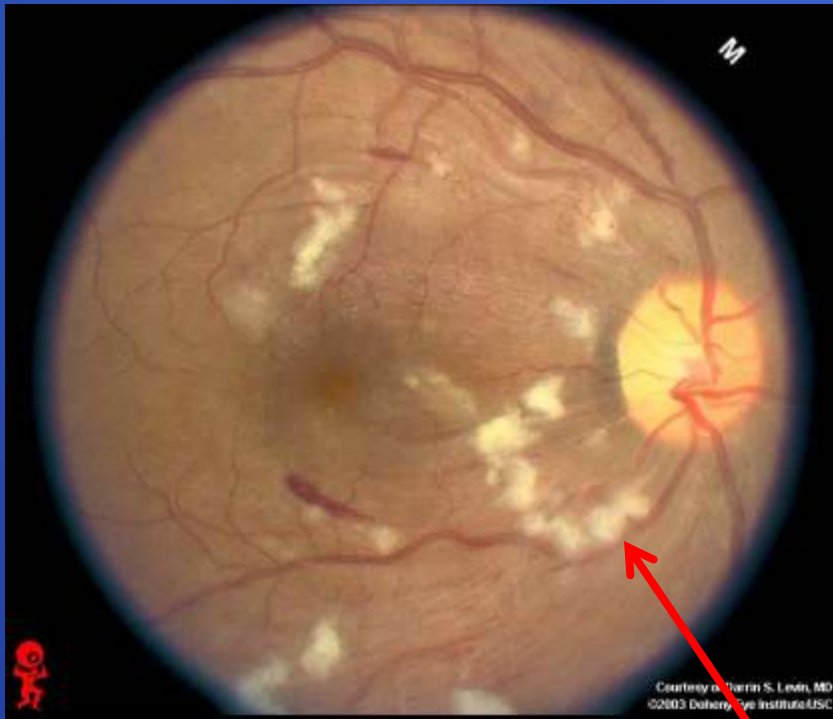
- Systolic > 130 , Diastolic > 85 mmHg
- 65 million Americans
- Heart, kidneys, brain, & Eye
- May cause damage to retina, choroid, and optic nerve
- Acute & Chronic changes
- Preeclampsia



Hypertension

- Ocular findings
 - Arteriolar narrowing & A-V Nicking
 - Cotton Wool spots
 - Retinal hemorrhages
 - Optic nerve swelling (edema)
 - Retinal ischemia & neovascularization
- May be associated with:
 - Branch retinal artery occlusion (BRAO)
 - Branch retinal vein occlusion (BRVO)
 - Central retinal vein occlusion (CRVO)
 - Retinal artery macroaneurysm (RAMA)

Hypertensive Retinopathy

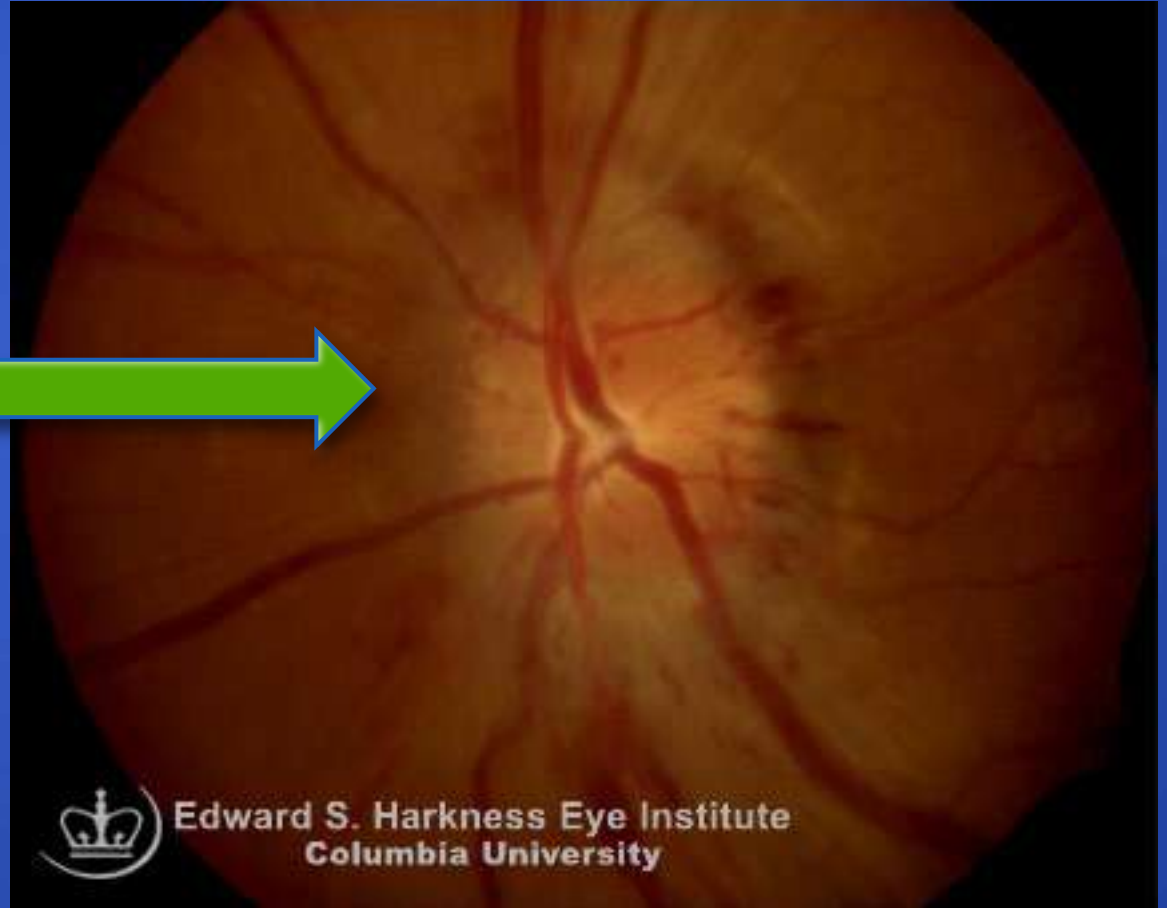
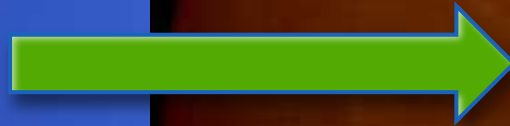


Images courtesy of Redatlas.org

Cotton wool spots

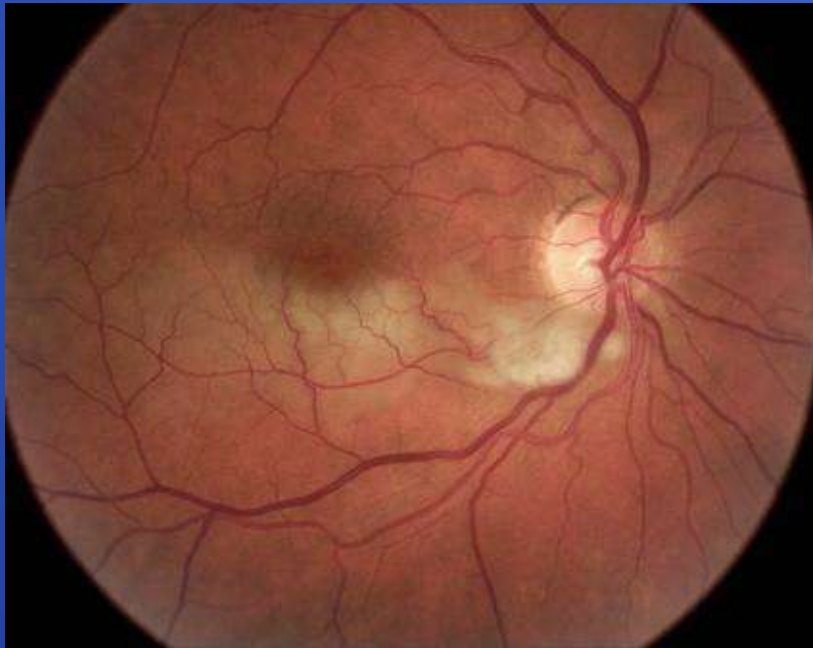
Hypertensive Retinopathy

Optic Nerve
Edema

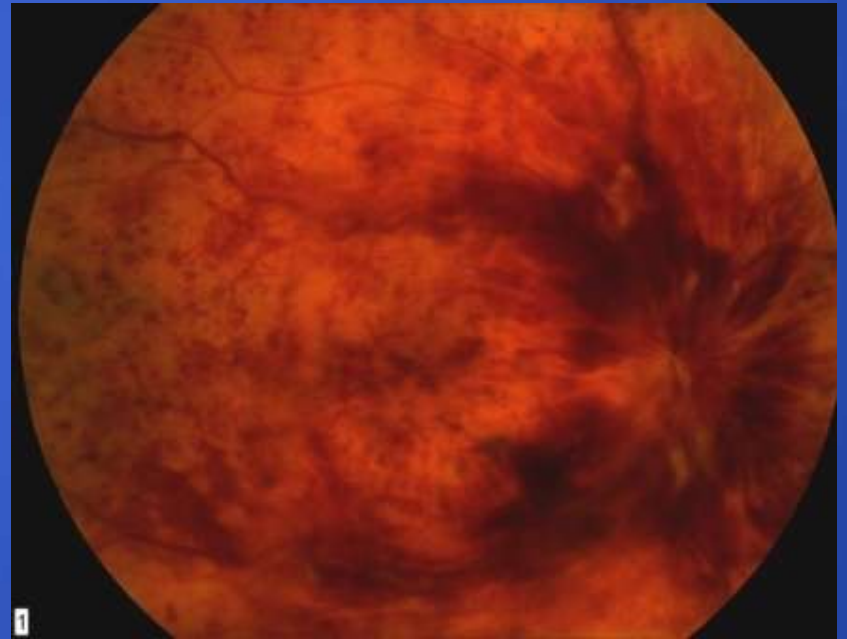


Edward S. Harkness Eye Institute
Columbia University

Hypertensive Retinopathy



BRAO



CRVO

Diabetes mellitus

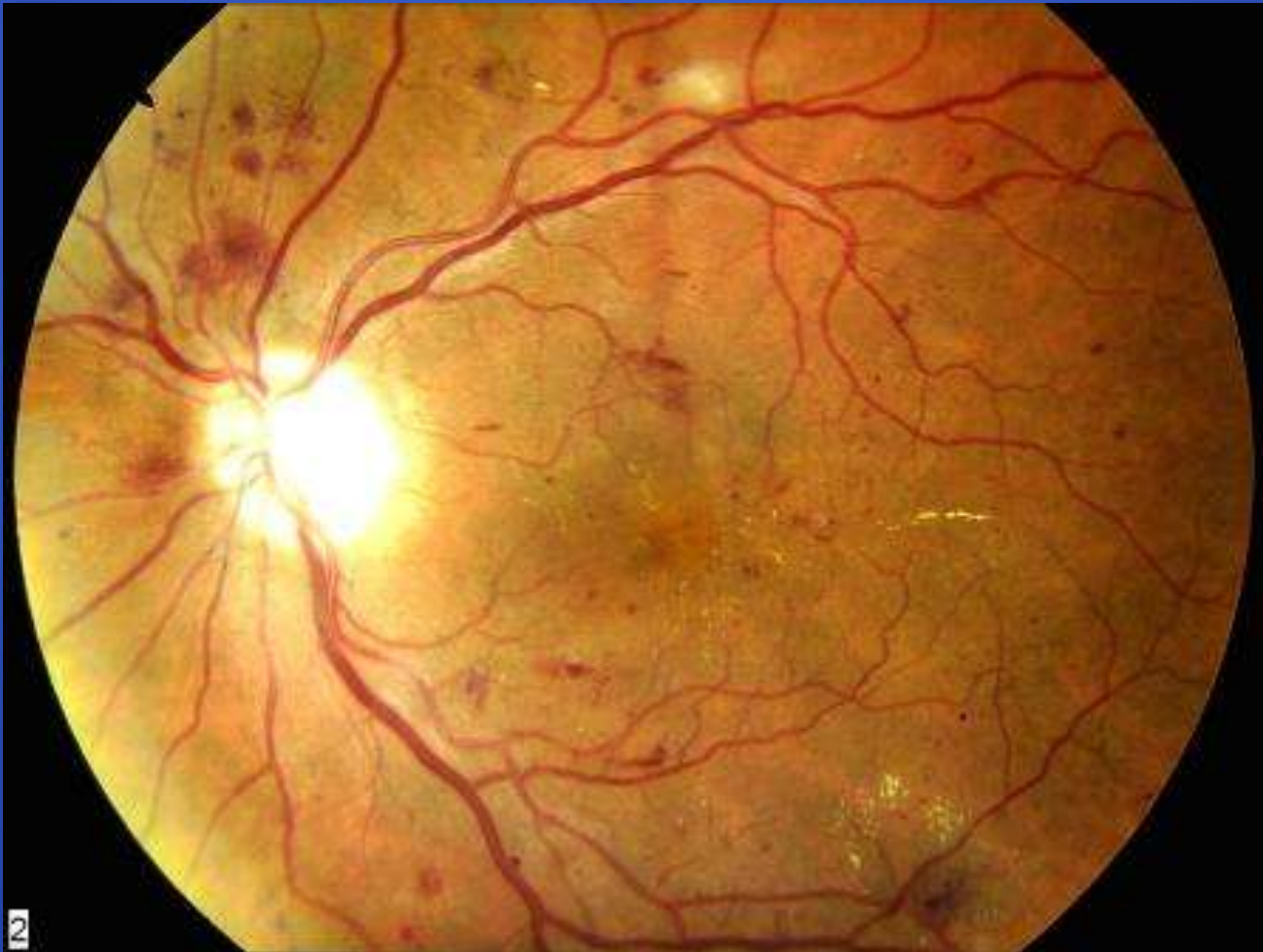
- Diabetic retinopathy (DR) is leading cause of blindness in 20-64yo in US
- Duration of DM is directly related to prevalence of retinopathy
 - After 20 yrs: **99% of type 1 and 60% of type 2** will have some degree of DR
- Pathologic changes include microvascular damage leading to hypoxia, vascular leakage & edema, ischemia, and neovascularization
- Prevention & Importance of systemic blood glucose, pressure, & lipid control: DCCT, UKPDS, & ACCORD trials

Diabetic Retinopathy

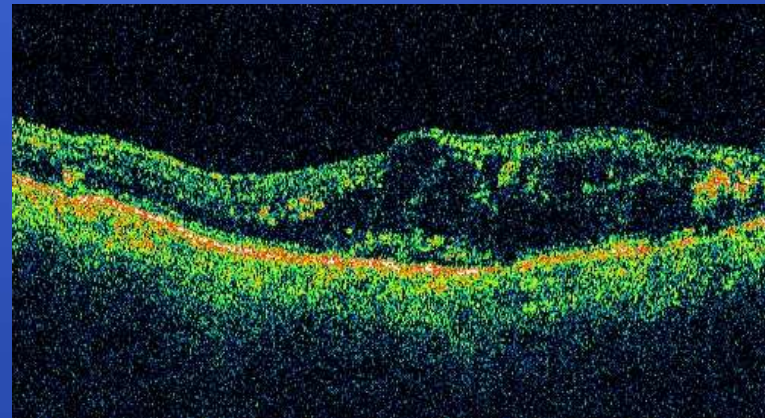
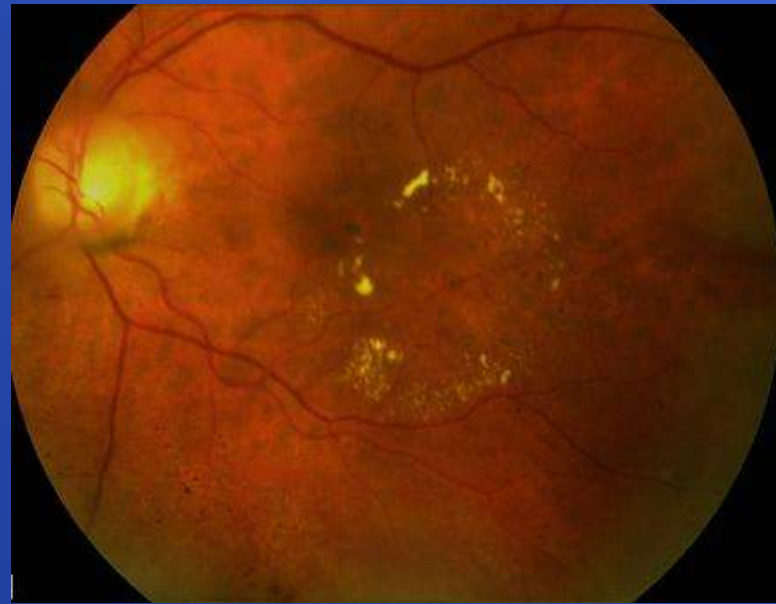
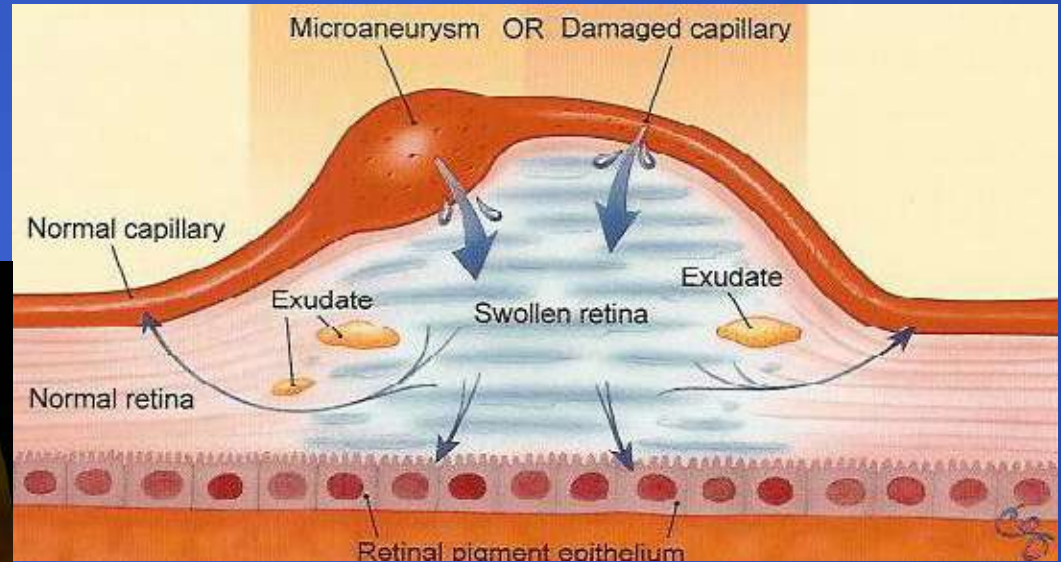
- Classification:
 - Non-Proliferative diabetic retinopathy (**NPDR**)
 - Proliferative Diabetic Retinopathy (**PDR**)
- Complications Resulting in Visual Loss
 - Macular edema (capillary leakage)
 - Macular ischemia (capillary occlusion)
- Sequelae from ischemia-induced neovascularization



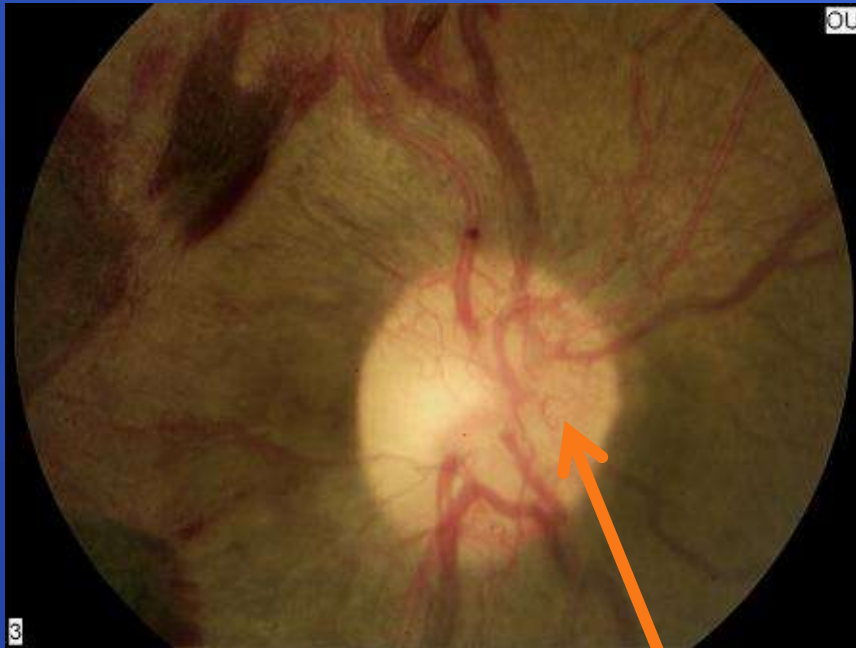
Diabetic Retinopathy: NPDR



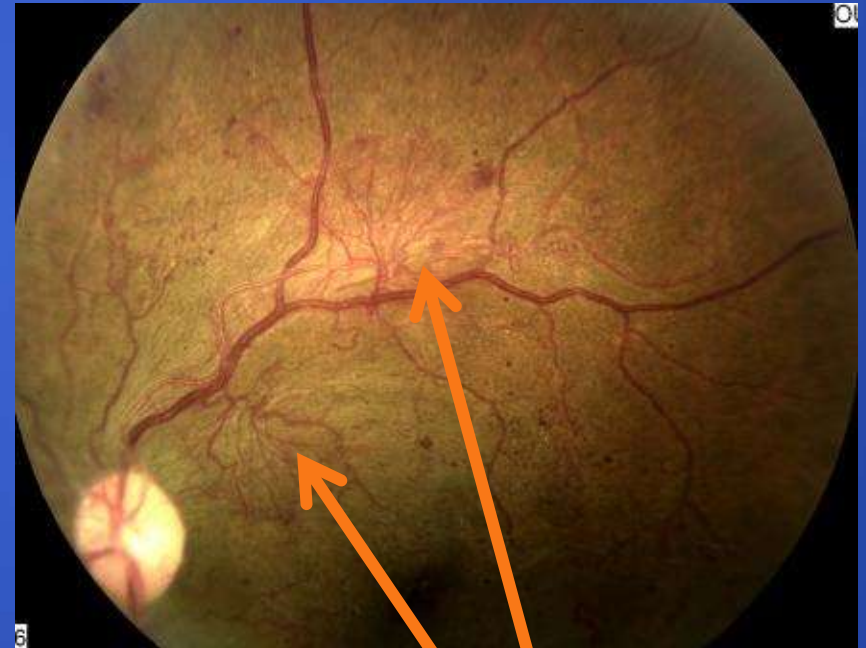
Diabetic Retinopathy: Macular Edema



Diabetic Retinopathy: PDR



NVD



NVE

Diabetic Retinopathy: PDR



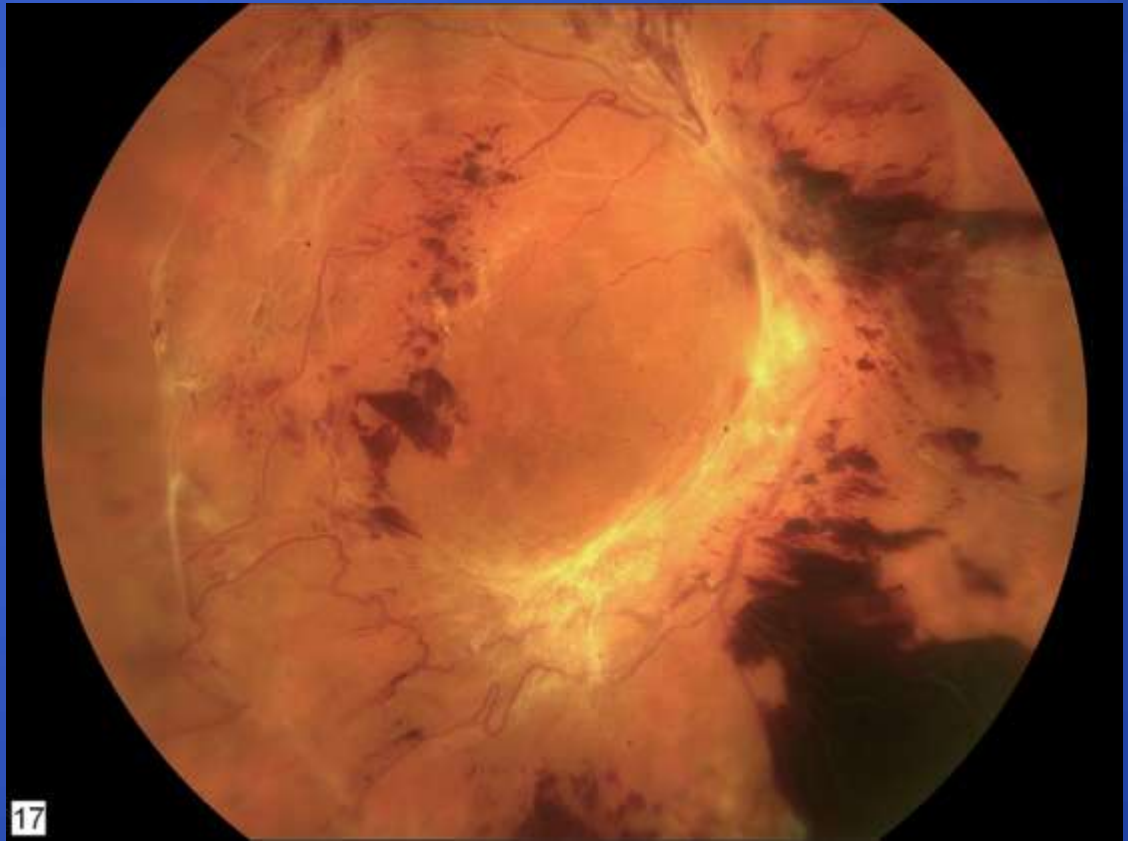
NVE



Diabetic Retinopathy: PDR



Vitreous Hemorrhage



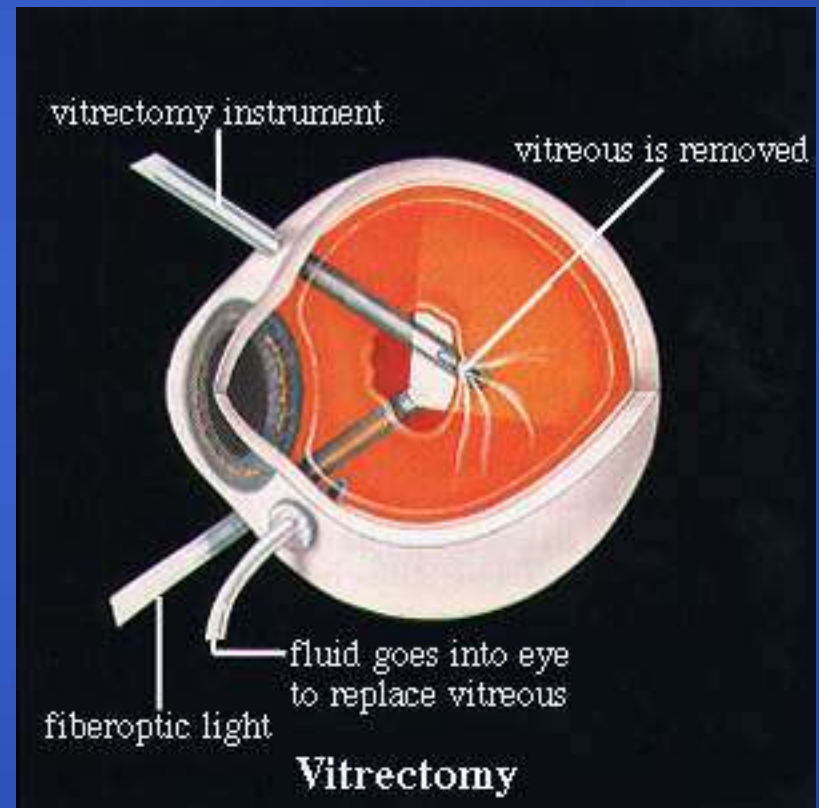
Tractional Retinal Detachment

Diabetic Retinopathy: Treatment

- Laser
- Pharmacologic (anti-VEGF meds)
- Surgery

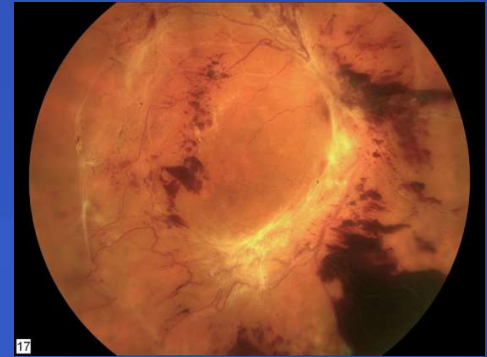
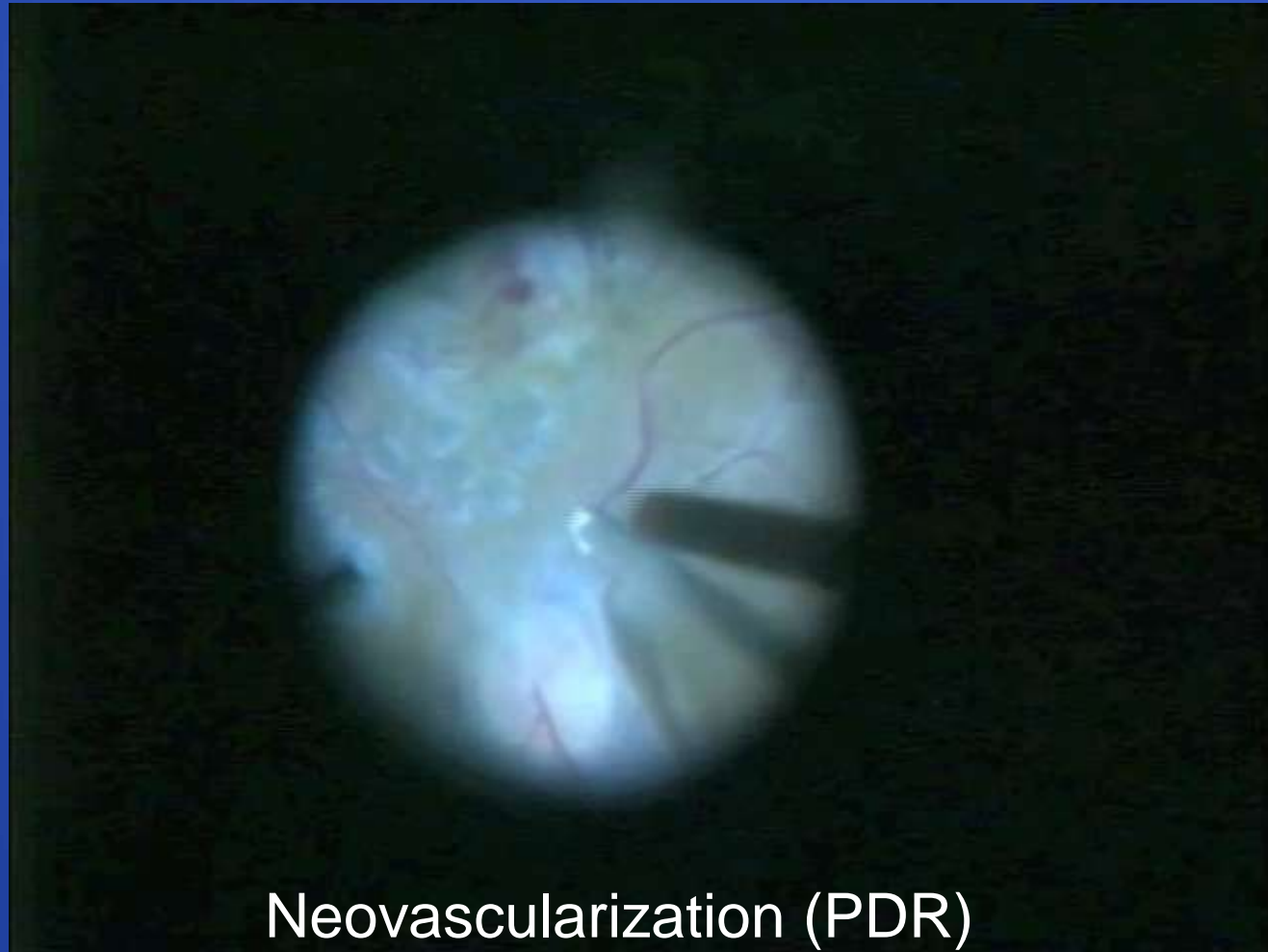


Laser Pan Retinal Photocoagulation



Vitrectomy Surgery

Diabetic Retinopathy: Vitrectomy Surgery



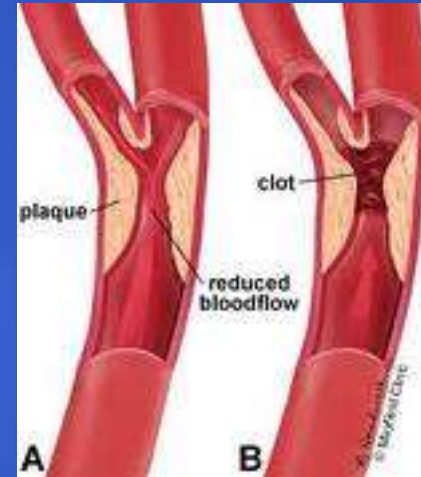
Scar tissue, membranes,
& blood on surface of
retina

Diabetic Retinopathy: Screening & Prevention

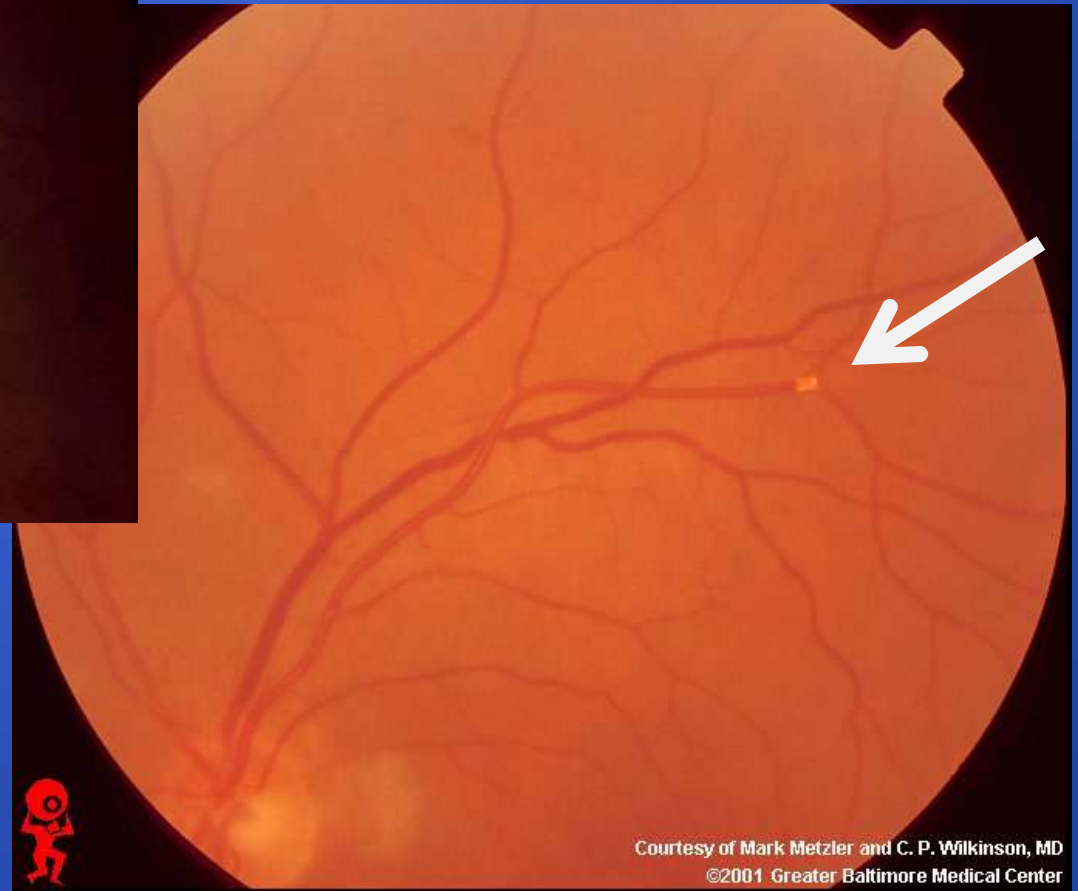
- Screening eye examination for all patients:
 - At time of diagnosis for type 2
 - Within 5 yrs of diagnosis for type 1
 - **Pregnancy**
 - Follow-up exams will be dependent on initial eye findings
- Blood glucose, Blood pressure, and Lipid optimization
- Stop smoking
- Exercise

Carotid Stenosis

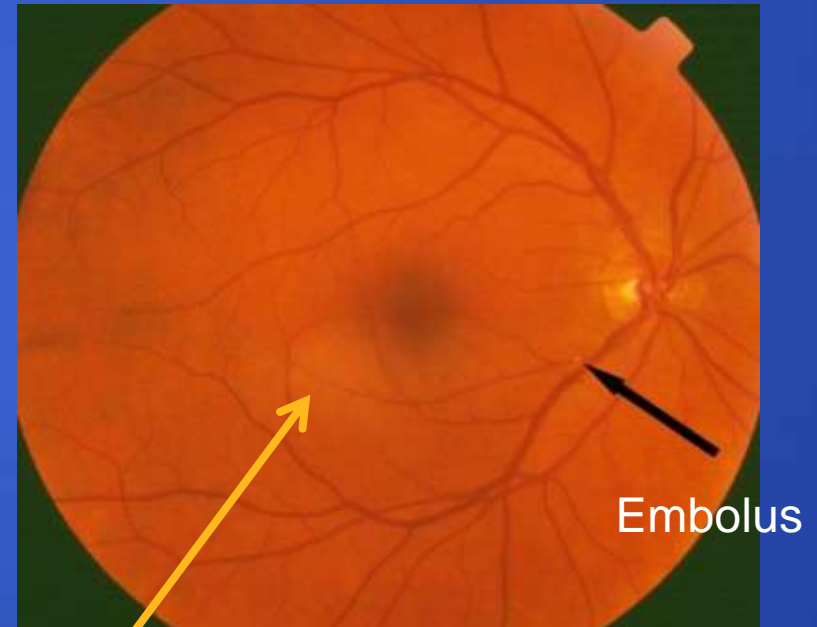
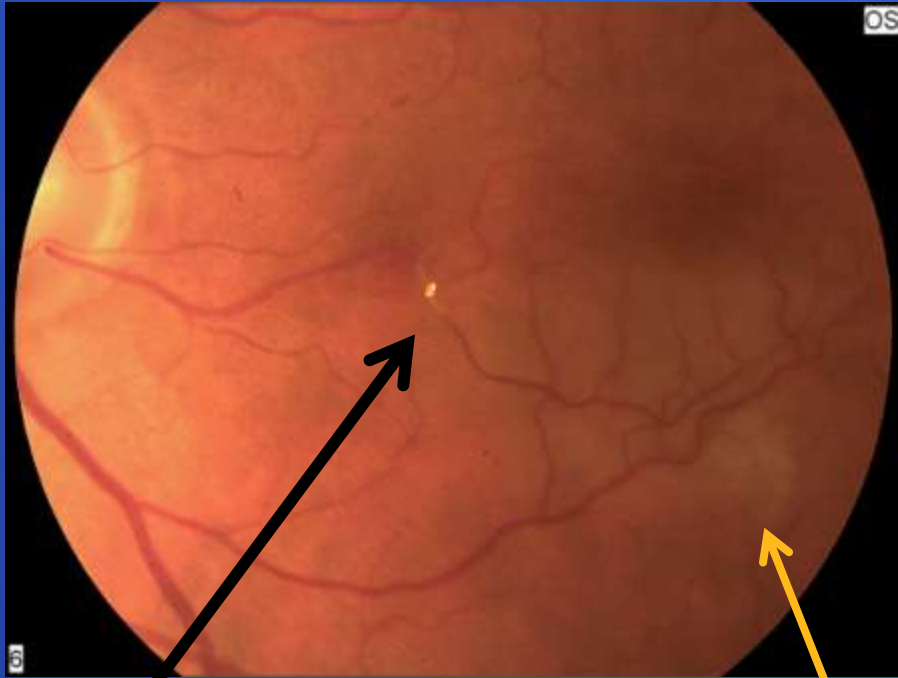
- Amaurosis fugax
- Hollenhorst plaque
- Retinal artery occlusion
- Ocular ischemic syndrome (& neovascular glaucoma)



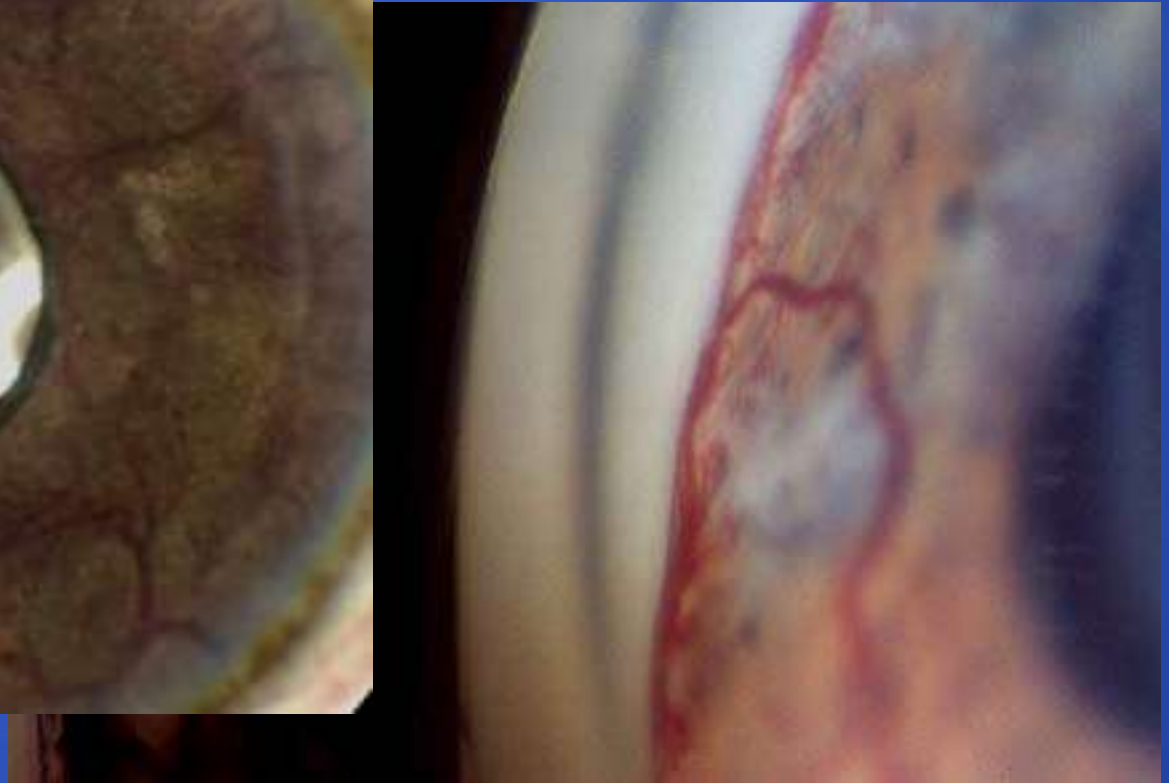
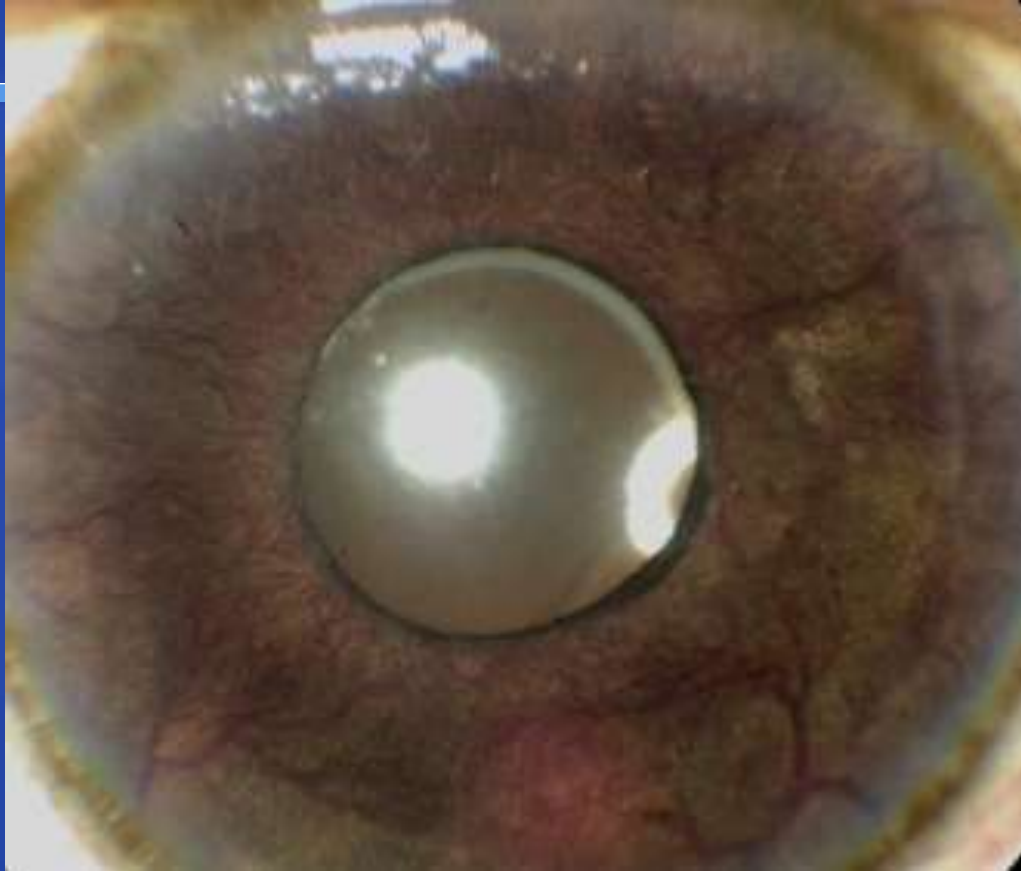
Hollenhorst plaque



Carotid Stenosis: Branch Retinal Artery Occlusion



Ocular Ischemic Syndrome

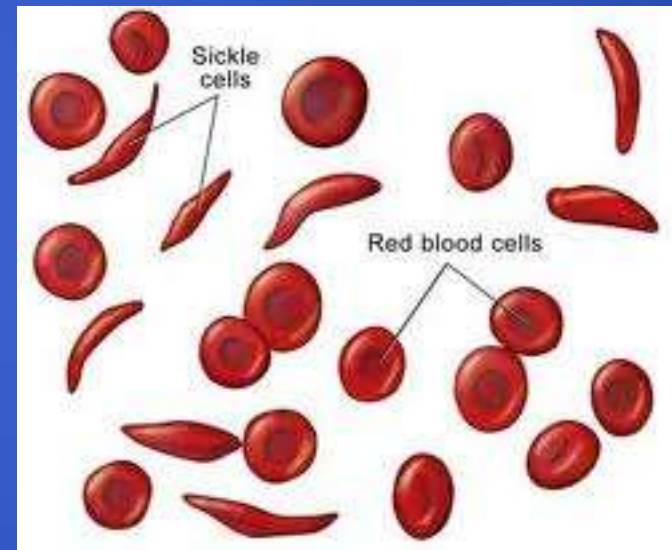


Pain
Red Eye
Loss of vision
Elevated Intraocular Pressure


Patients at risk for ischemic
CV disease, stroke, &
peripheral Vascular disease

Sickle Cell Disease

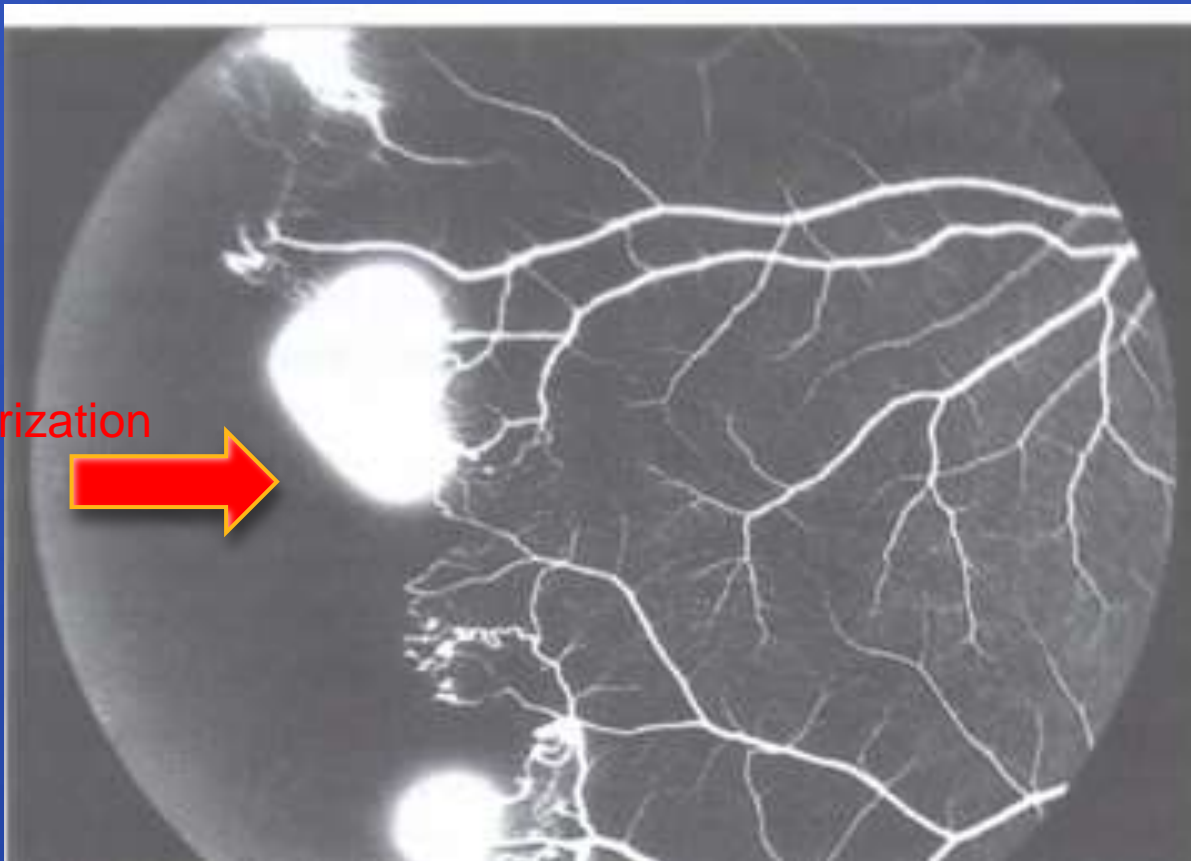
- Autosomal Recessive
- Genotype
 - 8% Sickle cell trait (HbAS)
 - 0.4% Sickle cell disease (HbSS)
 - 0.2% SC disease (HbSC)
 - Sickle Thalassemia
- Systemic Complications
 - Crises (painful episodes)
 - Acute chest syndrome



Sickle Cell Disease: Ocular Complications

- Frequency
 - HbSC (most common) – 33%
 - Sickle Thalassemia – 14%
 - HbSS – less frequently but have more severe systemic complications – 3%
- Pathogenesis:
 - Peripheral retinal nonperfusion – ISCHEMIA =
Neovascularization  Hemorrhage & Tractional
Retinal Detachment

Sickle Cell Disease



Capillary nonperfusion in peripheral retina

Sickle Cell Disease

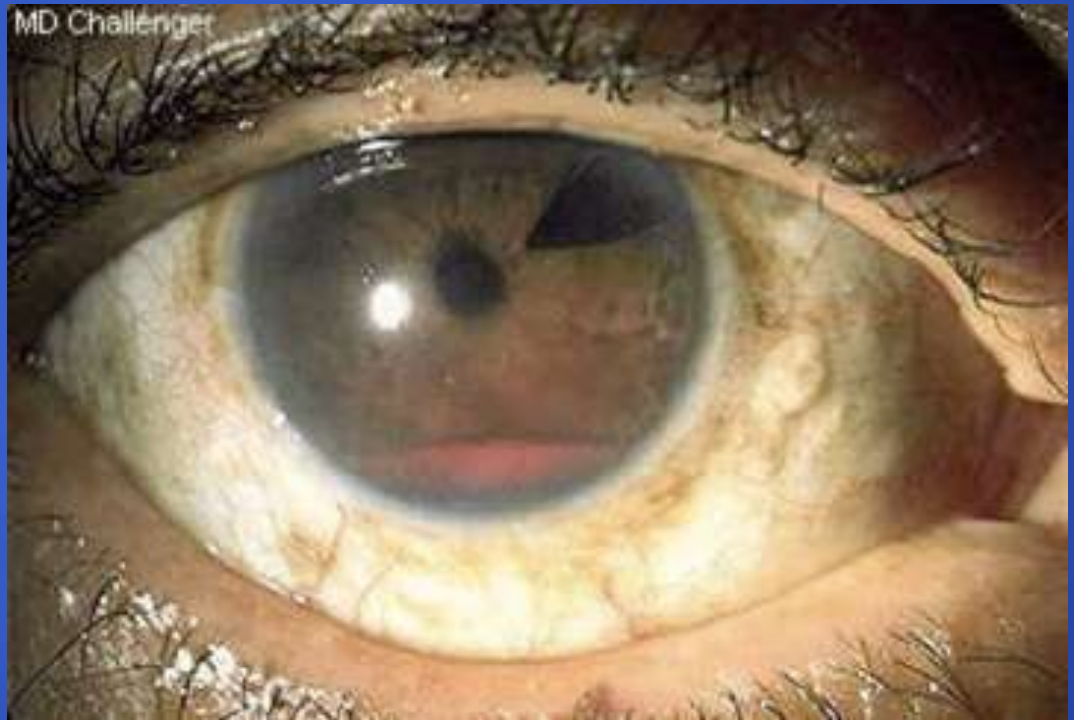


← Neovascularization

Dr. Shivam Maiti

Sickle Cell Disease: Special Situations

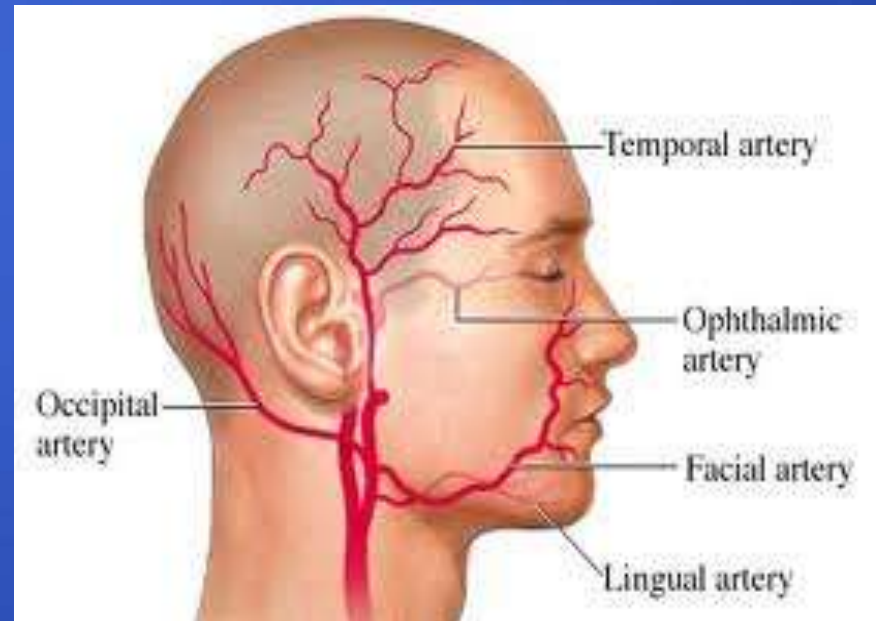
- High Risk for elevated intraocular pressure due to sickling of RBCs
- Require aggressive medical & sometimes surgical Rx to prevent optic nerve damage



Know Sickle Cell Status for patients with Traumatic Hyphema

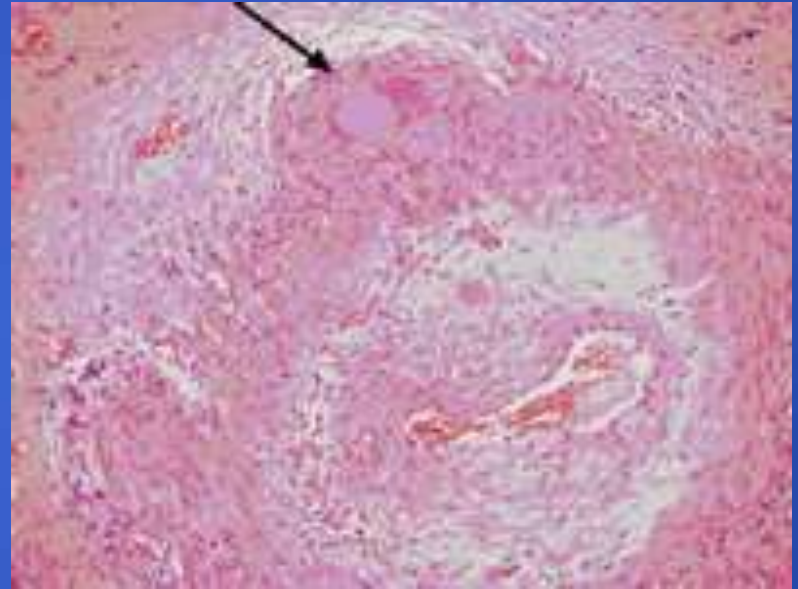
Giant Cell Arteritis

- AKA: Temporal Arteritis
- Systemic granulomatous vasculitis affecting medium- and large-sized vessels
- Age > 50 yo
- Symptoms
 - Headache
 - Scalp tenderness
 - Jaw claudication
 - Polymyalgia rheumatica
 - Acute vision loss



Giant Cell Arteritis

- Diagnosis:
 - Clinical history
 - Stat ESR &/or CRP
 - Temporal artery biopsy
- Treatment:
 - High-dose systemic steroids (**do not defer until after biopsy**)



Giant Cell Arteritis

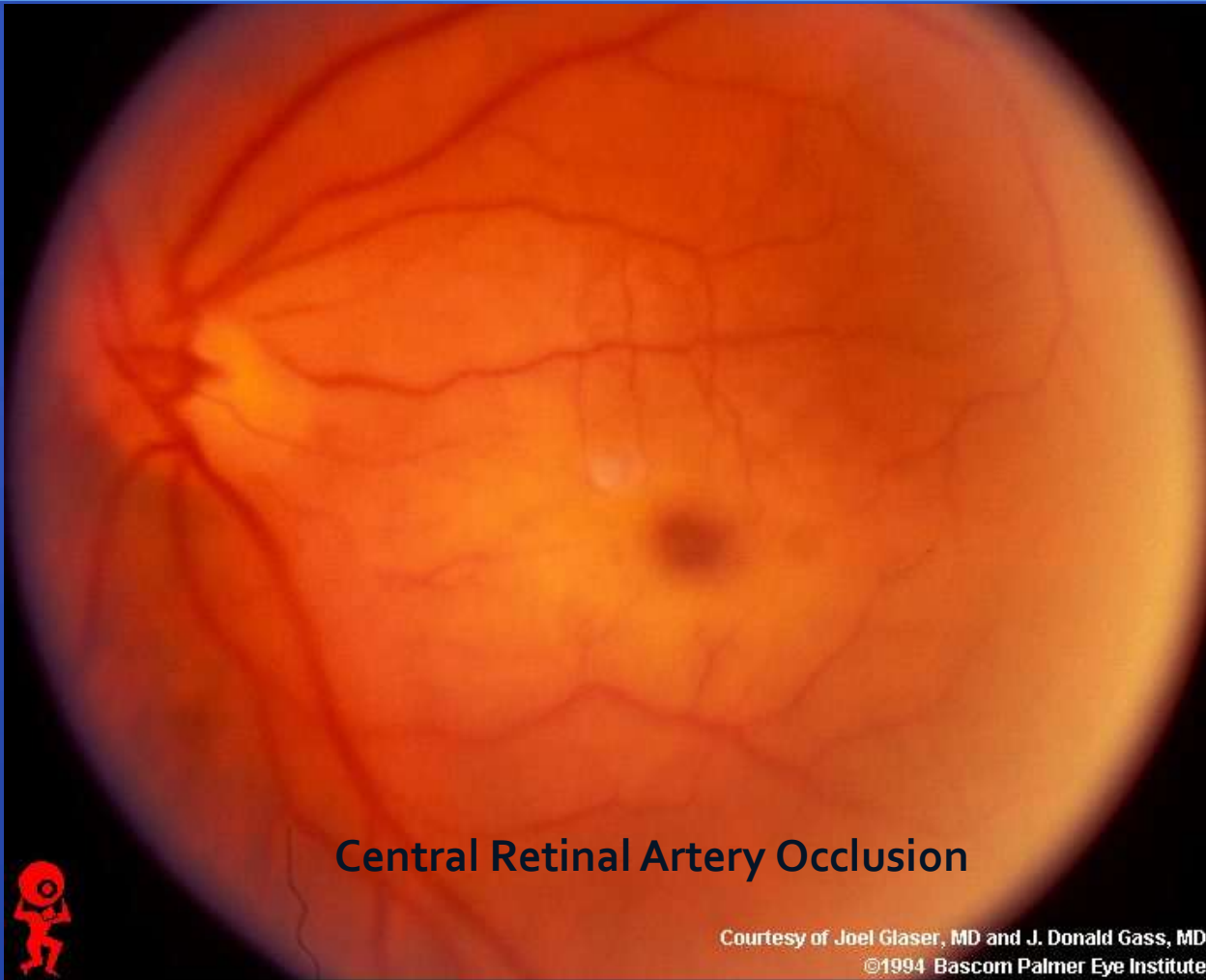


Dilated superficial temporal artery

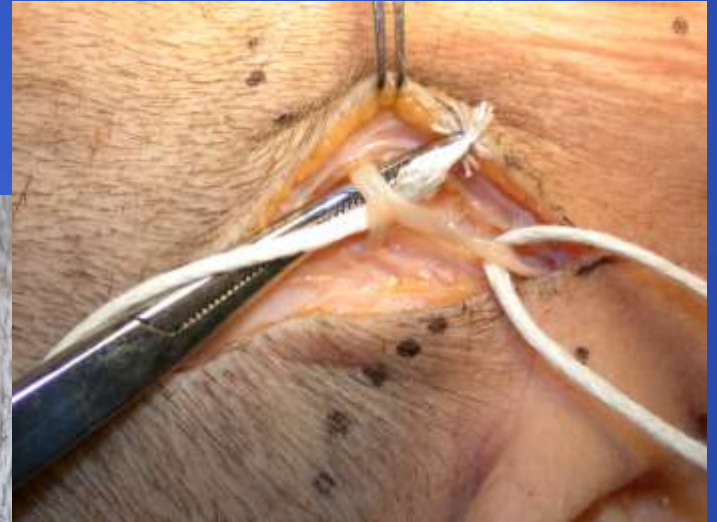


Scalp Necrosis

Giant Cell Arteritis



Temporal Artery Biopsy



Superficial Temporal artery

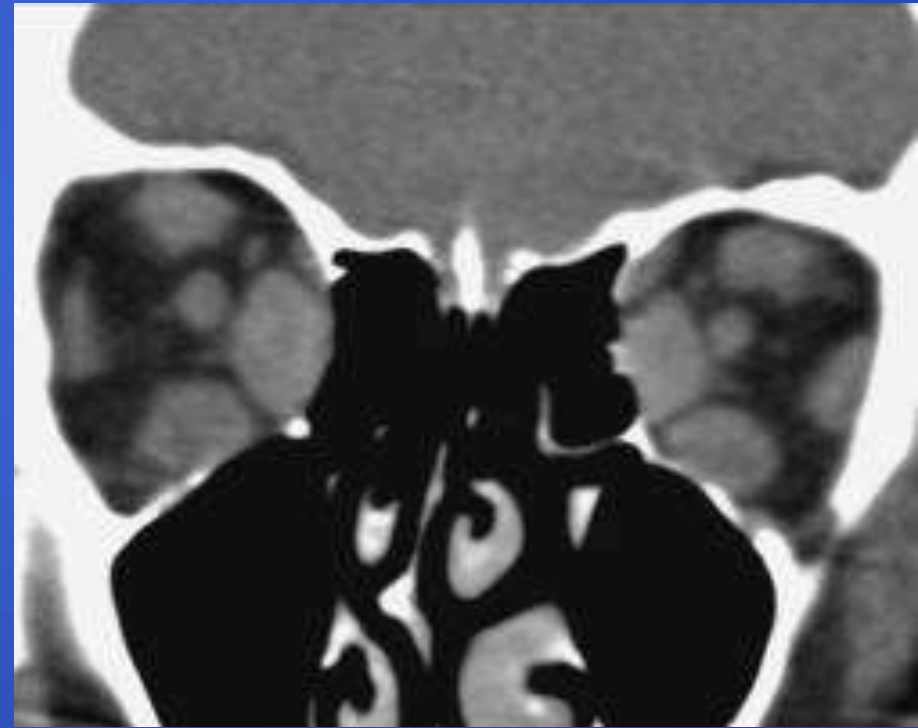
Thyroid Eye disease

- May occur with hyper-, hypo-, or euthyroid states
- Hyperthyroidism: goiter, tremor, pretibial myxedema, atrial fibrillation, etc
- Ocular Findings:
 - Proptosis (exophthalmos)
 - Lid Retraction -- **Thyroid stare**
 - Corneal exposure (dry eye, corneal ulcer)
 - Diplopia (due to eye muscle restriction)
 - Optic Nerve compression (optic neuropathy) – 5%



Thyroid Eye Disease: Pathophysiology

- Autoimmune process with cross-reaction against orbital and periorbital soft tissues



Enlargement of ocular rectus muscles

Thyroid Eye disease



Exophthalmos: “Thyroid Stare”



Thyroid Eye disease



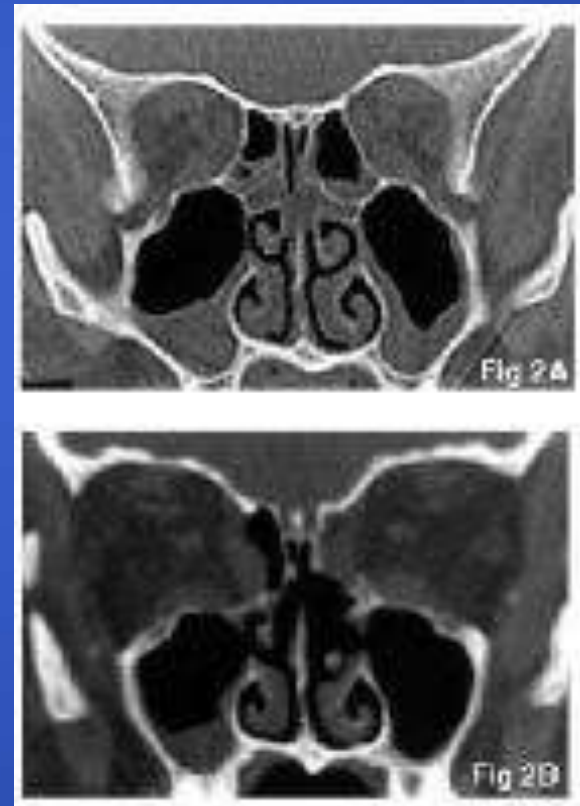
Chemosis & Dry Eye

Thyroid Eye disease

- CT scan orbits or Orbital Ultrasound
 - Look for enlargement of eye muscles
- Restrictive myopathy = Double Vision



Thyroid Eye disease: Orbital Decompression



(For TED-related Optic Neuropathy)

Thyroid Eye disease: Management

- Treatment Considerations:
 - Artificial tears & lubrication
 - Systemic steroids & external beam radiation (if vision threatening)
 - Surgery:
 - Orbital decompression
 - Eye muscle surgery
 - Eyelid Surgery
 - **Stop Smoking**

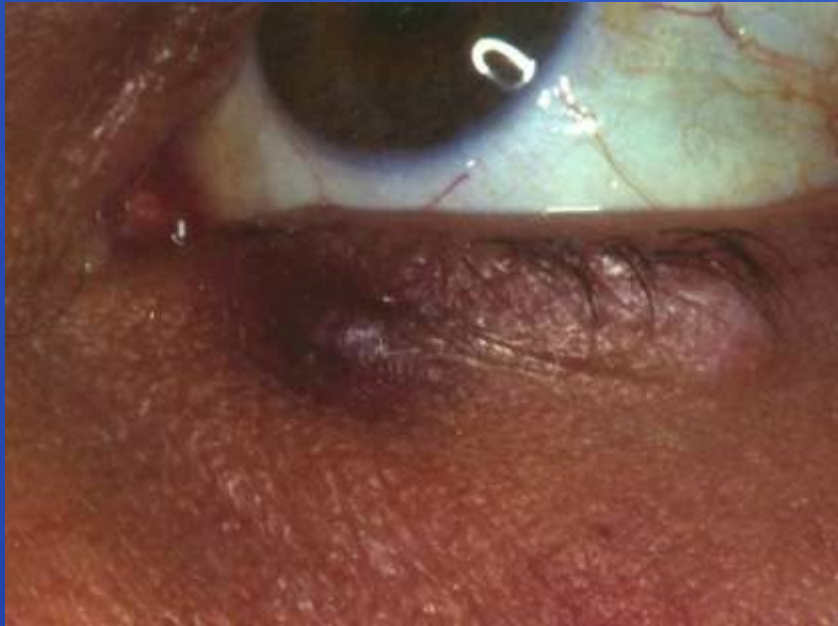
HIV & AIDS

- Eyelids: Kaposi sarcoma, molluscum contagiosum, Herpes zoster ophthalmicus
- Orbit: Cellulitis, B-cell lymphoma
- Cornea: Keratitis (microsporidium, HSV, HZV)
- Keratoconjunctivitis sicca (severe dry eye)
- Anterior uveitis
- HIV retinopathy
- Retinitis (CMV, VZV, toxoplasmosis)
- Choroiditis (pneumocystis, toxoplasmosis)
- B-cell intraocular lymphoma

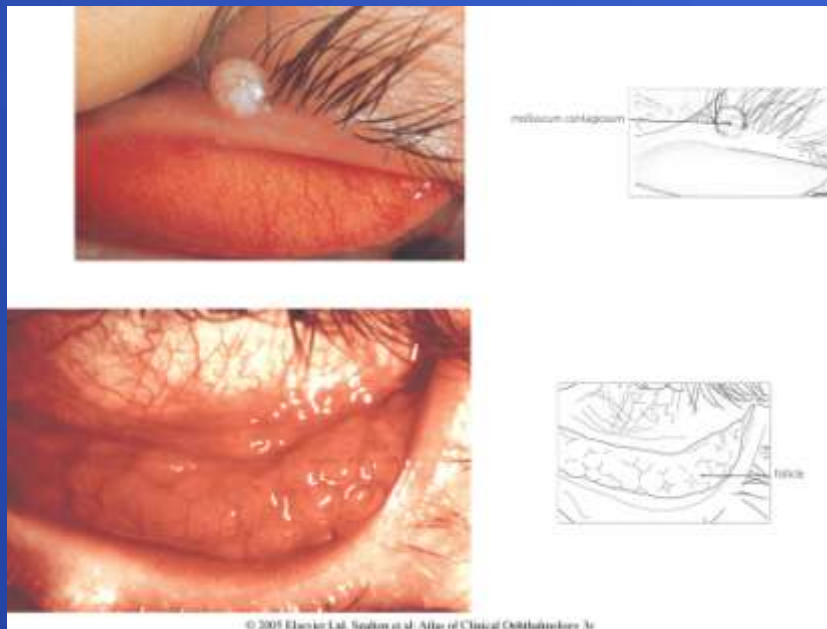
Kaposi Sarcoma

- Purplish red to bright red highly vascular lesions with surrounding telangiectatic vessels
- Associated with Human Herpes Virus-8 (HHV-8)
- 20-24% of AIDS-related Kaposi sarcoma will involve eye
- Eyelid & Conjunctiva
- Mostly local mass effects – pain, poor eyelid closure, etc
- Treatment: chemotherapy, surgical (if large to debulk)

Kaposi Sarcoma

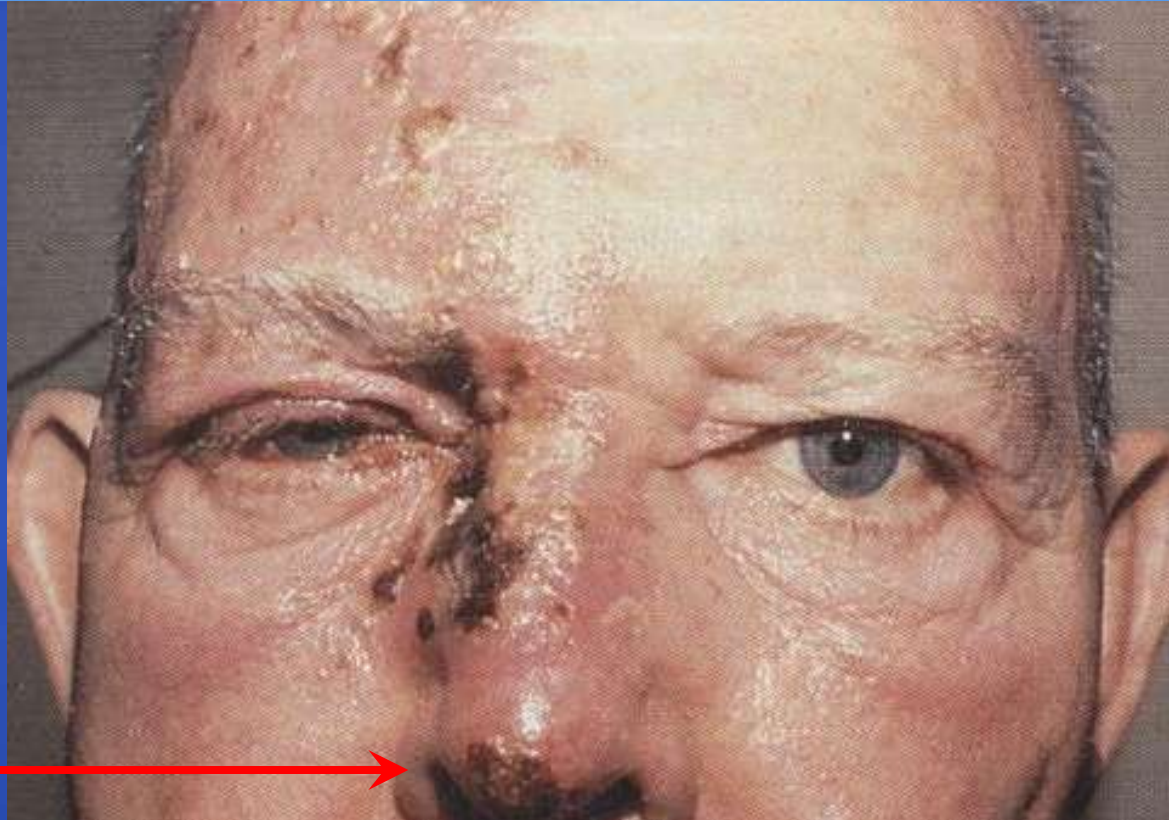


HIV/AIDS: Molluscum contagiosum



- Typically multiple lesions in HIV or AIDS

HIV/AIDS: Herpes Zoster

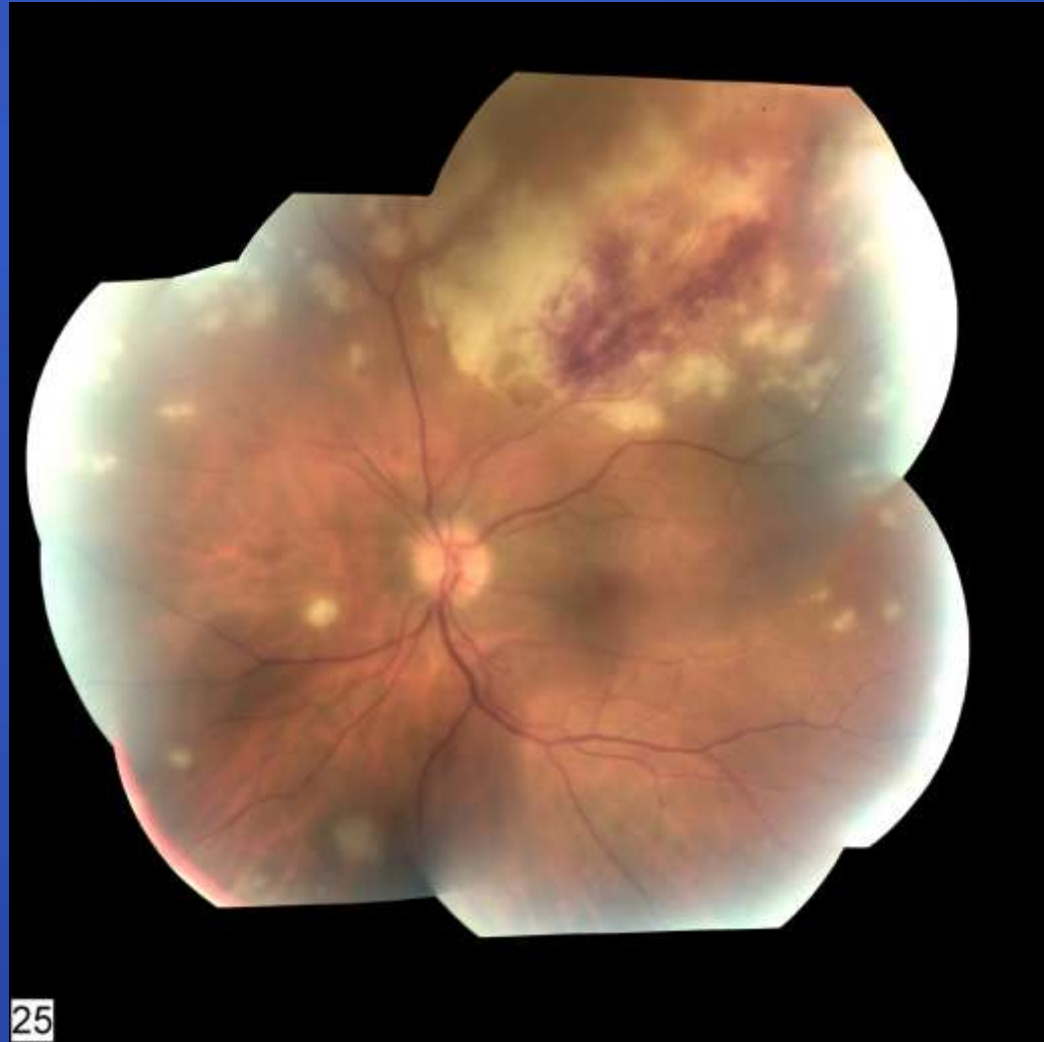


Hutchinson's
sign →

AIDS: CMV Retinitis

- Most common intraocular infection with AIDS
- Much reduced incidence since HAART (50% to 10% of pts)
- CD₄ count typically < 50 cells/mm³
- Retinal necrosis, exudation, & hemorrhage
- Treatment:
 - IV ganciclovir/foscarnet
 - Intravitreal ganciclovir/foscarnet; Ganciclovir intravitreal implant

AIDS: CMV Retinitis



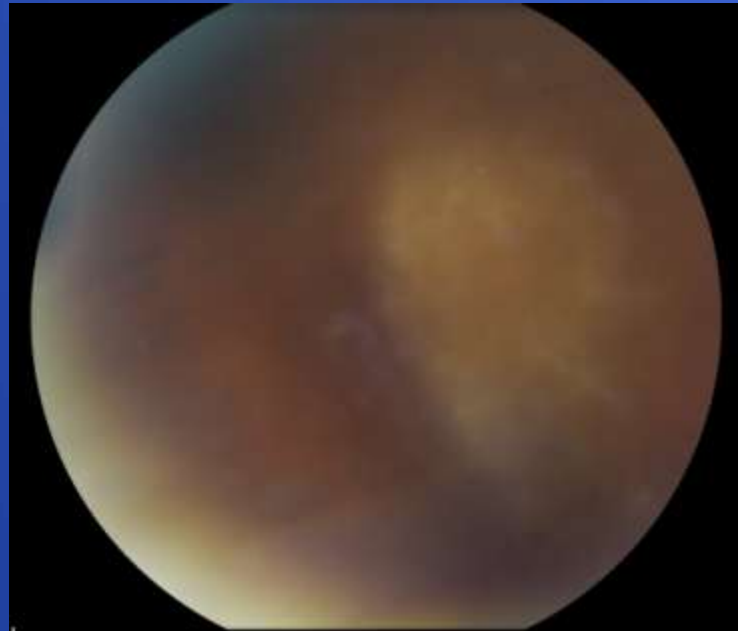
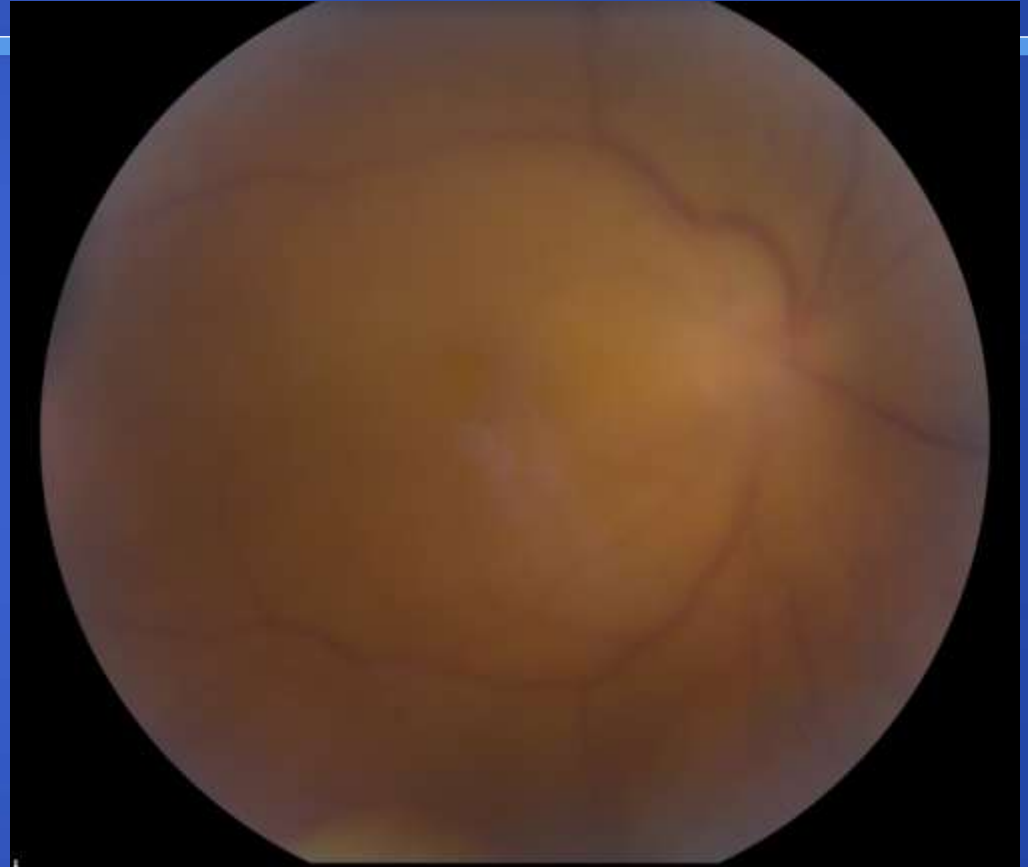
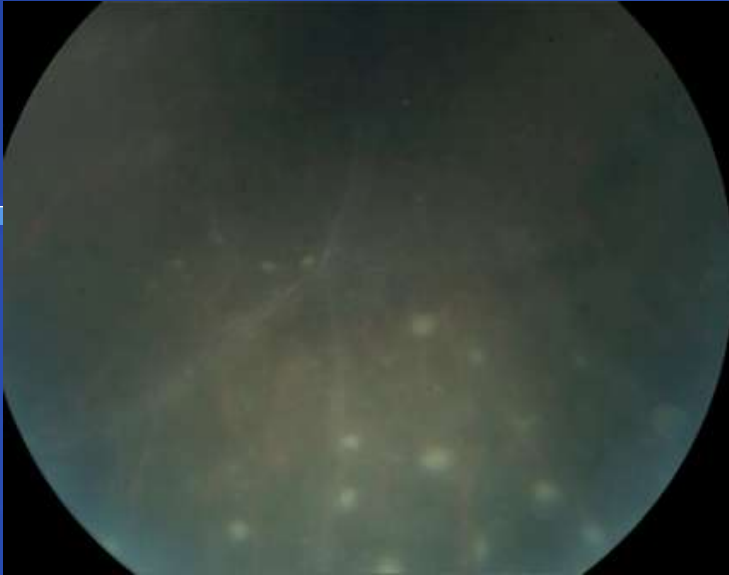
CD4 < 50

HIV/AIDS: Toxoplasmosis Retinitis



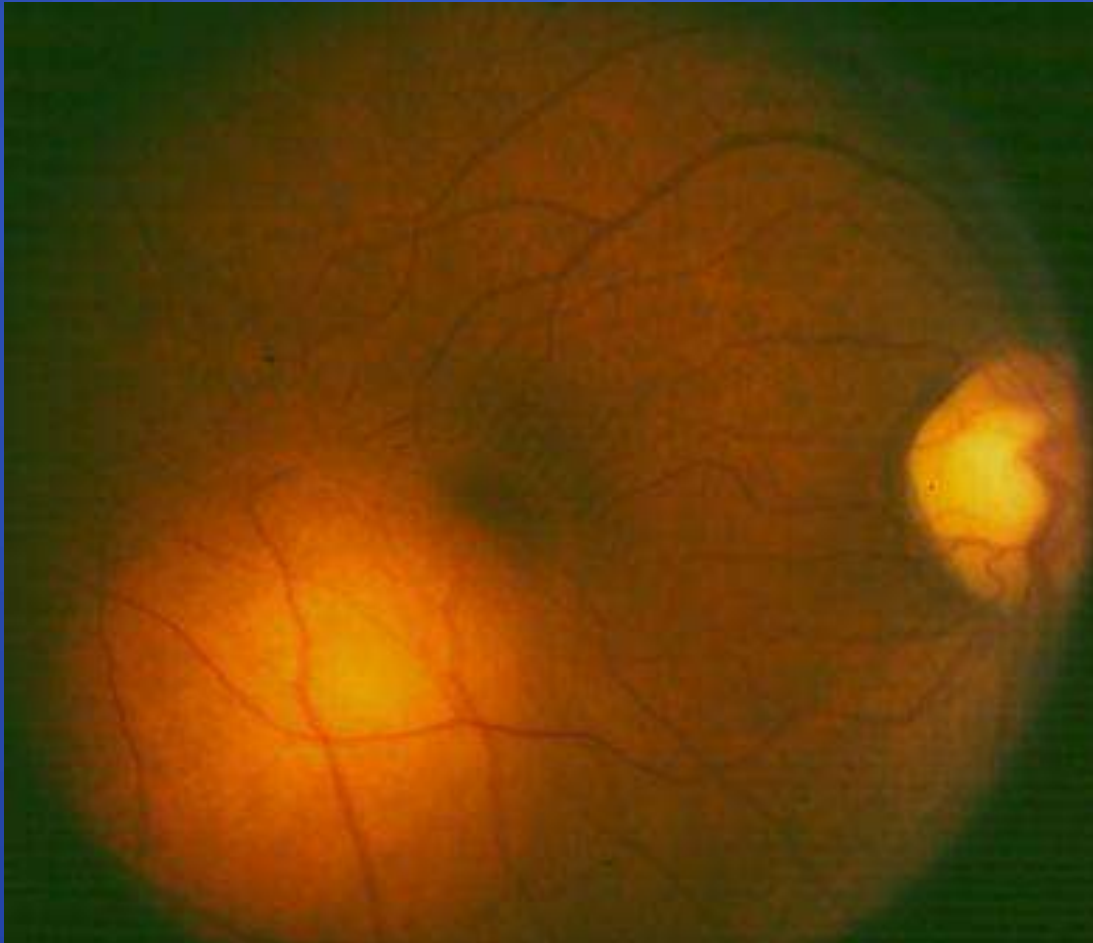
CD4<100

Syphilis



= Tertiary Syphilis
Need LP
Rx with IV Penicillin G

Tuberculosis



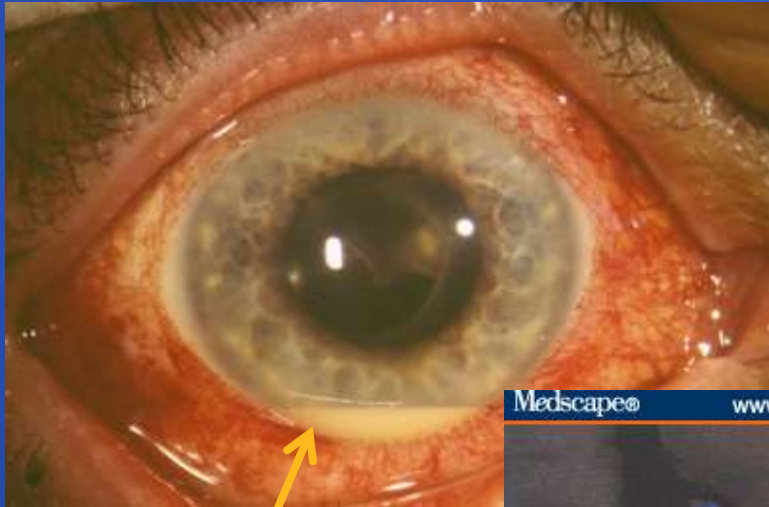
Uveitis
Choroidal granulomas
Periphlebitis

Granulomas = Choroidal Tubercles

Septicemia & Endogenous Endophthalmitis

- Hematologic seeding of the eye with infection
- Gram-positive, gram-negative, fungal etiologies
- Candida is most common causative organism
- Immunocompromised or immunosuppressed patients
- Chronic diseases (DM, Renal failure) & indwelling lines or invasive procedures, & intravenous hyperalimentation
- IV Drug Use
- Bilateral in 25%
- Clinical scenarios: Endocarditis, pneumonia, indwelling catheter (fungal), following surgery (cardiac, pulmonary, urologic)
- Treatment: IV Anti-bacterial/fungal
 - Adjunctive: +/- intravitreal antibiotics, Vitrectomy surgery

Septicemia & Endogenous Endophthalmitis



Hypopyon



Pneumonia



Bilateral Endophthalmitis

Septicemia & Endogenous Endophthalmitis



Ankylosing spondylitis

- Spondylarthropathy of the axial skeleton
- Typically affects males (4:1)
- 90% are HLA-B27 (+)
- Presents in early adulthood (15-35 yo) with pain & stiffness in lower back
 - Limitation of spinal flexion
- Juxta-articular osteoporosis & fusion of sacro-iliac joints
- “Bamboo spine”



Ankylosing spondylitis

- Ophthalmic features:
- Anterior uveitis in 30-40%
- Symptoms
 - Photophobia
 - Redness
 - Decreased vision
- Treatment:
 - Topical corticosteroids
 - Cycloplegia



Fusion of sacro-iliac joints

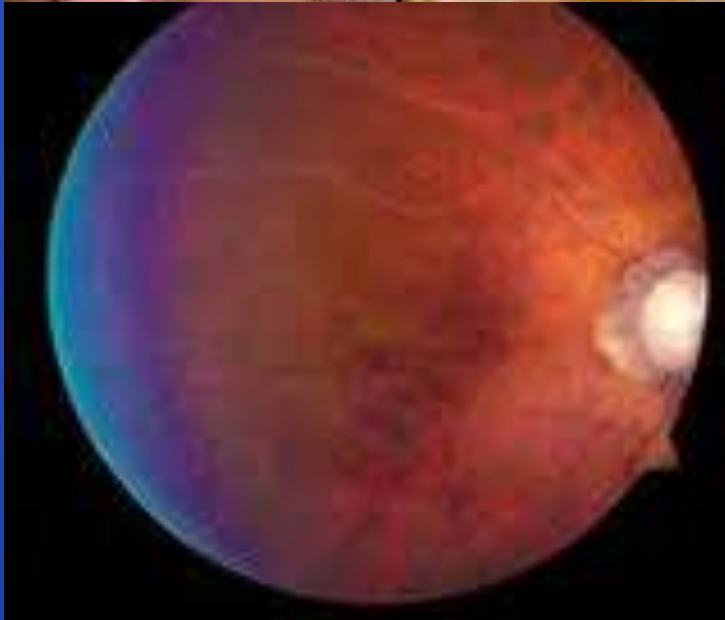
Ankylosing spondylitis



Behcet's Disease

- Vasculitis leading to chronic inflammation & ulceration
- Oral aphthae ulcers
- Genital ulcers
- Skin lesions (e.g. erythema nodosum)
- Eye inflammation (iritis, retinal vasculitis)

Behcet's Disease



Inflammatory Bowel Disease (IBD): Crohn's Disease & Ulcerative Colitis

- Ulcerative colitis: relapsing, non-transmural, restricted to colon
- Crohn's disease: relapsing, transmural, affects entire GI tract
- Ocular complications in 10%
 - Uveitis
 - Episcleritis
 - Scleritis

Women at higher risk
Associated with HLA-B27

Sarcoidosis

- Focal noncaseating granulomas
- AA females, 20-40 yo
- Elevated Calcium, ACE, abnormal CXR
- Lacrimal gland granulomas
- Anterior uveitis
- Retinal inflammation
- Ocular complications: glaucoma, cataract



Hilar Lymphadenopathy

Sarcoidosis



Lacrimal Gland Granuloma

Sarcoidosis

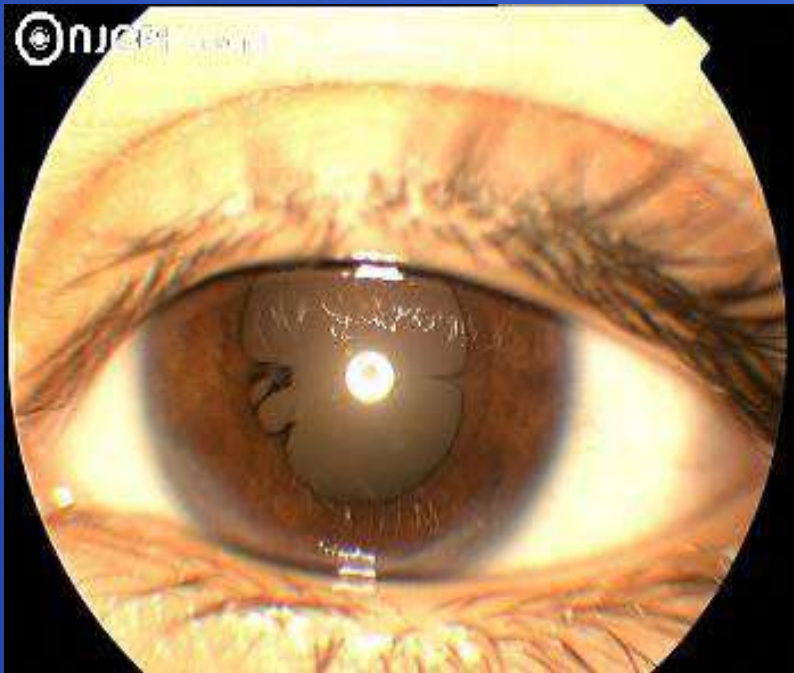


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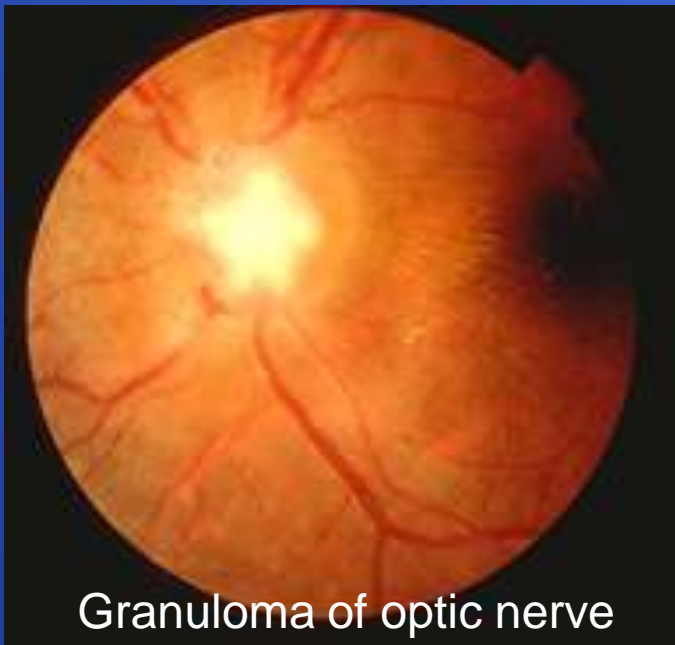
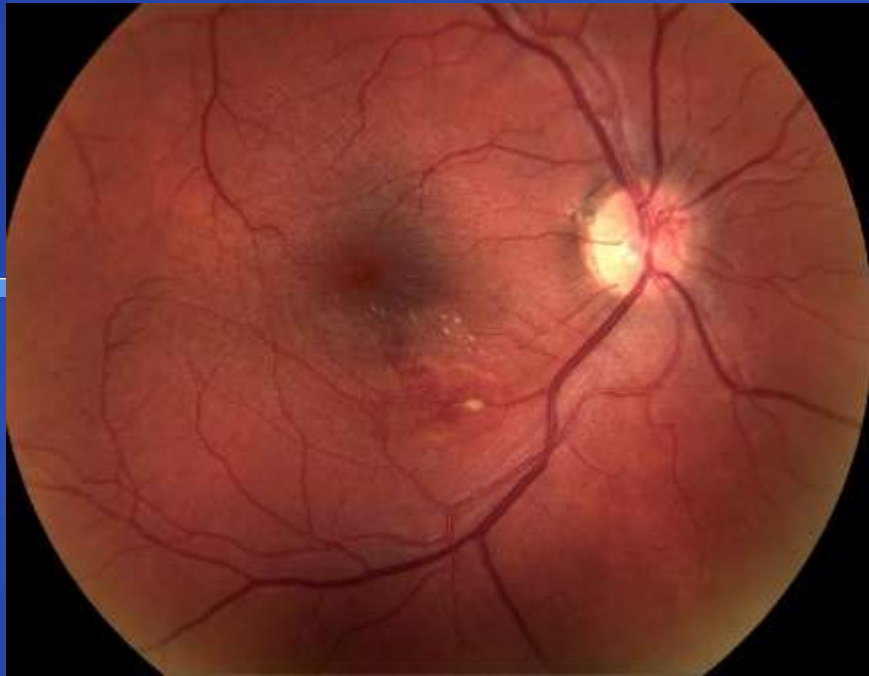
“Mutton fat” KP
(Keratic Precipitates)

Sarcoidosis



Posterior Synechiae of the iris

Sarcoidosis



Granuloma of optic nerve



Perivascular Inflammation

Rheumatoid Arthritis

- 25% may have ocular findings
- Dry eyes (15-25%)
- Episcleritis
- Scleritis
- Corneal ulcers
- uveitis

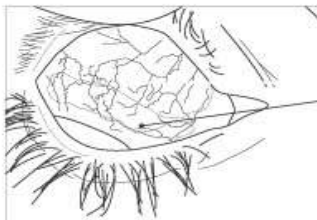
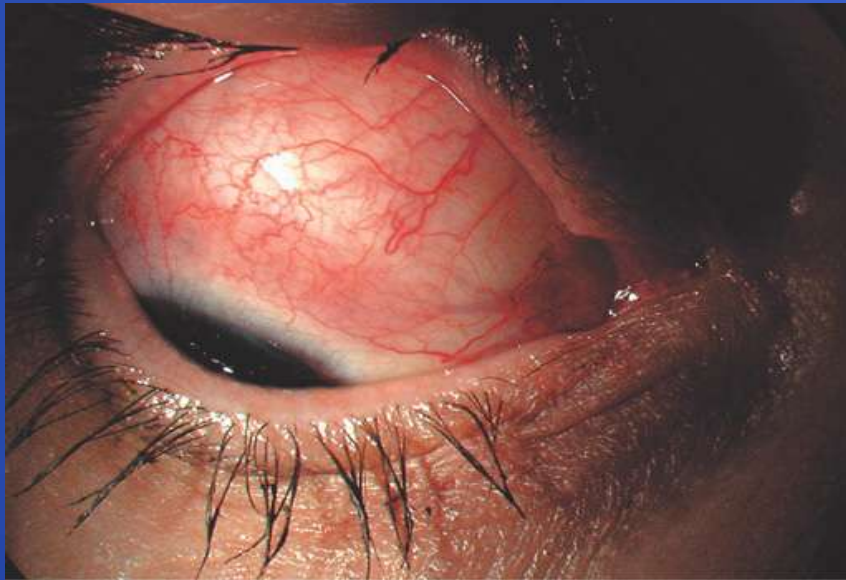


Rheumatoid Arthritis



Peripheral Ulcerative Keratitis

Rheumatoid Arthritis: Scleritis



diffuse anterior
scleritis.

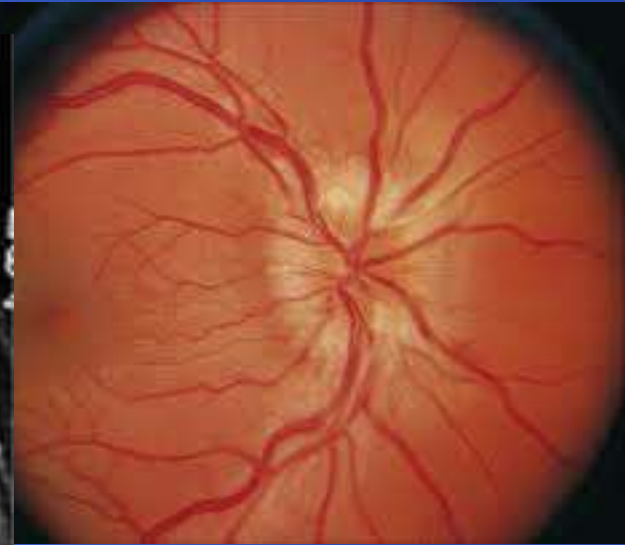
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nodule
dilated anterior
ciliary vessels

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Multiple Sclerosis: Optic Neuritis



50% of patients with MS will develop Optic Neuritis

20-30% of time will be presenting sign for MS

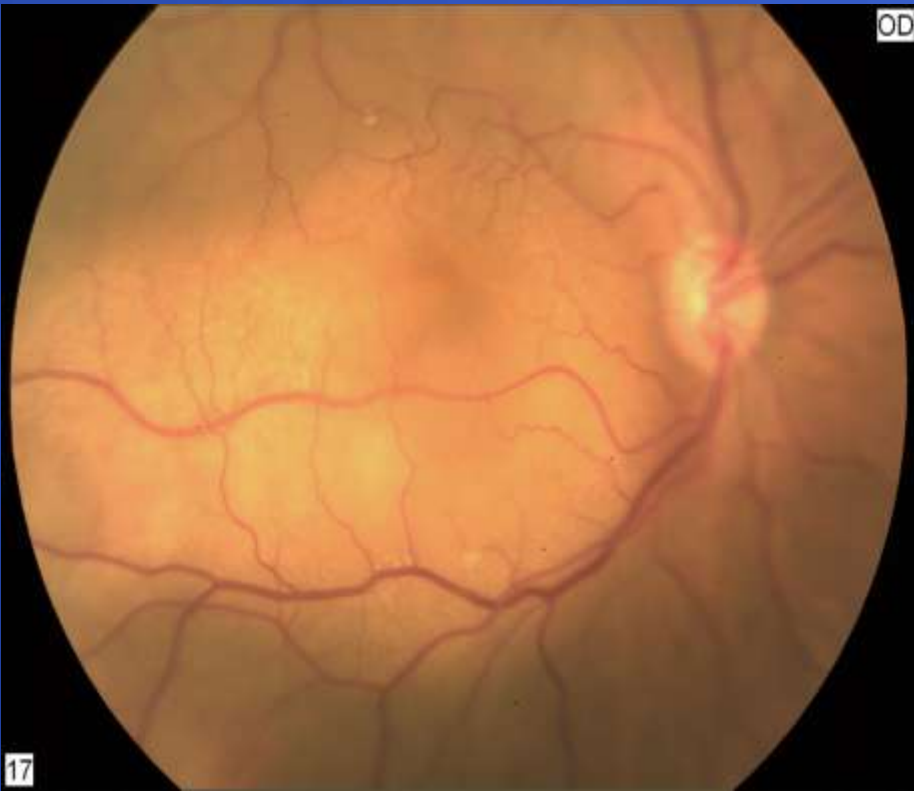
Metastatic Disease

- Most common intraocular malignancy in adults
- May be asymptomatic
- May produce decreased or distorted vision
- Most common primary: Lung, Breast
- 10% have unknown primary
- No prior history of Cancer in 25%

Metastatic Lung Cancer



Metastatic Breast Cancer



Elevated Amelanotic Mass in Macula



S/p ChemoRx

Myasthenia gravis

- Autoimmune neuromuscular disorder leading to fluctuating muscle weakness & fatiguability
- Circulating antibodies block Ach receptors at post-synaptic NM junction, inhibiting stimulative effect of neurotransmitter Ach
- Ptosis, double vision, problems chewing, talking, and swallowing
- Diagnosis: Tensilon test, single-muscle fiber EMG
- Treatment: Acetylcholinesterase inhibitor (Mestinon)

Myasthenia gravis



← Ptosis

Myasthenia – Fatigue and Recovery Test 'Simpson plus'



Fatiguability

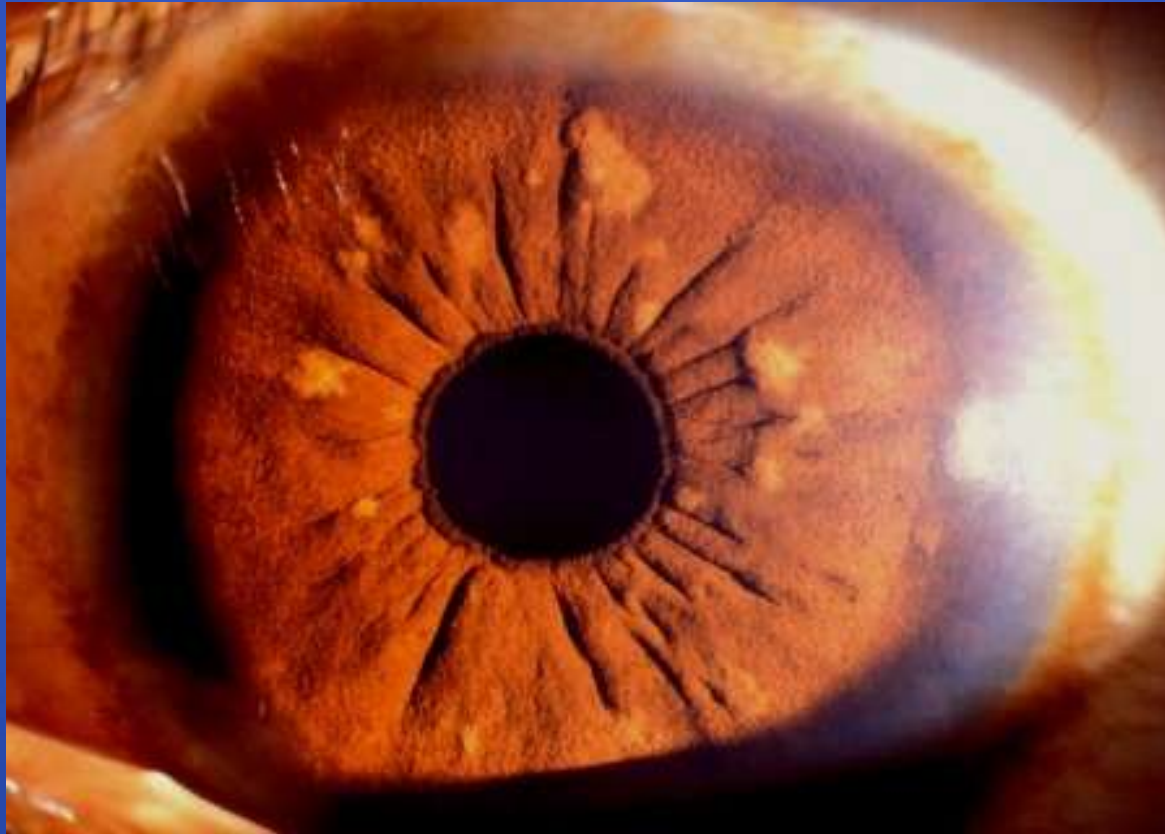


Neurofibromatosis-1

- Autosomal Dominant
- Chromosome 17
- Diagnostic Criteria
 - Café au lait spots
 - Intertriginous freckle
 - Neurofibroma
 - Optic nerve glioma
 - Lisch nodules
 - Osseous lesions
 - Family history in 1st degree relative



Neurofibromatosis-1



Seen in 90% of cases

Neurofibromatosis-1



S-Shaped Eyelid Neurofibroma

Neurofibromatosis-1

20% with NF-1
will have Optic
Nerve glioma

50% of pts with
optic nerve
glioma have NF-
1



Optic Nerve Glioma

Sturge-Weber Syndrome

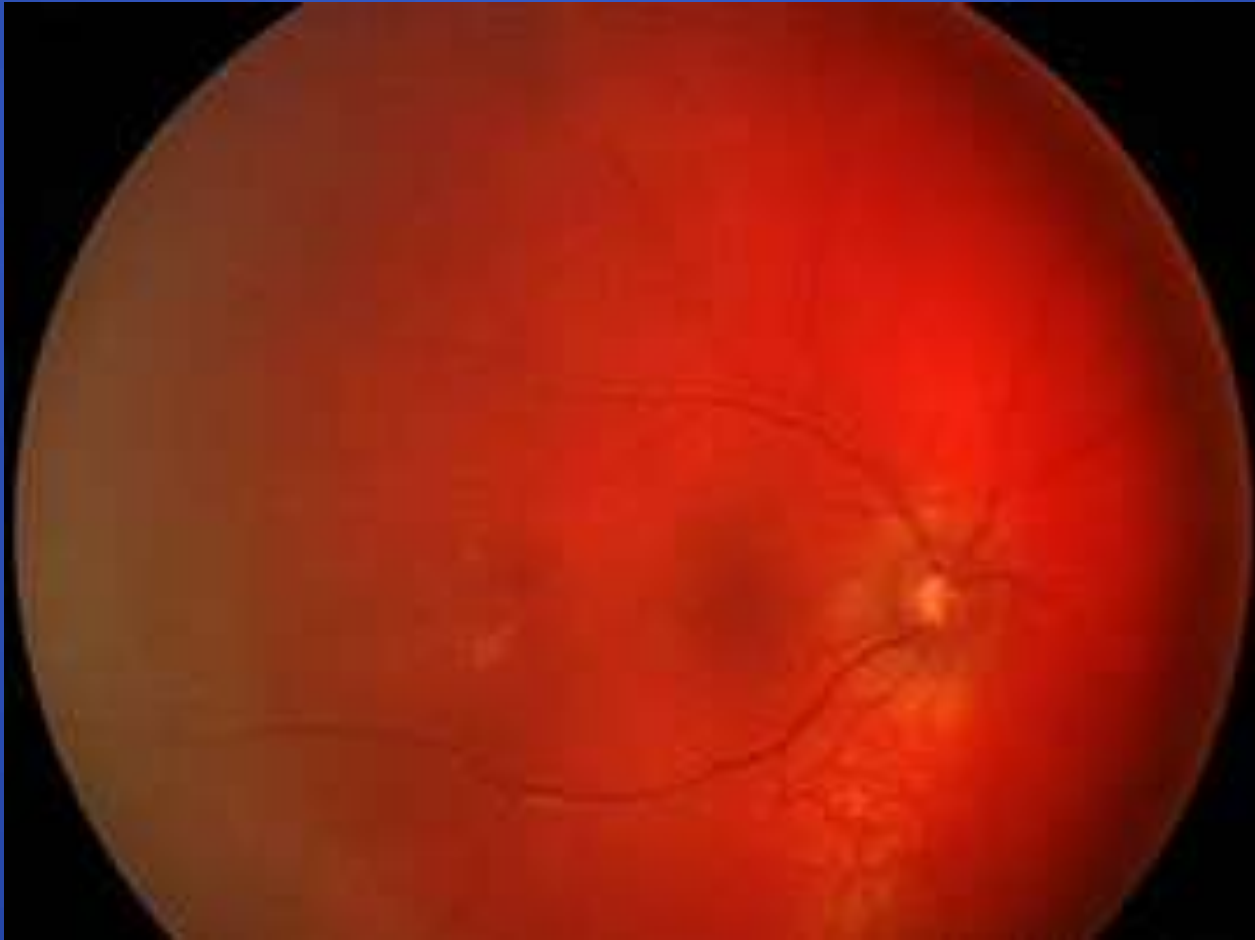
- Sporadically inherited phakomatoses
- Glaucoma
- Dilated & tortuous episcleral vessels
- Seizures
- CNS angiomas (Leptomeningeal hemangioma)
- calcification

Sturge-Weber Syndrome



Nevus flammeus (Port Wine Stain)

Sturge-Weber Syndrome: Choroidal Hemangioma



Systemic Medications

- Benign ocular conditions
 - Amiodarone – whorl keratopathy
- Toxic Retinopathies
 - Thioridazine, chloroquine, hydroxychloroquine, tamoxifen
- Toxic Optic Neuropathies
 - Ethambutol, isoniazid

Hydroxychloroquine: Ophthalmic Screening

- Used for rheumatoid arthritis, SLE, etc
- Ocular toxicity rare with usual dose 200 mg bid (5-7mg/kg/day)
- Toxicity related to cumulative dose (>460 g) & duration of use
- Ocular findings: bulls-eye retinopathy
- Recommended screening:
 - Baseline exam & Central VF testing
 - Annual examination & repeat central VF for pts using medicine > 5 yrs

Plaquenil toxicity: Bull's Eye Maculopathy



Thank You for your Attention

???Any Questions???

