Have I Gone Mad

Melissa Tripoli MD

Case Presentation

- Received a call from a neurology colleague to discuss a patient he is currently taking care of
- Explains this patient had been “flown in this morning for a stroke alert”
- Prior to this he was agitated, aggressive, and per his wife was speaking complete non-sense
- While in the ED he became combative, biting nurse
- He was subsequently intubated and now in the ICU

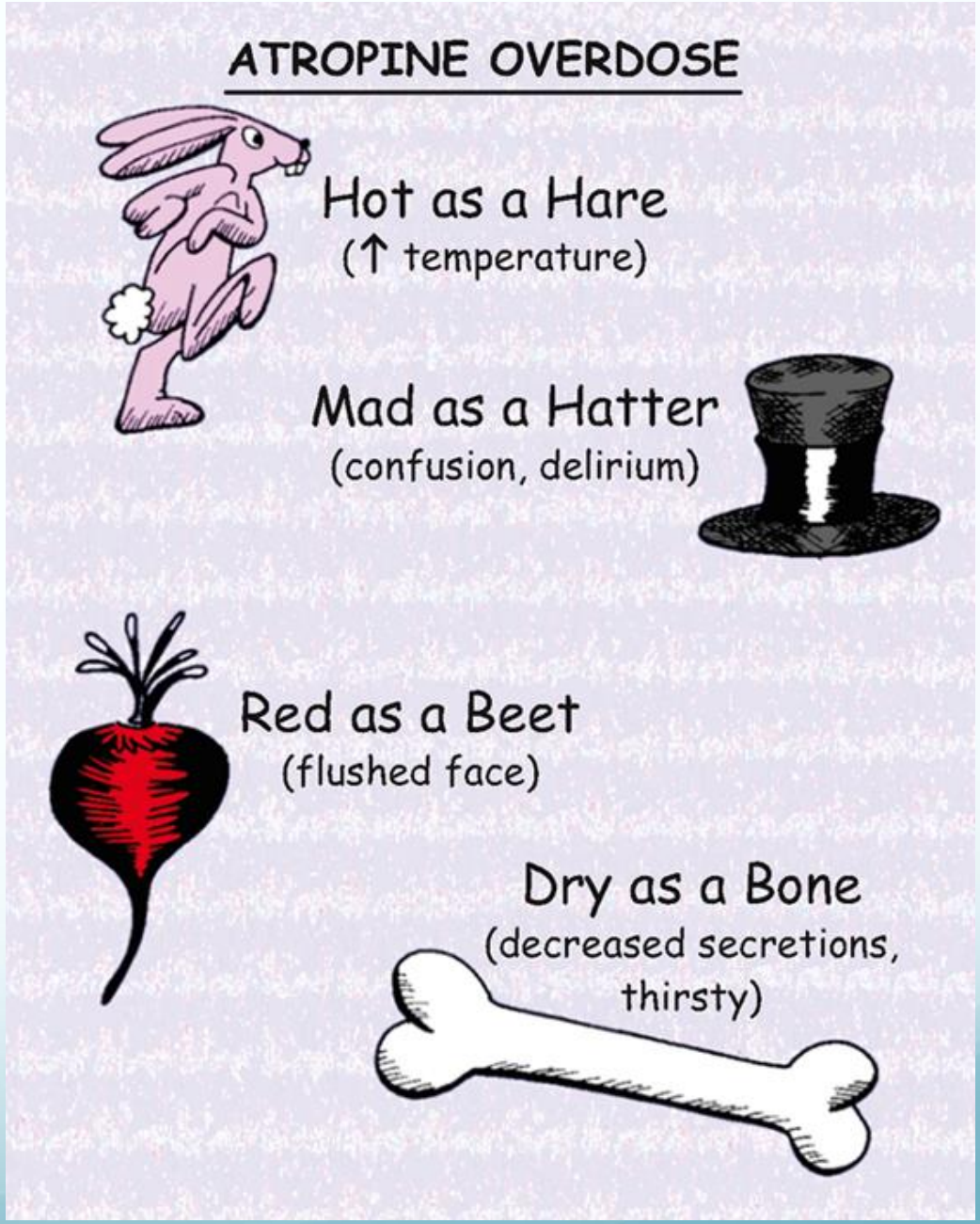
Story continues

- The neurologist adds, I am calling because the wife is very concerned about his eye
- He had retinal detachment surgery 3 days ago and he needs face down positioning
- Initially relieved you are not going to have to access double vision
- You think about the likely gas in the eye… and the helicopter ride

- Find out who the retinal surgeon is, who expresses surprise about the patients state because he was in great health 2 days prior
- Tell him that you will go check on the patient
- Briefly at the bedside note the pupil is dilated, trace injection, and subconjunctival hemorrhage but there are grossly no signs of infection, normal appearance for a post operative eye
- When updating his surgeon:

- My dear I know exactly what is wrong with this patient!!!
- Knowing that the patient recently had a retinal detachment repair, prior to this had normal cognitive status, what could be causing all of the patients symptoms that landed him in the ICU???

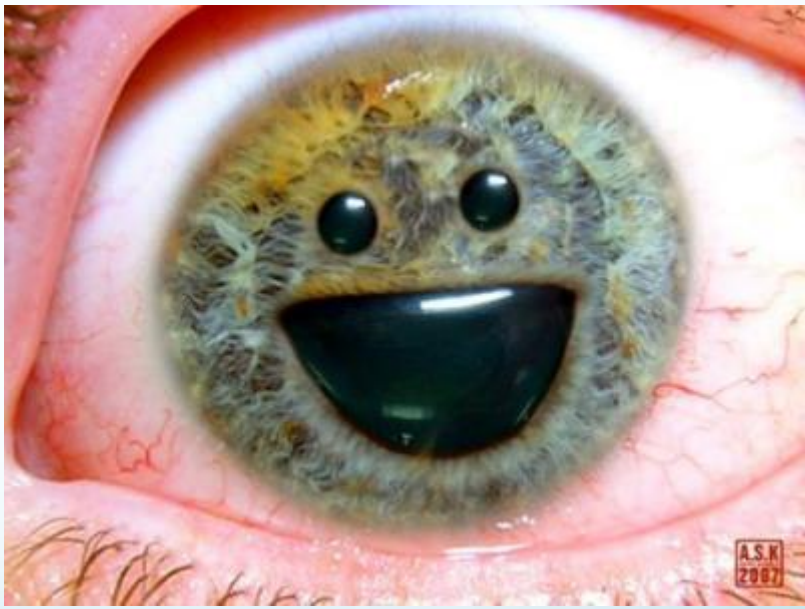
ATROPINE TOXICITY!!!



- Atropine is commonly given after retinal surgery or in cases of uveitis to keep the pupil dilated
- While rare cumulative dosage can lead to systemic overdose
- Was given Physostigmine and within 24 hours was extubated and in his normal state of health

Objectives

- **Discuss systemic medications that cause ocular side effects**
- **Detail necessary screening guidelines and provide information on when this is indicated**
- **Review systemic diseases that have ocular manifestations**
- **List screening/referral guidelines**



Where Medications Accumulate in the Eye

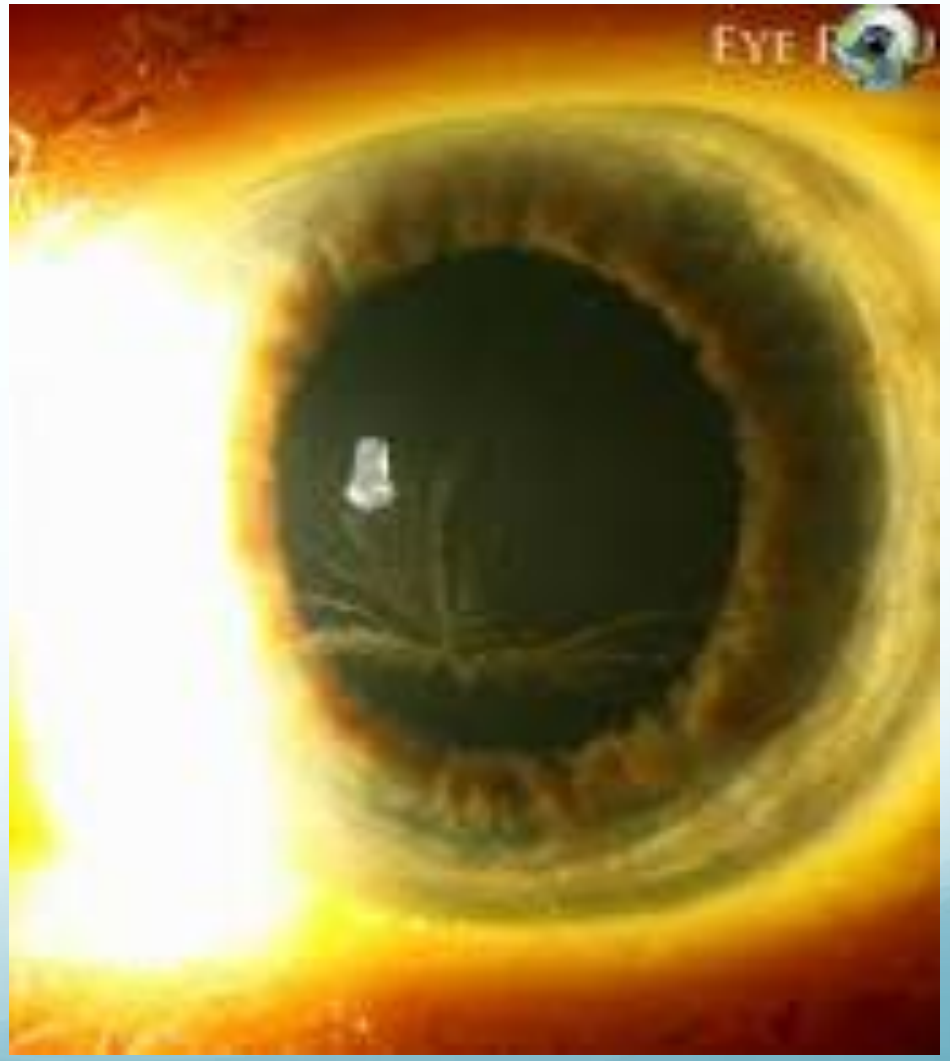
- Cornea – endothelium permeable to medications, once in the stroma can bind to glycosaminoglycans
- Bind to Lens proteins
- Accumulate in the vitreous cause damage to the retina

Amiodarone

- Corneal Deposits which leads to findings called verticillata
- Seen in 69 percent of patients on 200-400 mg daily
- Can be seen bilaterally
- Not thought to effect vision, however may be linked to halos around light
- Most resolve with cessation of medication, takes about 3-20 months

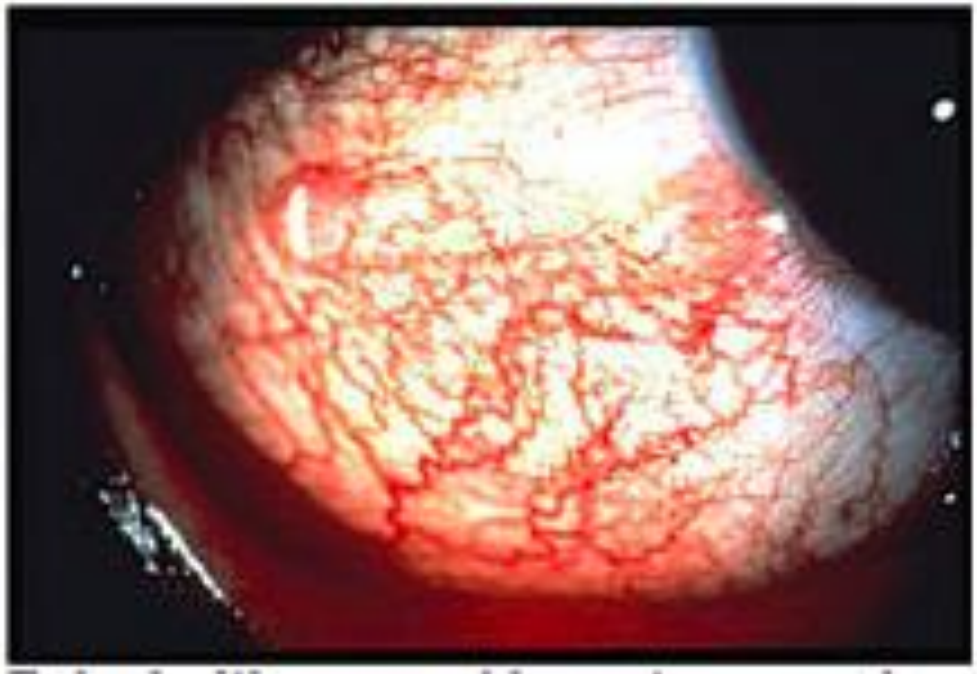
Verticillata

- Amiodarone
- Chloroquine
- Hydroxychloroquine
- Indomethacin
- Phenothiazines



Bisphosphonates

- Orbital Inflammation
- Uveitis
- Scleritis
- Normally occur pretty soon after starting the medication
- Patient with red, painful eye after starting drug, should stop medication and refer to ophtho



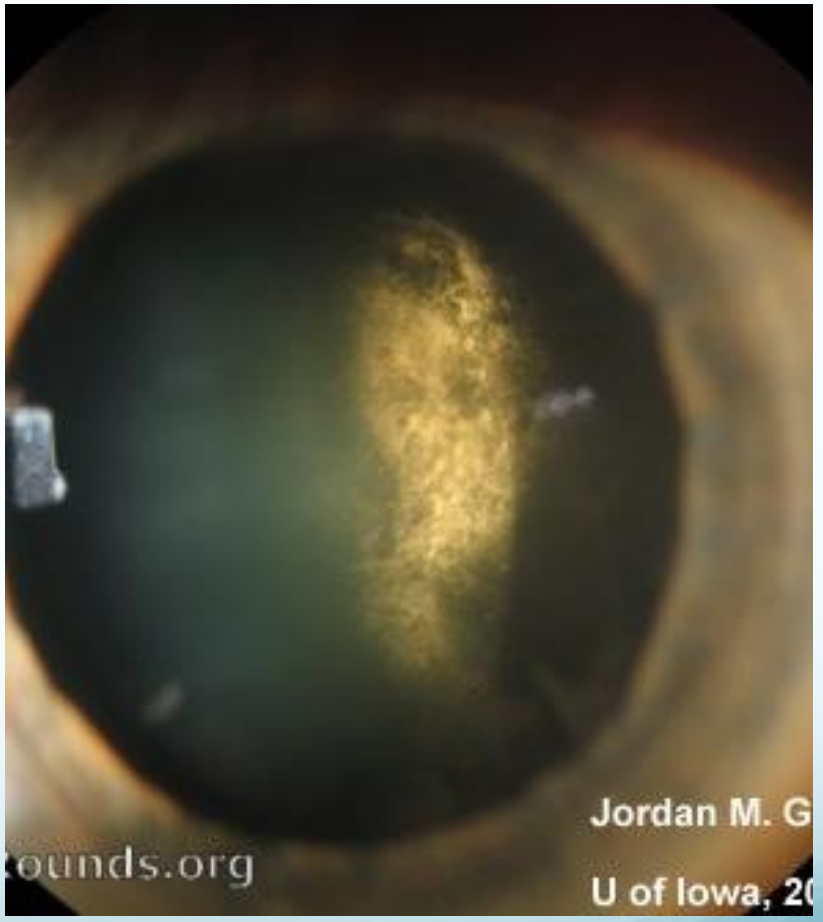
Episcleritis caused by osteoporosis medications.

Minocycline

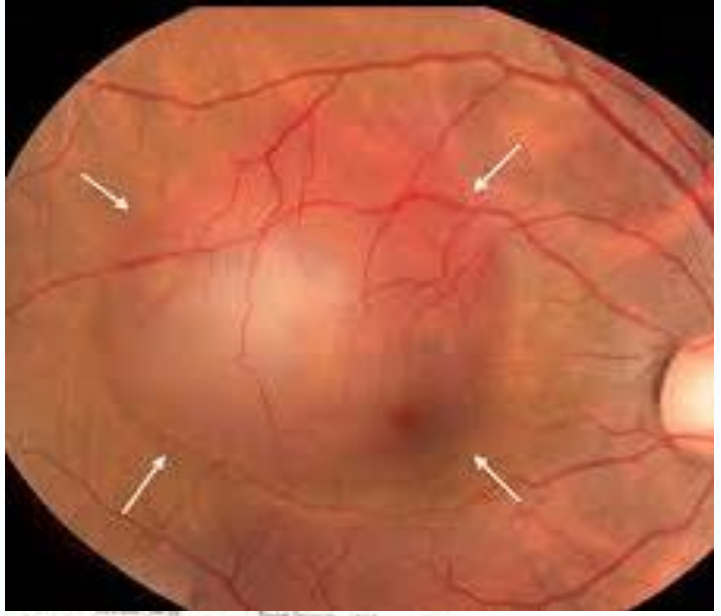
- Known to cause increased Intracranial Pressure
- Papilledema can lead to permanent vision loss if not recognized
- Patient would present suspicious for pseudotumor cerebri with headaches, visual obscurations, pulsatile tinnitus
- Need MRI/MRA

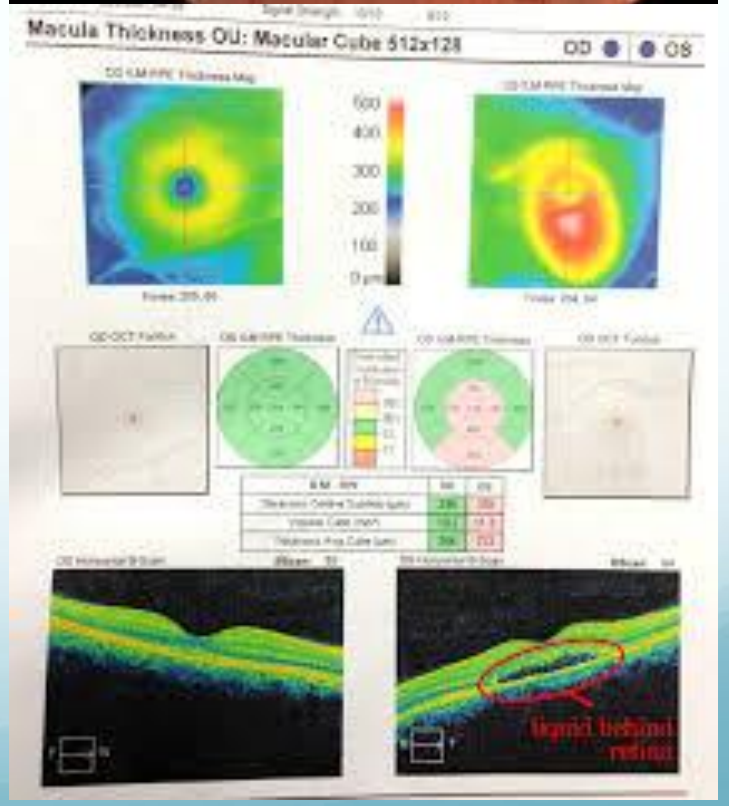
Steroids

- Posterior Subcapsular Cataract
- Unknown mechanism
- Younger patients more susceptible
- Even with steroid inhaler



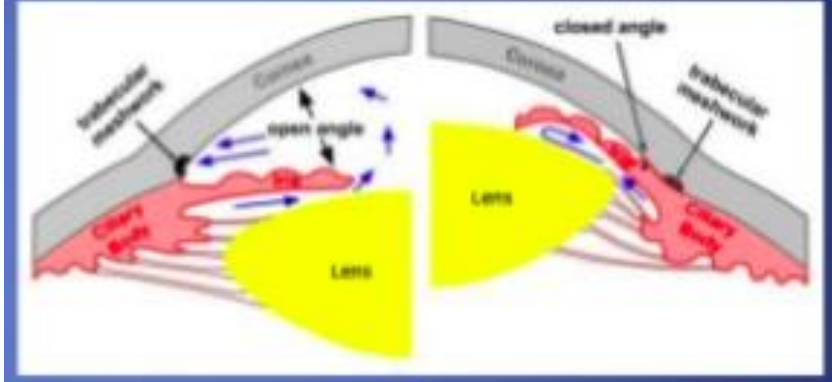
- Central Serous Retinopathy
- Typical presentation in young male
- Resolves with stopping medication
- Can lead to permanent scarring
- Blurred vision, distortion, scotoma

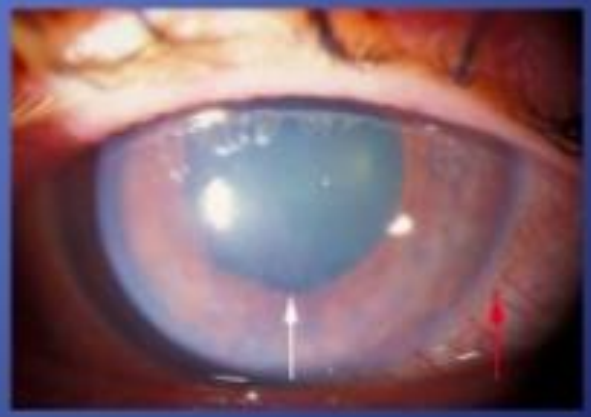




Topamax

- Ciliary Body swelling can lead to angle closure glaucoma and loss of vision
- Causes acute myopia (large amount) in first month
- Suprachoroidal efffusion
- Usually within the first two weeks of starting medication





Plaquenil

- Mainly central retinal damage, Asian patients can show a more damage in pattern more outside central vision
- Recommend a maximum daily dose of 5.0 mg/kg real body weight
- Risk is dose and duration dependent
- Very rare in first 5 years
- None reversible

Plaquenil Screening

- Should have baseline screening exam at time of starting disease
- Begin annual screening at 5 years
- Screening requires Spectral Domain OCT
- Difficult to monitor in patients with other retinal disease especially macular degeneration

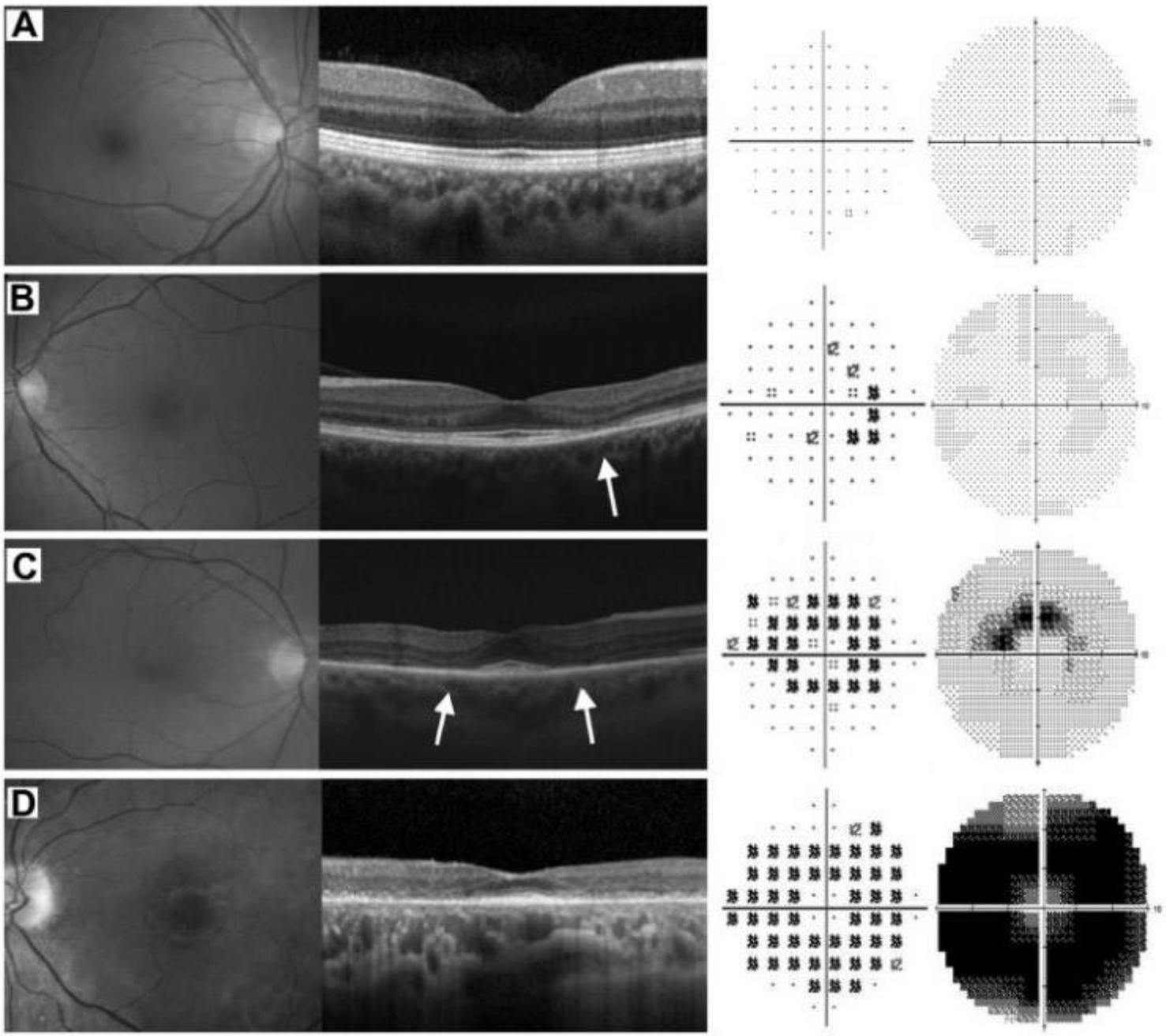

A
B
C
D

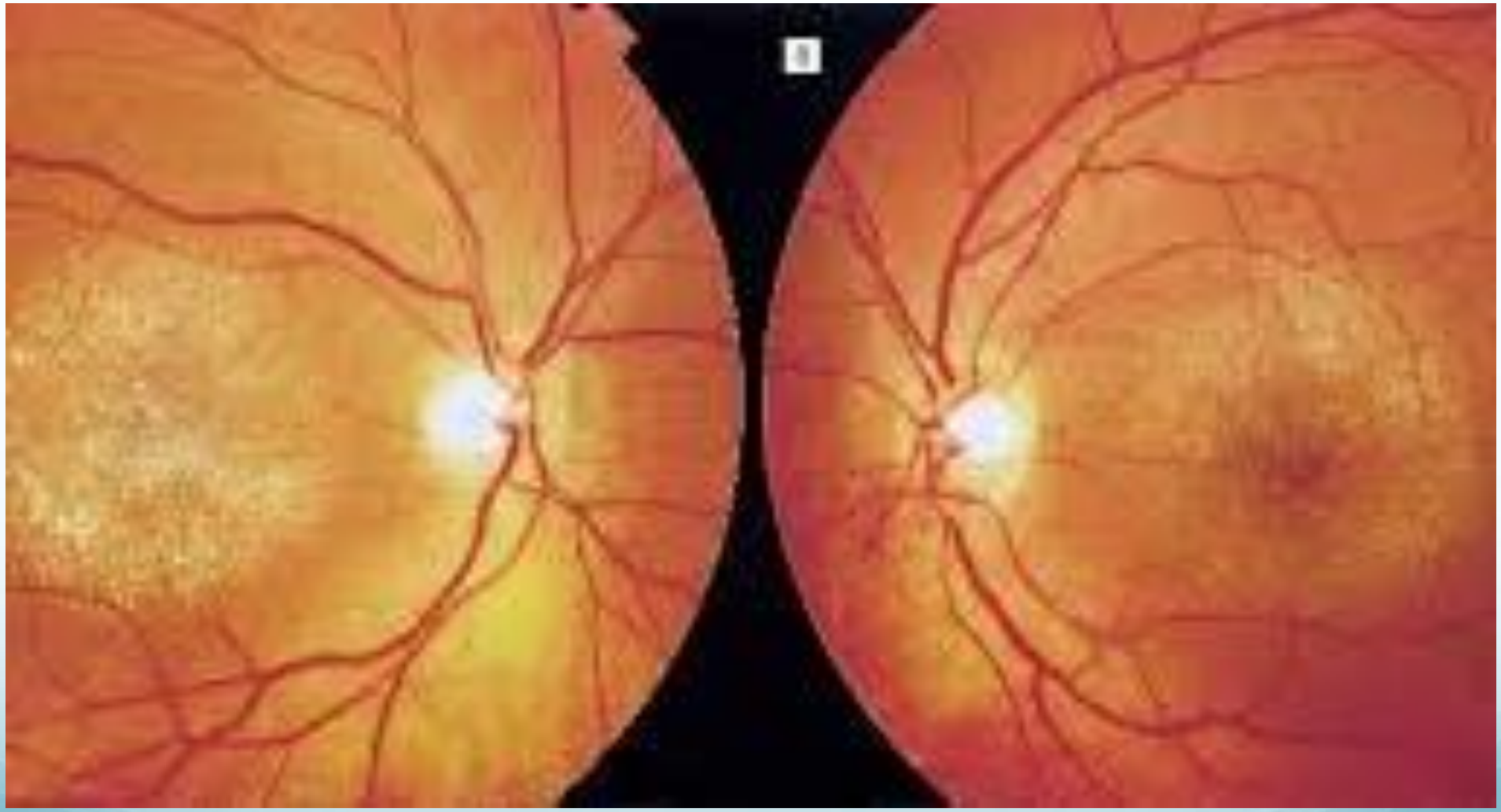
Table 1. Major Risk Factors for Toxic Retinopathy

Daily dosage	
HCQ	>5.0 mg/kg real weight
CQ	>2.3 mg/kg real weight
Duration of use	>5 Yrs, assuming no other risk factors
Renal disease	Subnormal glomerular filtration rate
Concomitant drugs	Tamoxifen use
Macular disease	May affect screening and susceptibility to HCQ/CQ

CQ = chloroquine; HCQ = hydroxychloroquine.

Tamoxifen

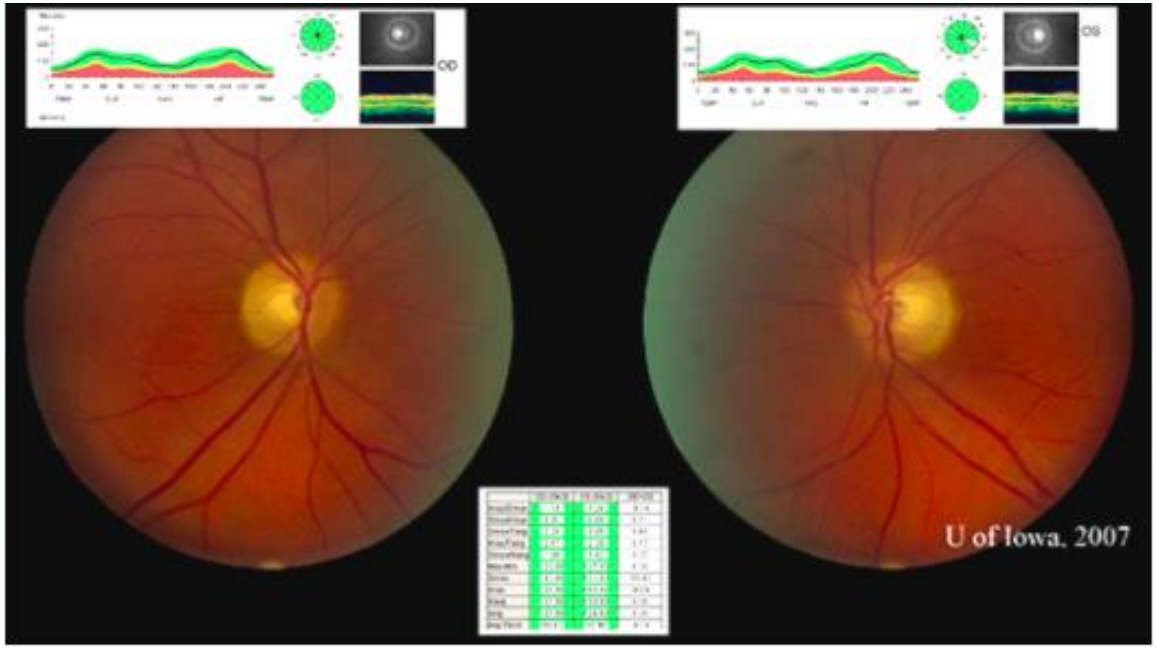
- Dose Dependent
- Less likely with 20 mg or less
- Common to effect lacrimal and meibomian glands – causing dry eye
- Increase rate of cataract – posterior sub-capsular
- White to yellow retractile bodies in the macula
- Tend to occur 1 year after starting medication and are cumulative
- Most common symptom would be photopsia



Tamoxifen Screening

- Baseline exam within the first year of treatment including color testing
- Repeat every 6 months
- Symptoms then need prompt ophthalmology referral
- Presence of crystals alone do not need to stop medication, but if has decline in central or color vision need to stop or decrease medication
- Finding will disappear once med is stopped or dose decreased
- Unless the findings have been present for an extended period of time

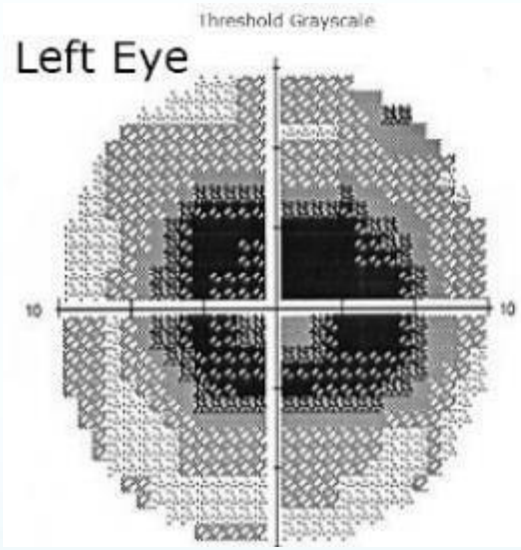
Ethambutol

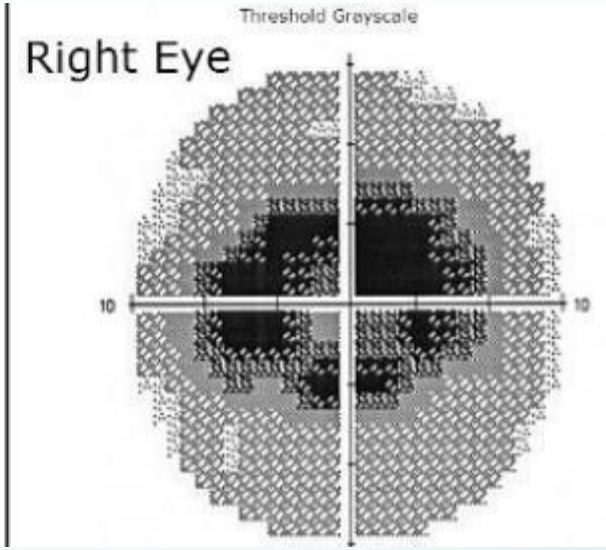


- Toxic Optic Neuropathy
- Subacute, painless, bilateral central vision loss
- Stocking and glove peripheral neuropathy
- Dose related
- Higher occurrence in those with renal disease

Ethambutol Testing Results

- Bilateral findings
- NO APD because symmetric
- Central Scotoma
- Optic nerve will likely look normal at first, start to have temporal hyperemia then temporal pallor
- Recommendations: Discussion with patient about side effects, discontinue and prompt referral is noted





TOXINS:	MEDICATIONS:	VITAMIN DEFICIENCIES:
• Arsenics • Carbon disulfide/tetrachloride • Ethyl alcohol • Ethylene glycol • Methanol • Thallium • Tobacco	• Amiodarone • Cyclosporine • Chlorambucil • Chloramphenicol • Cisplatin • Disulfiram • Ethambutol • Halogenated hydroxyquinolones • Isoniazid • Penicillamine • Sildenafil • Streptomycin	• B12 • B1 (Thiamin deficiency = beriberi) • B6 • Nicotinic Acid (Niacin deficiency = pellagra)

Vigabatrin

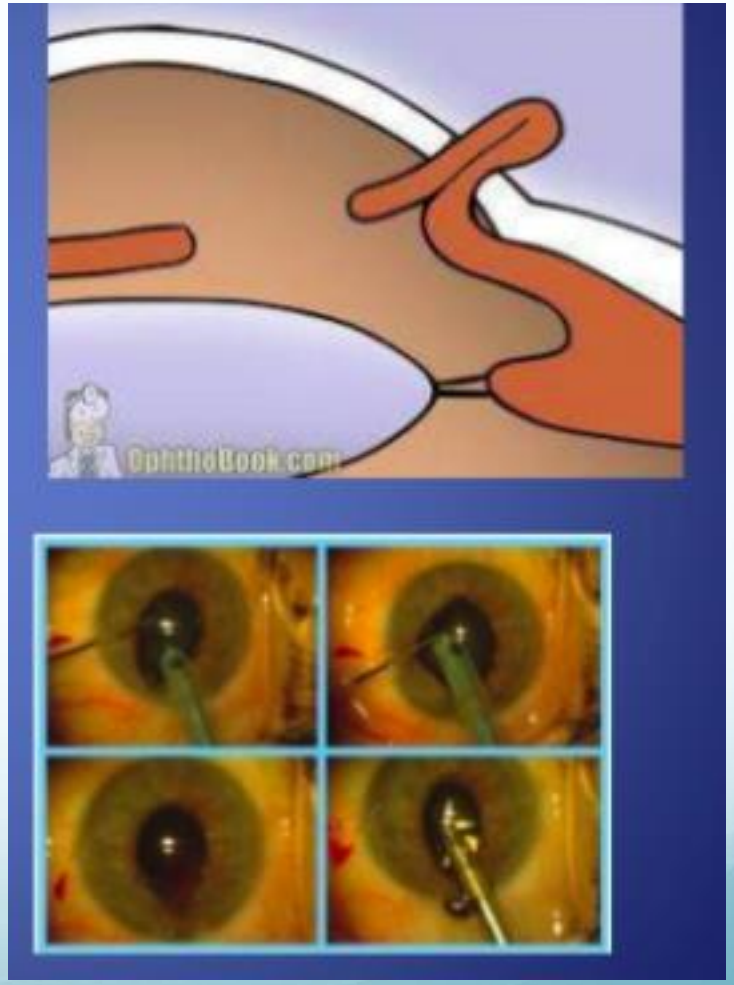
- One of the few things that can cause Binasal visual field defects (black box warning)
- Months to years after starting (average about 6 months)
- Persistent if medication is stopped however does not progress if continue medication
- Need ophtho exam prior to starting medication and then every 3 months after
- Also due to toxicity if seizures do not respond in 3 months should stop the medication

Viagra and Cialis

- Color Change
- Mostly blue or blue green tinge to images, may be pink or yellow
- Can notice for about 4 hours
- Non specific Visual distortions
- Incidence
  - 50 mg – 3%
  - 100 mg - 10%
  - 200 mg 40-50%
- Ischemic Optic Neuropathy – permanent severe vision loss

Tamsulosin

- Floppy Iris Syndrome
- Effects Cataract surgery, controlled with particular device during surgery
- Effect last even if patient had been on medication years ago
- Helpful to know prior to surgery



Systemic Diseases

Diabetes

- Leading cause of blindness worldwide in adults 20-65 years of age
- 35-40% prevalence among diabetics

D'REAM PROGRAM

Diabetic retinopathy (DR)
American Academy of Ophthalmology Staging Guideline

Normal Fundus

UK equivalence:
R0

Moderate Nonproliferative DR (NPDR)

Mild NPDR

Microaneurysms only

Moderate NPDR

More than just microaneurysms but less than severe nonproliferativediabetic retinopathy

R1

Severe NPDR

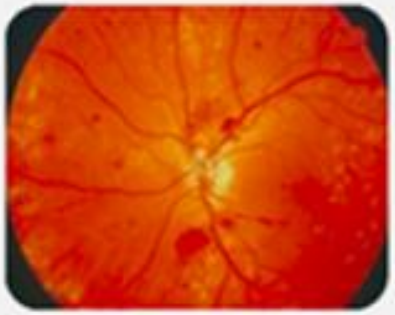
Severe Non proliferative Diabetic Retinopathy

Any of the following:

- More than 20 intraretinal hemorrhages in each of 4 quadrants
- Definite venous beading in 2+ quadrants
- Prominent IRMA in 1+ quadrant and no signs of PDR

R2

Proliferative DR (PDR)



Proliferative Diabetic Retinopathy

1 or more of the following:

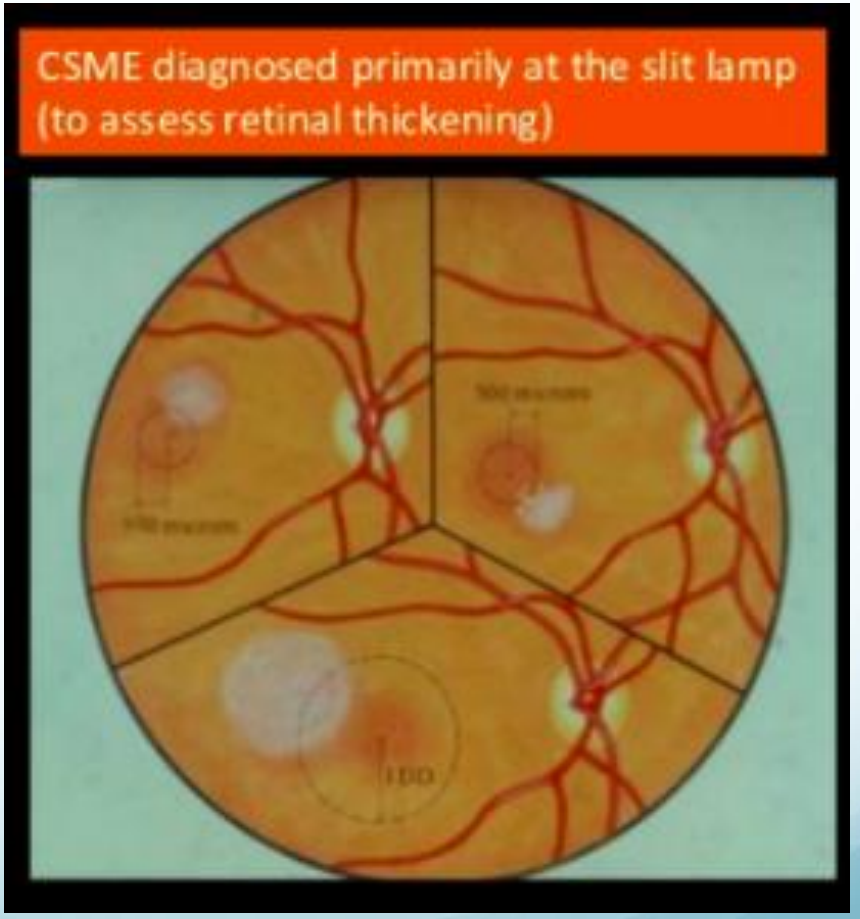
- Neovascularization
- Vitreous/preretinal hemorrhage

R3

American Academy of Ophthalmology, October 2002.

Macular Edema

- Retinal thickening at or within 500 microns of the center or
- Hard exudates at or within 500 microns of the center if accompanied by thickening
- Zone of retinal thickening 1 disc diameter located 1 disc diameter or less from the center



Screening – When should be seen by eye doctor

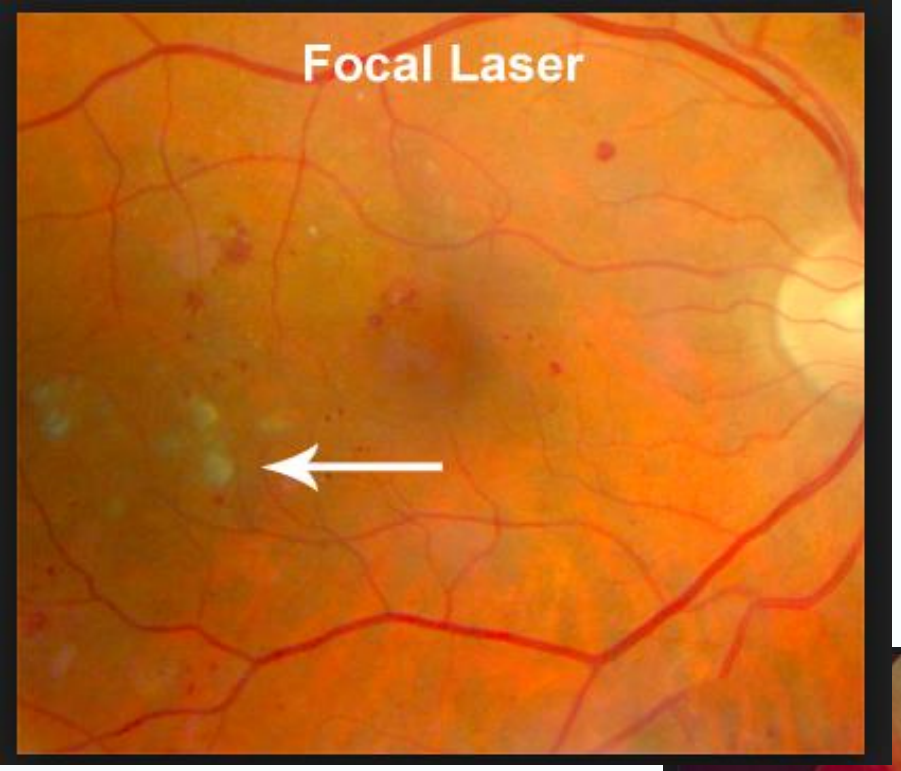
- Type 1 Diabetics – 5 years after diagnosis and then annually
- Type 2 Diabetics – At time of diagnosis and then annually
- Mild Non - Proliferative DM – 6 months to 1 year after initial diagnosis of retinopathy
- Moderate – severe non proliferative – 4- 6 months after DX
- Proliferative – 1-3 months after diagnosis of retintopathy

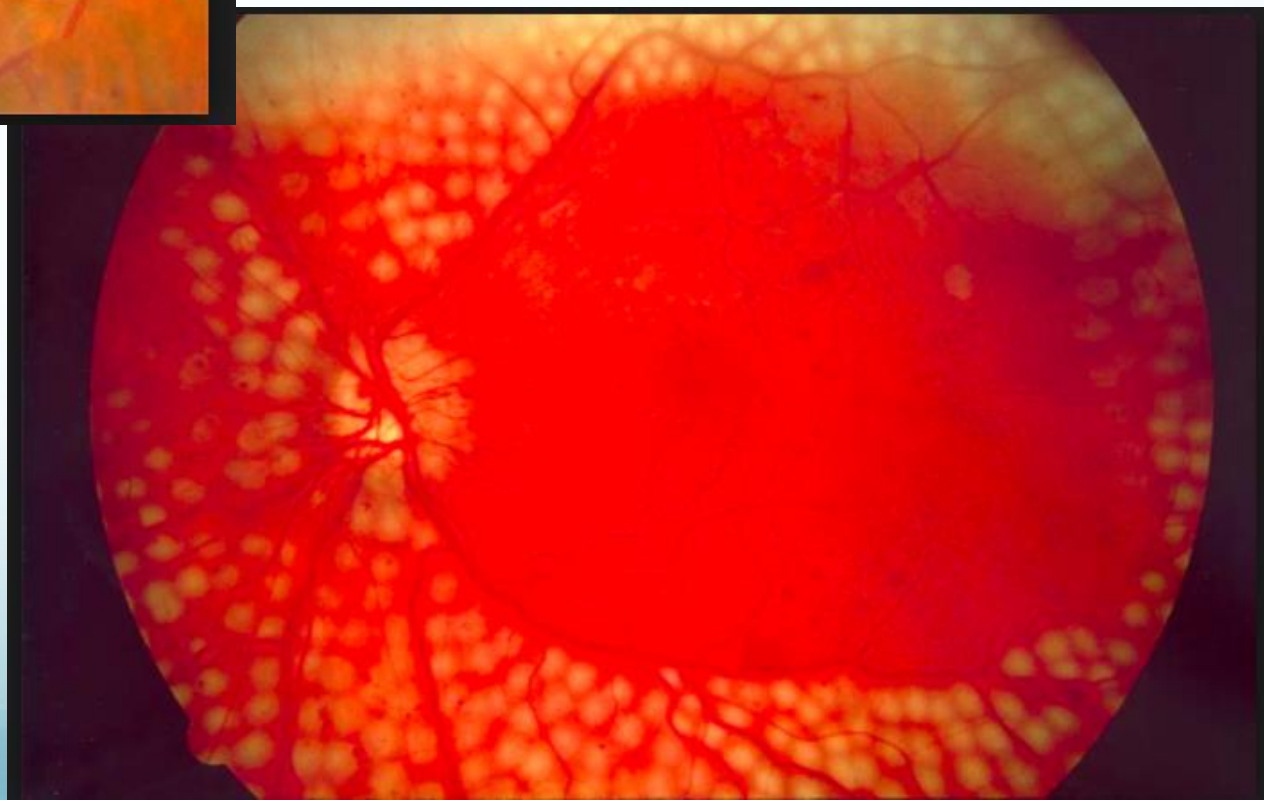
Screening in Pregnancy in those with pre-existing DM

- Should be examined soon after conception
- Mild disease check again in 3rd trimester – unlikely to progress
- Moderate – Every Trimester – most will progress but regress post delivery
- Severe or proliferative disease – Monthly – treat PDR with Laser, observe Macular edema
- Gestational diabetes does not carry risk of retinopathy

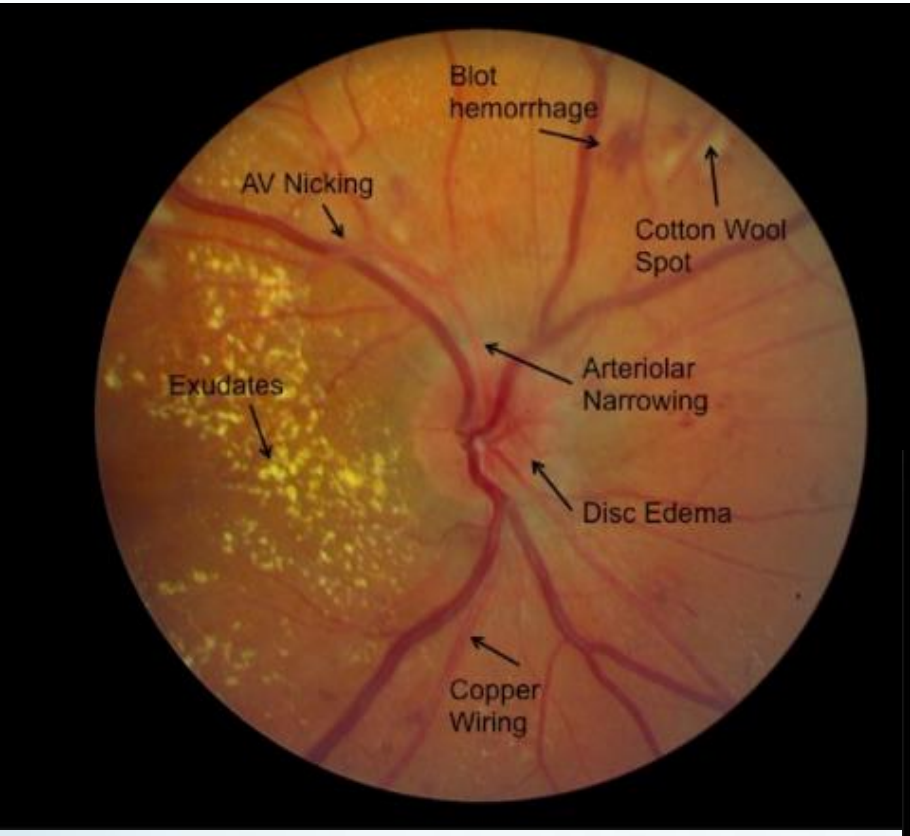
Treatment

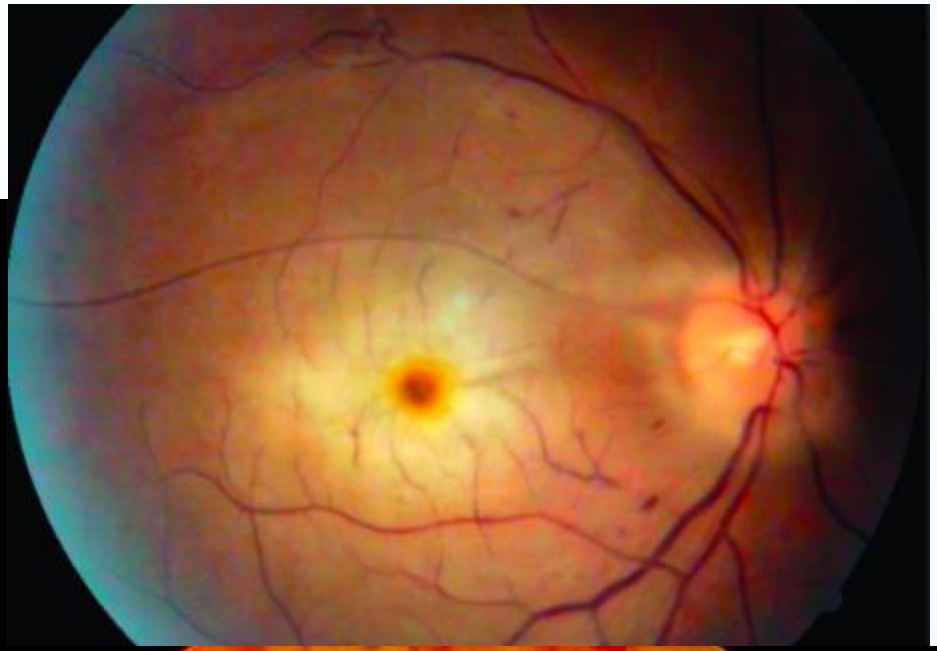
- Non-proliferative without Macular edema – monitor
- Non – proliferative with Macular Edema
  - Intra-ocular injection of Anti VEGF
    - Avastin, Lucentis, Eylea
  - Focal Laser
- Proliferative Retinopathy
  - Pan retinal Photocoagulation
  - Non Clearing Hemorrhage – Retinal Surgery – Vitrectomy

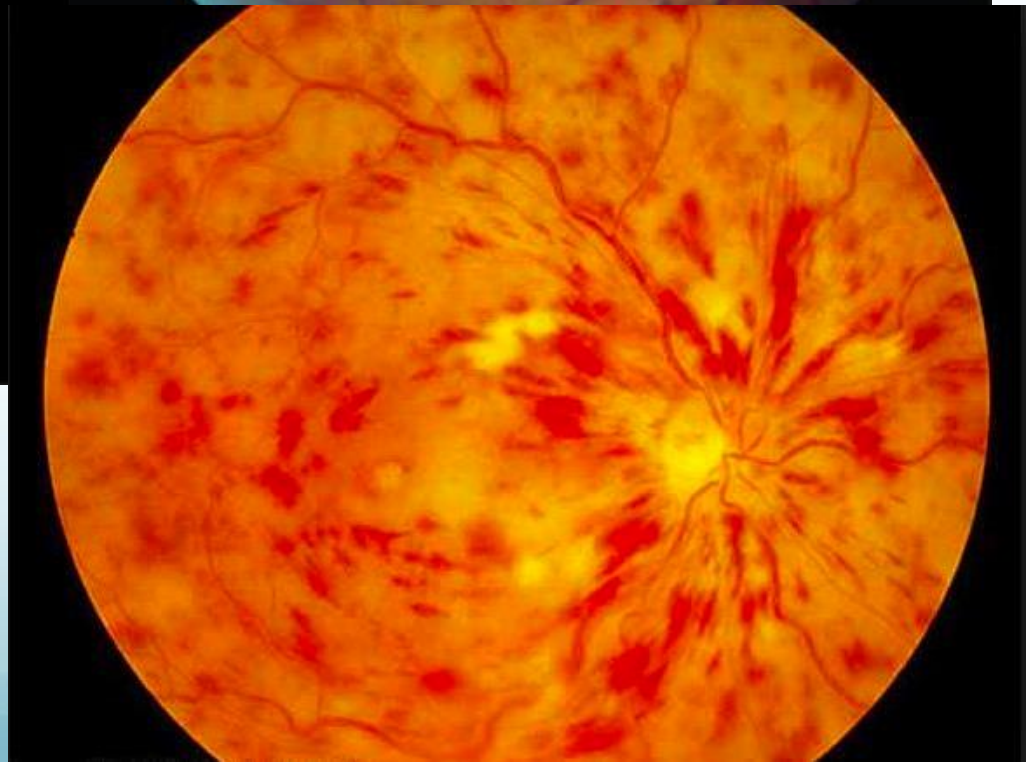

Focal Laser



Hypertension







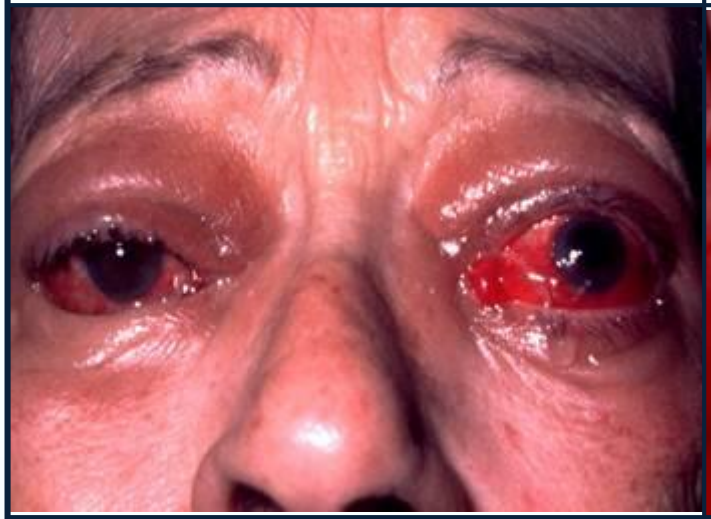
Recommend annual exam

Thyroid Eye Disease

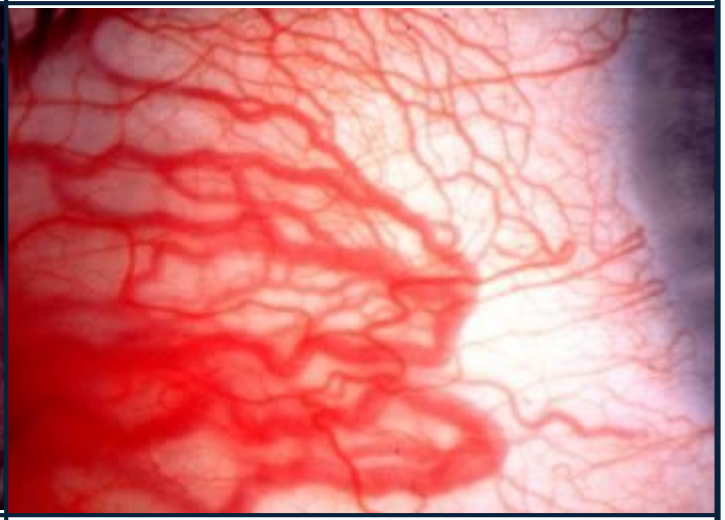
- 1. Soft Tissue Swelling
- 2. Eyelid retraction
- 3. Proptosis
- 4. Optic neuropathy
- 5. Restrictive Myopathy

Soft tissue involvement

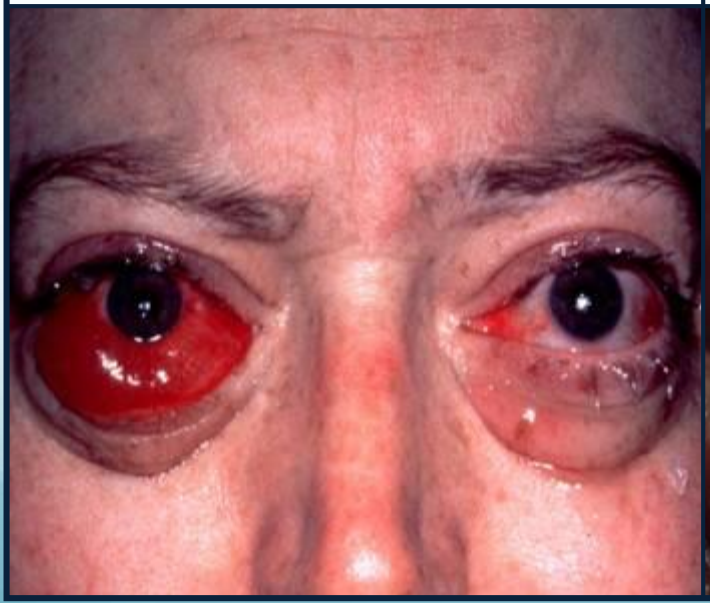
Periorbital and lid swelling



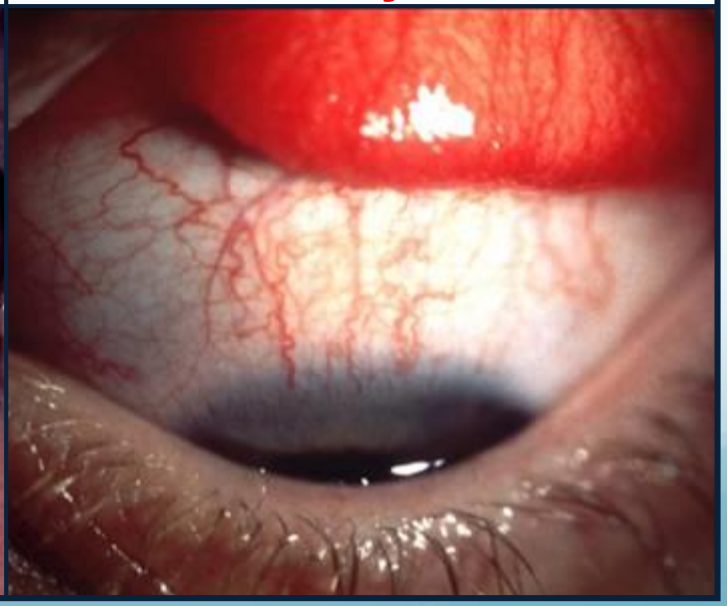
Conjunctival hyperaemia



Chemosis

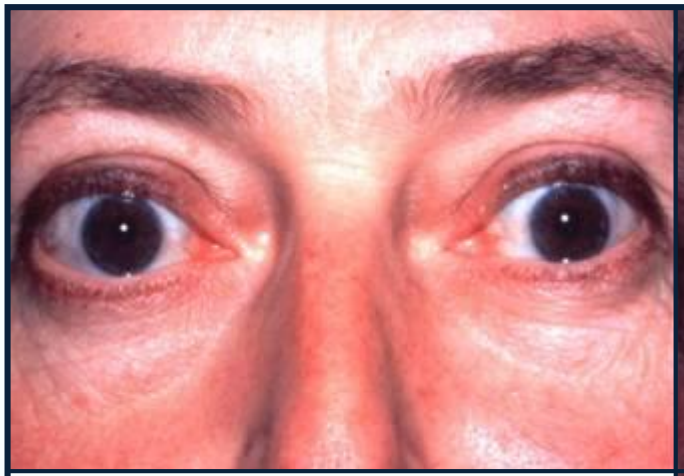


Superior limbic keratoconjunctivitis

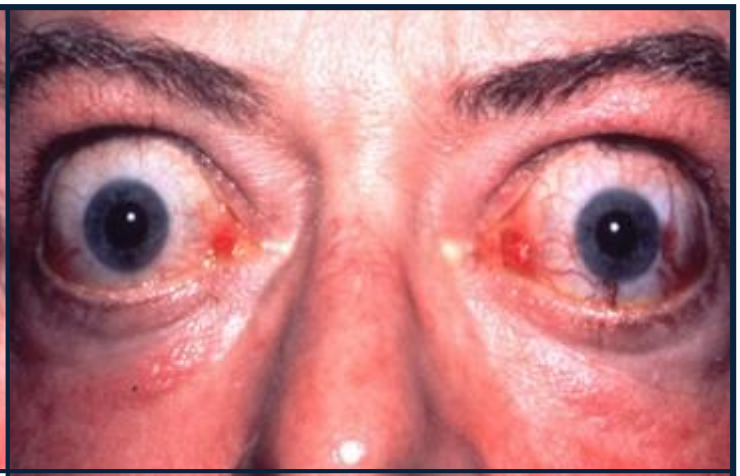


Signs of eyelid retraction

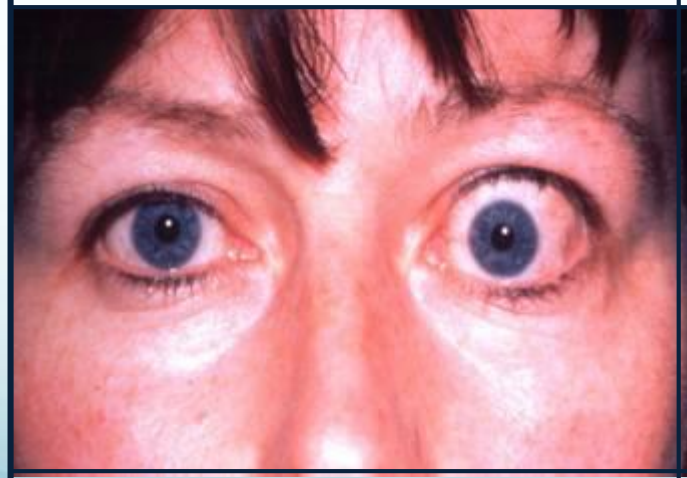
Occurs in about 50%



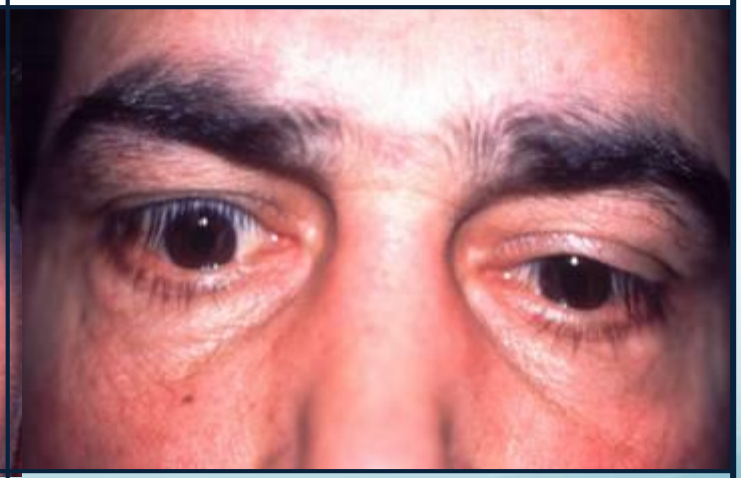
- Bilateral lid retraction
- No associated proptosis



- Bilateral lid retraction
- Bilateral proptosis



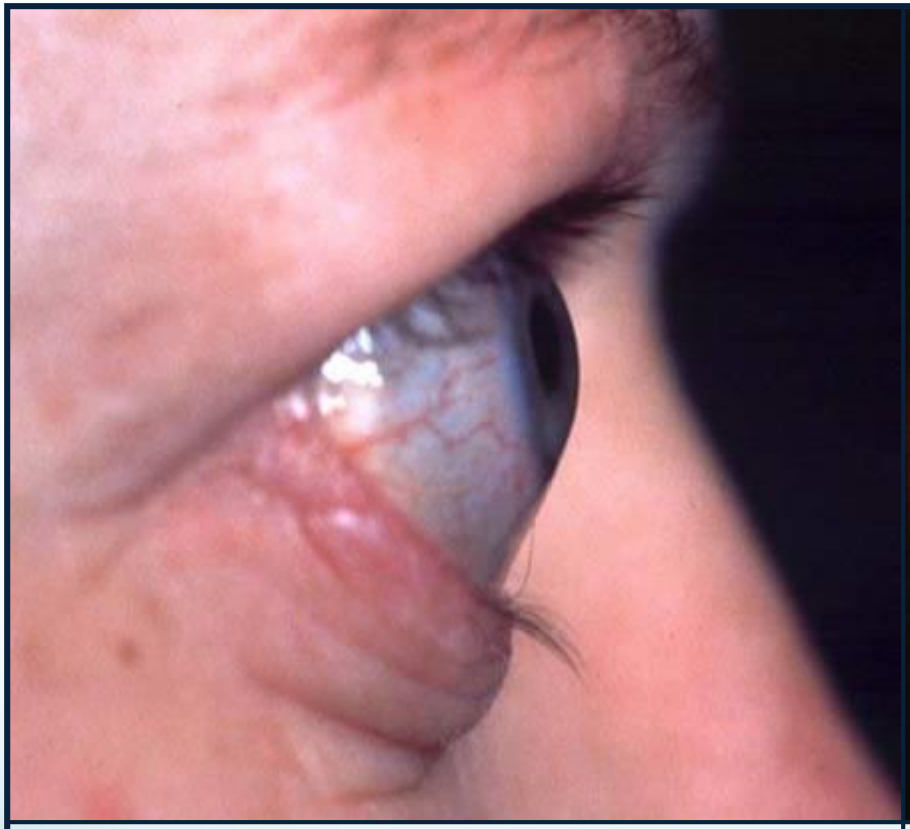
- Unilateral lid retraction
- Unilateral proptosis



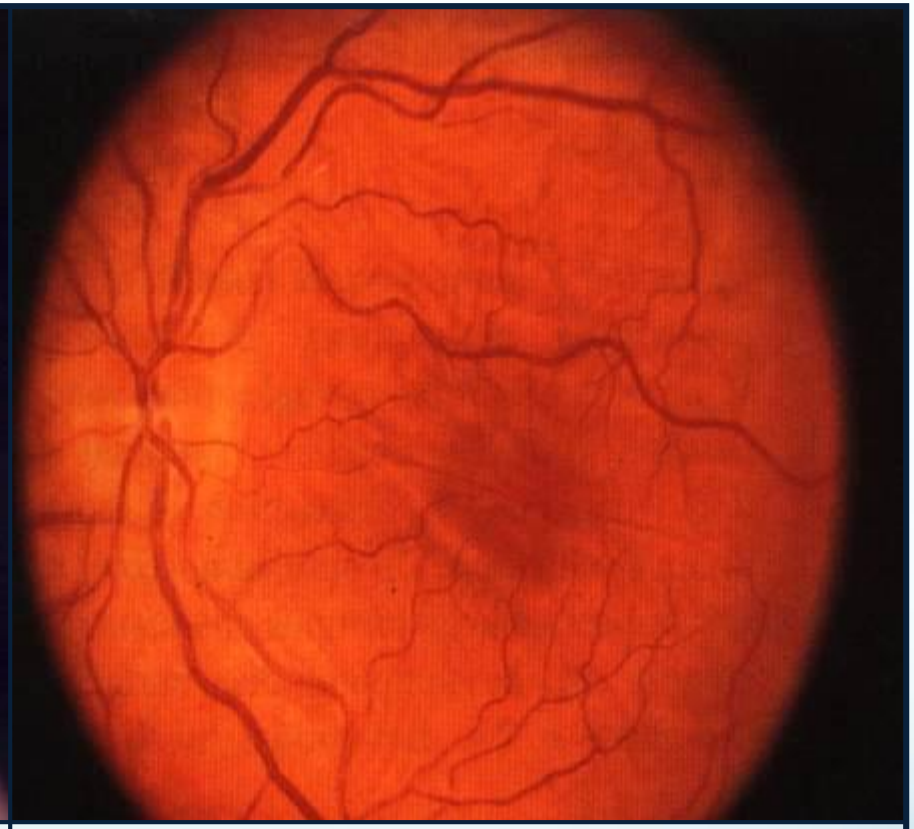
- Lid lag in downgaze

Proptosis

- **Uninfluenced by treatment of hyperthyroidism**



Axial and permanent in about 70%



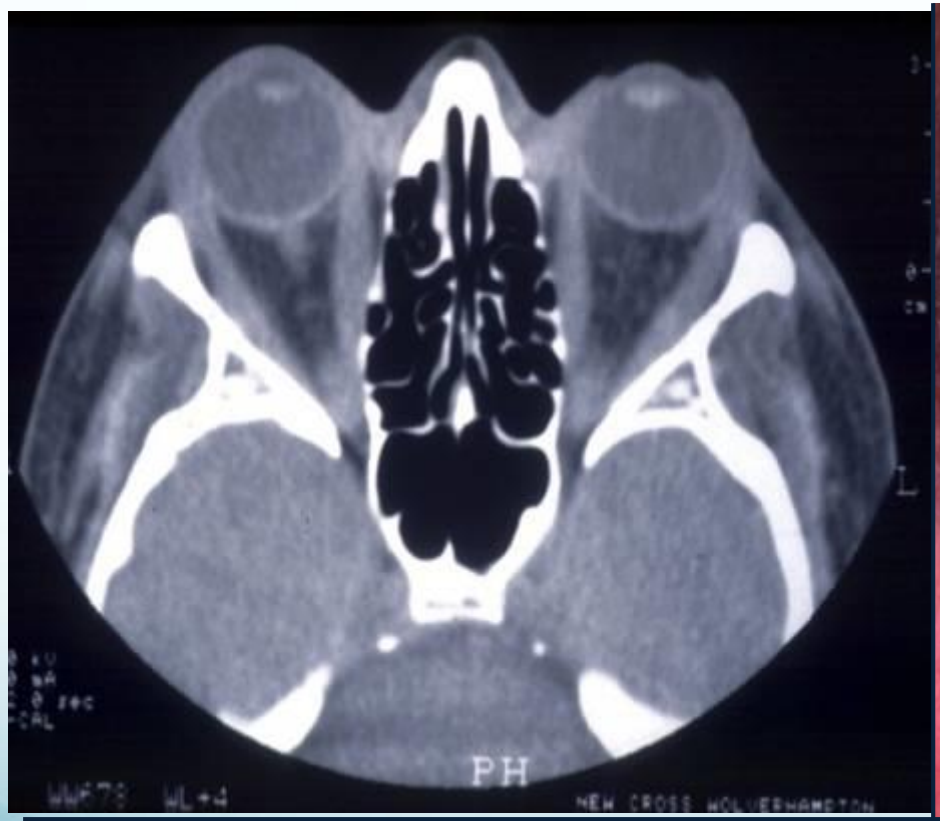
May be associated with choroidal folds

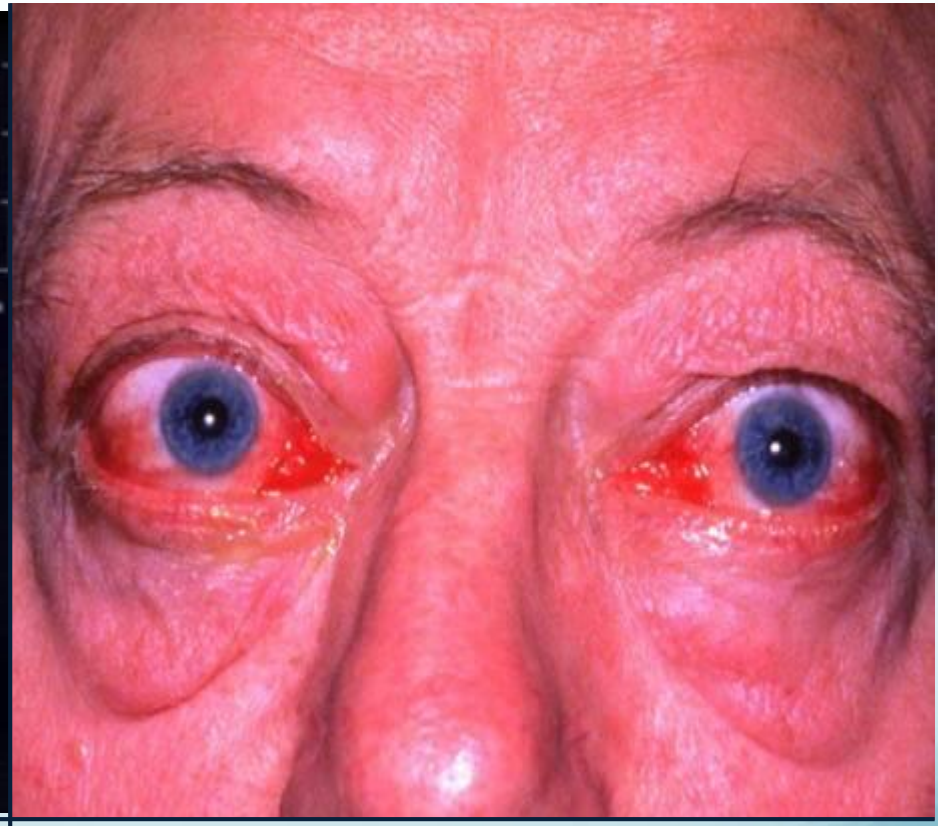
Treatment options

- **Systemic steroids**
- **Radiotherapy**
- **Surgical decompression**

Optic neuropathy

- Occurs in about 5%
- Early defective color vision
- Usually normal disc appearance



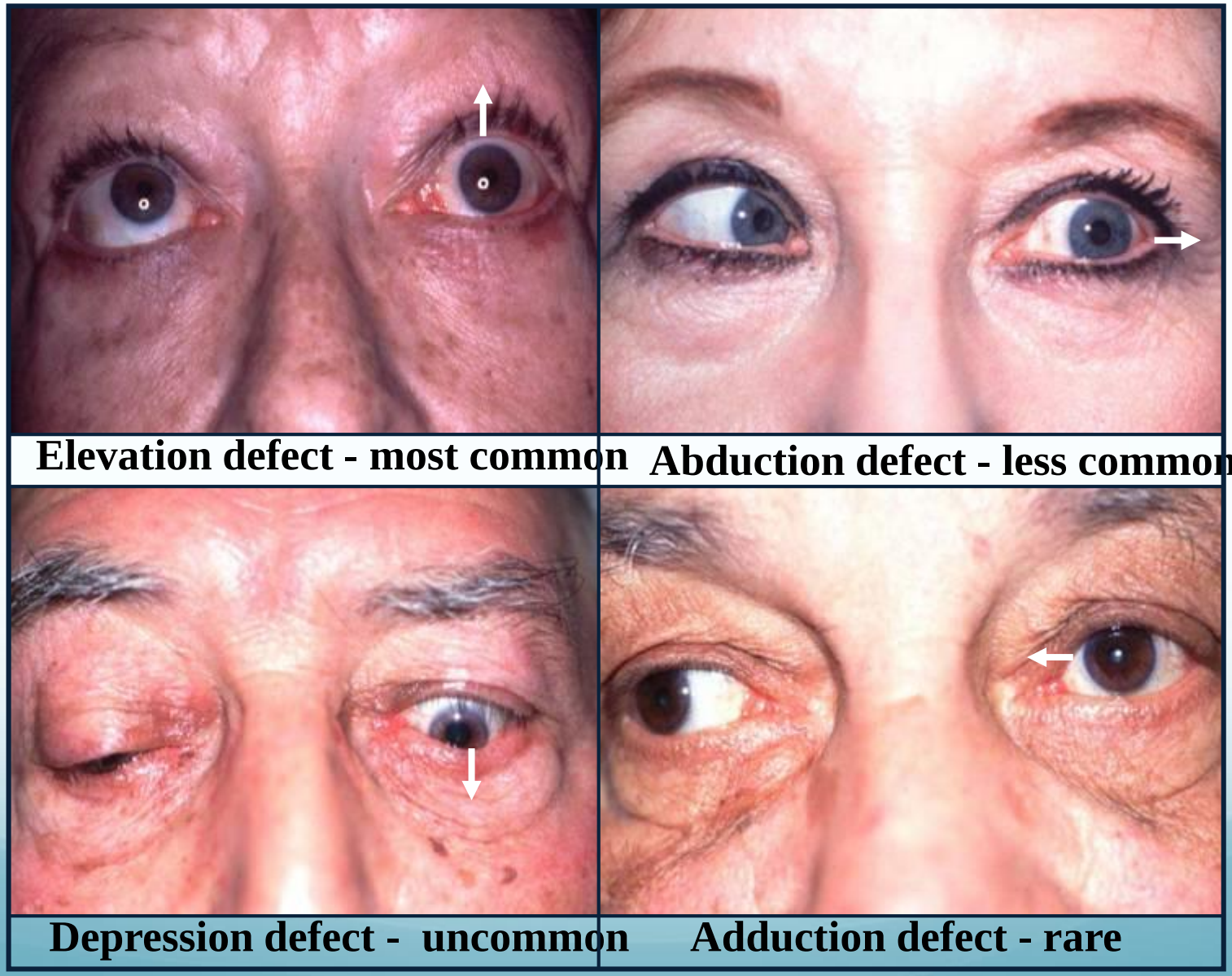


Caused by optic nerve compression at orbital apex by enlarged recti

Often occurs in absence of significant proptosis

Restrictive myopathy

- Occurs in about 40%
- Due to fibrotic contracture



- 30 percent of patients with Hyperthyroidism will develop Thyroid Eye Disease
- Most commonly seen in Hasimoto's
- Changes are not reversible once thyroid is controlled
  - Surgery – Decompression followed by eye muscle surgery followed by lid surgery

Summary

- Drug Screening Guidelines
- Patient education at initiation of medication
- Majority of medications: Referral with signs or symptoms
- Plaquenil – At time of drug initiation, then annually at 5 years
- Tamoxifen – When drug is started then every 6 months
- Ethambutol – When starting medications and then is develop vision symptoms

Diabetes

- Type 1 – 5 years after DX, then annually unless retinopathy is noted
- Type 2 – At time of diagnosis then annually
- Pre-existing DM Pregnancy – Soon after conception if retinopathy will need follow during pregnancy
- Gestational DM – No increased risk of retinopathy

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Thank You