Disclosures

Wilmer Eye Institute
Johns Hopkins Medicine

Horizon Therapeutics/Amgen (Advisory Boards)

Catalyst Pharmaceuticals (Advisory Board)

Argenx (Clinical Trial Site)

Learning Objectives

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By the end of this presentation, participants will be able to:

a. Diagnose thyroid eye disease

b. Develop appropriate treatment plans for patients with thyroid eye disease

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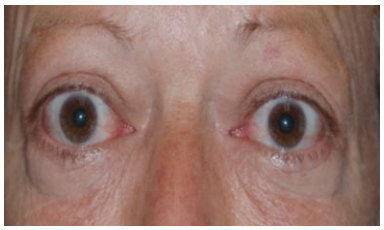
Case: 50-year-old woman presents with one month of changing facial appearance and blurred/double vision



Past Medical History

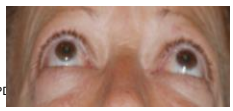
Graves disease with hyperthyroidism

- s/p radioactive iodine therapy

Social History

Current smoker- 1 ppd since age 18

Examination



Visual acuity
OD 20/20
OS 20/20

Pupils Briskly reactive OU, no RAPD

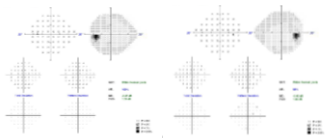
IOP 23/24

Color 10/10 OD and OS

Exophthalmometry
OD 23mm, OS 22mm
Base 113

EOM
Limitation of elevation and abduction OU

DFE unremarkable



Clinical Activity Score: 6
Periorbital pain/pressure
Pain with eye movement
Eyelid swelling
Eyelid redness
Conjunctival injection
Chemosis
Inflammation of caruncle/plica

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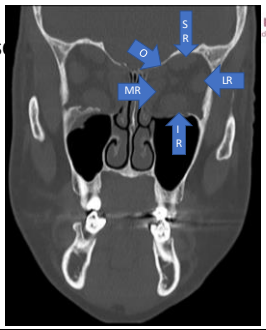
Questions

- What evaluation does she need?
- What treatment options do we have?

Evaluation

- Thyroid labs (TSH, fT4, TSI) / Endocrinology evaluation
- +/- Orbital Imaging (CT, MRI)

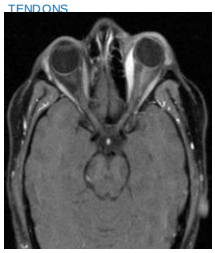
Thyroid Eye Disease



Orbital Imaging

THYROID EYE DISEASE- SPARES TENDONS

IDIOPATHIC ORBITAL INFLAMMATION- INVOLVES TENDONS

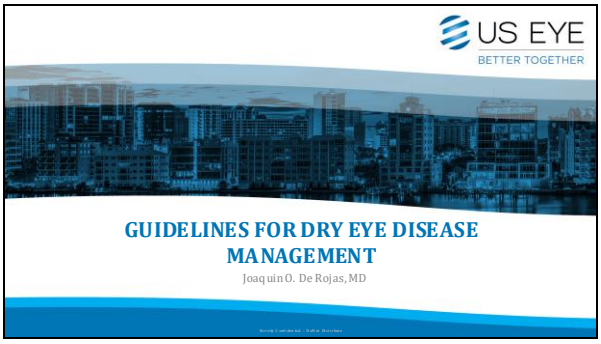


Thyroid Eye Disease: Management

- STOP smoking
- Treat thyroid abnormalities (Endocrinology)
- Selenium supplementation (Marcocci et al, European Group on Graves's Orbitopathy. Selenium and the course of mild Graves' orbitopathy N Engl J Med, 2011)
- Treatment of exposure keratopathy
- Steroids: IV > PO, EUGOGO protocol (Bartalena, et al,The 2021 European Group on Graves'orbitopathy (EUGOGO) clinical practice guidelines for the medical management of Graves' orbitopathy Eur J Endocrinol. 2021)
- Radiation (Sobel RK, et al, Orbital Radiation for Thyroid Eye Disease: AReport by the American Academy of Ophthalmology Ophthalmology, 2022)
- Teprotumumab (Smith TJ, et al, Teprotumumab for Thyroid-Associated Ophthalmopathy. N Engl J Med, 2017; Douglas RS, et al, Teprotumumab Efficacy, Safety, and Durability in Longer-Duration Thyroid Eye Disease and Re-treatment: OPTIC-X Study. Ophthalmology 2022)
- Surgical treatment
  - Orbital decompression
  - Strabismus surgery
  - Eyelid surgery

Take Home Points

- Thyroid eye disease is typically a clinical diagnosis, though orbital imaging and serum testing for thyroid function and thyroid stimulation antibodies can be helpful to confirm diagnosis
- Treatment options include:
  - Conservative measures
  - Steroid
  - Orbital radiation
  - Targeted immunotherapy (teprotumumab, other agents off label and in clinical trials)
  - Surgery


US EYE
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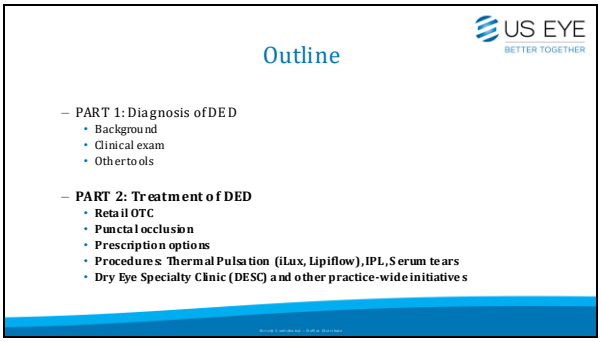
GUIDELINES FOR DRY EYE DISEASE MANAGEMENT
Joaquin O. De Rojas, MD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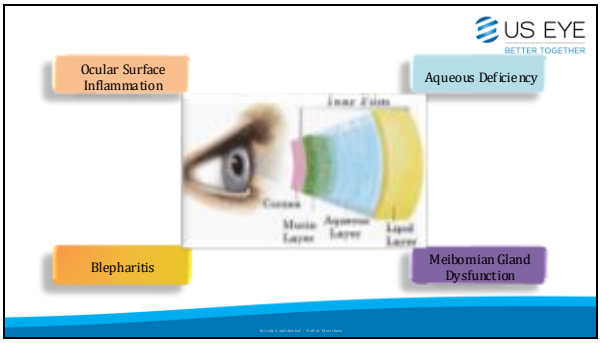
Outline
– PART 1: Diagnosis of DED
• Background
• Clinical exam
• Other tools
– PART 2: Treatment of DED
• Retail OTC
• Punctal occlusion
• Prescription options
• Procedures: Thermal Pulsation (iLux, Lipiflow), IPL, Serum tears
• Dry Eye Specialty Clinic (DESC) and other practice-wide initiatives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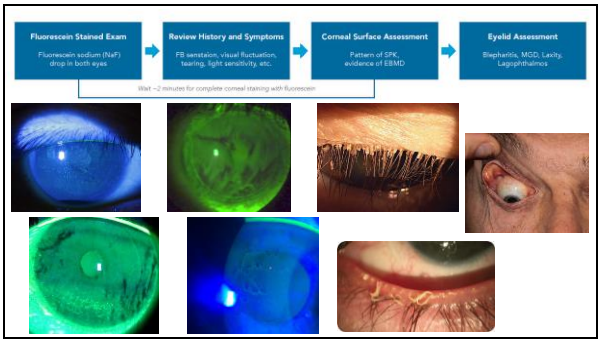
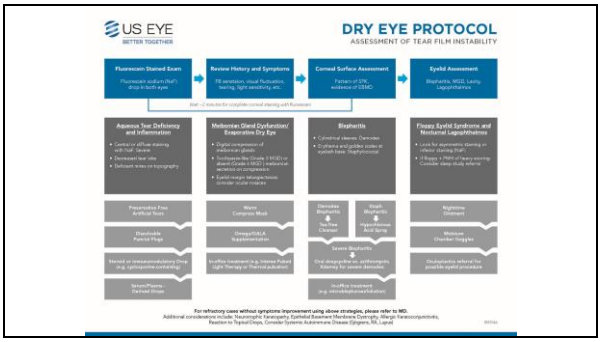
Ocular Surface Inflammation
Aqueous Deficiency
Blepharitis
Meibomian Gland Dysfunction


Fluorescein Stained Exam
Fluorescein sodium (NaF) drop in both eyes
Review History and Symptoms
FB sensation, visual fluctuation, tearing, light sensitivity, etc.
Corneal Surface Assessment
Pattern of SPK, evidence of EBMD
Eyelid Assessment
Blepharitis, MGD, Laxity, Lagophthalmos
Wait ~2 minutes for complete corneal staining with fluorescein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DRY EYE PROTOCOL
ASSESSMENT OF TEAR FILM INSTABILITY
Fluorescein Stained Exam
Review History and Symptoms
Corneal Surface Assessment
Eyelid Assessment
Aqueous Tear Deficiency and Inflammation
Meibomian Gland Dysfunction/ Evaporative Dry Eye
Blepharitis
Floppy Eyelid Syndrome and Nocturnal Lagophthalmos


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PART 2: TREATMENT

Aqueous Tear Deficiency and Inflammation

- Central or diffuse staining with NaF: Severe
- Decreased tear lake
- Deficient mires on topography

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Preservative Free Artificial Tears

Dissolvable Punctal Plugs




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Dissolvable Punctal Plugs

Steroid or Immunomodulatory Drop (e.g. cyclosporine-containing)





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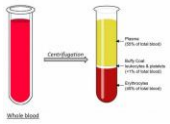
Preservative Free Artificial Tears

Dissolvable Punctal Plugs

Steroid or Immunomodulatory Drop (e.g. cyclosporine-containing)

Serum/Plasma - Derived Drops



PRP PROCEDURE

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- Takes about 15-20 minutes to complete
- Patients get their drops the same day
- 3 month supply (depending on how patient is using their drops) Most often 4Xs daily
- Drops DO need to be kept cold
- Patients often report improvement in symptoms after 3-4 weeks

Front

Back

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Meibomian Gland Dysfunction/ Evaporative Dry Eye

- Digital compression of meibomian glands
- Toothpaste-like (Grade 3 MGD) or absent (Grade 4 MGD) meibomian secretion on compression
- Eyelid margin telangiectasias: consider ocular rosacea

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Warm Compress Mask

Omega/GALA Supplementation

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Warm Compress Mask

Omega/GALA Supplementation

In-office treatment (e.g. Intense Pulsed Light Therapy or Thermal pulsation)

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IPL PROCEDURE

- Series of 4 recommended (appointments spaced every 2-4 weeks) then switch to maintenance treatments
- Initial appointment takes 45 minutes. Following appointments take about 15-20 Min
- No downtime after appointment
- If history of Herpes Zoster Opthalmicus the patient will need to be on antiviral before/after appointment

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MEIBOGRAPHY WITH LIPIVIEW

- Quick images in about 5 min
- Helpful prior to IPL, Lipiflow, or iLux
- Great for patient education regarding MGD
- Easy for patients to see and understand

Front

Intense Pulsed Light (IPL) FAQs

What is IPL for Dry Eye?
Intense Pulsed Light (IPL) therapy is a highly effective treatment for dry eye disease and ocular rosacea. This treatment aims to improve the symptoms of dry eye disease commonly caused by abnormal blood vessels and meibomian gland dysfunction.

Center For Sight is among the first practices in the area to offer IPL for dry eye, offering our patients a painless and quick treatment for the uncomfortable gritty and burning sensation often felt with dry eye disease.

How does it work?
The IPL device delivers intense pulses of non-coherent light transmitted to the skin through a cooled applicator. The light pulses target the abnormal blood vessels which are causing inflammation, and subsequent symptoms of dry eye disease. IPL also clears the debris blocking the meibomian glands and decreases bacterial growth.

Research has demonstrated that IPL treatment improves tear breakup time, meibum quality and gland expressability. We are delighted to offer this treatment option to our patients who have not experienced improvement through the use of other dry eye therapies.

Am I a candidate for IPL treatment?
You may be a candidate for IPL treatment if you experience symptoms of dry eye disease to the degree they are impacting your vision and/or quality of life. You will be referred to one of our dry eye specialists for an evaluation and treatment.

How many treatments will I need?
Most patients need four sessions, spaced three to four weeks apart. Each session takes approximately 15 minutes. Many patients elect to continue maintenance treatments every 6-12 months to remain symptom-free.

Back

Dry Eye Care at Center For Sight

What to expect on your treatment day?
Your IPL treatment will take approximately fifteen minutes to complete. Following treatment, you may experience some redness around your eyes, which will subside shortly. IPL is a very gentle procedure and there is no need to alter your daily routine.

Schedule an appointment today to determine if IPL treatment can help you experience relief from painful dry eye symptoms.

Meet Our Dry Eye Team

Priya Mathews, M.D.
Dr. Mathews is a board-certified, fellowship-trained cataract, refractive, and corneal surgeon. She also serves as the Director of Cornea and Ocular Surface Disease at Center For Sight.

Joaquin De Rojas, M.D.
Dr. De Rojas is a board-certified, fellowship-trained cataract, refractive and corneal surgeon who also serves as the Director of Refractive Surgery at Center For Sight.

Maureen Traina, PA-C
Maureen Traina is a Florida-licensed Physician Assistant (PA-C) who currently serves as an Ophthalmic PA at Center For Sight. Maureen focuses on performing treatments for dry eye disease.

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Blepharitis

- Cylindrical sleeves: Demodex
- Erythema and golden scales at eyelash base: Staphylococcal

Blepharitis

- Cylindrical sleeves: Demodex
- Erythema and golden scales at eyelash base: Staphylococcal

Demodex Blepharitis → Tea-Tree Cleanser

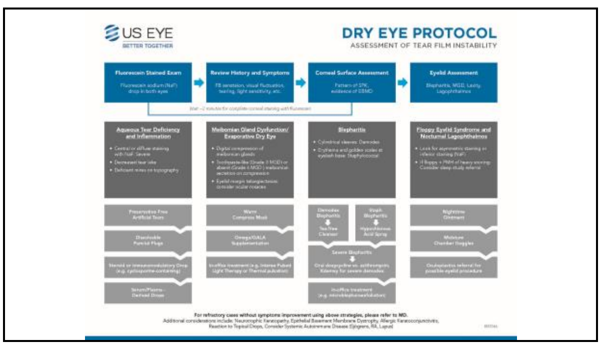
Staph Blepharitis → Hypochlorous Acid Spray

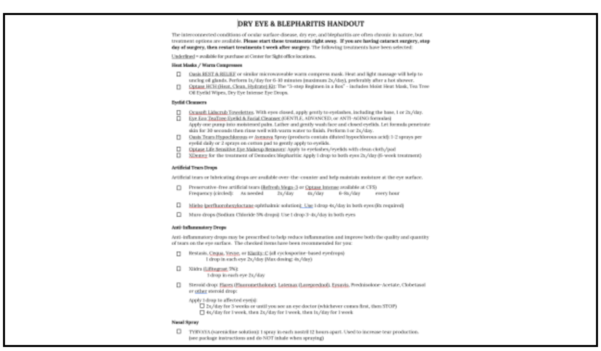
Severe Blepharitis → Oral doxycycline vs. azithromycin; Xdemvy for severe demodex

In-office treatment (e.g. microblepharoexfoliation)

Floppy Eyelid Syndrome and Nocturnal Lagophthalmos

- Look for asymmetric staining or inferior staining (NaF)
- If floppy + PMH of heavy snoring: Consider sleep study referral





DRY EYE & BLEPHARITIS HANDOUT

The interconnected conditions of ocular surface disease, dry eye, and blepharitis are often chronic in nature, but treatment options are available. **Please start these treatments right away. If you are having cataract surgery, stop day of surgery, then restart treatments 1 week after surgery.** The following treatments have been selected:

Underlined = available for purchase at Center for Sight office locations.

Heat Masks / Warm Compresses

- ☐ Oasis REST & RELIEF or similar microwaveable warm compress mask. Heat and light massage will help to unclog oil glands. Perform 1x/day for 6-10 minutes (maximum 2x/day), preferably after a hot shower.
- ☐ Optase HCH (Heat, Clean, Hydrate) Kit: The "3-step Regimen in a Box" - includes Moist Heat Mask, Tea Tree Oil Eyelid Wipes, Dry Eye Intense Eye Drops.

Eyelid Cleansers

- ☐ Ocusoft Lidscrub Towelettes. With eyes closed, apply gently to eyelashes, including the base, 1 or 2x/day.
- ☐ Eye Eco TeaTree Eyelid & Facial Cleanser (GENTLE, ADVANCED, or ANTI-AGING formulas) Apply one pump into moistened palm. Lather and gently wash face and closed eyelids. Let formula penetrate skin for 30 seconds then rinse well with warm water to finish. Perform 1 or 2x/day.
- ☐ Oasis Tears Hypochlorous or Avenova Spray (products contain diluted hypochlorous acid): 1-2 sprays per eyelid daily or 2 sprays on cotton pad to gently apply to eyelids.
- ☐ Optase Life Sensitive Eye Makeup Remover: Apply to eyelashes/eyelids with clean cloth/pad
- ☐ XDemvy for the treatment of Demodex blepharitis: Apply 1 drop to both eyes 2x/day (6-week treatment)

Artificial Tears Drops

Artificial tears or lubricating drops are available over-the-counter and help maintain moisture at the eye surface.

- ☐ Preservative-free artificial tears (Refresh Mega-3 or Optase Intense available at CFS)
  Frequency (circled): As needed 2x/day 4x/day 6-8x/day every hour
- ☐ Miebo (perfluorohexyloctane ophthalmic solution): Use 1 drop 4x/day in both eyes (Rx required)
- ☐ Muro drops (Sodium Chloride 5% drops): Use 1 drop 3-4x/day in both eyes

Anti-Inflammatory Drops

Anti-inflammatory drops may be prescribed to help reduce inflammation and improve both the quality and quantity of tears on the eye surface. The checked items have been recommended for you:

- ☐ Restasis, Cequa, Vevye, or Klarity-C (all cyclosporine-based eyedrops)
  1 drop in each eye 2x/day (Max dosing: 4x/day)
- ☐ Xiidra (Lifitegrast 5%):
  1 drop in each eye 2x/day
- ☐ Steroid drop: Flarex (Fluorometholone), Lotemax (Loteprednol), Eysuvis, Prednisolone-Acetate, Clobetasol or other steroid drop:
  Apply 1 drop to affected eye(s):
  - ☐ 2x/day for 3 weeks or until you see an eye doctor (whichever comes first, then STOP)
  - ☐ 4x/day for 1 week, then 2x/day for 1 week, then 1x/day for 1 week

Nasal Spray

- ☐ TYRVAYA (varenicline solution): 1 spray in each nostril 12 hours apart. Used to increase tear production. (see package instructions and do NOT inhale when spraying)

Antibacterials and Ointments

Antibacterial drops:

- ☐ Moxifloxacin or Ofloxacin 1 drop 3x/day while contact lens is in place.
- ☐ Other antibiotic drop(s):

Ointments: Put a small amount of ointment on a clean fingertip or Q-tip. Gently apply the ointment to the everted eyelid edge (ointment will enter eye after blinking).

- ☐ Erythromycin or Bacitracin-Polymyxin B ophthalmic antibacterial ointment at bedtime
- ☐ Over-the-counter lubricating gel or ointment at bedtime. Recommended brands: Refresh PM, Genteal gel, Systane Nighttime, or Lacrilube
- ☐ Muro ointment (Sodium Chloride 5% ointment) at bedtime.

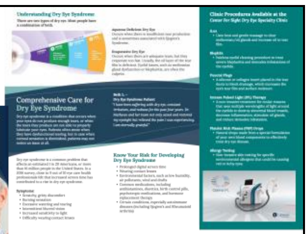
Oral antibiotics (take by mouth):

- ☐ Doxycycline 20-50 mg pill 2x/ day x 3-4 months (take with food to decrease upset stomach)
- ☐ Azithromycin x 5 days ("Z-Pak"): 5-day course pack, then repeat every month for 3-4 months.
- ☐ Azithromycin 250 mg every day for 30 days, followed by Z-Pak monthly for 3 months.

Other Treatments

- ☐ Omega-3 oral supplement to promote a healthy oil in tears. Recommended: HydroEye Softgels
- ☐ Vitamin C oral supplement (1000-2000 mg/day) to promote corneal healing.
- ☐ Moisture chamber goggles for use at bedtime. Recommended: Eyeseals 4.0 Hydrating Sleep Mask. First, apply nighttime gel/ointment (see above), then place moisture chamber over eyes prior to sleep. Recommended if you use CPAP or nasal cannula, or if your eyelids do not fully close when you sleep.
- ☐ Punctal plugs or Lacrifill: Small inserts placed into your tear drainage sites to increase natural tear buildup, thereby lubricating your eyes. May need replacement at 6 months.
- ☐ **Amniotic Membrane Graft** (ScellerEYES or Prokera Slim): Biological bandage device placed by your doctor to facilitate corneal healing in severe ocular surface disease and related conditions. If placed, use with antibiotic drops.
- ☐ **Intense Pulsed Light Therapy, iLux, or LipiFlow**: Electronic device that uses heat and massage to unclog the oil glands within your eyelids to alleviate inflammation, improve dry eye, and lengthen the life of your oil glands. After the procedure, use a steroid drop 1 drop 2x/day (see "Steroid drop" above) and continue warm mask therapy daily (see above). Treatment may be repeated.
- ☐ **Blephex**: A quick and painless eyelid cleaning procedure performed in-office to treat severe blepharitis and demodex infestation of eyelashes. Continue daily eyelid cleansing at home after procedure. May be done alone or in conjunction with iLux (see above). Treatment can be repeated every 6 months.
- ☐ **Platelet-Rich Plasma or Serum drops**: For severe ocular surface disease. May be formulated using your own blood components in our office or at a specialty pharmacy. Use 1 drop in affected eyes 4x/day. Please keep unused bottles frozen and used bottles refrigerated (shelf life 5-7 days in refrigerator, 5-6 months in freezer)
- ☐ Oxervate (cenegermin-bkbj): Specialty drops used to improve corneal nerve function in severe ocular surface disease with neurotrophic keratitis. 1 drop 6x/day at 2-hour intervals for 8 weeks. Prior approval from insurance is needed.
- ☐ Allergy testing for environmental allergens +/- sublingual therapy: A quick and easy 15-minute procedure that can be done in-office. This may be recommended to you if you have chronic itchy or red eyes or other symptoms of allergies. Please refrain from using any allergy medications at least 3 days prior to testing.

DRY EYE SPECIALTY CLINIC AT CFS



Make sure to show your patients what you offer (and let them research on their own!)

Thank You!

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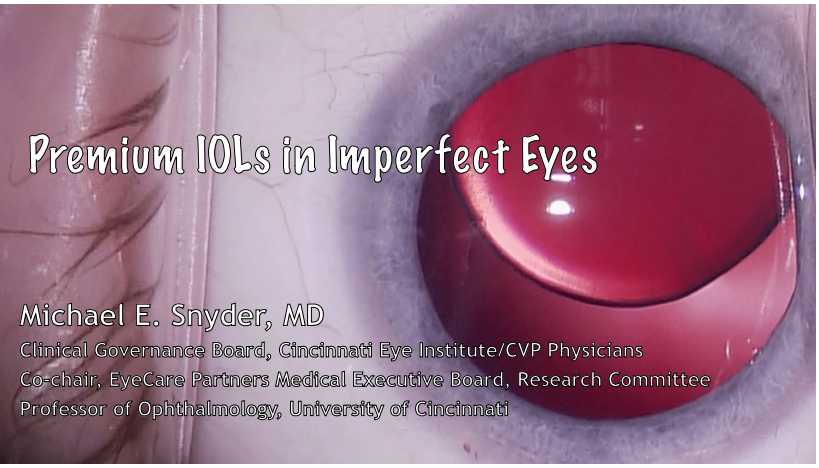
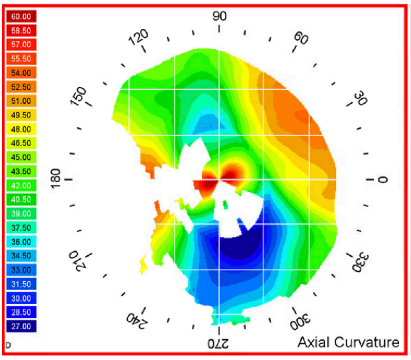
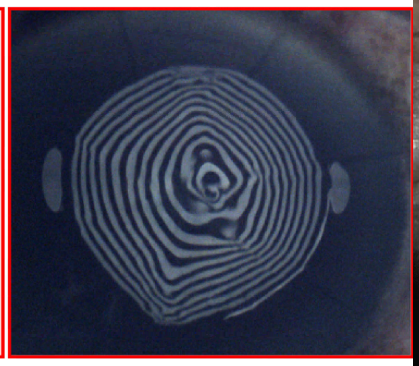


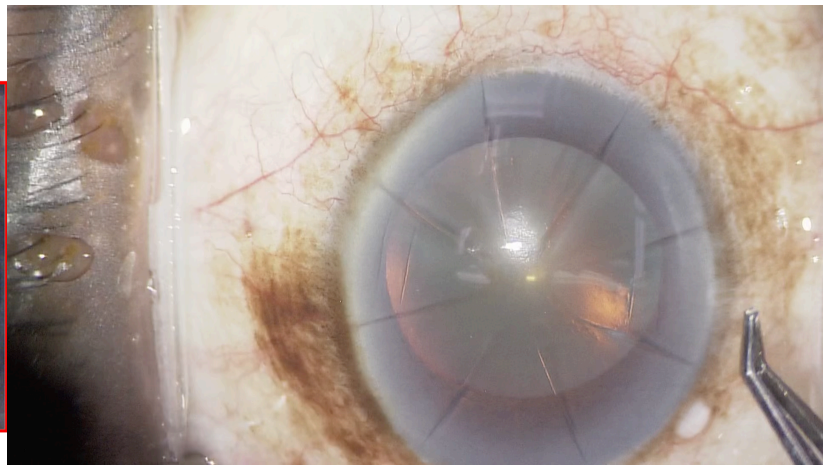
Disclosures

- DORC: Consultant
- Gore: Consultant
- Haag-Streit: Consultant
- Humanoptics: Consultant, Royalties
- Johnson and Johnson Vision: Research
- Plexitome: Research
- VEO Ophthalmics: Board member, Royalties (TKP)

Marked Irregular Astigmatism, Post RK

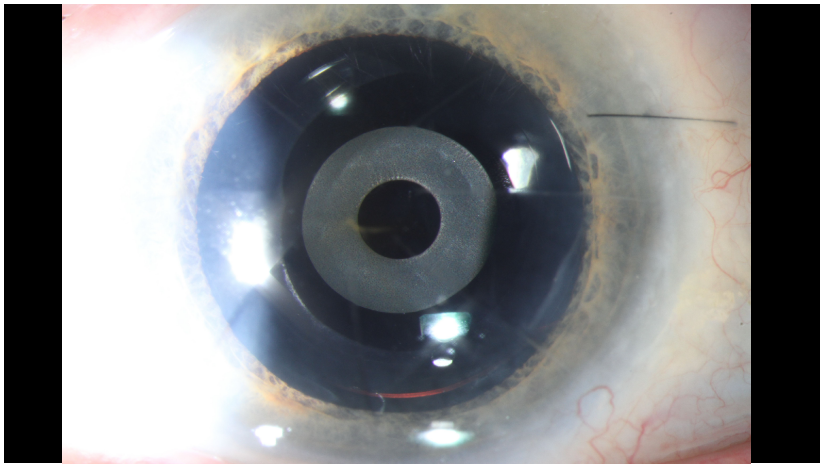


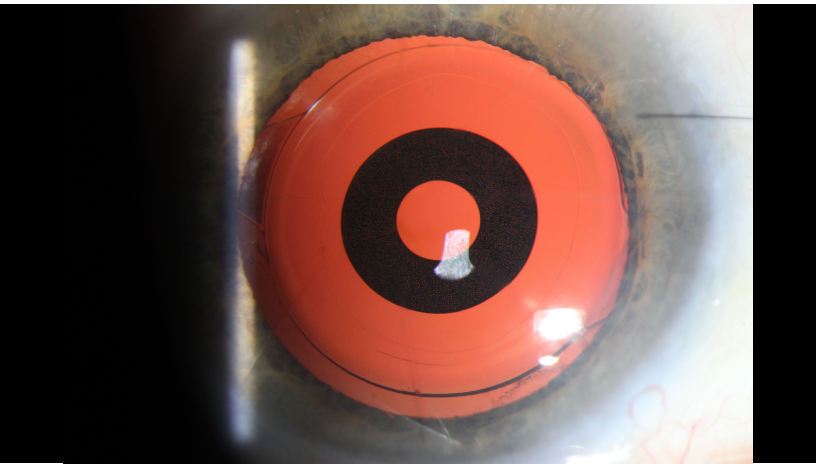




Marked Irregular Astigmatism, Post RK

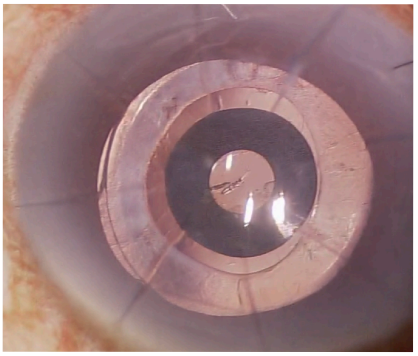
- BSCVA and UCVA = 20/50, J3
- HAPPY!

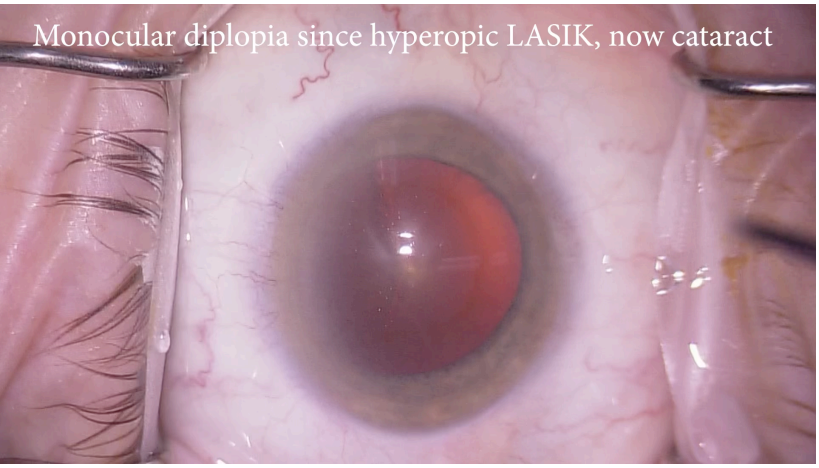




Marked Irregular Astigmatism, Post RK

- BSCVA and UCVA = 20/50, J3
- HAPPY!
- Gets PCO…
- …has YAG elsewhere, cracks optic with YAG…
- BCVA 20/100,
- Very unhappy :-(
- Gets PK…





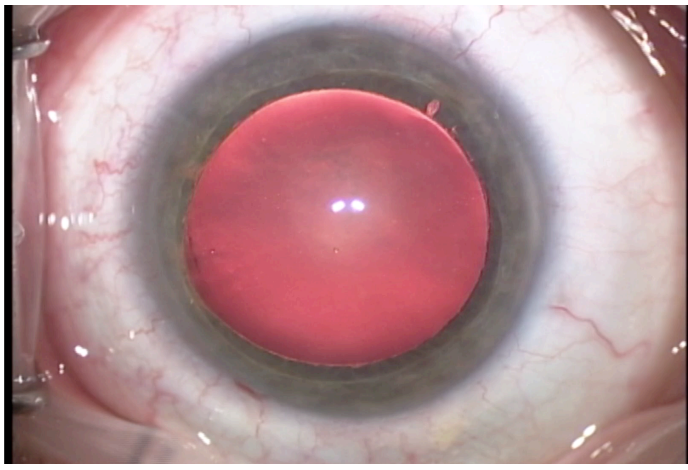
No More Diplopia!
UCVA 20/20, J1+

Mild Halo
"…not perfect in the distance…"

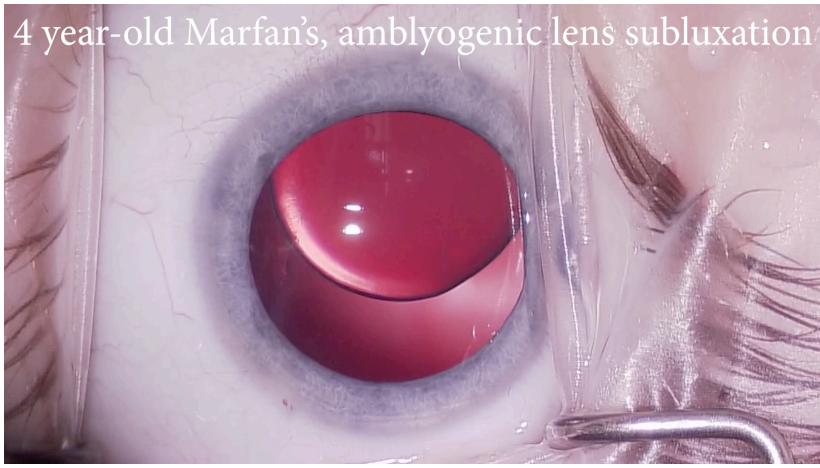
Giant Bag…

- Single Piece IOL haptic-to-haptic diameter is smaller than the bag?

Megalo-Anterior Segment With Giant Bag!



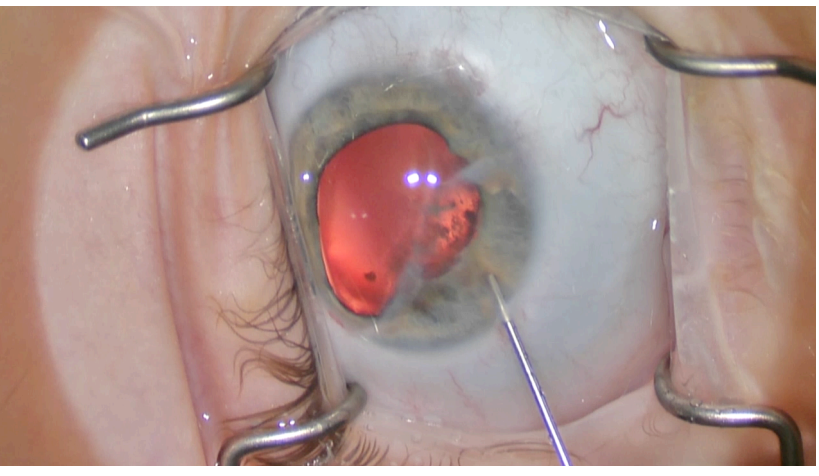
Zonular Dialysis



Cionni MCTR Tips

- Dispersive OVD for Vitreous Tamponade
- Dispersive PVD for Equatorial Stenting
- I/A only for Young Lenses
- Shrink Ring to Fit Small Bags
- Kids Adapt to Multifocality Really Well

Pupillary Abnormality & Zonular Dialysis (& Corneal Scar)

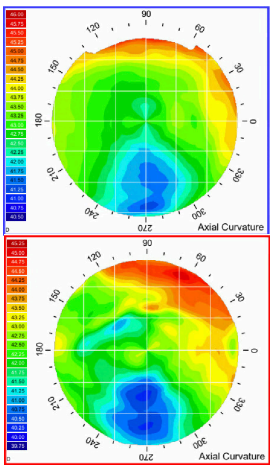


Post-Myopic Lasik Regular and Irregular Astigmatism

- Nuclear > Cortical Cataract

Post-op Range										
Rx LAL A = 119.1 Target = Plano	IOL Power	K:	41.90	K:	42.30	K:	42.83	K:	43.21	K:
	21.5	=	+1.29	=	+0.92	=	+0.40	=	+0.02	=
	22.0	=	+0.97	=	+0.59	=	+0.07	=	-0.31	=
	22.5	=	+0.65	=	+0.26	=	-0.26	=	-0.64	=
	23.0	=	+0.33	=	-0.07	=	-0.59	=	-0.97	=
	23.5	=	-0.00	=	-0.40	=	-0.92	=	-1.30	=

Post-op Range										
Rx LAL A = 119.1 Target = Plano	IOL Power	K:	41.03	K:	41.46	K:	41.90	K:	42.34	K:
	21.5	=	+1.22	=	+0.78	=	+0.36	=	-0.07	=
	22.0	=	+0.89	=	+0.46	=	+0.03	=	-0.41	=
	22.5	=	+0.56	=	+0.14	=	-0.30	=	-0.75	=
	23.0	=	+0.23	=	-0.20	=	-0.63	=	-1.08	=
	23.5	=	-0.10	=	-0.53	=	-0.96	=	-1.41	=



Pt Underwent Phaco/LAL OU

- POM1: UCDVA: 20/20-2 OU, UCIVAL: 20-30-2 OU,UCNVA: J2+ OU
- Week 3 Mx: OD: -1.25 + 1.00 x 173; OS: -1.75 + 1.25 x 005
- LAL Treatment OU x 2

- Final result: UCDVA: 20/15 OU! UCNVA: J1+ OU!

Don't celebrate too soon…

Excerpts from letter POM5:

"Unfortunately the weather has been affecting my eyes…"

Don't celebrate too soon…

Excerpts from letter POM5:

"Unfortunately the weather has been affecting my eyes…"

"I paid over $12K for these lenses and I do not want seasonal issues."

Don't celebrate too soon…

Excerpts from letter POM5:

"Unfortunately the weather has been affecting my eyes…"

"I paid over $12K for these lenses and I do not want seasonal issues."

"I have several friends who paid a lot less for the traditional lenses and have none of my issues."

Don't celebrate too soon…

You please some of the people all of the time…

…you can please most of the people most of the time…

…but you can't please all of the people all of the time!

Don't celebrate too soon…

You please some of the people all of the time…

…you can please most of the people most of the time…

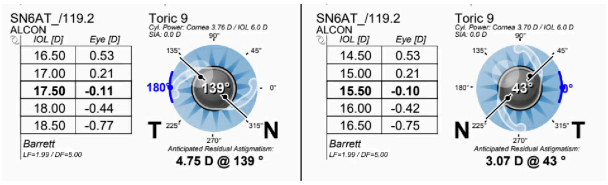
…but you can't please all of the people all of the time!

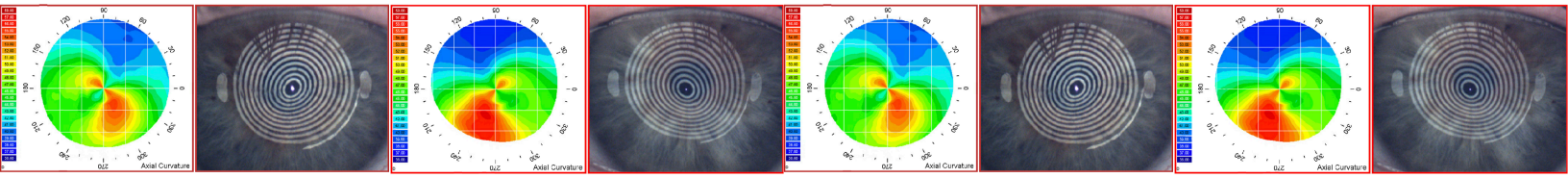
And some people you just cannot please!

Regular & Irregular Astigmatism…

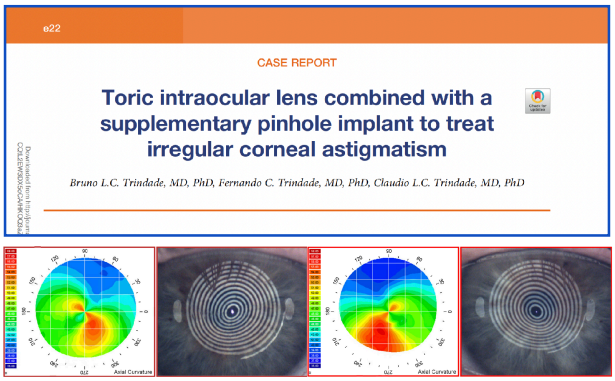
- -1.50 + 4.25 x 179
- -2.50 + 4.25 x 174

Regular & Irregular Astigmatism…





Possible High Toric IOL and Pinhole?



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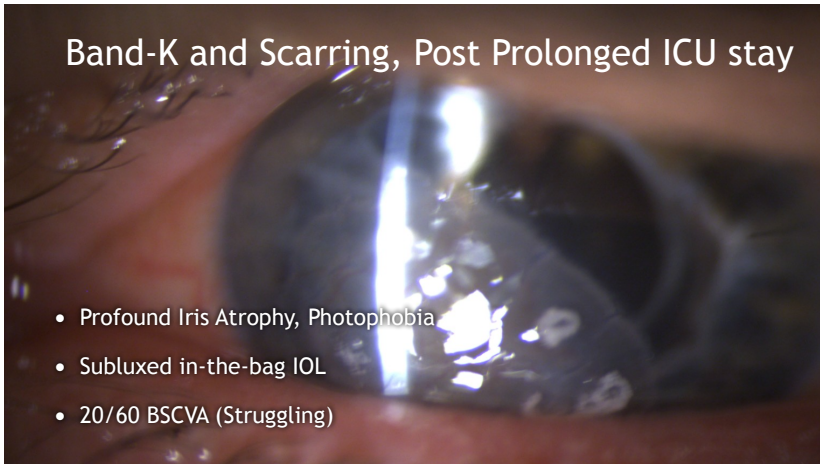
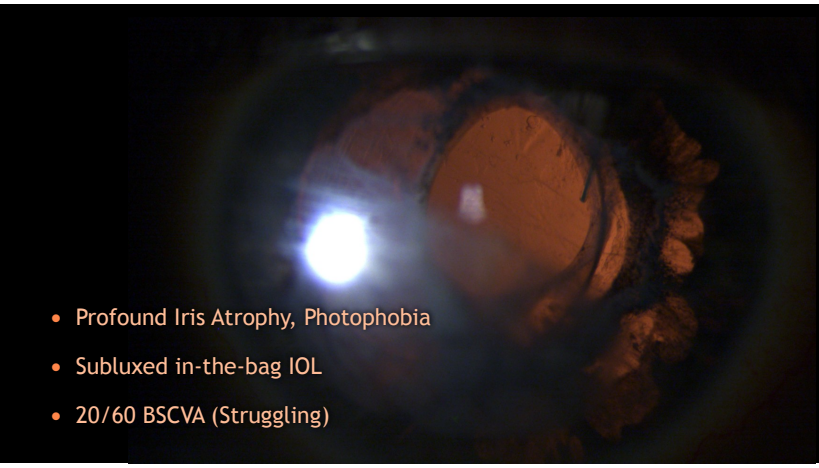
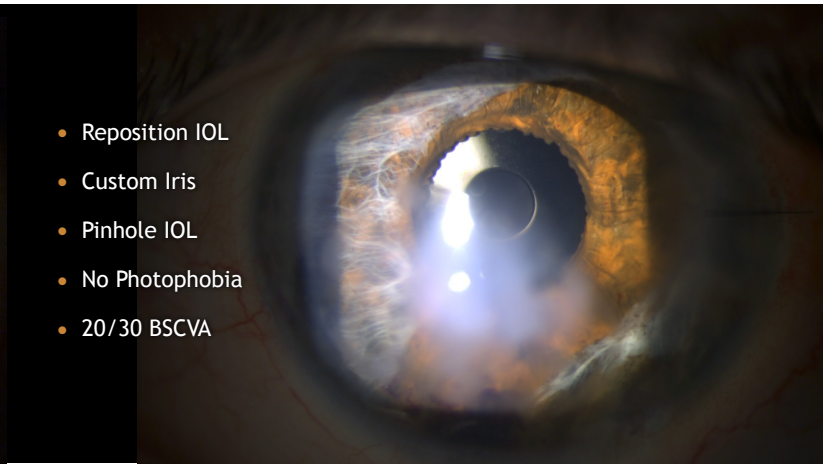
CASE REPORT

Toric intraocular lens combined with a supplementary pinhole implant to treat irregular corneal astigmatism

Bruno L.C. Trindade, MD, PhD, Fernando C. Trindade, MD, PhD, Claudio L.C. Trindade, MD, PhD







Overriding Principles

Qs?

Overriding Principles

- Regular Topography (Even if Some Scarring):
  - OK for Toric IOL and/or presbyopia correction
- Irregular Astigmatism:
  - No MFIOL
  - Consider Pinhole IOL, possible Crystalens if mild
- Irregular Pupil/Corectopia
  - Will it be regular at the end of the case? *It should be!* (Repair or Prosthesis)
  - Everything is still on the table! (Except Crystalens, if Iris Prosthesis)
- Zonulopathy
  - IOL needs to be centered by the end of the case. NO CRYSTALENS!
- Kiddos?
  - They adapt very well to multifocality.
  - Today's problem is amblyopia; tomorrow's problem is ametropia…
- Intact Bag? More Options…
  - PCCC if Megalo-bag

Urgencies in Ophthalmology, a general overview

- Hilary A. Beaver, MD
- Associate Professor of Clinical Ophthalmology
- Weill Cornell Medical College, Houston Methodist Hospital
- Adjunct Associate Professor
- University of Texas Medical Branch at Galveston

Disclosures

Amgen
- Advisor

All images from University of Iowa unless otherwise stated

Urgencies are not the same as emergencies

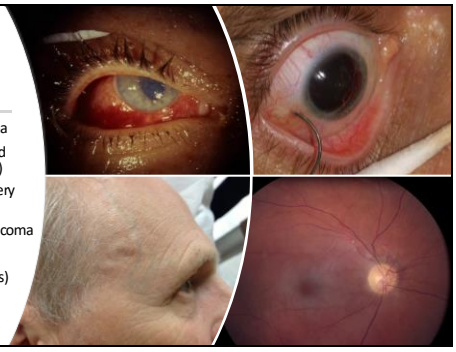
Routine acute eye conditions are also alarming
- Patient and family
- Referring physician

Triage history gives you control
- Age, timing of complaint, quality Sx, mechanism of injury
- Appearance of the eye
- Vision: the vital sign of the eye
- Pain: quality, severity, location

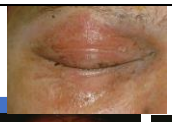
Nail Gun

5 True Ophthalmic Emergencies

- Open globe trauma
- Pupil involved third nerve palsy (CN III)
- Central retinal artery occlusion
- Angle closure glaucoma
- Chemical injury
- (Giant Cell Arteritis)



Chemical injury
identify chemical agent



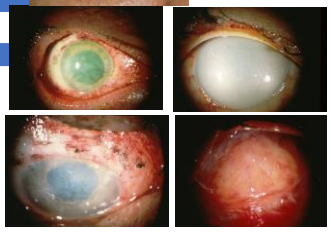
Roman candle:
Thermal + chemical

Alkali worse than acid

- Penetrates eye, saponifies vs. coagulates
- Vascular occlusion

Clinical findings

- Skin burns
- Corneal (conjunctival) epithelial defect
  - May not stain with fluorescein
- Limbal ischemia (guarded >1/3, poor > 1/2)
- Corneal haze, loss of iris detail
  - Collagen shrinkage
  - Endothelial pump
- AC reaction or hyphema
- Cataract
- Elevated IOP



Copious irrigation

- 30+ minutes, saline or LR
- pH 7.0

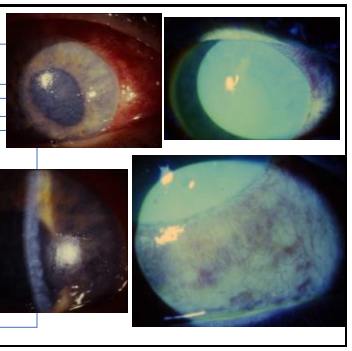
Sweep fornices

Rx acute

- Topical steroid (+/- > 1 week)
- Mydriatics (no vasoconstrictors)
- Collagen protection
  - Vitamin C PO, topical 10% (production)
  - Tetracycline PO (< collagenase)
- Topical sodium citrate 10% (< PMN recruitment)
- IOP control
- Lubricants
- Bland antibiotic ointment

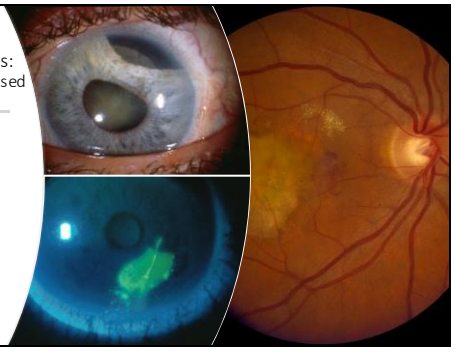
Rx chronic

- IOP control
- Amniotic membrane
- Serum tears
- Limbal stem cell transplant



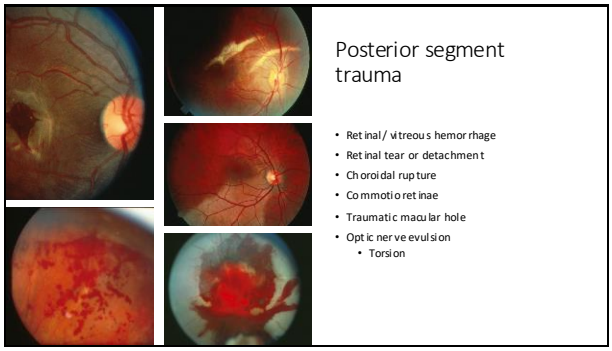
5 Ocular Urgencies: Symptom/History based

- Other trauma
  - Ocular/globe
  - Orbit/adnexa
- Sudden vision loss
- Red eye
- Eye pain
- Double vision



Anterior segment trauma

- Pupil sphincter tears
  - Anisocoria
  - Dilated pupil
- Traumatic iritis
  - Inflammation, pain, injection
  - Cyclitis (ciliary body)
- Angle Recession
- Iridodialysis
  - Separation iris root
- Hyphema



Posterior segment trauma

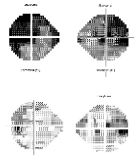
- Retinal/vitreous hemorrhage
- Retinal tear or detachment
- Choroidal rupture
- Commotio retinae
- Traumatic macular hole
- Optic nerve evulsion
  - Torsion

Orbit trauma




- Eyelid lacerations
  - Lid margin
  - Canalicular trauma
- Orbital fracture
  - Muscle entrapment more emergent
    - Young, elastic bone
- Orbital hemorrhage
- Orbital emphysema
- Traumatic enucleation

Acute, subacute vision loss



Vitamin A deficiency

"Blurred vision" with no referral history needs evaluation

Sudden awareness or sudden onset

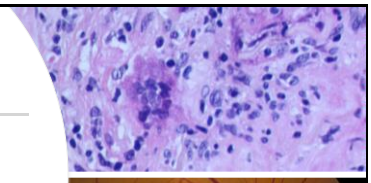
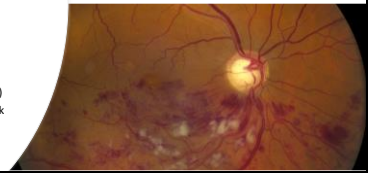
Acute on chronic disease

- Ocular surface disease: Dryeye, punctate keratopathy
- Retinal hemorrhage: diabetes, subretinal NVM
- Nutritional: restricted intake, alcohol abuse, vomiting, GI surgery or disease
- Compressive etiology: painless progressive loss of vision

Acute, urgent disease

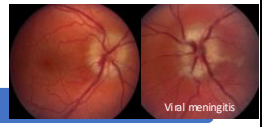
- Vascular etiologies
- Optic neuropathies

Vascular vision loss

- Retinal
  - Arterial or venous occlusion
  - Vitreous hemorrhage
- Choroidal
  - Macular degeneration
  - Central serous chroidopathy
- Optic nerve ischemia
  - Arteritic (giant cell arteritis)
  - Non-arteritic (vasculopathic disease)
- CNS: stroke or transient ischemic attack
  - Homonymous hemianopsia
  - Occipital blindness

Optic neuritis



Idiopathic optic neuritis

Multiple sclerosis

- Young, white, less severe, most improve within weeks-months

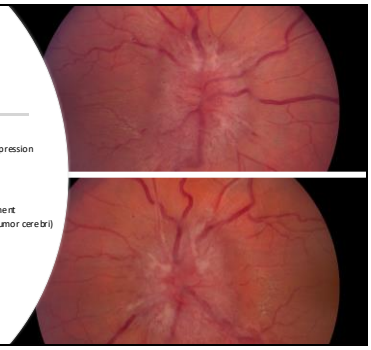
Neuromyelitis optica (NMO)

- Older, non-white, more severe, no improvement
- Transverse myelitis, vomiting, narcolepsy, hiccups

Myelin oligodendrocyte glycoprotein (MOG)

Optic neuropathy

- Optic nerve compression
  - Thyroid eye disease- extraocular muscles compression
  - Tumor- optic nerve, chiasm
- Optic disc edema
  - Malignant hypertension- with ischemia
    - +/- retinal vascular or choroidal involvement
  - Idiopathic intracranial hypertension (pseudotumor cerebri)
  - Intracranial mass
  - Infectious (Lyme, cat scratch, syphilis, TB)
  - Inflammatory (sarcoidosis)
- Nutritional (B12, folate)



Vision loss can always be retinal detachment

The red eye complaint

Anatomical location

- Orbital red eye
- Ocular red eye

Carotid cavernous fistula

Etiology

- Allergic
- Infectious
- Inflammatory
- Vascular

Sarcidosis

"Ocular" red eyes

- Anterior segment
  - Lids and lashes
  - Conjunctiva/Episclera/ Sclera
  - Cornea
  - Anterior chamber
  - Iris
- Posterior segment - less likely "red"
  - Vitreous
  - Retina
  - Choroid
  - Retinal vessels

Vernal conjunctivitis

Chalazion

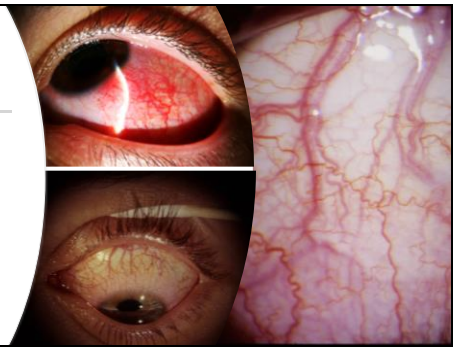
Conjunctivitis

- Allergic/ atopic/ vernal
- Infectious
  - Viral
    - Adenovirus
    - Herpes simplex or zoster
  - Bacterial
    - Purulent
    - Hyperpurulent (Gonorrheal)
    - Mucopurulent (Chlamydia)
  - Parasitic
    - Pthirus pubis (Pubic lice)
    - Demodex

Adenovirus with membranes and preauricular node

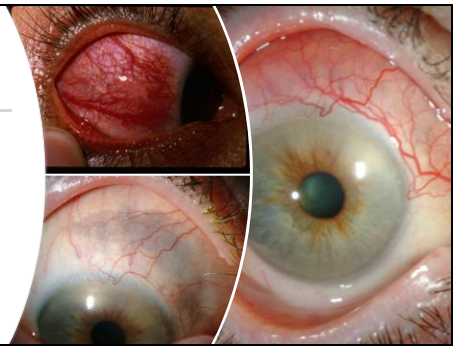
Episcleritis

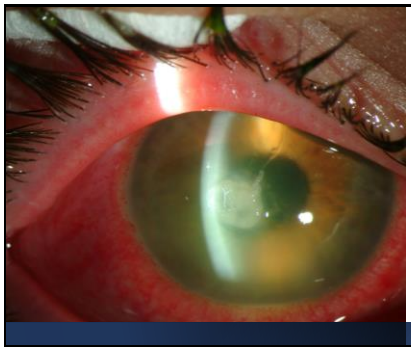
- Etiology
  - Idiopathic
  - Inflammatory
    - Sarcoid
  - Infectious
    - Syphilis, TB
- Presentation
  - Diffuse
  - Localized
  - Nodular



Scleritis

- Etiology
  - Idiopathic
  - Inflammatory
  - Infectious
- Location
  - Anterior
  - Posterior

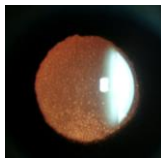




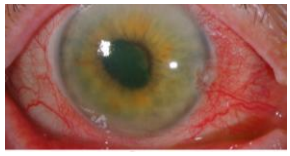
Keratitis

- Dry eye
- Abrasion and foreign bodies
- Microbial keratitis
  - Contact lens use
  - Corneal scraping, culture
    - Large, central
    - Epithelium non-intact
    - Suppurative

Uveitis: intraocular inflammation Anterior (vs posterior)



- Idiopathic (70%)
- Inflammatory
- Infectious
  - Syphilis, TB
- Secondary
  - Endophthalmitis
    - Post surgical vs. Endogenous
  - Blebitis
    - Glaucoma filtering surgery
  - Spill over
    - Episcleritis/scleritis/keratitis



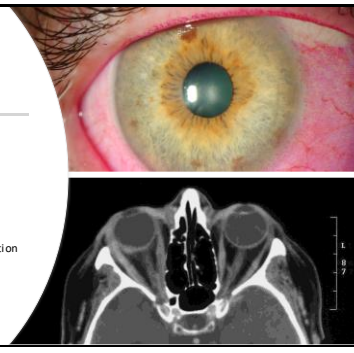
Panophthalmitis, Houston Methodist

Posterior uveitis

- Intermediate uveitis (pars planitis)
- Vitritis
- Retinitis
- Choroiditis
- Retinal vasculitis
  - Arterial
  - Venous
- Endophthalmitis
- Panophthalmitis

Eye pain

- Onset: acute, subacute, recurrent
- Potential trauma: Metal on metal/stone
- Contact lens use
- Quality of pain
  - Burning: dry eye
  - Itching: allergy
  - Irritation: meibomian gland dysfunction
  - Boring pain: scleritis
  - Photophobia: uveitis
- Severity
- Associations: headache or facial pain



Eye pain with headache: neurology or otolaryngology

Trigeminal pain:
- Cluster headache, paroxysmal hemicrania, SUNCT, hemicrania continua

Referred pain
- Migraine
- Tension headache
- Sinusitis

https://medlineplus.gov/ency/images/ency/fullsize/19224.jpg

Eye pain with adnexal disease

- Herpes Zoster Ophthalmicus
- Sinus disease
- Orbital inflammation
  - Dacrocystitis: nasolacrimal sac
  - Dacroadenitis: lacrimal gland
  - Orbital myositis: muscle
  - Idiopathic orbital pseudotumor
  - Inflammatory and infectious (IGG4, sarcoidosis)

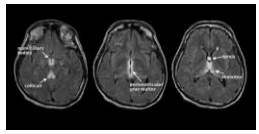
- Thyroid eye disease

Double vision

Evaluation
- Monocular vs. Binocular diplopia
- Vertical or horizontal

DDX: is it isolated
- Cranial neuropathy
- Skew- inpatient neurology
- Wernicke- other Sx
  - 2 of 3: eye, cerebellar, cognitive

Acute on chronic
- Decompensated phoria
- Convergence/divergence insufficiency



https://arcr.niaaa.nih.gov/sites/default/files/202012/article07-02_0.png

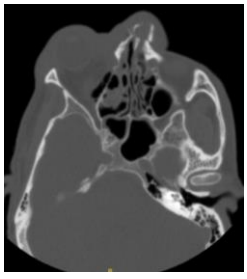
Case: 47 year-old male s/p aggravated assault

- Mace, fists, kicked x 2
  - 10/10 pain
- Va: 20/125 OD, 20/30 OS
- External: proptosis, ecchymosis, brow laceration
- Motility: diffuse decrease OD
- Ta: 23 mm Hg OD, 10 OS
- SLE: subconjunctival hemorrhage, 60% corneal abrasion
- Fundus: commotio retinae OD

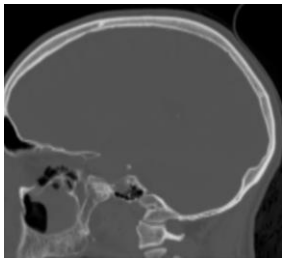
- Visual fields: full OU
- Pupils: symmetrical, no APD

CT Head, maxillofacial

- Nasal fractures
  - Lateral deviation nasal bridge
  - Displaced fracture nasal septum
  - Fracture lamina papyracea
- Right orbit
  - Medial and inferior floor blowout fracture
  - Small extraconal hematoma
  - Orbital emphysema
- Hemorrhage right maxillary sinus

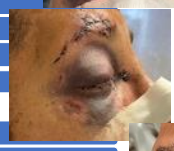


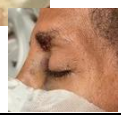
Case and images from Houston Methodist Hospital



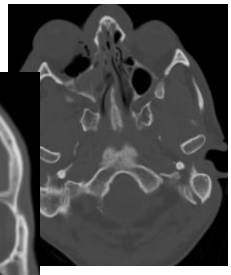
Instructed: no nose blowing
But… he forgot

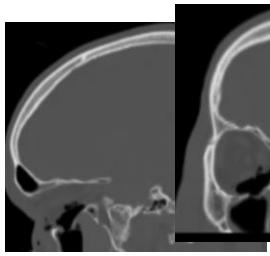
- Increased pain 8 ➡ 10/10
- Decreased vision: 20/400 OD
- External: increased proptosis OD
- Pupils: minimally reactive (narcotics)
  - Red saturation decreased OD 40% /100 %OS
  - Light saturation = OU
- Motility: -2 horizontal, -3 vertical OD, diplopia
- CVF: centrally subjectively worse
- Ttono: 9 OD/12 OS mm Hg





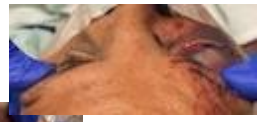
Repeat CT Head





Oculoplastics consult

- Increased pain, decreased motility, vision, red saturation
- Decision: needle decompression
  - 23G short Atkinson retrobulbar needle
  - 3-5 cc syringe, **no plunger, with saline**

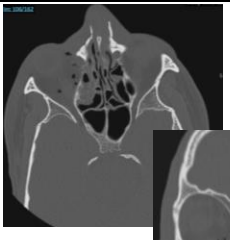


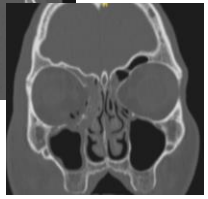
Post procedure: immediate improvement

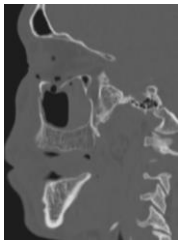
- Proptosis
- Pain
- Diplopia
- Visual field

- CT decreased pneumo-orbit

Post decompression CT







Overview of ophthalmic emergencies

- Identify emergent vs urgent presentations
  - Elicit triage history to guide you
- Name 5 true ophthalmic emergencies
- Describe 5 presentations of ophthalmic urgencies

Thank you for your time and attention

Courtesy of Culver Boldt, MD

Five meds that could blind you: (the Lee med HATE list)

- Andrew G. Lee, MD
- Professor of Ophthalmology, Neurology, & Neurosurgery, Weill Cornell Medical College
- Chair, The Methodist Hospital (Houston, TX)

Methodist | University of Iowa Health Care | UTMB The University of Texas Medical Branch | Texas A&M Health Science Center College of Medicine | Cornell University Joan and Sanford I. Weill Medical College | BCM Baylor College of Medicine | The University of Texas MD Anderson Cancer Center Making Cancer History®

Why are we here?....

I care about feedback….

- Yes, fill out your evaluations
- Yes, say how great it was
- But I care more about you and your patients….
- Stop me at AAO & tell me how you saved someone by using the Force (Neuro-OP)
- That's powerful feedback

Financial disclosure

- I have no proprietary interest in any of the content of this presentation

- I also have no personal experience with the pharmaceutical agents described (…not that there is anything wrong with that)

Objectives: Meds that I H.A.T.E. in neuro-op clinic

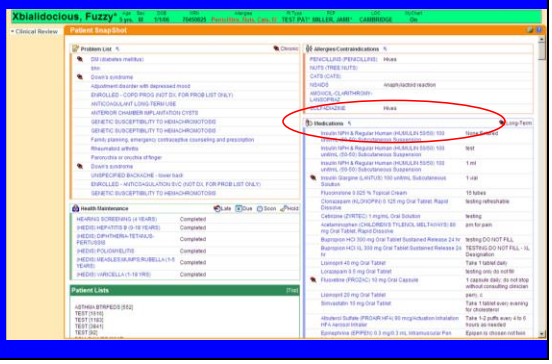
1. Hydroxychloroquine/chloroquine retinopathy
2. Amiodarone optic neuropathy: Anterior ischemic optic neuropathy
3. Tetracycline: pseudotumor cerebri
4. Ethambutol optic neuropathy

The Erectile dysfunction agents (Viagra): Anterior ischemic optic neuropathy

Inappropriate medication lists….

- "See list
- "Some type of lung medicine"
- "heart medicine"
- "Some kind of antibiotic"

Our frenemy the EMR



Why is toxicity dangerous?

- The prescribing physician sometimes does not warn the patient appropriately
- The screening eye doctor sometimes does not know that they are supposed to be screening
- Eye doctors are asking less & less about medicines
- The risk factors for toxicity are not a typical part of the eye history
- The fundus findings of toxicity often occur in the ends stage when it is too late

A big problem

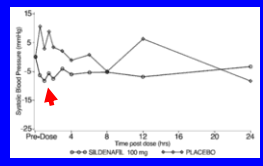
- "One of the top five reasons ophthalmologists go to court is from an adverse drug reaction"
- "If the Academy is taking a position on Plaquenil then ophthalmologists are held to that standard. We'd better be aware of it."
- F.W. Fraunfelder MD (EyeNet May 2011)

What's in a name?

- Hydroxychloroquine = Plaquenil
- Amiodarone = Corderone, Pacerone
- Tetracycline = somet type of acne medicine
- Ethambutol = Myambutol
- Erectile dysfunction agents (Viagra = sildenifil but also consider Levitra, Cialis)
- It is harder and harder to keep up with the names of new medicines

Viagra
Biologically plausible mechanism: SBP drop 5-10 mm Hg at 2-4 hours after dose

- Non-arteritic AION
  - Hypotension
  - Hypoperfusion
- ED agents
  - Hypotension
  - Sympathomimetics
- My take: There is a weak but biologically plausible mechanism for NAION in ED agents

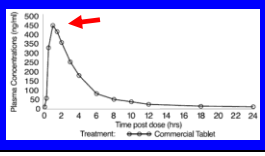


Mechanism: Exclude chance alone

- 43 cases NAION in FDA database
- ED agents used in vasculopathic males
- Risk factors for impotence (DM, cardiac)
- 1 billion doses given
- 23 million prescriptions
- 13,000 males in preclinical testing: No NAION cases

Temporal relationship

- Coherent with pharmacokinetics, half-life, or peak onset of drug (e.g., peak/trough)
- ED taken at night
  - Nocturnal hypotension presumed cause NAION
  - Many cases not within ½ life (peak 2-4 hours)
- My take: Weak temporal relationship



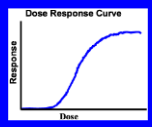
Analogy from animal or human

- No evidence for AION or testing in animals
- 43 cases (known) in FDA database
- Case-control data weak
- Uniformity in cases lacking
- My take: Weak analogy from existing reports, no animal model

Coherence with current knowledge ("class effect")

- Toxic optic neuropathy looks different
  - Bilateral
  - Biologic gradient (dose response)
  - Papillomacular bundle
  - Central/cecocentral scotoma
  - Retrobulbar optic neuropathy
- Analogy: Amiodarone optic neuropathy
- My take: Weakly coherent for toxic optic neuropathy

Dose responsiveness

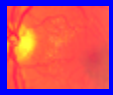


- Increased dose = increased toxicity
- Examples
  - Ethambutol (15 mg/kg < 25 mg/kg) toxicity
  - Hydroxychloroquine/chloroquine retinopathy
- Pharmacokinetics
  - e.g., Renal disease increases toxicity if renal excretion
  - Liver disease increases toxicity if hepatic metabolism
  - Weight (mg/kg dose), obese vs. lean body weight
- My take: There is little dose effect seen in cases

Effect specificity (r/o chance)

- The more specific the effect, the more likely the cause is due to the effect
- Reduced likelihood of alternate etiologies
- Examples: Stevens Johnson syndrome
  - Amiodarone corneal vortex keratopathy
  - Hydroxychloroquine bull's eye maculopathy
  - Tamoxifen crystalline retinopathy
- My take: NAION is not a very specific effect for toxicity



Recovery/rechallenge

- Rechallenge cases exist
  - One case (tadalafil)
- Recovery not reported
- Examples
  - Stevens-Johnson syndrome rechallenge
  - Recovery of vision after stopping HCQ

Case-control study

- Vaphiades M & McGwin G.
- 38 cases NAION & 38 age matched controls
- Males with NAION were not more likely to report Viagra or Cialis use than controls
- NANOS Annual Meeting, Tuscon AZ Feb 25, 2006.

Retraction Watch

Tracking retra process

Retractile dysfunction? Author says journal yanked paper linking Viagra, Cialis to vision problem after legal threats

with one comment

The *British Journal of Ophthalmology* has retracted a 2006 paper which purported to show a link between drugs for erectile dysfunction and a rare form of sudden vision loss called non-arteritic anterior ischaemic optic neuropathy, more commonly known as "Viagra blindness."

That wouldn't be terribly interesting, except for this: One of the authors of the paper, a researcher at the University of Alabama named Gerald McGwin Jr., told us that the journal retracted the article because it had become a tool in a lawsuit involving Pfizer, which makes Viagra, and, presumably, men who'd developed blindness after taking the drug.

> The article just became too much of a pain in the rear end. It became one of those things where we couldn't provide all the relevant documentation [to the university, which had to provide records for attorneys]

Ultimately, however, McGwin said that the *BJO* pulled the plug on the paper.

> It was really the journal's decision to take it out of the literature.

NAION & phosphodiesterase type 5 inhibitors (sildenafil)

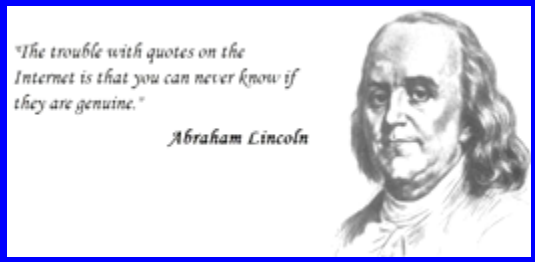
- J Sexual Medicine 2015;12:139-51
- 103 centers (US and Europe)
- 43 definite NAION cases with PDE5i exposure in prior 30 days (five half lives)
- **OR = 2.15** (95% CI: 1.06, 4.34
- Possible NAION cases included (n = 64) OR = 2.36 (95% CI: 1.33, 4.19

Viagra: My take on causality

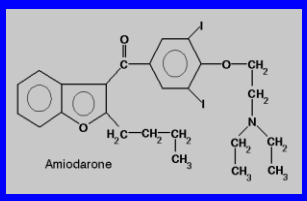
- Biologic mechanism: Weakly plausible
- Temporal relationship: Weak (variable)
- Analogy: Few
- Coherence: Weak
- Dose responsiveness: None
- Effect specificity: Not specific
- Rechallenge: Rare
- Recovery (dechallenge): None

Bottom line: Someone needs to tell the patient….

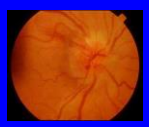
What will happen if you don't tell them about ED agents & NAION….



Amiodarone:
A medical or medico-legal problem?



amiodarone
Lawyer



Largest lawsuit in ophthalmology

- $22.8-million judgment against Wyeth-Ayerst Pharmaceuticals (Philadelphia, PA) in 1997 for amiodarone
- Labeling changed to emphasize the possible occurrence of amiodarone-associated ON
- Shifted pharmaceutical product liability issue to a malpractice problem

Deseret News

Court allows $20M in punitive damages to man blinded by heart medicine

JUSTIA US Law

Search

Nelson v. American Home Products Corp., 92 F. Supp. 2d 954 (W.D. Mo. 2000)

U.S. District Court for the Western District of Missouri - 92 F. Supp. 2d 954 (W.D. Mo. 2000)
March 24, 2000

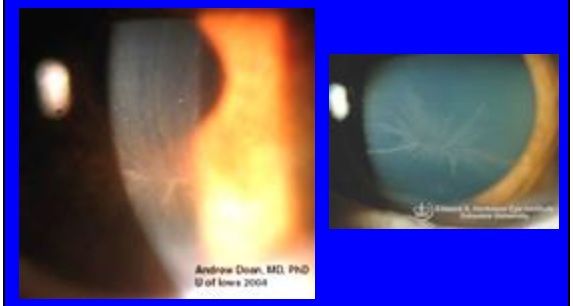
92 F. Supp. 2d 954 (2000)

Roger G. NELSON, and Lou Nelson Plaintiffs,
v.
AMERICAN HOME PRODUCTS CORPORATION, and Wyeth-Ayerst Laboratories Company, Defendants.

Amiodarone keratopathy: A causal relationship (Austin Bradford Hill criteria)

- Temporally associated with drug onset
- Analogy: seen in majority of patients on drug
- Dose-dependent effect
- Specific corneal appearance
- Can't be attributed to alternative etiologies
- Coherence: Pathologic drug deposition in epithelium
- Dechallenge: Typically resolves after discontinuation but do not discontinue drug for keratopathy (benign)

Amiodarone keratopathy: Dose responsive, specific finding, challenge data supported



How about amiodarone optic neuropathy?

- Macaluso et al
  - 73 optic neuropathy patients on amiodarone
  - Insidious onset, slow progression
  - Bilateral & protracted disc swelling
  - Resolved within several months after discontinuing
- Nagra et al
  - Three patients
  - Loss of visual acuity & visual field
  - Bilateral disc swelling slowly improved after discontinuation

Amiodarone optic neuropathy

- Amiodarone saves lives (stopping drug may kill people)
- Not dose-dependent phenomenon
- Seen in minority of patients on drug
- No proven pathogenic mechanism
- Can look just like non-arteritic anterior ischemic optic neuropathy
- Patients with other vasculopathic risk factors
- May not resolve after discontinuation of drug

Randomized prospective double masked trial showed no AION

- Mindel et al. Am Heart J. 2007;153(5):837-842
- Amiodarone (n = 837) vs placebo (n = 832)
- Median follow-up 45.5 months
- End point = bilateral vision loss
- No subject was removed from study because of bilateral vision loss
- Conclusion: Bilateral vision loss from amiodarone toxic optic neuropathy occurs infrequently if at all

What to tell the patient

- There is a risk of amiodarone optic neuropathy
- The risk factors for taking amiodarone overlap with the vasculopathic risk factors for NAION
- I will call your cardiologist about your medicine
- You need to make a risk benefit decision with cardiology

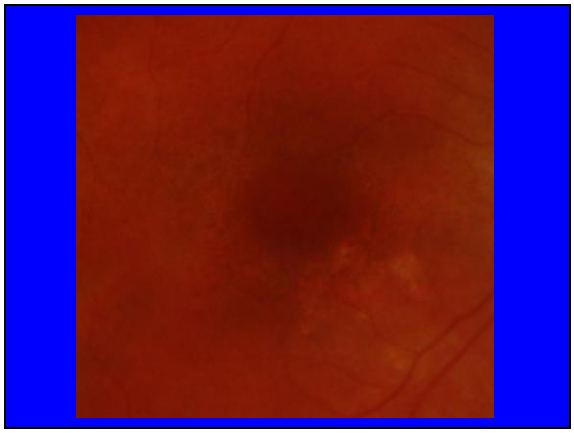
55 yo thin WF with SLE on hydroxychloroquine (HCQ)

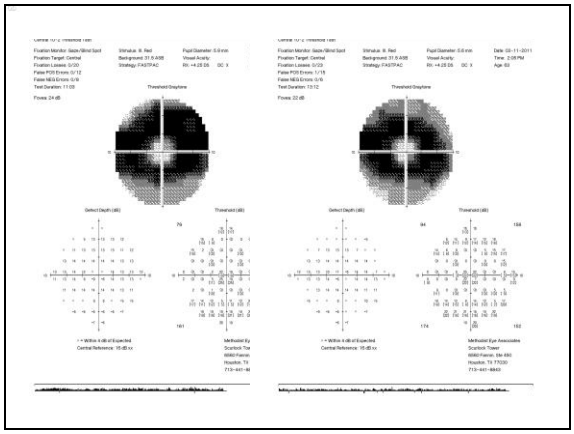
- 20 years of HCQ (Plaquenil)
- 2.5 mg/kg
- 2.688 kg cumulative dose
- No renal or liver disease
- No prior maculopathy

How much is a kilogram?

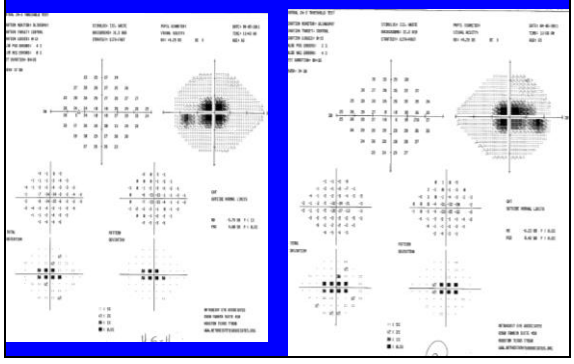
Hydroxychloroquine toxicity

- Toxicity mechanism poorly understood
- Ring-shaped perifoveal zone spares central 2-3 degrees & extends out to 10 degrees
- "Bull's eye" halo around the fovea
- Bilateral & often irreversible
- May progress even after drug discontinued

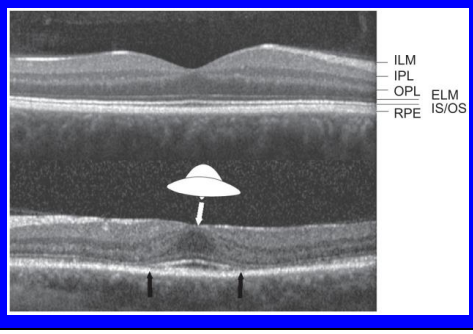


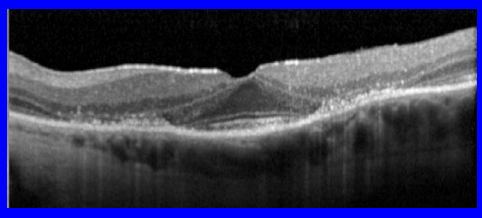


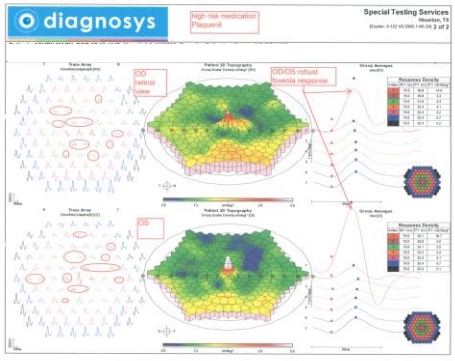
HVF 24-2 (especially Asians)

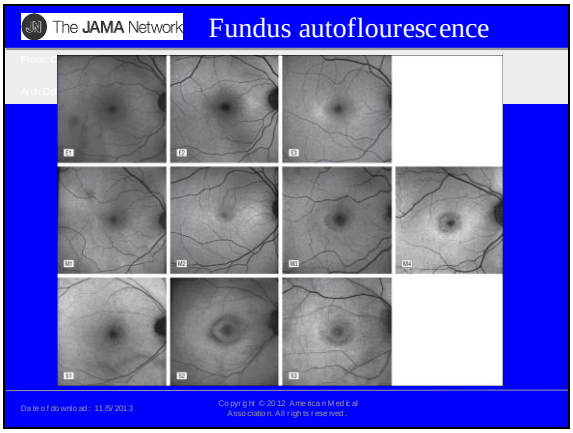


HCQ (Plaquenil) screening SD OCT

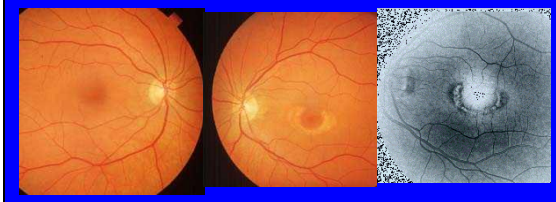






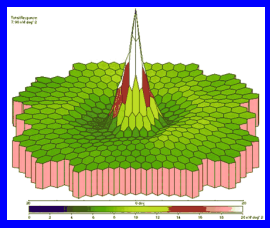


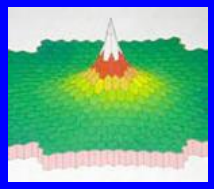
Chloroquine is worse!
Bull's eye maculopathy



http://www.uwo.ca/ophthalmol/GR/98-99/unknowndate.htm

MERG may be more sensitive





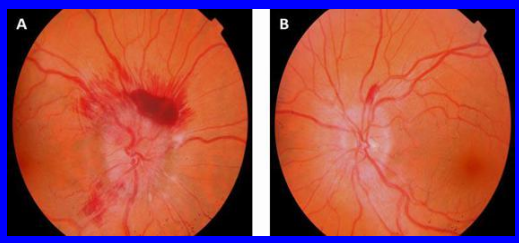
Criteria	Low risk	Higher risk
Dosage	< 6.5 mg/kg 5 mg/kg	➢6.5 mg/kg ➢total 1 kg
Duration	< 5 years	> 5 years
Habitus	Lean/average fat	High fat level
Renal/liver disease	Absent	Present
Concomitant retinal disease	Absent	Present
Age	< 60 years	> 60 years

Some recommendations

Marmor et al. Ophtahlmol 2011: 118:415-422.

- MERG, SD-OCT, FAF more sensitive than VF
- 10-2 HVF + one of the above
- If 10-2 HVF abnormal then complaints "should be taken seriously" (Asians 24-2)
- MERG may be "used in place of VF"
- Amsler grid no longer recommended
- Beware Tamoxifen

A 15 y/o thin, male with HA, blurred vision OU and….



Which of the following medications can cause this finding?

Accutane (vitamin A analog) & tetracycline

- Pseudotumor Cerebri warning
- "Accutane use has been associated with a number of cases of pseudotumor cerebri" Some cases involved concomitant use of tetracyclines
- Concomitant treatment with tetracyclines should therefore be avoided "

Ethambutol toxicity

1. Painless, progressive, bilateral visual acuity loss
2. Proven causality, dose related optic neuropathy
3. Color loss (e.g. blue-yellow dyschromatopsia)
4. Central or cecocentral scotomas
5. Initially normal optic nerve (retrobulbar) followed by temporal optic disc pallor OU

Ethambutol screening

- Screen high risk patients (high dose > 15 mg/kg/day, renal failure, long duration): Follow q month (longer for low risk)
- Warn patients about toxicity
- Baseline exam & visual field
  - Color testing
  - Dilated fundus exam
  - Automated 24-2 or 10-2/Amsler (self check)
  - If any change come in right away

Homeland security risk stratification for ethambutol toxicity: Dose! Dose! Dose!

Do not confuse the screening strategies

- "Imp: No evidence of EMB toxicity
- Plan: 1 year"
- This is NOT the correct screening strategy
- PS: Weight loss will change dose (s/p lung transplant or MAI or TB patients lose weight over time unintentionally)

(e) During medical consultations in the course of anti-TB treatment including EMB, all patients should be assessed clinically for symptoms of visual disturbance. Enquiring monthly about visual symptoms is advisable.

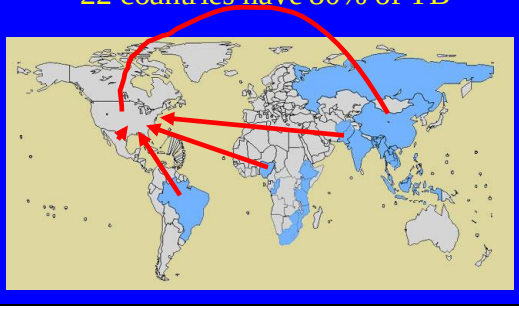
(f) Directly observed treatment (DOT), apart from ensuring treatment adherence, also allows health care workers to monitor the patients closely for such symptoms.

Table 2. British Thoracic Society Guidelines - Chemotherapy and management of tuberculosis in the United Kingdom: recommendations 1998*.

Special precautions and pretreatment screening point (1)

Because of the possible (but rare) toxic effects of ethambutol on the eye, it is recommended that visual acuity should be tested by Snellen chart before it is first prescribed. The drug should only be used in patients who have reasonable visual acuity and who are able to appreciate and report visual symptoms or changes in vision. The notes should record that the patient has been told to stop the drug immediately if such symptoms occur, and to report to the physician. The general

You are going to see more ethambutol toxicity 22 countries have 80% of TB



Scary math: 100,000 blind

J Neuroophthalmol. 2008 Dec;28(4):265-8. doi: 10.1097/WNO.0b013e31818f138f.

Ethambutol optic neuropathy: how we can prevent 100,000 new cases of blindness each year.

Sadun AA, Wang MY.

Objectives: Meds that I H.A.T.E.

1. **H**ydroxychloroquine/chloroquine retinopathy
2. **A**miodarone optic neuropathy: Anterior ischemic optic neuropathy
3. **T**etracycline: pseudotumor cerebri
4. **E**thambutol optic neuropathy

PS: The Erectile dysfunction agents (Viagra): Anterior ischemic optic neuropathy

Thanks for your attention

Thanks for your attention

Methodist

BCM
Baylor College of Medicine

UTMB
The University of Texas Medical Branch

CORNELL UNIVERSITY Joan and Sanford I. Weill Medical College

The University of Iowa Health Care