Complex Cases Potpourri

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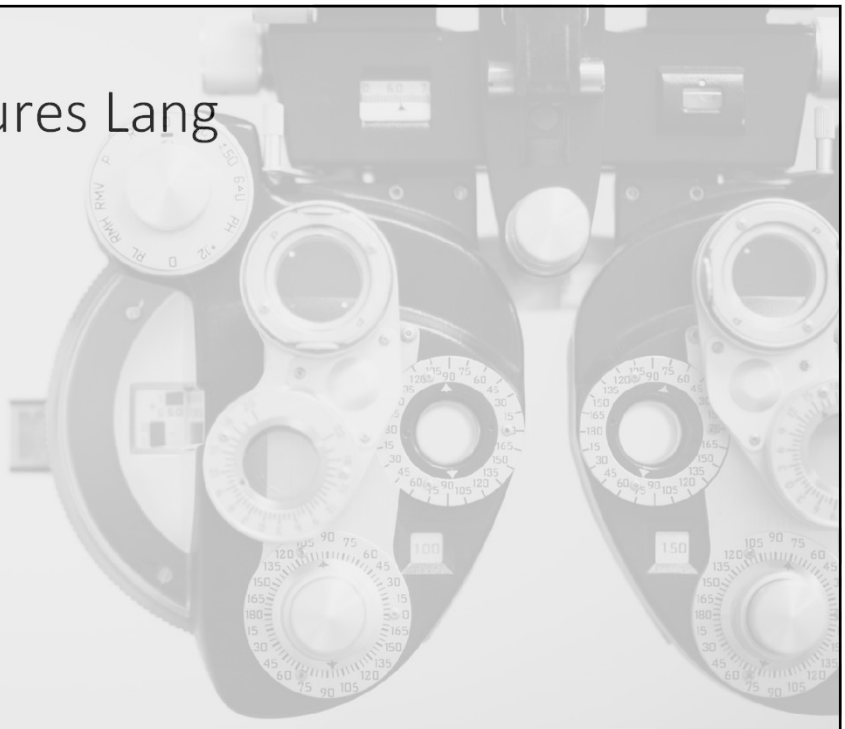
Intrepid

Dry Eye CONSULTANTS

Financial Disclosures Lang

- Allergan
- Avellino
- Aldeyra
- Dompe'
- Kala
- Novartis
- AOS
- Scope
- Sun Pharma
- Tarsus
- Quidel
- Horizon
- Aerie
- Ocular Theraputix
- Orasis
- Oyster Point



Case

12yo Male

Rx shift and decreased BCVA OS

MRx 2019

Pl	20/20
Pl -0.50 x120	20/20

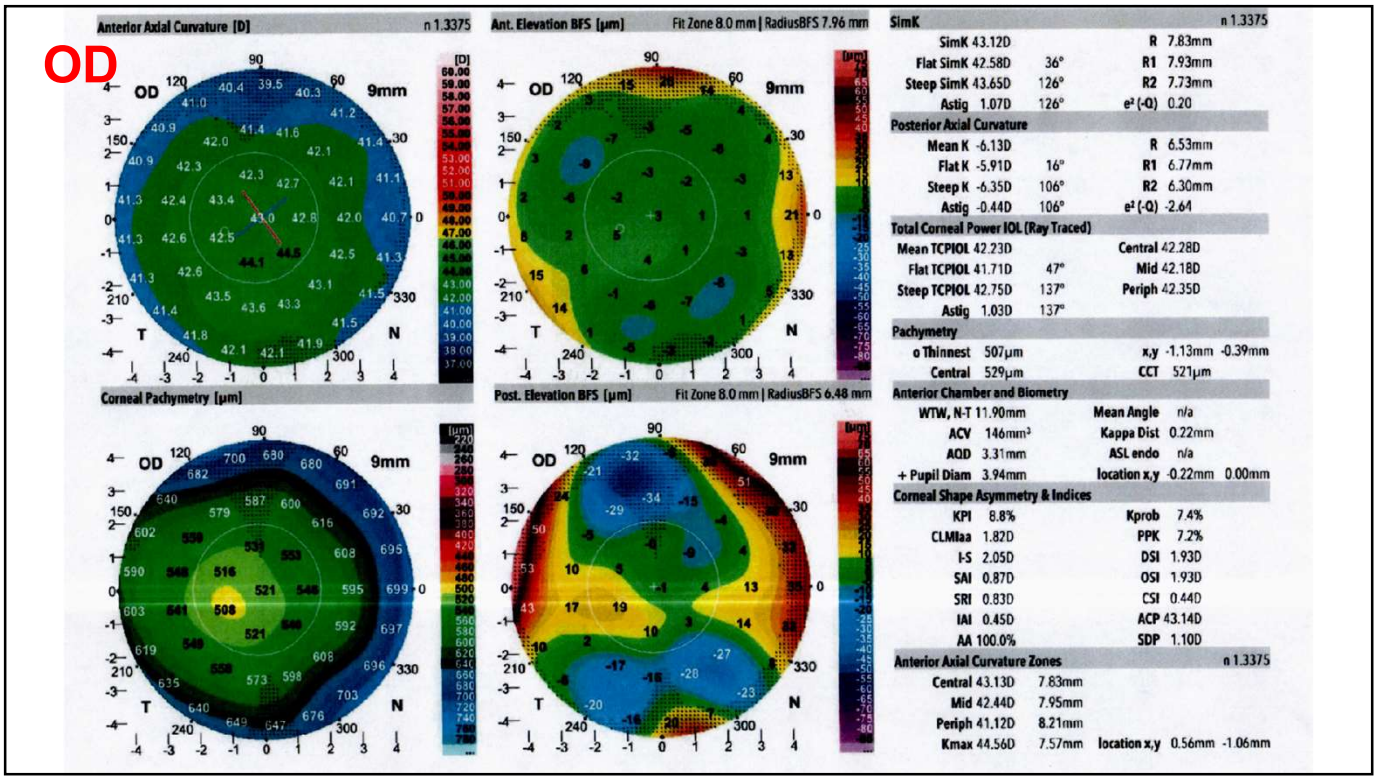
MRx 2021

Pl-0.50x180	20/20
Pl-1.25x 130	20/30

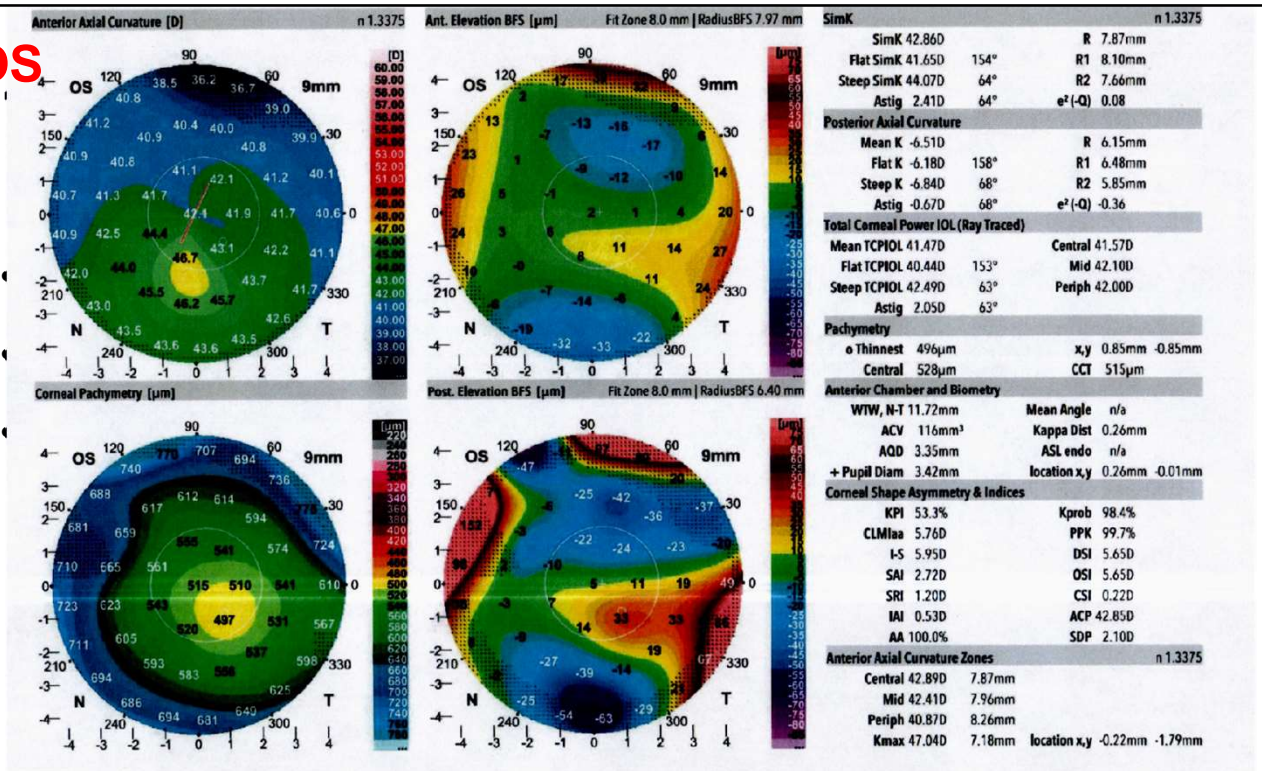
K's 2021

42.58/43.65

41.65/44.07



OS



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Cross Linking on 12 yo Male

OD

OS

OU

Close Observation

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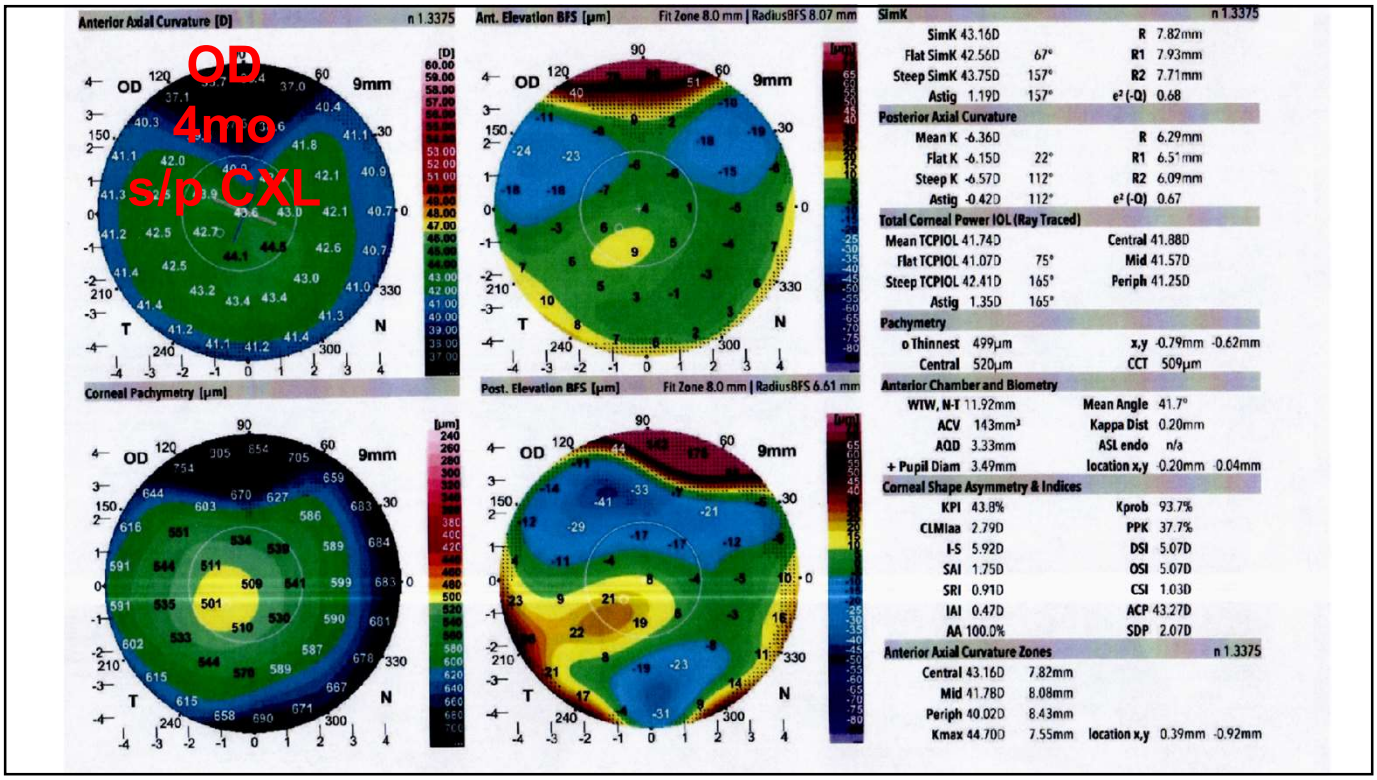
Posterior Stroma

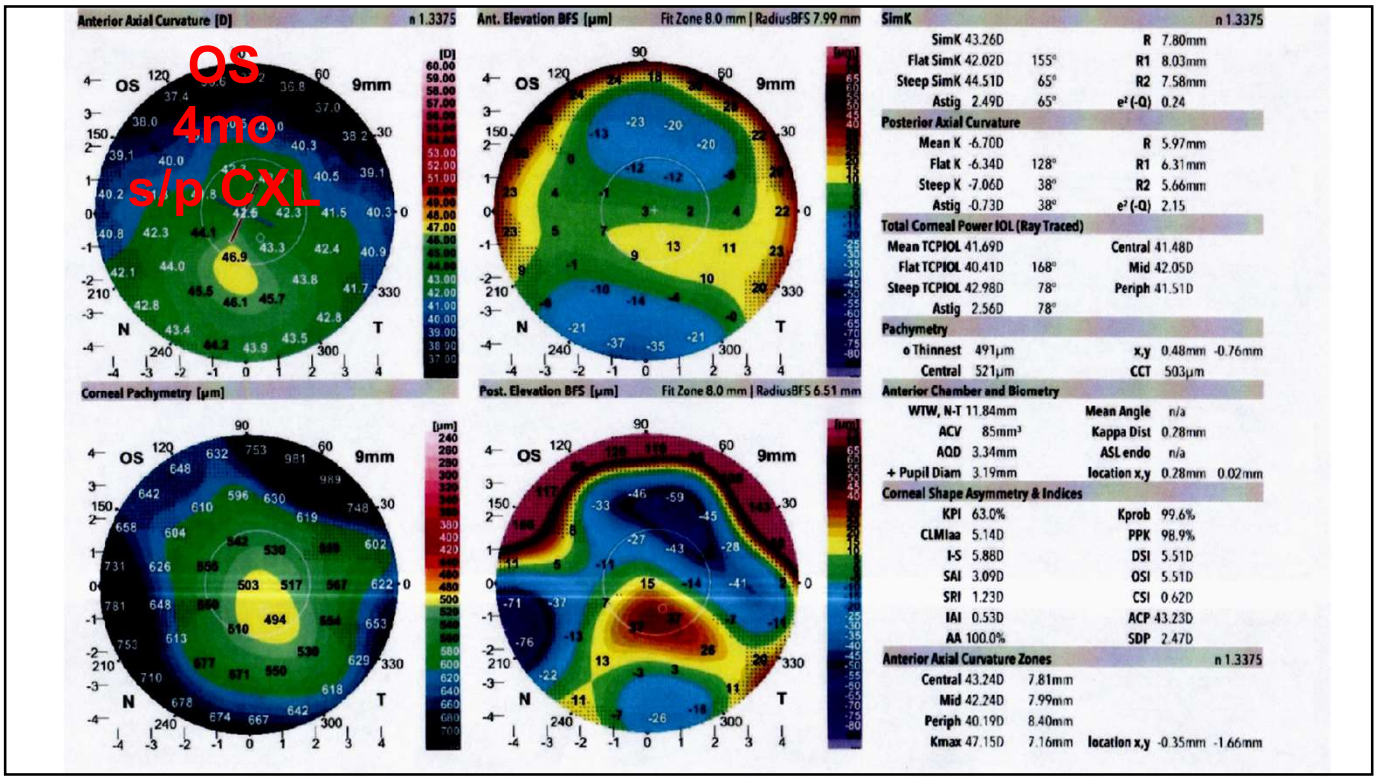
12yo Male

Now What?
- CXL?

- Treat OD too?
  - Monocular KCN?

- Other Therapies or Options





Posterior Stroma

Patient has an identical twin…

Posterior Stroma

Genetic Risk
Keratoconus and Genetics

Patient

FINAL RESULTS

CONDITION TESTED	RESULT	DETAIL	EXPLANATION
Keratoconus (KC)	High genetic risk	67 polygenic risk score	Tested for variants within 75 genes found to be associated with keratoconus.
TGFBI Corneal Dystrophies (CD)	Negative for TGFBI Corneal Dystrophies	No pathogenic variants detected	Tested Negative for 70 known variants associated with TGFBI corneal dystrophies.

This AvaGen Genetic Test result should be considered with other clinical criteria, the patient's family history and communicated in a setting that includes appropriate genetic counseling

Keratoconus (KC) Risk Assessment

Based on the polygenic risk score of 67, this patient's risk for KC is High.

THE POLYGENIC KC RISK SCORE: The AvaGen Genetic Eye Test provides a polygenic risk score for individuals tested for their genetic risk for KC. The risk score is the cumulative sum of individual risk contributed by several independent SNPs that were identified in our genetic association study by screening thousands of variants in 75 genes related to corneal structure and function. KC is a complex genetic disease that involves genetic and environmental components as well as their interactions that contribute to the development of the disease. Genetics is an important contributor in KC risk, but it is not the only contributing factor that determines risk for KC.

Twin

FINAL RESULTS

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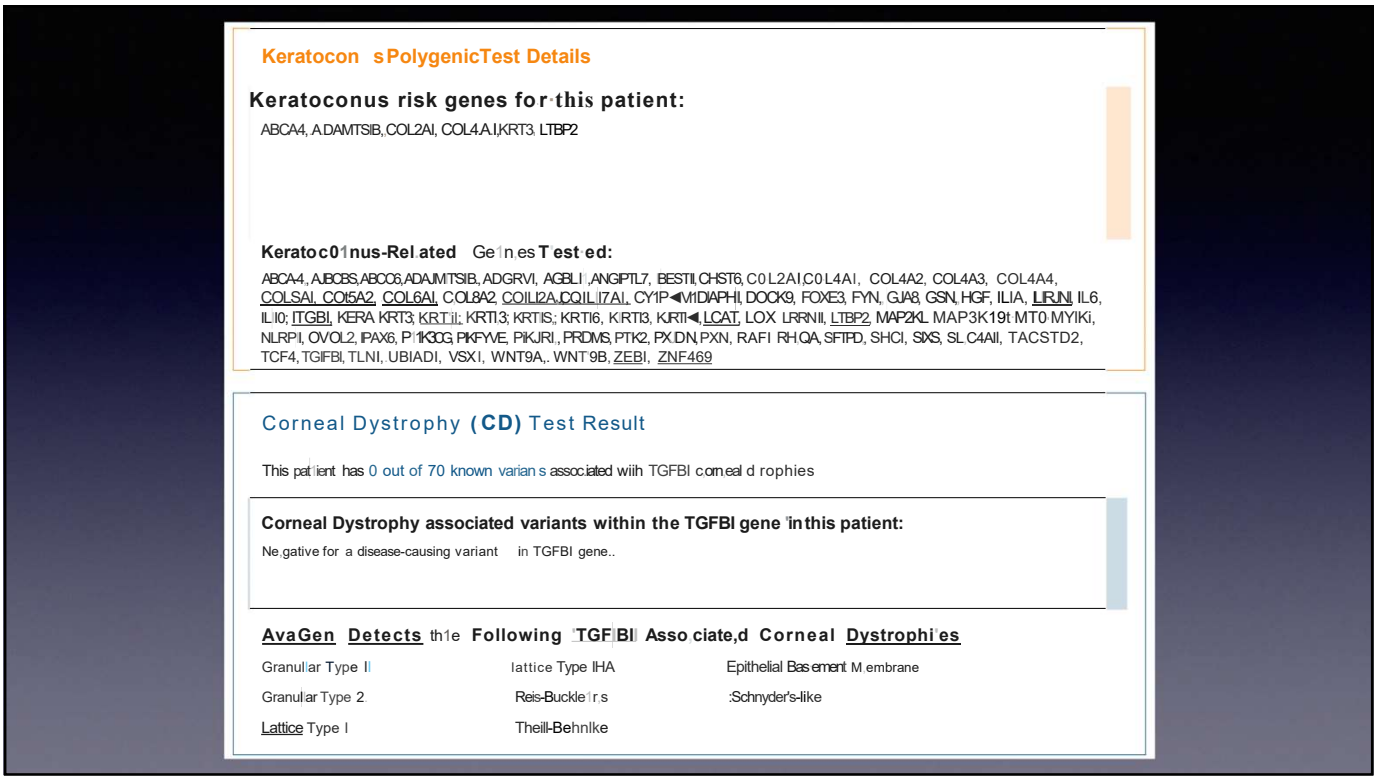
They ARE Identical Twins!



Keratocon sPolygenicTest Details

Keratoconus risk genes for this patient:

ABCA4, ADAMTSIB, COL2AI, COL4A1, KRT3, LTBP2

Keratoc01nus-Rel ated Ge In es T est ed:

ABCA4, AJBCBS, ABCC6, ADAJMTSIB, ADGRVI, AGBLI , ANGPTL7, BESTI, CHST6, C0L2AI, C0L4AI, COL4A2, COL4A3, COL4A4, COLSAI, COt5A2, COL6AI, COL8A2, COILI2A, CQILI7AI, CY1P◀VtDIAPHI, DOCK9, FOXE3, FYN, GJA8, GSN, HGF, ILIA, LIRJNI, IL6, ILI0; ITGBI, KERA KRT3; KRTiL; KRTI3; KRTIS,; KRTI6, KRTI3, KJRTI◀, LCAT, LOX LRRNII, LTBP2, MAP2KL MAP3K19t MT0 MYIKi, NLRPI, OVOL2, IPAX6, P 1K3CG, PIKFYVE, PIKJRI , PRDMS, PTK2, PX DN, PXN, RAFI RHQA, SFTPD, SHCI, SIXS, SL C4AII, TACSTD2, TCF4, TGIFBI, TLNI, UBIADI, VSX I, WNT9A,. WNT 9B, ZEBI, ZNF469

Corneal Dystrophy **(CD)** Test Result

This pat ient has 0 out of 70 known varian s assoc iated wiih TGFBI corn eal d rophies

Corneal Dystrophy associated variants within the TGFBI gene in this patient:

Ne gative for a disease-causing variant in TGFBI gene..

AvaGen Detects th1e **Following TGFBI Asso ciate,d Corneal Dystrophi es**

Granul ar Type II	lattice Type IHA	Epithelial Bas ement M embrane
Granul ar Type 2	Reis-Buckle r s	:Schnyder's-like
Lattice Type I	Theill-Behnlke	

Posterior Stroma

Now What?

CXL for Twin?

Nature vs Nurture?

Behaviors, Habits?

Preventative Care for KCN?

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What Would YOU Do?

Treat Both Eyes, and Twin

Treat ONE eye, and NOT Twin

Treat Both Eyes, and NOT Twin

Treat ONE eye and Twin

None of the above

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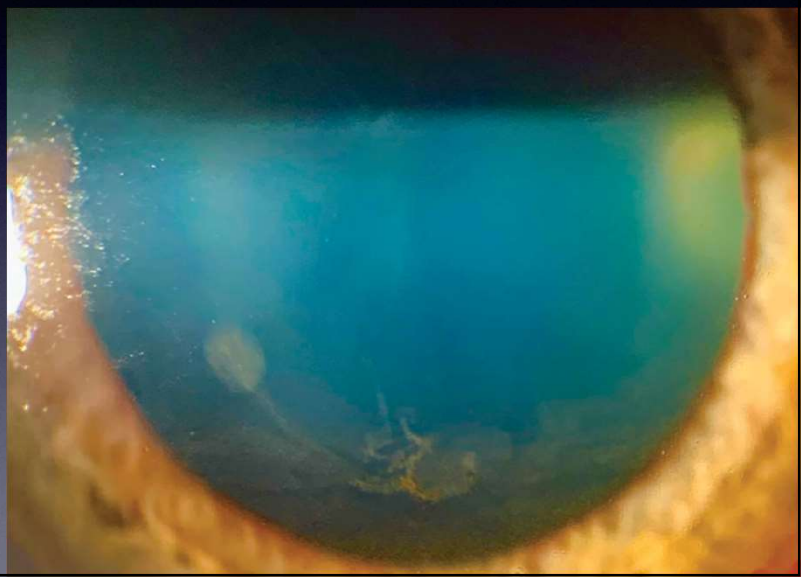
CASE

- 50YO M
- No CC



Verticillata

- There are a multitude of differentials with regard to the corneal finding known as verticillate or whorl epitheliopathy .
- The standard acronym is CHAI-T+F
  - (Chloroquine, Hydroxychloroquine, Amiodarone, Indomethacin, Tamoxifen, Fabry disease).

Verticillata

- Corneal verticillata can appear for a host of reasons, including signs of serious underlying metabolic disease, such as Fabry disease and cystinosis.
- It can also occur as a side effect of certain medications, amiodarone being the most common.

Verticillata

- It is pertinent for eye care providers to consider glaucoma medications, specifically ROCK inhibitors, when investigating the source of this clinical finding.
- ROCK inhibitors (Rho-Kinase) might play an increasingly bigger role in eye care as we continue to harness their effect on the corneal endothelium and epithelium. Maybe our upcoming board preparatory classes should serve their CHAI-T (+F) on the “rocks”?

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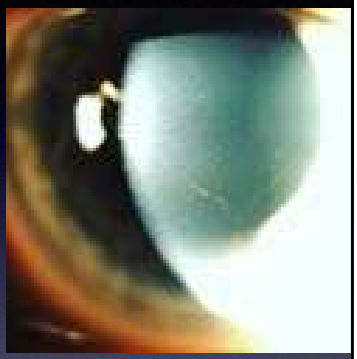
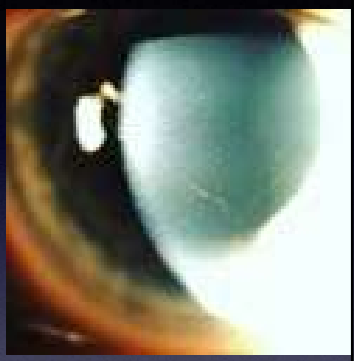
Fabry's Disease



Fabry's Disease

- Fabry disease is a lysosomal storage diseases.
- The function of an enzyme that processes biomolecules known as sphingolipids, leading to these substances building up in the walls of blood vessels and other organs.
- It is inherited in an X-linked manner.
- Blood test that measures the activity of the affected enzyme called alpha-galactosidase
- Genetic testing is also sometimes used, particularly in females

Fabry's



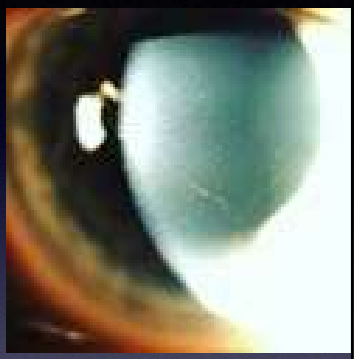
Fabry's Disease; Non-ocular Manifestations

- Neuropathic pain,
- Dermatologic manifestations such as telangiectasias and angiokeratomas,
- Renal failure,
- Strokes,
- Deafness.
- Neuropathic pain is a common association, with typical onset in childhood.
- Patients frequently do not live beyond the fourth or fifth decade of life.

WHICH Systemic Condition?

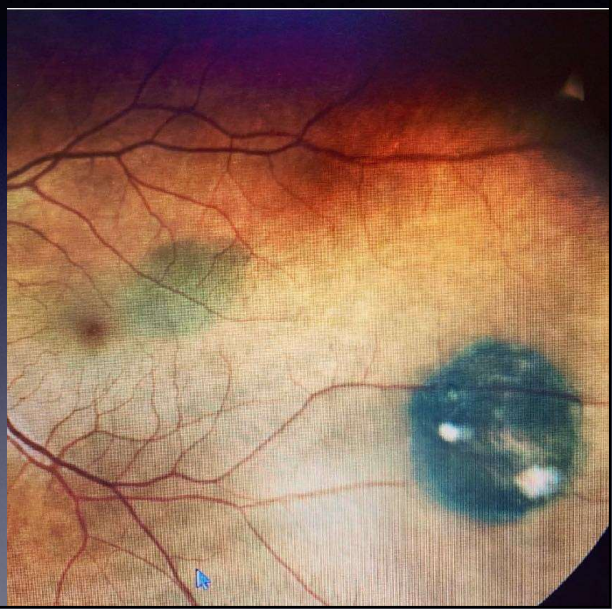
Fabry's Disease

The treatment for Fabry disease varies depending on the organs affected by the condition, and the underlying cause can be addressed by replacing the enzyme that is lacking.



Case V1.0

- 46 yo F
- No CC

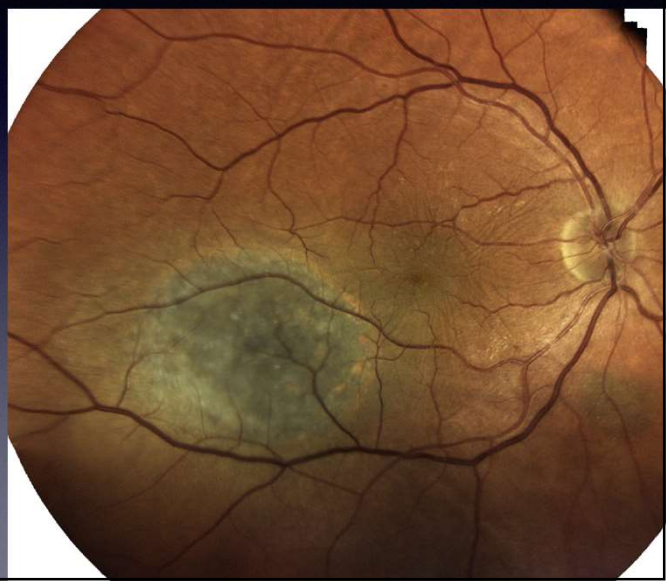


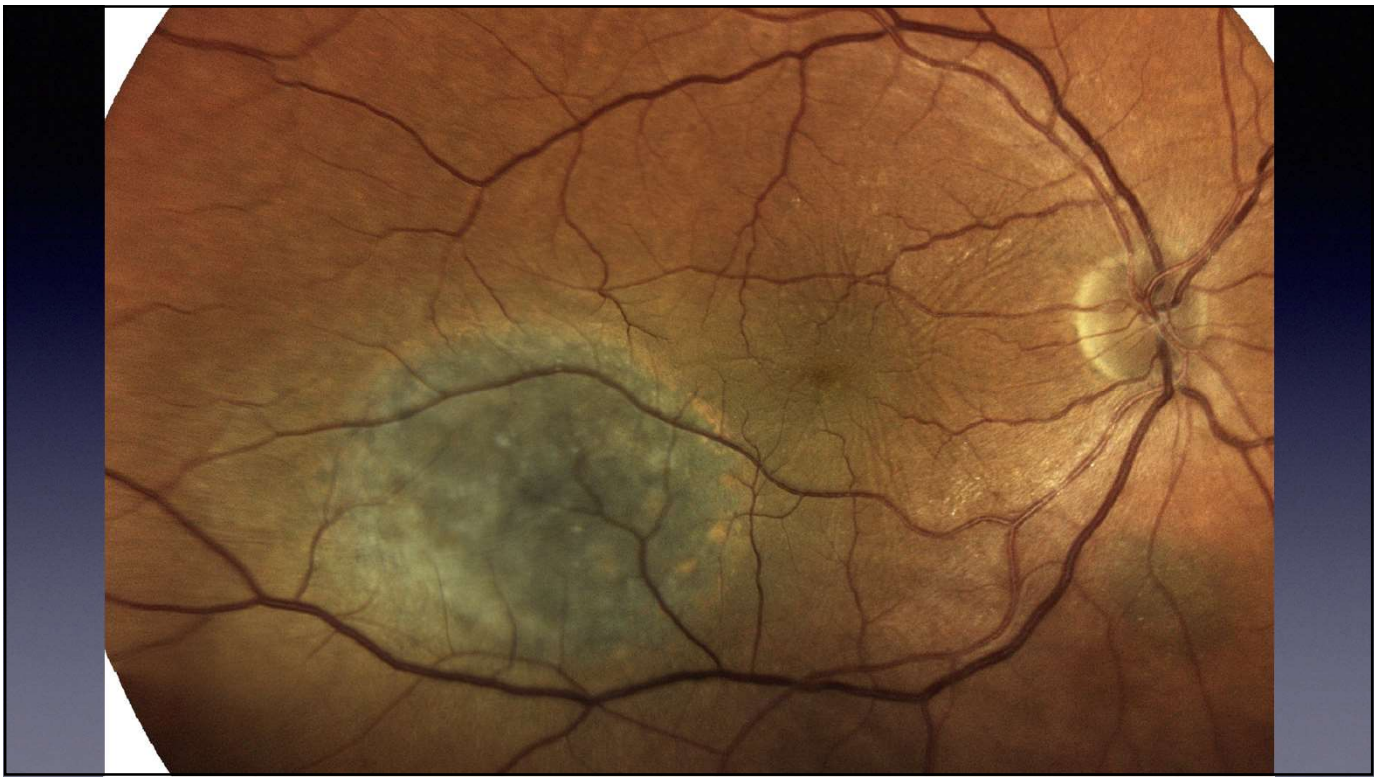
Case V1.5

- 63 yo M
- Blurry VA, “Cataract” OD

Case V1.5

- 63 yo M
- Back from Hilton Head
- Blurry VA, “Cataract” OD
- 20/80 BCVA





Choroidal Melanoma

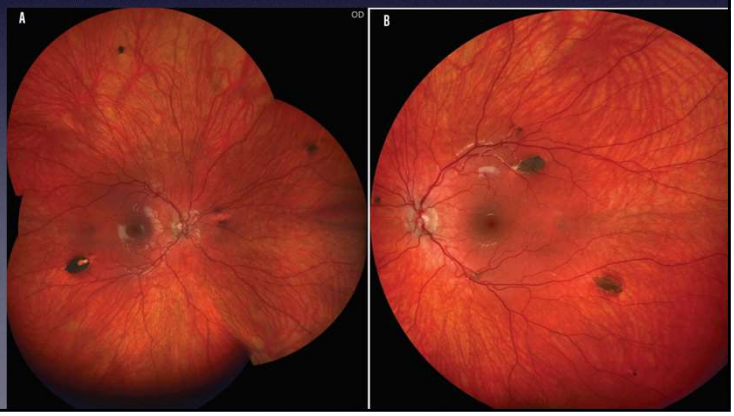
- Choroidal Melanoma
  - 6 in 1,000,000 Caucasian individuals
- Choroidal nevi → Melanoma
  - The annual rate of malignant transformation is estimated to be;
    - 1 in 8,845

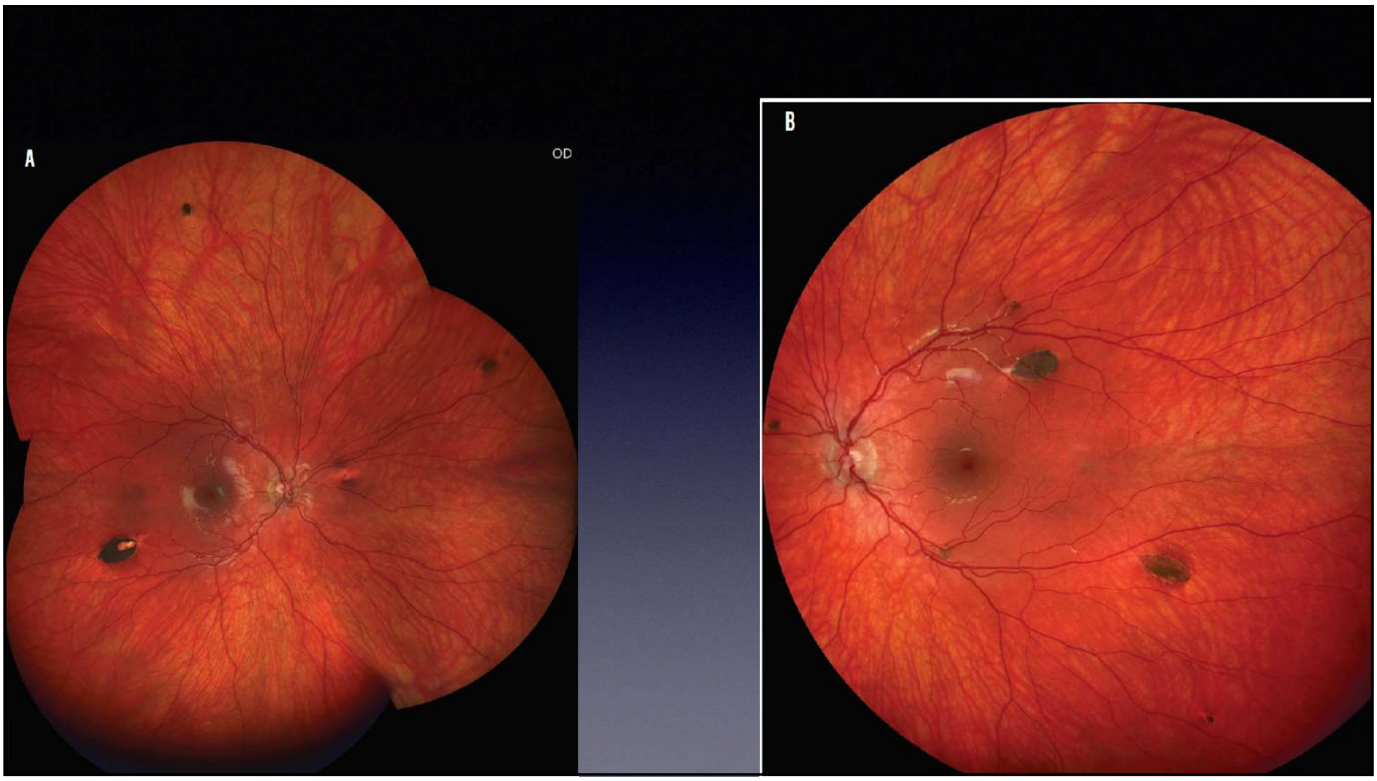
Choroidal Melanoma

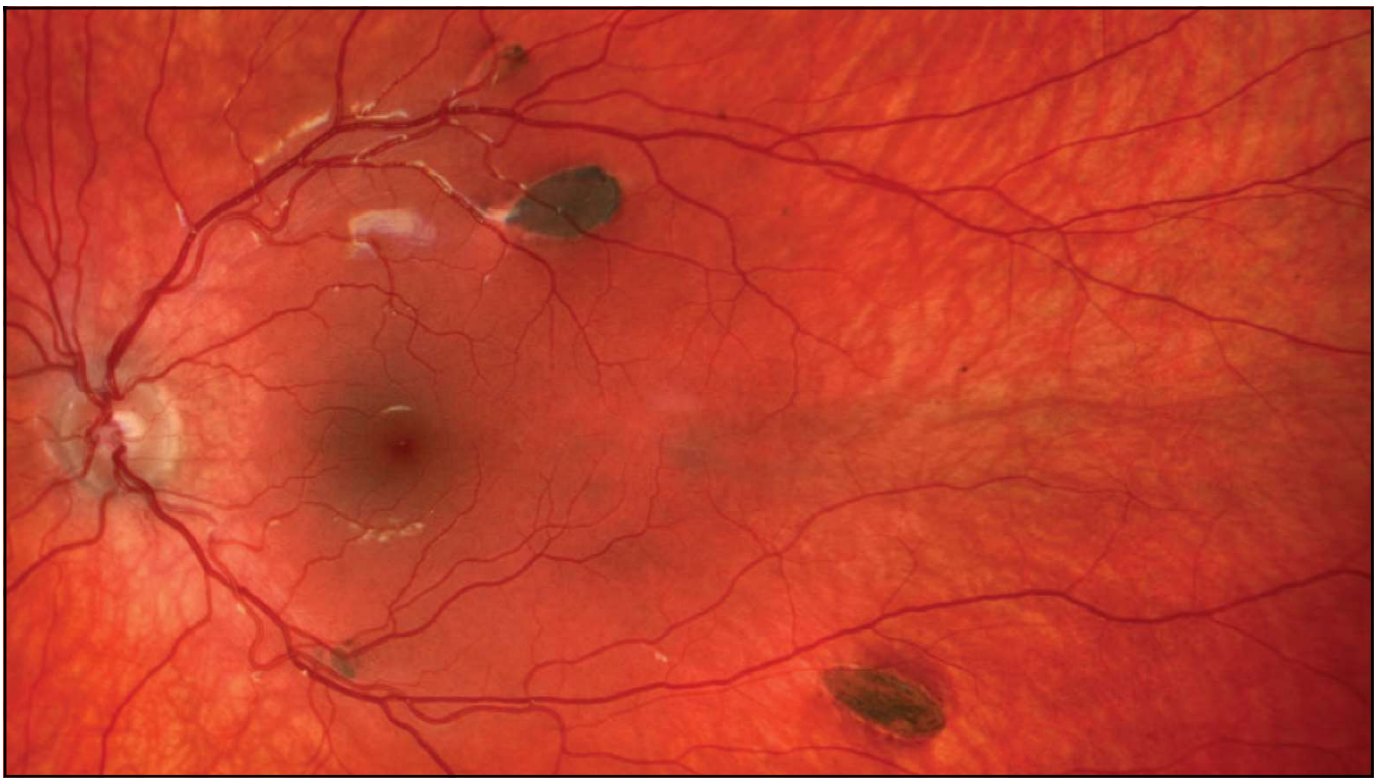
- **"To Find Small Ocular Melanoma Using Helpful Hints Daily" (TFSOM-UHHD)**
  - **Thickness** greater than 2 mm
  - Subretinal **Fluid**
  - **Symptoms**
  - **Orange** pigment present
  - **Margin** within 3 mm of the optic disc
  - **Ultrasonographic Hollowness** (versus solid/flat),
  - **Absence** of **Halo** and absence of **Drusen**.
    - (A halo refers to a pigmented choroidal nevus surrounded by a circular band of depigmentation.)

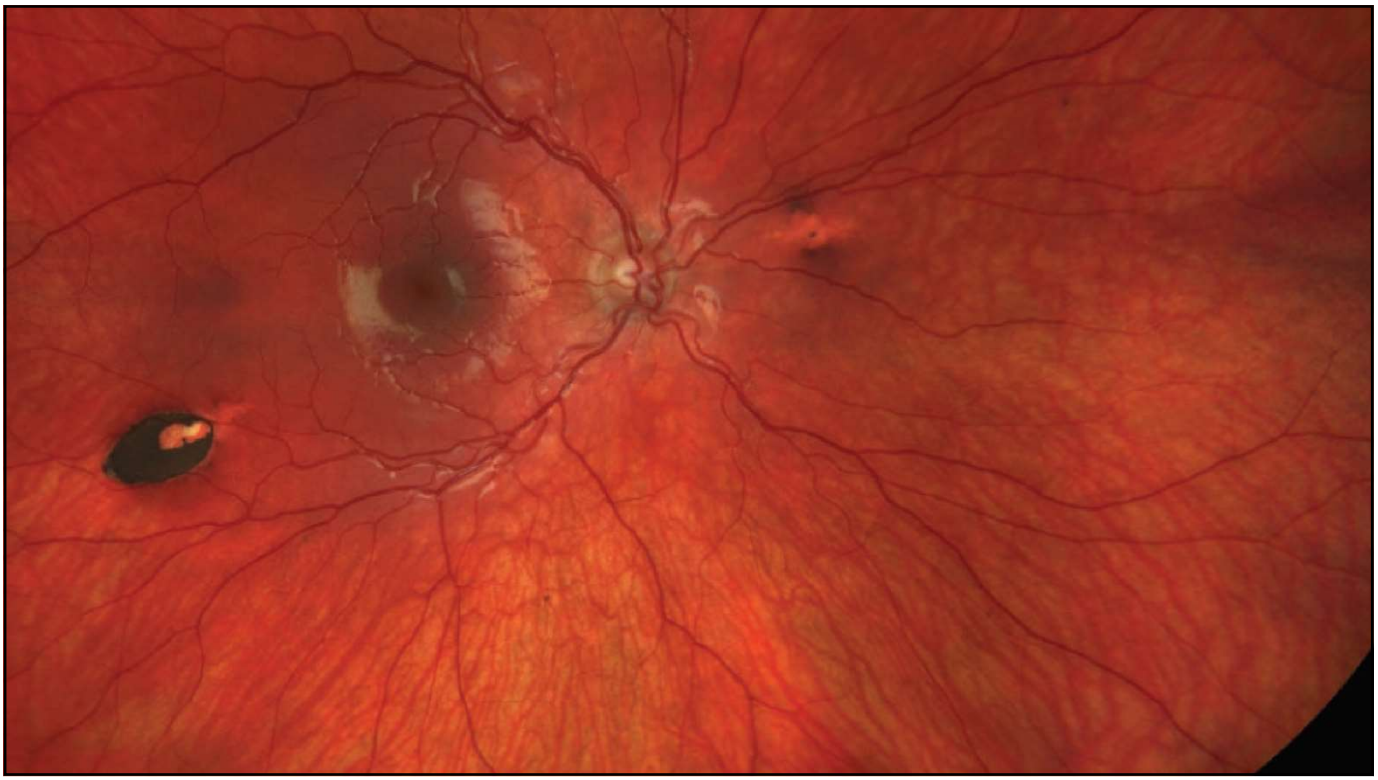
Case 2.0

- 7 yo M
- 1st Exam
- CC; Blur at Distance
  - Myopia
    - -1.00 OU 20/20




A
OD
B





FAMILIAL ADENOMATOUS POLYPOSIS

- The hallmark pathologic finding of familial adenomatous polyposis (FAP) is the development of hundreds to thousands of polyps in the colon and rectum by the second decade of life.
- Pigmented fundus lesions are the most common and earliest **extracolonic** manifestations of FAP.
- These lesions are asymptomatic and have little visual significance other than to prompt further evaluation for **FAP**.

FAMILIAL ADENOMATOUS POLYPOSIS

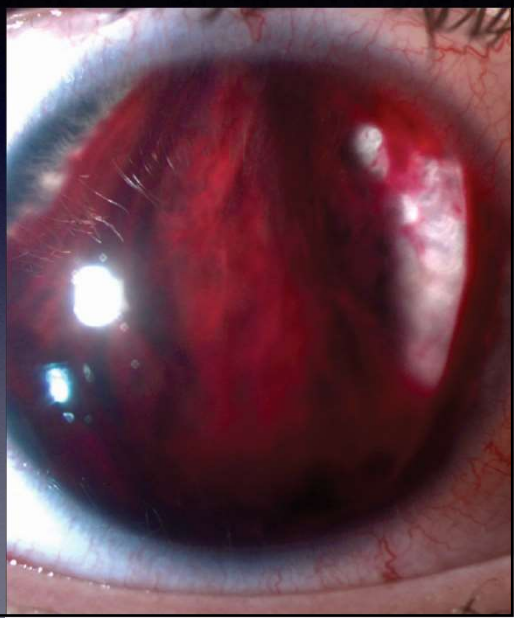
- These polyps eventually transform in colorectal cancer (**7% risk by age 21, 87% by age 45, and 93% by age 50**)
- With no family history of colon cancer, the patient's parents were skeptical about the diagnosis and it took some convincing for them to follow through with genetic testing, but taking this extra step likely saved his life.

FAMILIAL ADENOMATOUS POLYPOSIS

- The patient is now 13 years of age and has had yearly colonoscopies with multiple colon polyps removed every year, including one duodenal polyp.

Case

- 12yo M
- Pain & Loss of Vision



Hyphema

- Pt. reported to our clinic emergently one morning after experiencing a kickball injury the night before.
- After initially noting only a slight blur to his vision on the night of the injury, upon waking the following morning, the patient had only light perception vision in the affected eye, precipitating a very concerned call to us from his mother.

Hyphema

- Two of the main sequelae in cases such as this are caused by;
  - Increased IOP
  - Corneal blood staining

Hyphema

- Approximately 30% of patients presenting with traumatic hyphema have elevated IOP.
  - The pathophysiology behind this is rooted in **obstruction** of the trabecular meshwork by blood components.
- Increased IOP is seen in;
  - **10%** of eyes with less than a 50% hyphema
  - **25%** if there is greater than 50% hyphema
  - **50%** if the hyphema is complete (100%)

Hyphema

- Late traumatic glaucoma may develop weeks to years after the initial injury.
- The incidence of late-onset glaucoma from hyphema ranges from 0% to 20%.
- There tend to be two periods of elevated IOP,
  - **2 months to 2 years** after injury
  - **10 to 15 years** after injury.

Hyphema

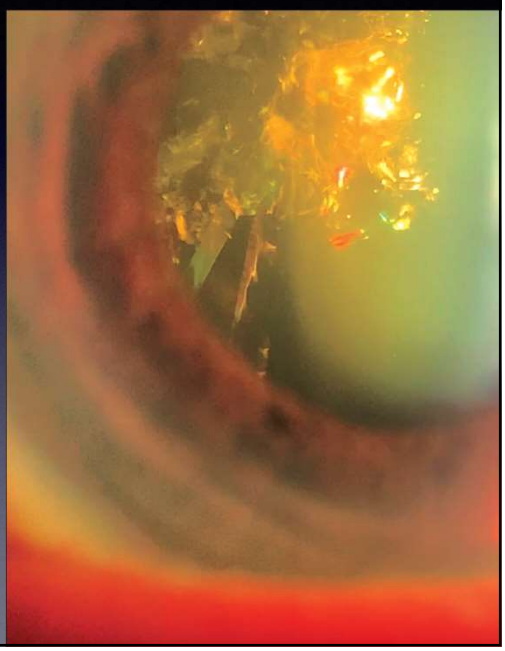
- Corneal blood staining starts centrally and appears as a yellow hue in the deep stroma.
- Blood staining may also cause endothelial decompensation and amblyopia in young patients.

Hyphema

- Reasons to consider **surgical consultation** for traumatic hyphema include;
  - The patient has sickle cell disease or trait, **and** the mean IOP is greater than **24** over the first 24 hours or, if treated, the IOP **spikes repeatedly over 30**
  - The treated IOP is greater than **60 for 2 days**
  - The treated IOP is greater than **25 with a total hyphema for 5 days**
  - There is corneal blood staining
  - The hyphema fails to resolve to **less than 50%** of anterior chamber volume by **8 days.**

Case

- 75yo M
- CC;
  - Glare at night
  - Needing more light to read



CHRISTMAS TREE CATARACT

- This type of cataract is most commonly related to an accelerated breakdown of denatured proteins induced by **elevated calcium** levels in the lens. Peptides and amino acids accumulate in the reticular meshwork of the lens, and **cysteine** is concentrated to a level at which crystallization occurs.
- It's essentially a kidney stone inside the eye.
- Although these cataracts are often not visually significant, they can progress and impair vision.

CHRISTMAS TREE CATARACT

- Sometimes associated with autosomal-dominant myotonic dystrophy (DM). There are two main types: DM1 and DM2. There is an extremely broad spectrum of manifestations and disease severity in DM.
- Approximately 75% of patients develop symptoms between the **second and fourth decade.**
- The most common initial symptom is myotonia or delayed relaxation (prolonged contraction) of skeletal muscles.

CHRISTMAS TREE CATARACT

- A retrospective review of 23 patients with DM1 revealed the presence of Christmas tree cataract in 13 patients (56%).
- They were unilateral in 10 of the 13 patients and bilateral in three.
- Average age of diagnosis was 47 years.

CHRISTMAS TREE CATARACT

- The cataract was the first sign of the disease for 11 patients and was detected during a routine eye examination.
- There was an abnormally large interval between diagnosis of the cataract and DM (10 years).
- This delay was explained by the fact that none of the patients presented with any of the typical symptoms of DM when the cataract was diagnosed.

CHRISTMAS TREE CATARACT

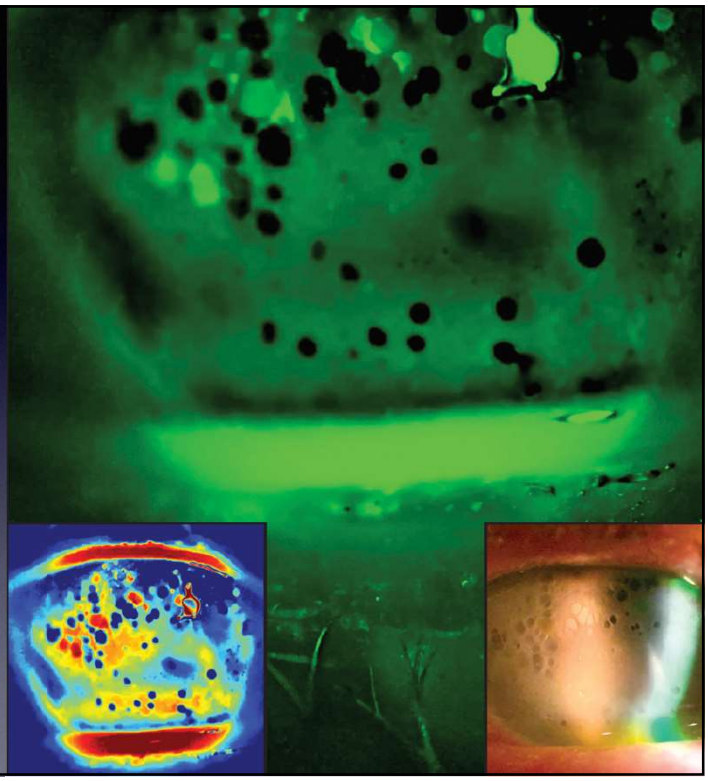
- Christmas tree cataracts are typically detected in nearly all patients with DM1
- Only 16.7% of individuals with Christmas tree cataracts are diagnosed with DM
- In other words, most Christmas tree cataracts are idiopathic,
  - **BUT** they are extremely common in patients diagnosed with DM.

CHRISTMAS TREE CATARACT

- Other manifestations and associations of DM include ;
  - cardiac dysrhythmia, gastrointestinal symptoms, higher risk of cancer, primary hypogonadism, insulin resistance, increased cholesterol and hypertriglyceridemia, abnormal liver function test, and balding.

Case

- 85yo F
- CC;
  - Painful eye
  - Longstanding poor vision



BULLOUS KERATOPATHY

- Bullous keratopathy is characterized by stromal edema and anterior corneal bullae
- Rooted in the loss of corneal endothelial cell integrity and function.
- Patients with this corneal pathology present with decreased vision and ocular pain caused by the epithelial manifestation of the disease, specifically the ruptured and intact epithelial bullae.

BULLOUS KERATOPATHY

- In children, normal endothelial cell density is greater than 3,500 cells/mm2.
- This density naturally declines with age to approximately 2,400 cells/mm2 in adulthood.
- Edema occurs when the cell density drops below 1,000 cells/mm2

BULLOUS KERATOPATHY

- Conditions or events that give rise to bullous keratopathy include
- Fuchs corneal endothelial dystrophy, viral endothelialitis, exfoliation syndrome, traumatic injury, and endothelial injury caused by intraocular procedures such as cataract or glaucoma surgery.
- Bullous keratopathy may occur in around 1% to 2% of patients undergoing cataract surgery,
- a significant number when you consider that approximately 10 million patients undergo cataract surgery worldwide each year

BULLOUS KERATOPATHY

- With the increase in intraocular implants such as those used in MIGS,
- and with the anterior chamber now being used as a depot for medication,
- it is more important than ever that optometrists stay vigilant in monitoring the corneal endothelium for abnormal or expedited cell loss.

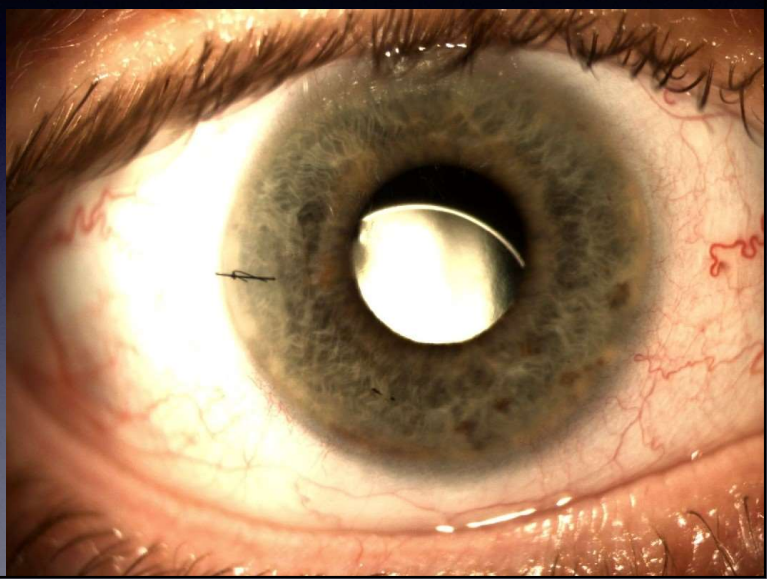
BULLOUS KERATOPATHY

- It is notable that patients with dry eye disease also have an accelerated rate of corneal endothelial cell loss.
- Those with lower subbasal nerve density, in particular, are at higher risk for accelerated endothelial cell loss.
- This observation stresses the importance and role of the neurosensory system in corneal disease, including but not exclusive to dry eye disease.

BULLOUS KERATOPATHY

- Keratoplasty is the primary treatment option for most patients with bullous keratopathy.
- The surgical strategy has evolved from full thickness penetrating keratoplasty to lamellar, endothelium-only strategies such as Descemet-stripping automated endothelial keratoplasty and Descemet membrane endothelial keratoplasty.
- Further evolution now includes nontransplant options such as Descemet stripping only or DSO. T
- The use of a rho-kinase inhibitor, as an endothelial “encourager” in conjunction with surgical endothelial cell implantation procedures or as an independent therapy, has also shown promise.

Case



DISLOCATED IOL

- The World Health Organization estimated the number of cataract surgeries performed in 2010 to be 20 million and that number was expected to reach 32 million by last year.
- Obviously, this device has become commonplace in eye care, but as with anything, there are some instances when an IOL will have to be modified, replaced, or repaired.

DISLOCATED IOL

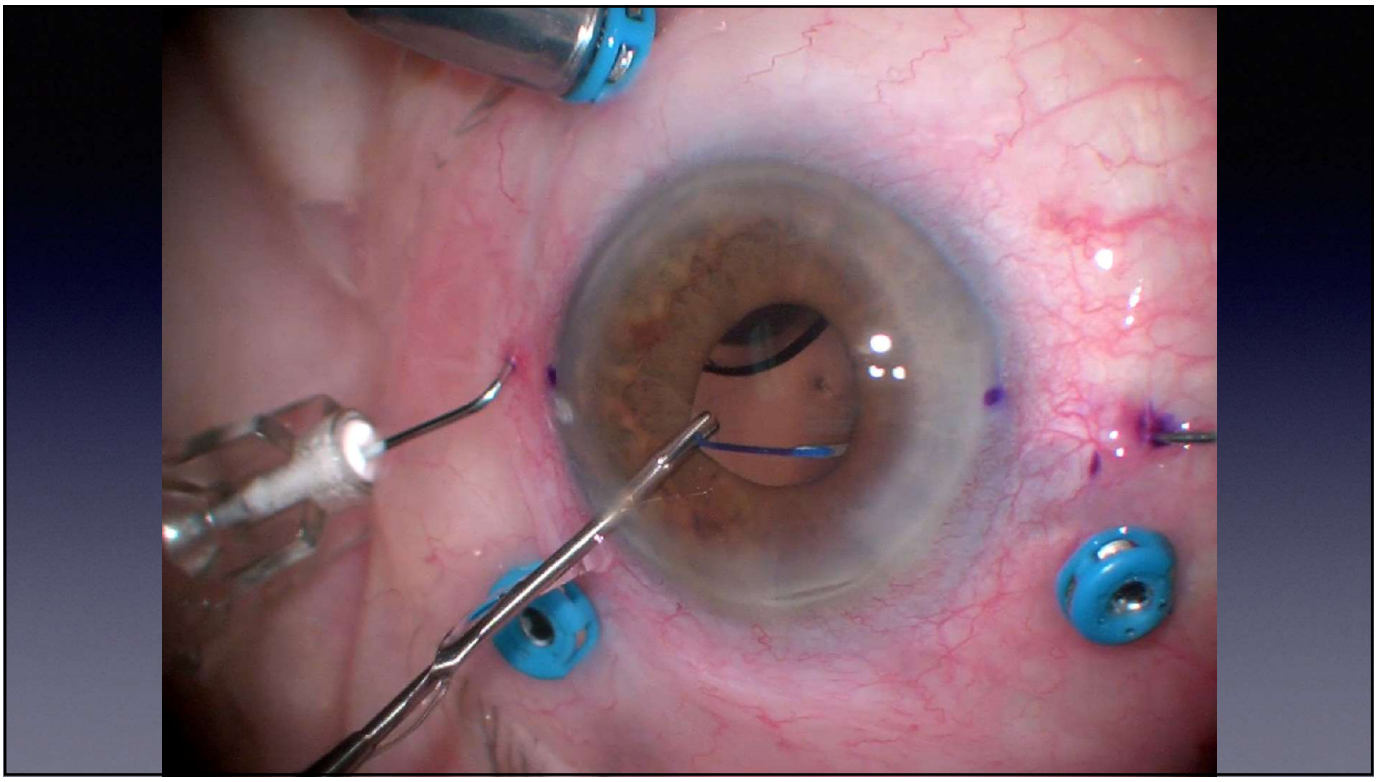
- IOL dislocation isn't common, but several risk factors can help predict if and when "the sun will set."
- Pseudoexfoliation is probably the strongest risk factor for IOL dislocation.
- Pseudoexfoliation can lead to zonular complications intraoperatively. It can also lead to progressive anterior capsulorhexis contraction, which can in turn dislocate the IOL-bag complex.
- Other risk factors for IOL dislocation included trauma, high myopia, multiple intraocular surgeries, capsulotomy, uveitis, Marfan syndrome, and retinitis pigmentosa.

DISLOCATED IOL

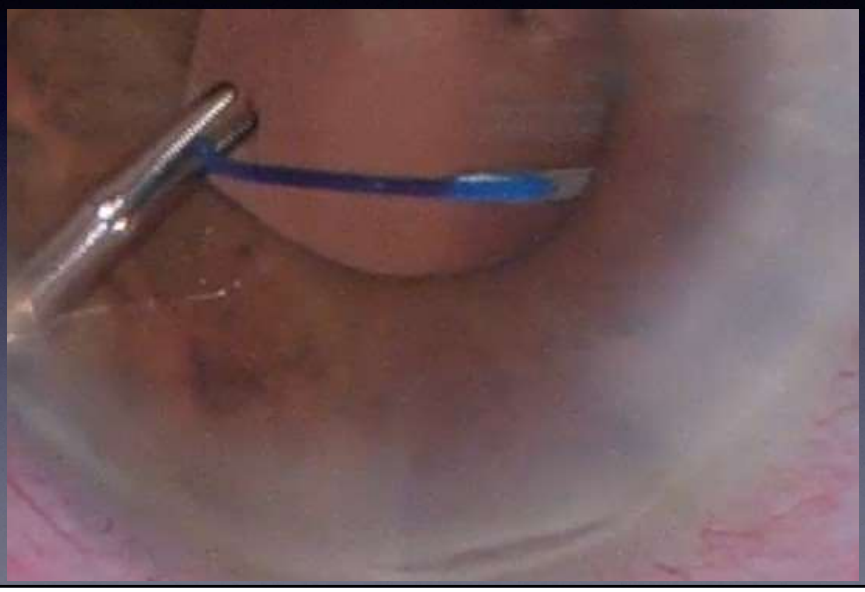
- Methods for IOL repositioning and repair have evolved as surgeons seek the simplest, safest, and most efficient way to restore vision for these patients.
- Surgical options include replacing the posterior chamber lens with an anterior chamber IOL, suturing the dislocated lens to the iris, or securing it to the sclera with either sutures or glue.
- Each of these methods has its own complications, such as endothelial compromise, suture erosion, and breakage of the adhesive or the suture

Yamane Technique

- In this procedure, the surgeon uses a transconjunctival approach with two 30-gauge thin-walled needles.
- The haptics of a three-piece IOL are inserted into the needles and externalized.
- The haptic tips are then cauterized (melted) to make a flange or bulge at the end of the haptics.
- Finally, the flange is pushed back and fixed into the sclera. The flange prevents the haptics of the IOL from falling back into the globe. T
- his procedure has been shown to provide good IOL positioning with firm haptic fixation and without the need for sutures or glue.



Yamane technique

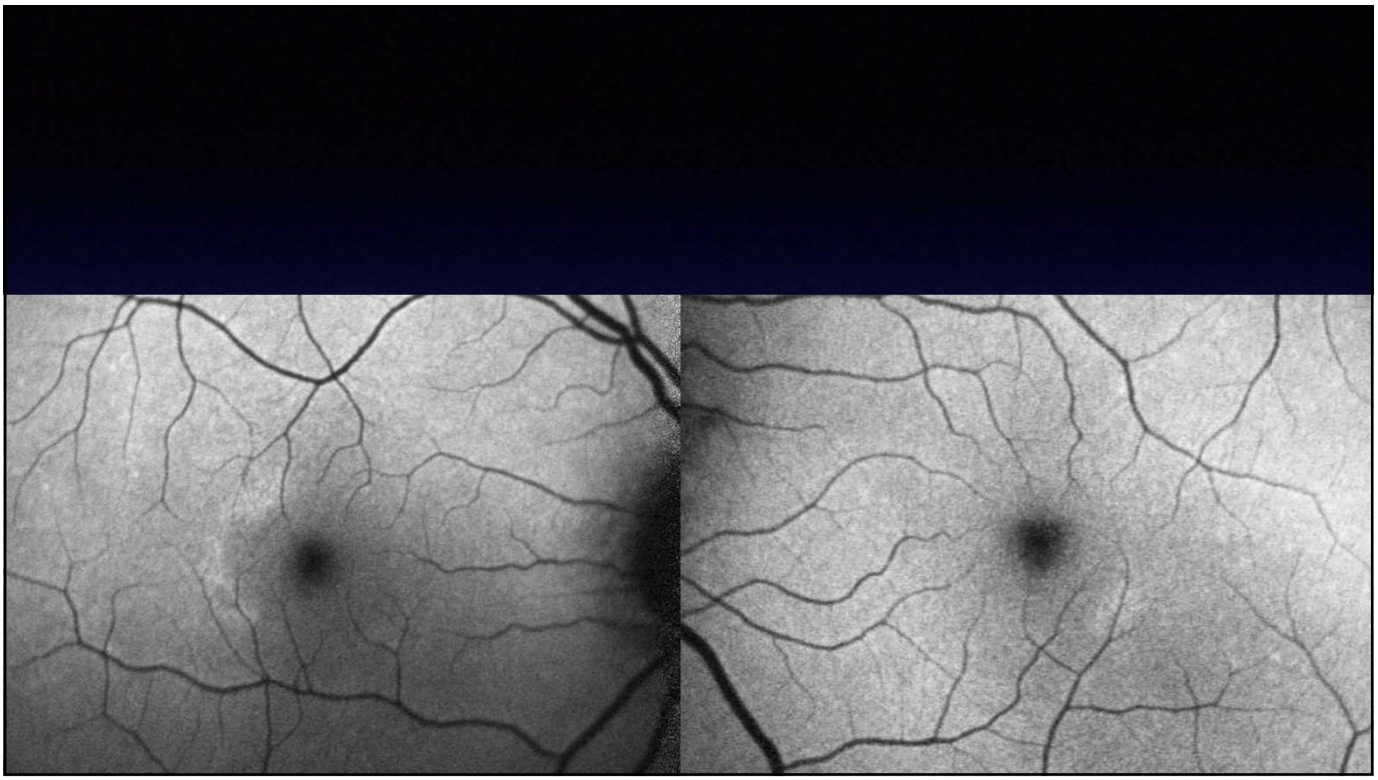


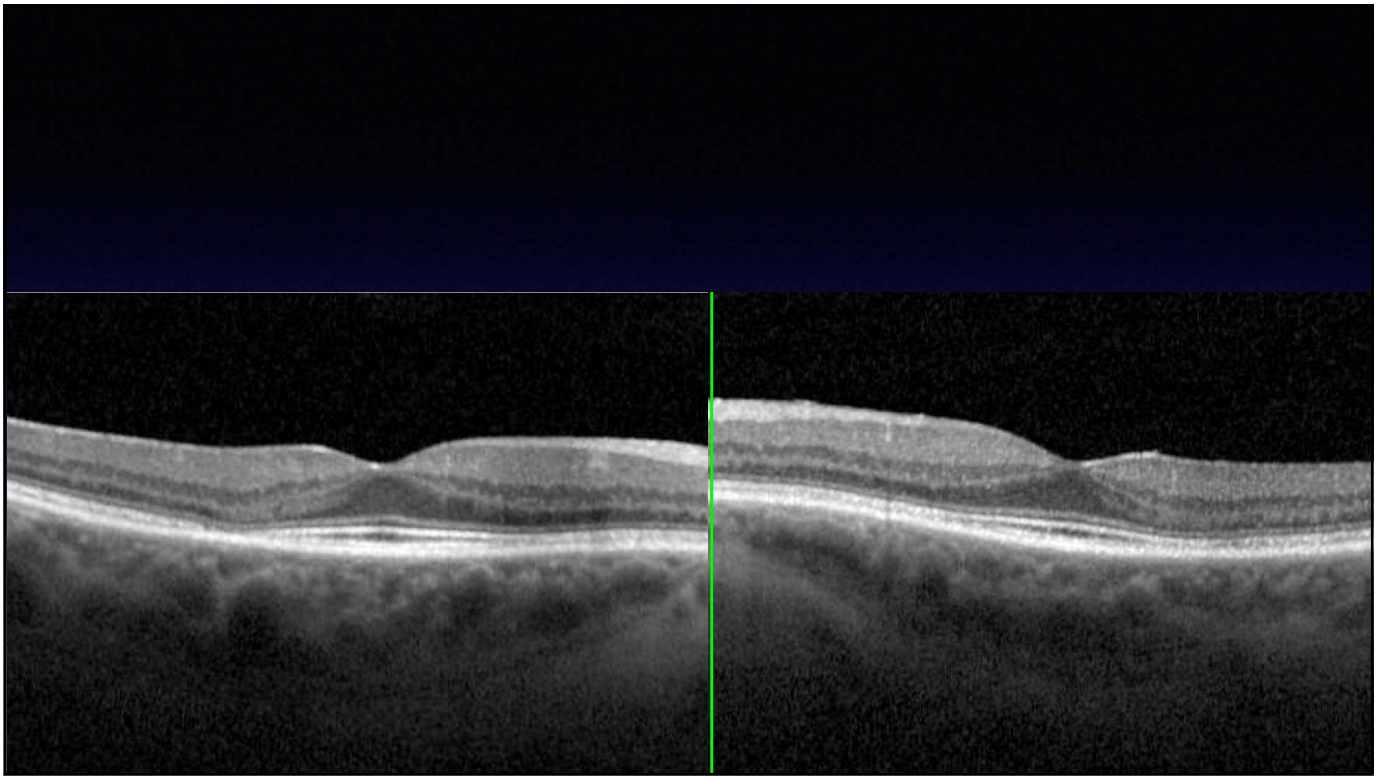
Case

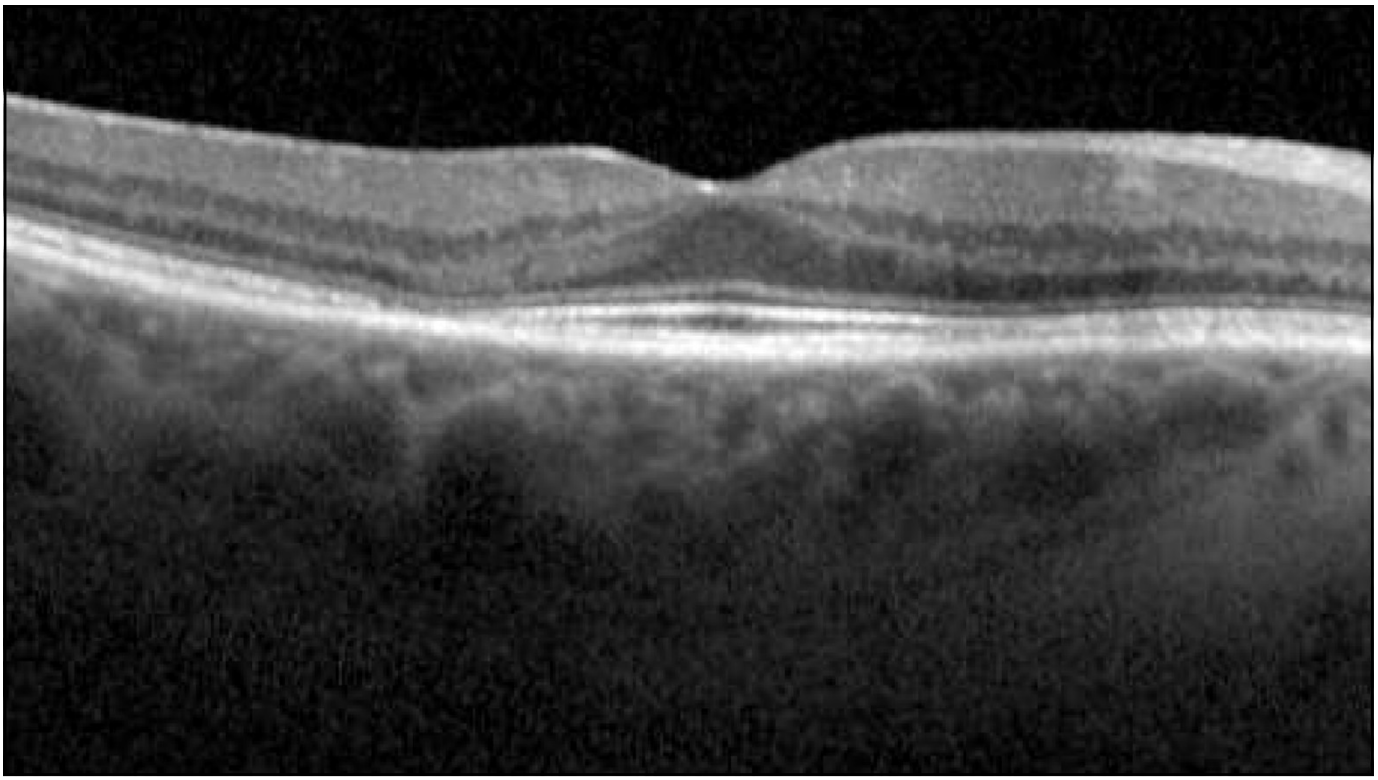
- Dry Eye Consult
- 35yo F
- CC; Blurred vision

Case

- CC; Blurred vision
- Lupus, Sjogrens
- “Sparkly” Vision
- Kidney issues







Chloroquine and Hydroxychloroquine Retinopathy

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

Michael F Marmor [1], Ulrich Kellner [2], Timothy Y Y Lai [3], Ronald B Melles [4], William F Mieler [5]; American Academy of Ophthalmology

Chloroquine and Hydroxychloroquine Retinopathy

- Asian patients often show an extramacular pattern of damage.
- DOSE: We recommend a maximum daily HCQ use of ≤5.0 mg/kg real weight, which correlates better with risk than ideal weight.
- There are no similar demographic data for CQ, but dose comparisons in older literature suggest using ≤2.3 mg/kg real weight.

Chloroquine and Hydroxychloroquine Retinopathy

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

Chloroquine and Hydroxychloroquine Retinopathy

- A baseline fundus examination should be performed to rule out preexisting maculopathy.
- Begin annual screening after 5 years for patients on acceptable doses and without major risk factors.

Chloroquine and Hydroxychloroquine Retinopathy

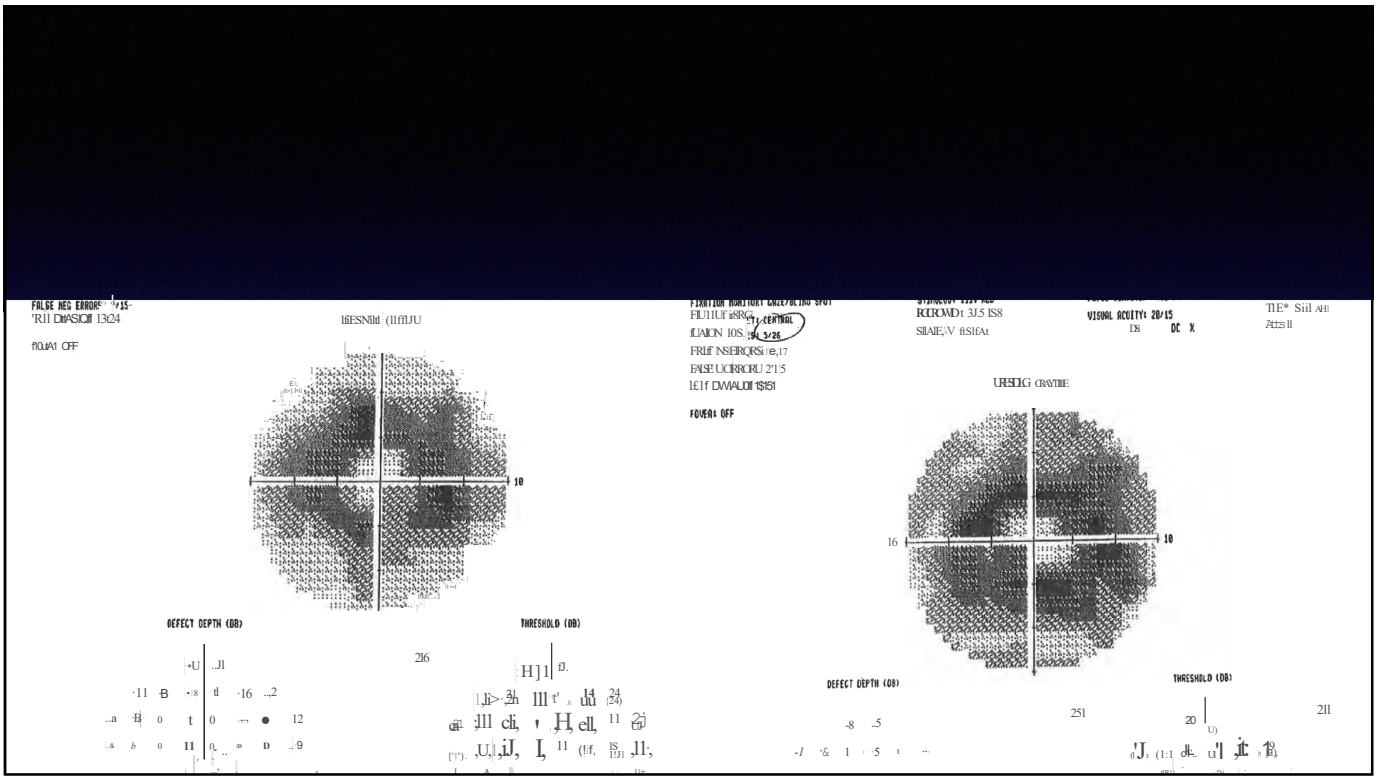
- High dose and long duration of use are the most significant risks. Other major factors are concomitant
- renal disease
- tamoxifen.

Chloroquine and Hydroxychloroquine Retinopathy

- The primary screening tests are
  - Automated visual fields (10-2 STD)
  - Spectral-domain optical coherence tomography (SD OCT).
    - The multifocal electroretinogram (mfERG) can provide objective corroboration for visual fields, and fundus autofluorescence (FAF) can show damage topographically

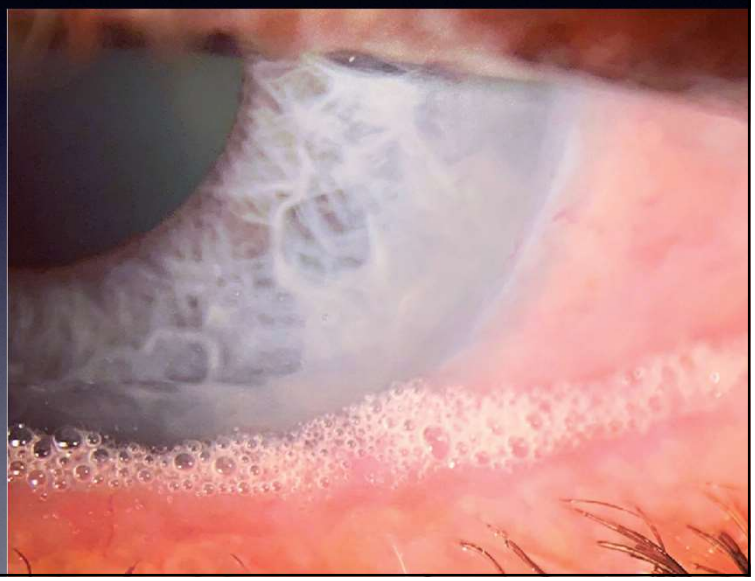
Chloroquine and Hydroxychloroquine Retinopathy

- Retinopathy is not reversible, and there is no present therapy.
- Recognition at an early stage (before any RPE loss) is important to prevent central visual loss.
- However, questionable test results should be repeated or validated with additional procedures to avoid unnecessary cessation of valuable medication.



Case

- 70 yo M.
- CC;
  - Burning
  - Fluctuating Vision



SAPONIFICATION

- This enzymatic reaction, called saponification, appears as foamy soap bubbles
- When bacterial overload and activity reaches a dysfunctional level. The true definition of saponification is the act, process, or result of making soap.
- This finding has been described for some time by clinicians and has been associated with blepharitis, specifically posterior blepharitis, and is better defined as meibomian gland dysfunction… is the most common form of dry eye.

SAPONIFICATION

- In the movie Fight Club, the Paper Street Soap Company uses rendered fat and lye to make soap.
- Soap is an excellent cleaner because of its ability to act as an emulsifying agent.
- We can appreciate how dissolving and mixing oils is detrimental to ocular surface health.
- Bacteria are achieving a similar breakdown of lipids (using lipases instead of lye) on the ocular surface.

SAPONIFICATION

- This enzymatic effect may be the root of therapeutic benefit in MGD, rosacea, and patients with acne.
- Lid hygiene is a major factor in helping to regulate the microbiome.
- I do not recommend baby shampoo, as I find it too irritating to the ocular tissues.
- It's also counterproductive to add more soap to an already soapy environment

SAPONIFICATION

- Epstein et al published a poster that demonstrated the effectiveness of hypochlorous acid (Avenova, AvenovaEyecare) for the inactivation of bacterial lipase.
- They noted complete inactivation of lipase, while several other common lid products appeared to have minimal effect.
- Some also postulate that tetracyclines downregulate lipase activity.
  - This enzymatic effect is at the root of their therapeutic benefit in MGD, rosacea, and patients with acne.

Questions???

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