Ocular Side effects of systemic medications

COPE Course ID: 85635-PH

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CHIEF OF OPTOMETRY, GREENVILLE HCC

No disclosures or conflicts of interest for anything presented in this lecture.

Case 1

42 yo white male

Cc: Patient reports vision is getting blurry up close within the last 6 month.

Reports color is more dull in the left eye. Recently diagnosed with MS and started on copaxone.

- **VA:**
  - **20/20**
  - **20/20**
  - **Pupils: ERRL (-) R APD**
  - **EOMS: SAFE**

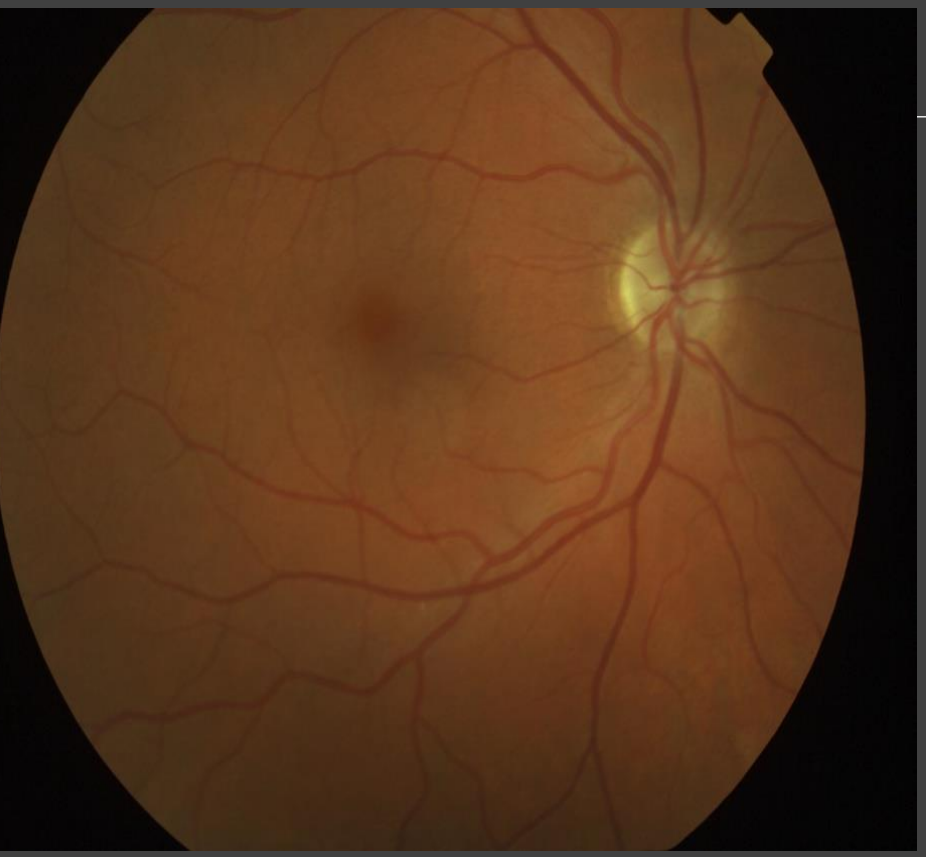
Color vision: Ishihara

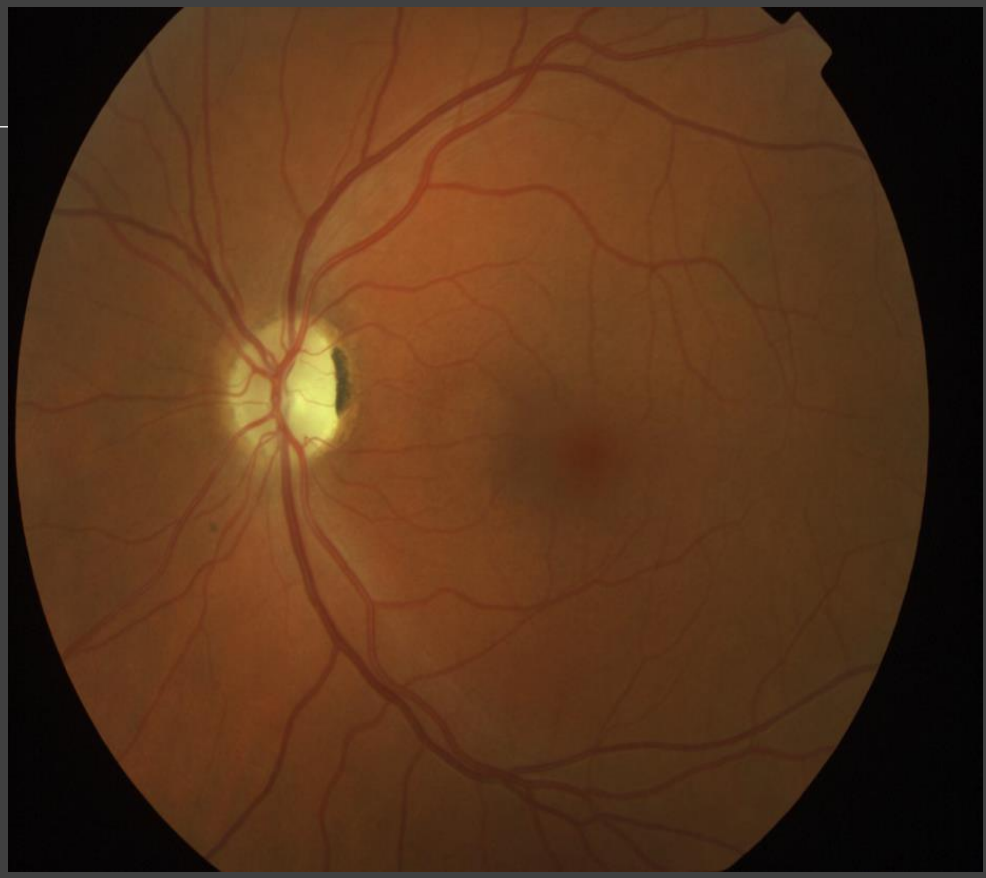
- **14/14 OD**
- **10/14 OS**

CVF: FTFC OD/OS

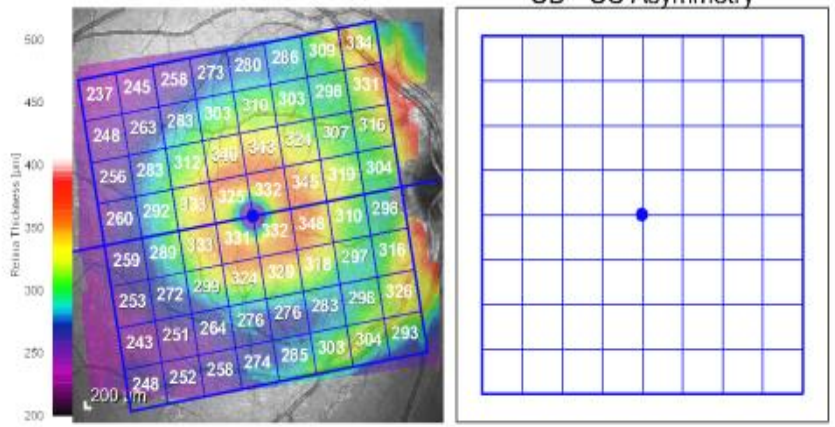
Anterior segment normal

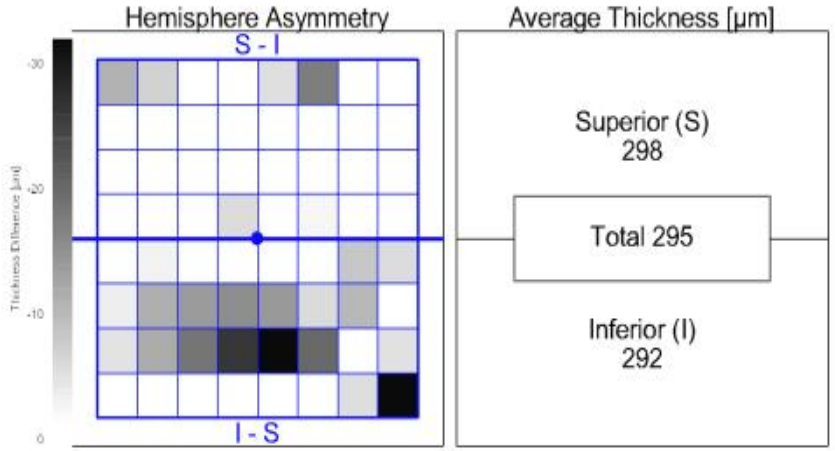
Pt was dilated……



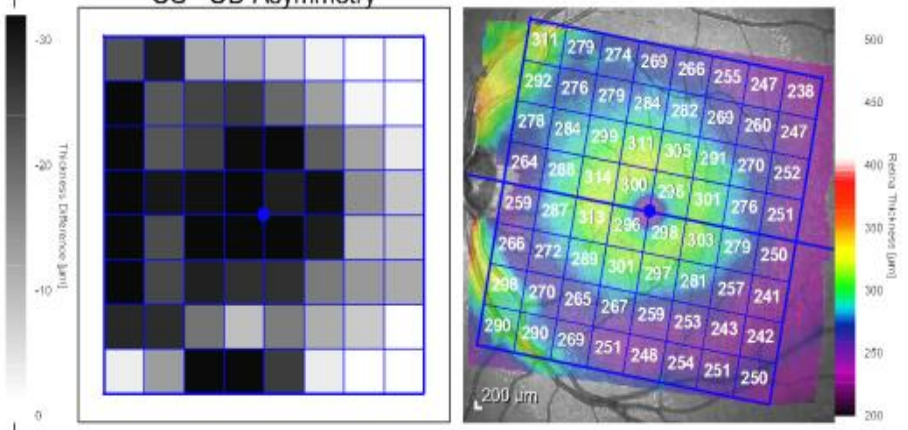


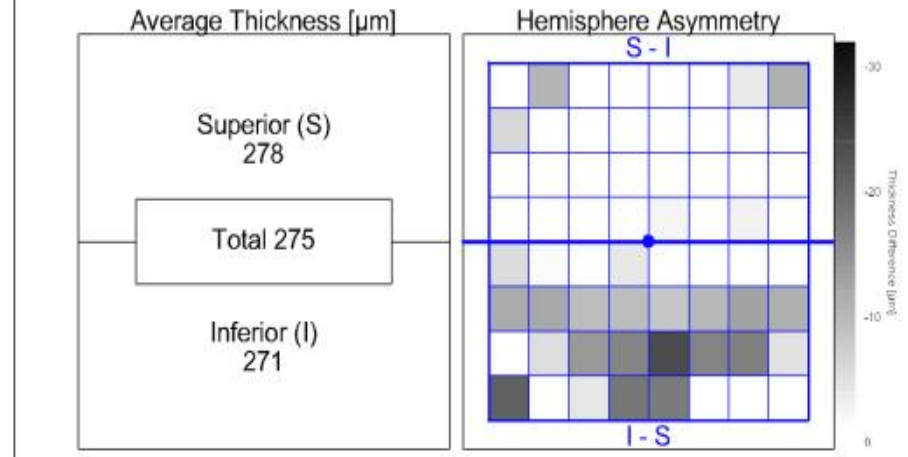
OD


OD - OS Asymmetry
200 µm


Hemisphere Asymmetry
S - I
I - S
Average Thickness [µm]
Superior (S)
298
Total 295
Inferior (I)
292

OS


OS - OD Asymmetry
200 µm

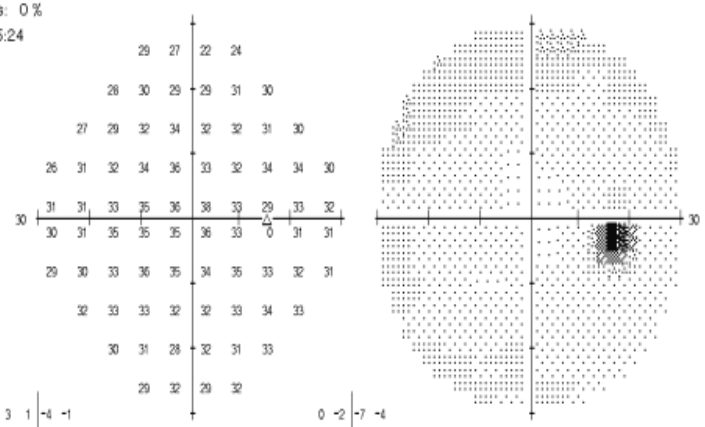

Average Thickness [µm]
Superior (S)
278
Total 275
Inferior (I)
271
Hemisphere Asymmetry
S - I
I - S

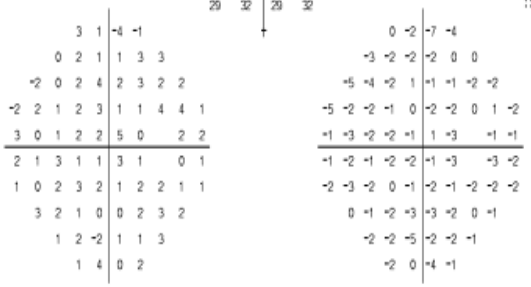
Fixation Monitor: Gaze/Blind Spot
Fixation Target: Central
Fixation Losses: 0/16
False POS Errors: 0 %
False NEG Errors: 0 %
Test Duration: 05:24
Fovea: OFF

Stimulus: III, White
Background: 31.5 ASB
Strategy: SITA-Standard

Pupil Diameter: 5.8 mm
Visual Acuity:
RX: +1.75 DS DC X

Date: 10-01-2012
Time: 1:21 PM
Age: 42





GHT
Within Normal Limits

VFI 100%

MD +1.62 dB
PSD 1.47 dB

:: < 5%
< 2%
< 1%
< 0.5%

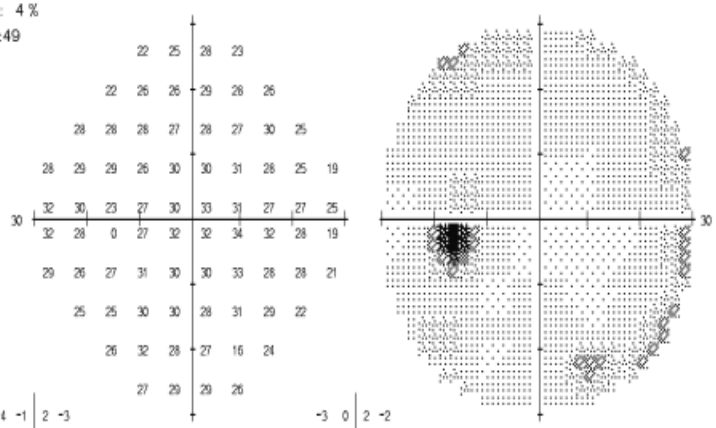
VA MEDICAL CENTER
718 SMYTH RD 3RD FLOOR
MANCHESTER, NH 03104
603-624-4366

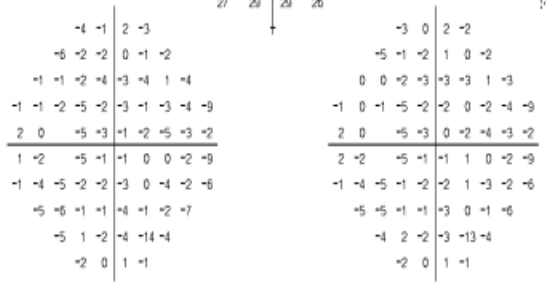
Fixation Monitor: Gaze/Blind Spot
Fixation Target: Central
Fixation Losses: 0/18
False POS Errors: 1 %
False NEG Errors: 4 %
Test Duration: 06:49
Fovea: OFF

Stimulus: III, White
Background: 31.5 ASB
Strategy: SITA-Standard

Pupil Diameter: 4.9 mm
Visual Acuity:
RX: +1.25 DS DC X

Date: 10-01-2012
Time: 1:29 PM
Age: 42





GHT
Within Normal Limits

VFI 97%

MD -2.44 dB P < 5%
PSD 2.77 dB P < 10%

:: < 5%
< 2%
< 1%
< 0.5%

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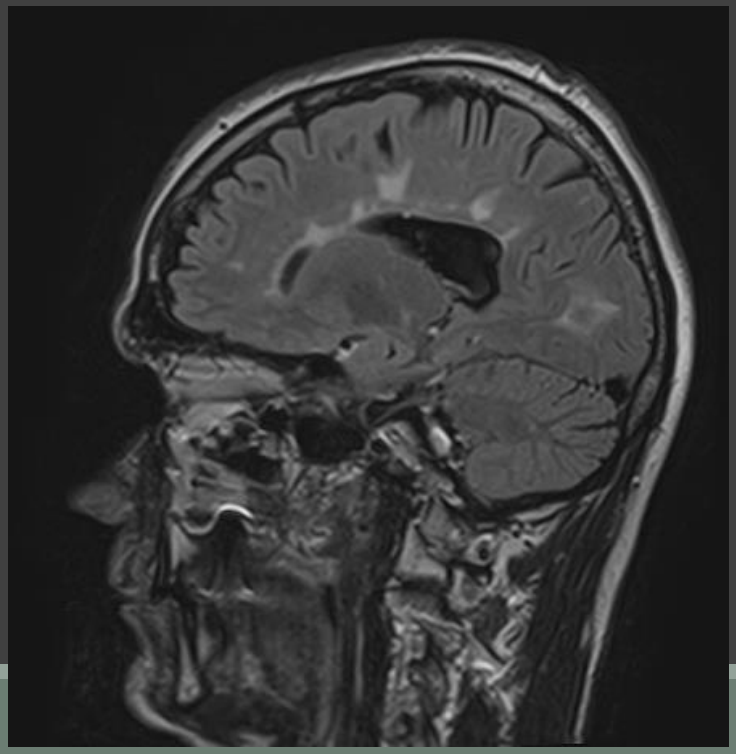
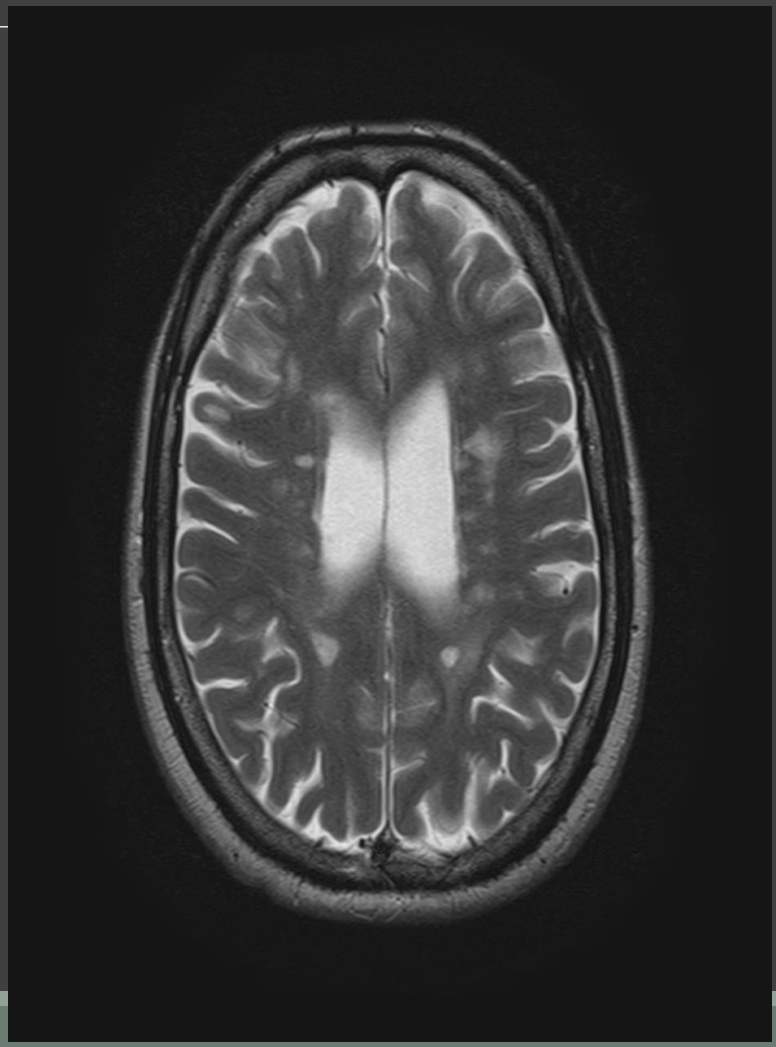
MRI with contrast.

- **Revealed white matter lesions consistent with MS.**





Optic Neuritis

- **Age range: ~18-45**

- **Pts will present with a sudden, painful vision loss that can progress to severe vision loss within a week.**

http://www.nature.com/eye/journal/v25/n7/fig_tab/eye201181f3.html

Signs and Sxs of Optic Neuritis

- Pain and tenderness of the globe near insertion of the superior rectus.
- Marcus Gunn Pupil (+ APD)
- Color desaturation
- Light comparison variation
- Pulfrich's stereo phenomenon
- Uhthoff's sign
- VF defects – mostly central.
  - NFL may be compromised

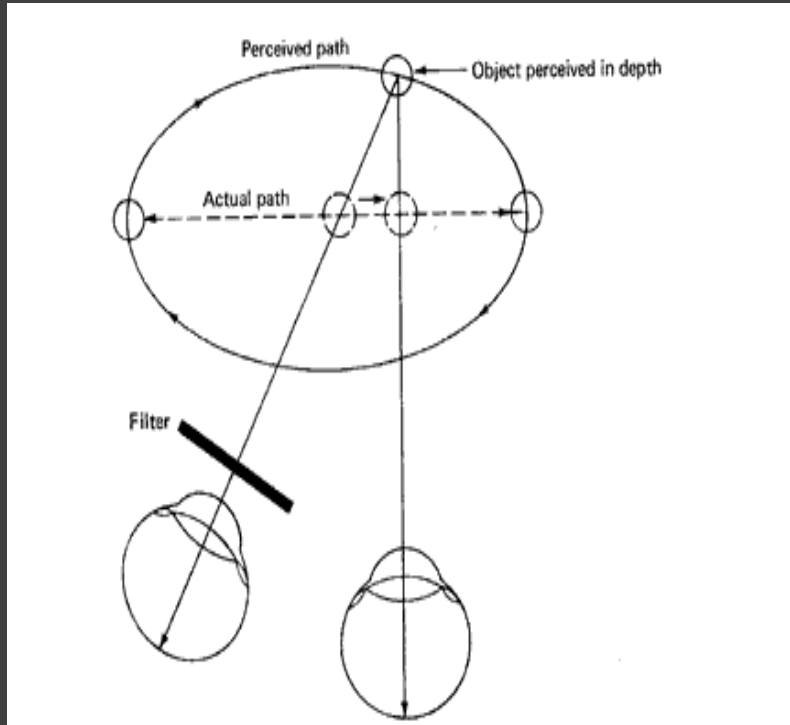


Fig. 13.7. The Pulfrich phenomenon. The attenuated eye perceives the pendulum ball as lagging behind the position as seen by the unattenuated eye. This is consistent with the ball actually traveling in an elliptical path, as shown.

Alexander, Primary Care of the Posterior Segment. 1994.

http://whensantagotstuckupthespaceship.blogspot.com/2008/12/pulfrich-effect.html

Treatment options in MS

Injectable medications

- Avonex (interferon Beta-1a)
- Betaseron (interferon Beta-1b)
- Copaxone (glatiramer acetate)
- Extavia (interferon beta-1b)
- Glatopa (glatiramer acetate)
- Plegridy (peginterferon beta-1a)
- Rebif (interferon beta-1a)
- Kesimpta(ofatumumab)

Oral medications

- Aubagio (teriflunomide)
- Gilenya (fingolimod)
- Tecfidera (dimethyl fumarate)
- Mavenclad (cladribine)
- Mayzent (Siponimod)
- Ponvory (ponesimod)
- Tascenso (fingolimod)
- Vumerity (diroximel fumarate)
- Zeposia (ozanimod)

Treatment options in MS

Infused medications:

- **Briumvi (ublituximab)**
- **Lemtrada (alemtuzumab)**
- **Novantrone (mitoxantrone)**
- **Ocrevus (ocrelizumab)**
- **Tysabri (natalizumab)**

Gilenya (fingolimod)

- **Class of medication called a sphingosine 1-phosphate receptor modulator.**
- **Works by retaining white blood cells (lymphocytes) in the lymph nodes and preventing them from crossing the blood brain barrier into the CNS.**

http://www.pharmafile.com/news/154480/oral-multiple-sclerosis-drug-gilenya-fingolimod-uk

Ocular Side effects of oral Gilenya

- **Amongst all of the Phase II, Phase III, and extension studies of fingolimod, sixteen study patients developed macular edema during the study period.**
- **One patient had associated branch retinal vein occlusion with macular edema. Four patients had a prior history of uveitis.**

https://www.nanosweb.org/files/public/MS_drug_may_increase_risk_for_RVO1NOTRACK2lf.pdf

Ocular Side effects of oral Gilenya

- **Only 2 of the patients on the currently approved 0.5mg tablet developed macular edema (ME), (0.2%), while the incidence was 1.1% in patients on the non-approved 1.25mg dosage.**
- **Twelve patients with ME presented with blurred vision or decreased acuity and 75% presented within the first four months of treatment. ME usually resolved after discontinuation of fingolimod.**

https://www.nanosweb.org/files/public/MS_drug_may_increase_risk_for_RVO1NOTRACK2lf.pdf

Recommended guidelines from NANOS (North American Neuro-ophthalmology society) and AAO ONE Neuro-ophthalmology committee

1. A screening evaluation for pre-existing uveitis or macular or retinal vascular disease prior to starting, or within the first few weeks of starting fingolimod should be considered.

2. A single re-evaluation at 3-4 months of therapy is recommended. All of the reported cases of ME occurred within this initial time frame, so the role of further repeated evaluation has not been established.

3. Patients should be advised that the incidence of macular edema is low (~2/1000) with the current recommended dosage, but if there is a past history of uveitis, the incidence may be as high as 20%. Diabetes and retinovascular disease may be additional risk factors, but the additional possible risk they produce for macular edema remains unknown at this time.

Recommended guidelines from NANOS (North American Neuro-ophthalmology society) and AAO ONE Neuro-ophthalmology committee

4. A visual acuity check and a complete eye exam including a dilated fundus exam is a reasonable ophthalmic screening protocol. As up to 25% of ME noted during the studies was asymptomatic, lack of subjective symptoms does not necessarily indicate absence of ME.

5. Patients with abnormalities on exam or unexplained decreased visual acuity might benefit from diagnostic imaging with macular OCT.

Case 2

79 yo white female

Presents for a complete exam. Last exam was 1 year ago at a retina practice.

MHX: misdiagnosed with Lupus 14 years ago and started on Plaquenil for the arthritis. Pt reports she never really had significant arthritis.

Within 9 months, her color vision started to diminish and she was sent to a retina doctor.

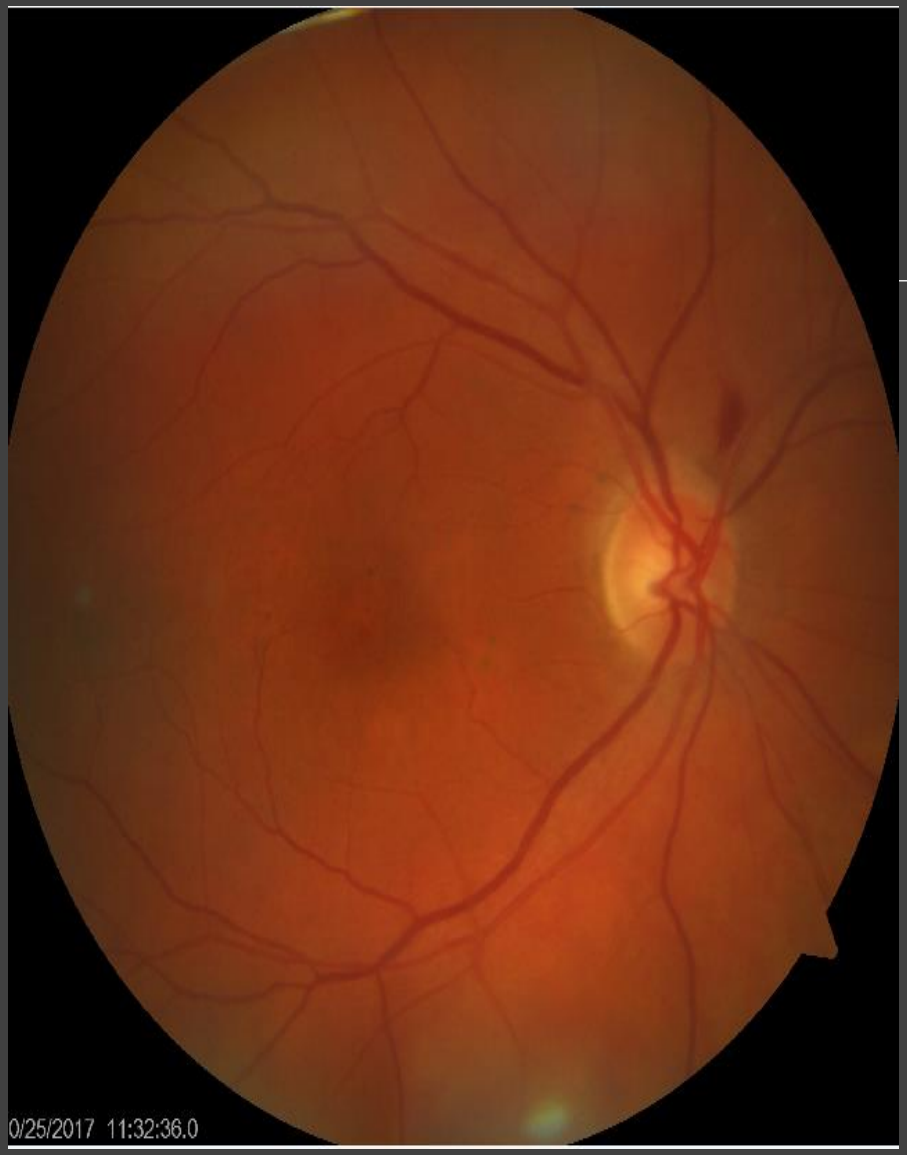
VA:

- **OD: 20/25**
- **OS: 20/25**

Pupils:

ERRL (-) APD

Anterior segment WNL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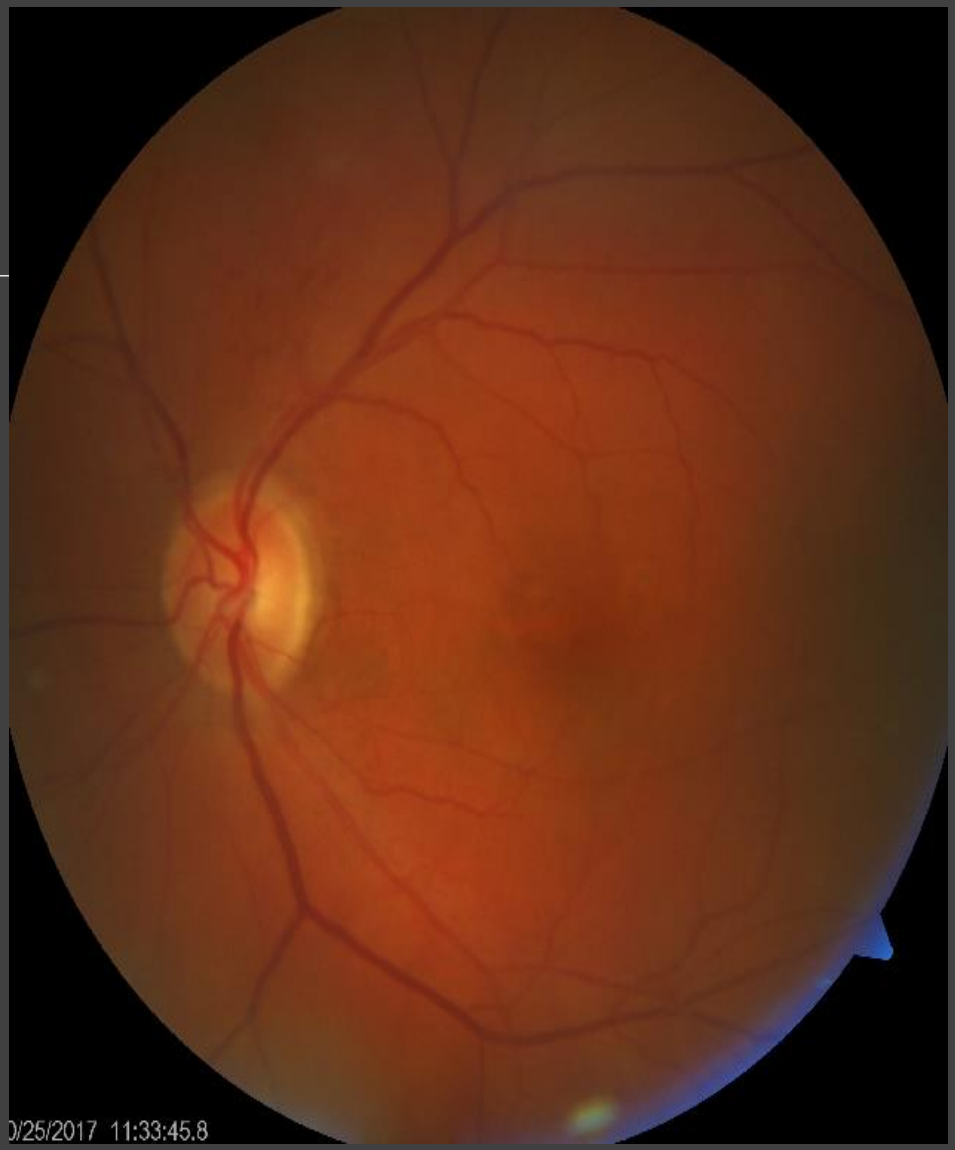
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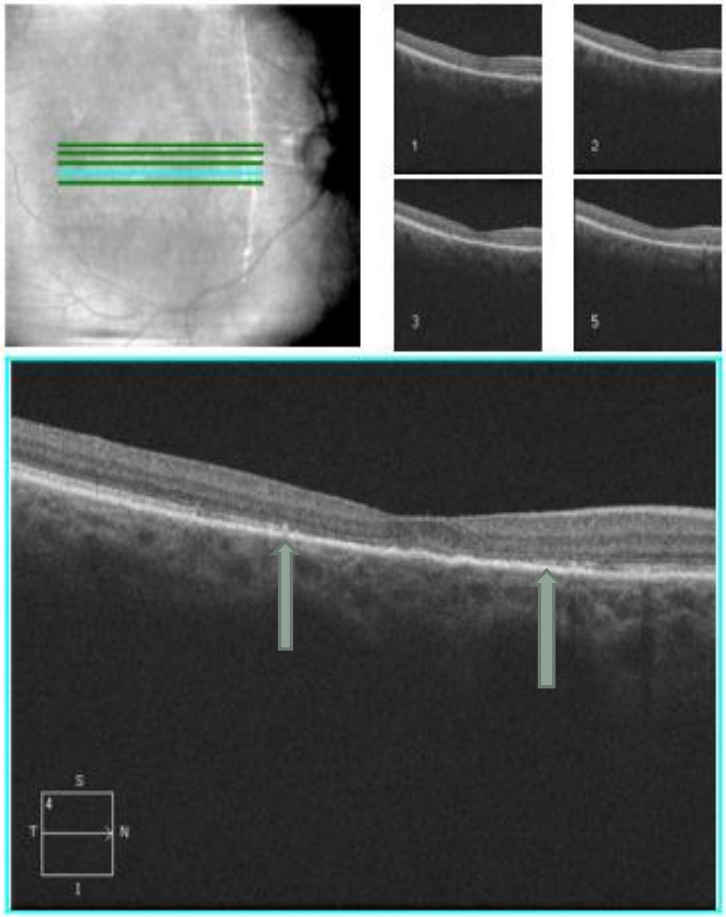
High Definition Images: HD 5 Line Raster

OD ● ○ OS

Scan Angle: 0° Spacing: 0.25 mm Length: 6 mm



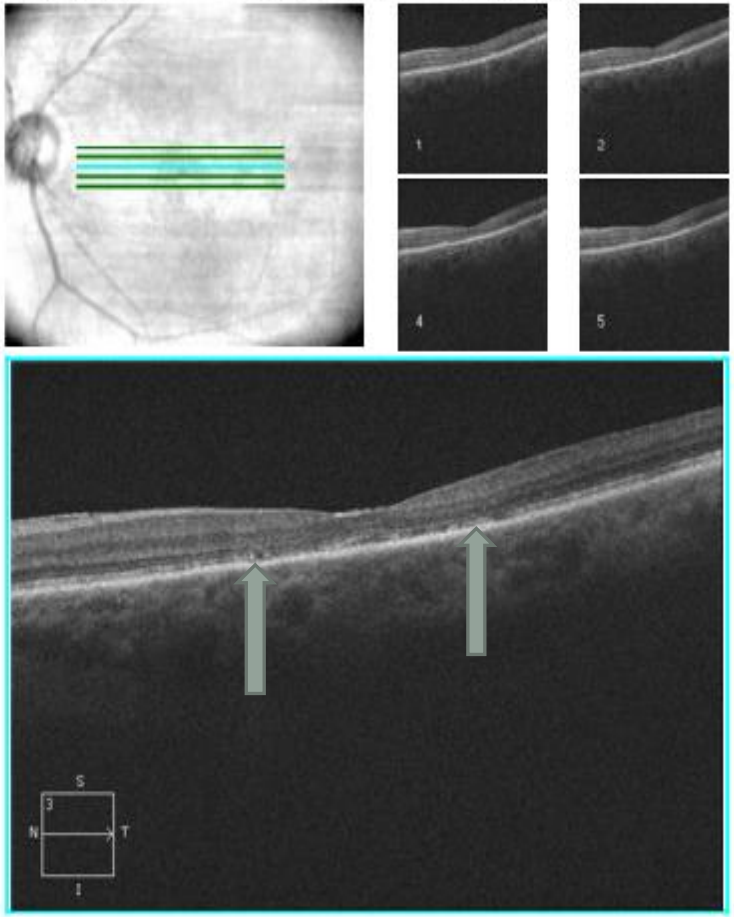
Comments

Doctor's Signature

High Definition Images: HD 5 Line Raster

OD ○ ● OS

Scan Angle: 0° Spacing: 0.25 mm Length: 6 mm



Comments

Doctor's Signature

Central 10-2 Threshold Test

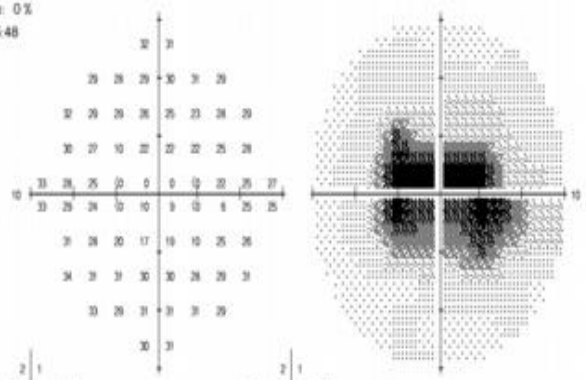
Fixation Monitor: Gaze/Blind Spot
Fixation Target: Central
Fixation Losses: 0/15
False POS Errors: 0 %
False NEG Errors: 0 %
Test Duration: 05:48

Stimulus: III, White
Background: 31.5 ASB
Strategy: SITA-Fast

Pupil Diameter: 4.8 mm
Visual Acuity:
RX: +2.50 DS DC: X

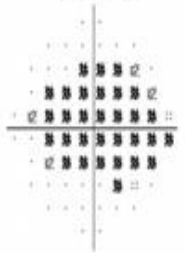
Date: 10-25-2017
Time: 9:54 AM
Age: 79

Fovea: OFF

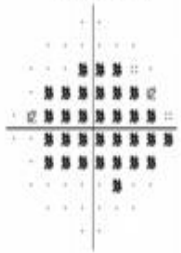


MD -8.26 dB P < 1%
PSD 10.64 dB P < 1%

Total Deviation

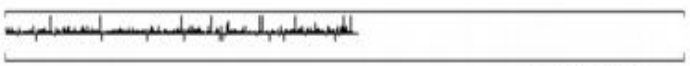


Pattern Deviation



:: < 5%
Ø < 2%
▓ < 1%

MCPHS EYE AND VISION CENTER
10 LINCOLN SQUARE
WORCESTER, MA 01608
508-373-5830



HFA II 750-40053-5.1.1/5.1.1

Central 10-2 Threshold Test

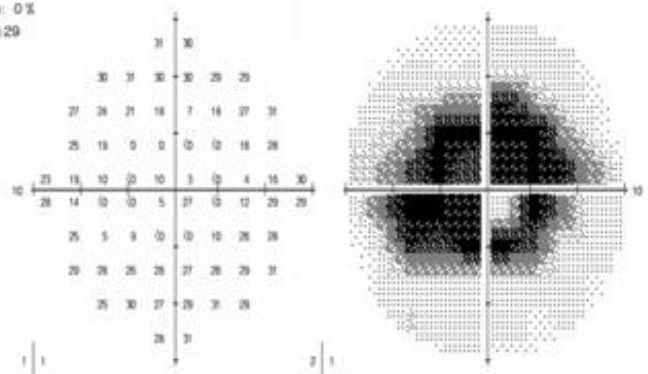
Fixation Monitor: Gaze/Blind Spot
Fixation Target: Central
Fixation Losses: 0/18
False POS Errors: 2 %
False NEG Errors: 0 %
Test Duration: 08:29

Stimulus: III, White
Background: 31.5 ASB
Strategy: SITA-Fast

Pupil Diameter: 5.3 mm
Visual Acuity:
RX: +3.25 DS DC: X

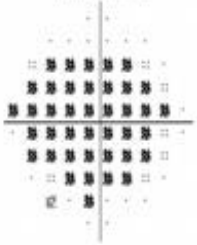
Date: 10-25-2017
Time: 9:43 AM
Age: 79

Fovea: OFF

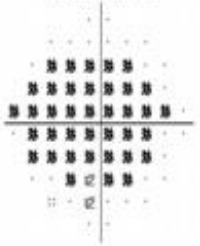


MD -13.62 dB P < 1%
PSD 12.87 dB P < 1%

Total Deviation



Pattern Deviation



:: < 5%
Ø < 2%
▓ < 1%

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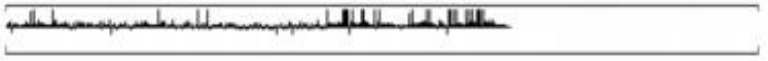
508-373-5830



HFA II 750-40053-5.1.1/5.1.1

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Evaluation of Hydroxychloroquine Retinopathy With Multifocal Electroretinography

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From the University of Texas Southwestern (SCS), Dallas, Texas; and the New England Eye Center (TRH, JSS, MLAQ), New England Medical Center, Boston, Massachusetts

Abstract

BACKGROUND AND OBJECTIVE— To describe the changes revealed by multifocal electroretinography (ERG) in patients taking hydroxychloroquine.

PATIENTS AND METHODS— Six patients being treated for various inflammatory conditions with hydroxychloroquine for periods ranging from 8 months to 7 years were consecutively evaluated. Each examination included measurement of Snellen visual acuities, Amsler grid assessment, and automated visual field testing. In some cases, funduscopic examinations were complimented by photography and fluorescein angiography. Multifocal ERG was performed for all patients.

RESULTS— Three patients (six eyes) were found to have distinctive abnormalities on multifocal ERG consisting of pericentral depression of ERG signals. The abnormalities on multifocal ERG corresponded with the patients' subjective descriptions and the visual field depiction of their pericentral scotomas. All affected patients had been taking hydroxychloroquine for at least 7 years. One patient with generalized depression on multifocal ERG had possible hydroxychloroquine retinopathy. Two patients (three eyes) had relatively normal results on multifocal ERG.

CONCLUSION— Multifocal ERG objectively demonstrates depression of signals in the perifoveal region in visually symptomatic patients with long-term hydroxychloroquine use. Even patients with normal visual acuity and no fundus abnormalities can have abnormal results. Although we have not yet identified patients with abnormalities on multifocal ERG before the onset of symptoms, multifocal ERG may be useful in monitoring patients at risk and may provide an earlier opportunity to identify maculopathy.

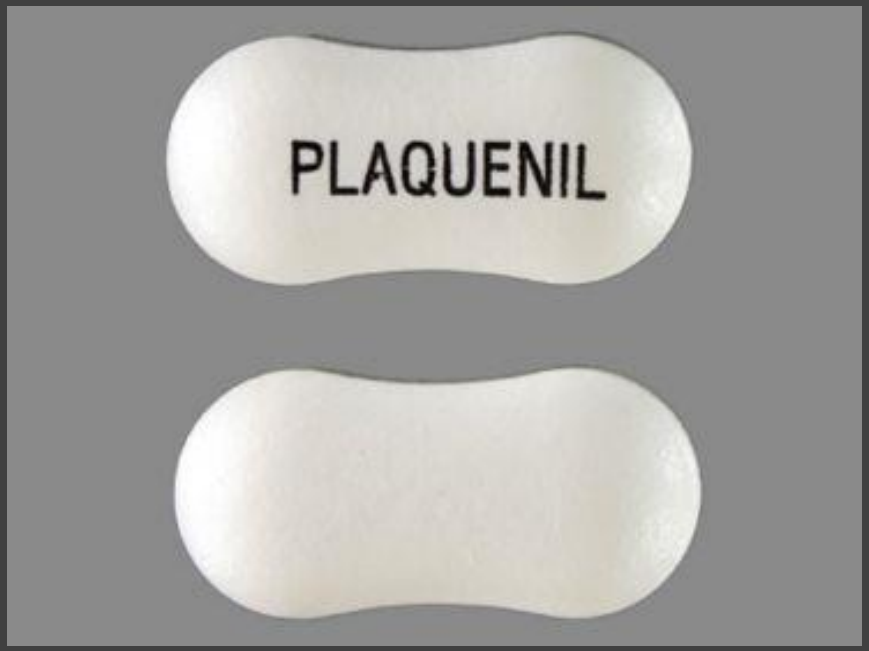
INTRODUCTION

Originally used as antimalarial agents, chloroquine and hydroxychloroquine are now being used as effective treatment for various connective tissue diseases, especially systemic lupus erythematosus and rheumatoid arthritis.[1] In 1959, chloroquine retinopathy was first described in three cases with classic bull's eye retinopathy, which was attributed to lengthy treatment.[2] Affected patients present with difficulty reading and blurred distance vision, along with increased granularity or patchy depigmentation in a ring-shaped pattern circumscribing the macula.[3,4]

Johnson and Vine examined nine patients taking a cumulative dose of hydroxychloroquine of greater than 1,000 g and noted that eight patients taking 400 mg/d had no evidence of

Plaquenil mechanism of action

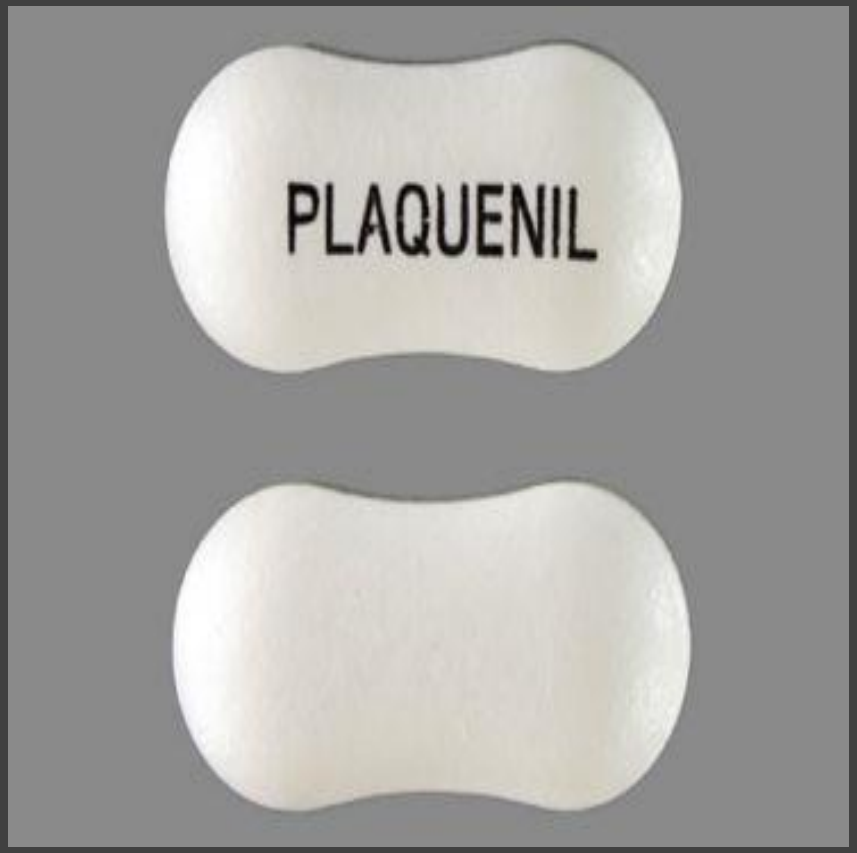
- **Proposed mechanism of action is interference with the "antigen processing" in macrophages and other antigen-presenting cells**
- **Results in down-regulation of the immune response against auto-antigenic peptides.**



http://drugs.healthgrove.com/l/851/Plaquenil

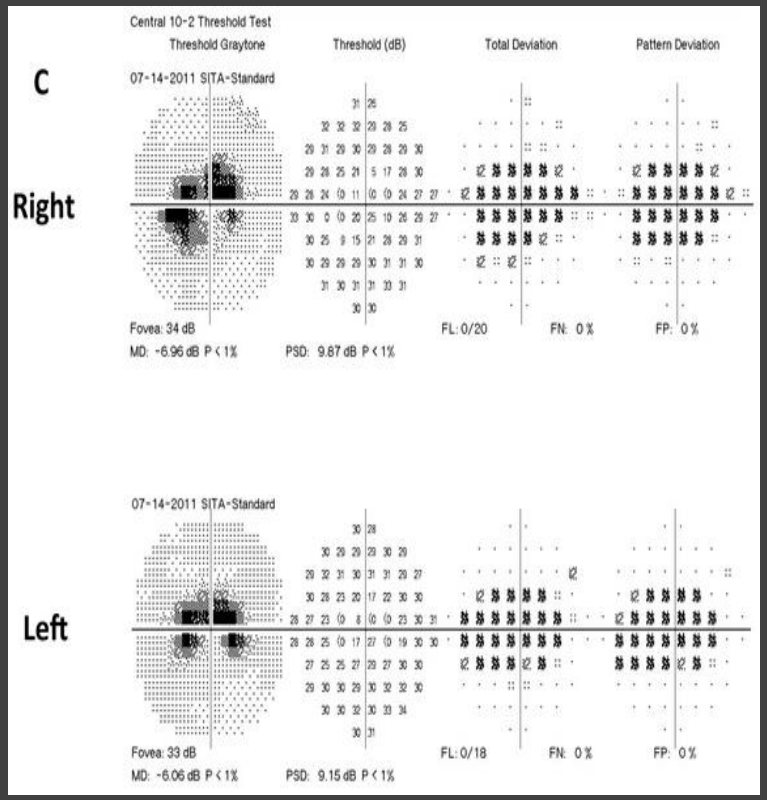
Antimalarial Agents: potential side effects

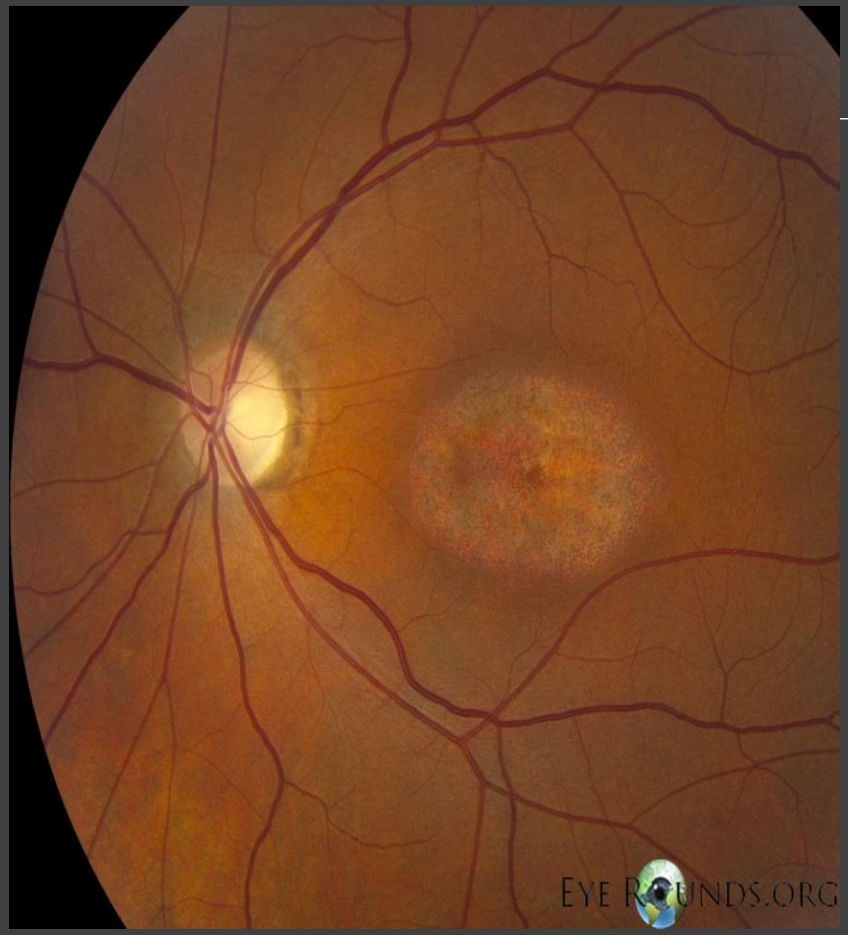
- **Punctate or verticillate corneal deposits**
- **Decreased visual acuity**
- **Difficulty with night vision (nyctalopia)**
- **Reduced color vision (especially blue/yellow)**



Antimalarial Agents: potential side effects

- **Development of persistent central or paracentral scotoma**
  - **May occur without obvious fundus findings**
- **Parafoveal RPE changes**
  - **Pigment clumping/atrophy**
  - **"Bull's eye" maculopathy: RPE depigmentation surrounded by a ring of hyperpigmentation with sparing of foveola**





C

Right

Central 10-2 Threshold Test

Threshold Graytone | Threshold (dB) | Total Deviation | Pattern Deviation

07-14-2011 SITA-Standard

Fovea: 34 dB

MD: -6.96 dB P < 1%

PSD: 9.87 dB P < 1%

FL: 0/20

FN: 0 %

FP: 0 %

Left

07-14-2011 SITA-Standard

Fovea: 33 dB

MD: -6.06 dB P < 1%

PSD: 9.15 dB P < 1%

FL: 0/18

FN: 0 %

FP: 0 %

2011 monitoring Guidelines

- **Dilated fundus exam at baseline, not for screening**
- **No longer recommend color vision or amsler grid testing**
- **10-2 SS VF still recommended**
- **When possible: FAF, mERG or macular OCT.**
- **Annual screening recommended after 5 years of the medication.**

Newest Guidelines - 2016

- **Updated again based on higher than previously believed prevalence of toxicity in long-term users.**
- **Risk is highly dependent on the daily dose by weight.**
- **Previously, this medication was prescribed using Ideal weight, but toxicity levels are better when using actual weight.**
- **Lower risk was achieved when doses were <5mg/kg real weight.**

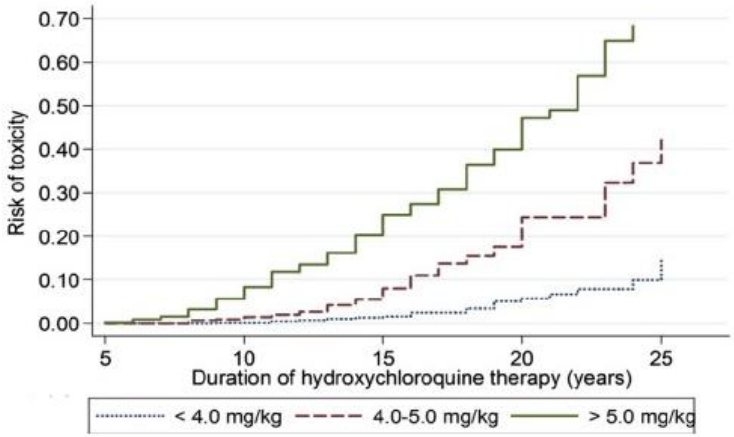


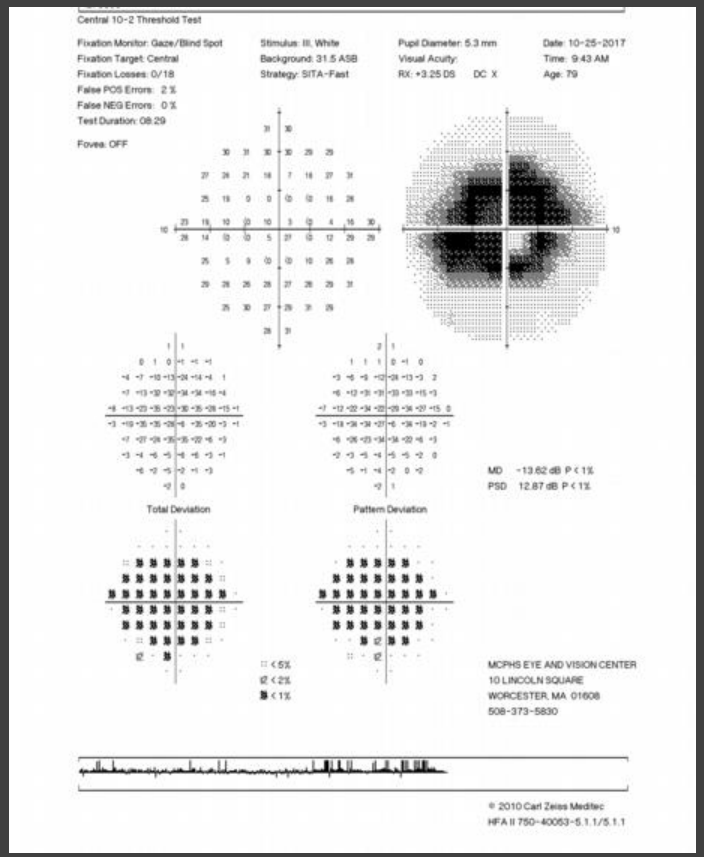
Figure 4. Kaplan–Meier curves showing the cumulative risk of retinopathy over time, with different levels of hydroxychloroquine (HCQ) use. When use is between 4.0 and 5.0 mg/kg, the risk is very low within the first 5 to 10 years, but it increases markedly thereafter. Reprinted with permission from Melles RB, Marmor MF. The risk of toxic retinopathy in patients on long-term hydroxychloroquine therapy. JAMA Ophthalmol 2014;132:1453–60.[2]

https://www.aao.org/clinical-statement/revised-recommendations-on-screening-chloroquine-h

Newest Guidelines - 2016

- **At recommended doses, the risk of toxicity up to 5 years is under 1% and up to 10 years is under 2%. This rises to almost 20% after 20 years.**

- **Also, "bull's eye" pattern of maculopathy is infrequent in Asian patients. Monitor with 24-2 SS or 30-2 SS instead of only 10-2 SS VF.**



https://www.aao.org/clinical-statement/revised-recommendations-on-screening-chloroquine-h

Newest Study information

- **Patients with renal disease can have an unpredictably high blood level as the medication is cleared by the kidney, so dosages have to be adjusted to account for this.**

****Patients who take tamoxifen concurrently have a 5 fold risk of toxicity****

https://www.aao.org/clinical-statement/revised-recommendations-on-screening-chloroquine-h

Newest Guidelines - 2016

No longer recommended:

- **Fundus examination for screening**
  - **Bull's eye macula is a late stage sign**
- **Time-domain OCT**
- **FFA**
- **Full field ERG**
- **Amsler Grid**
- **Color vision**

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.

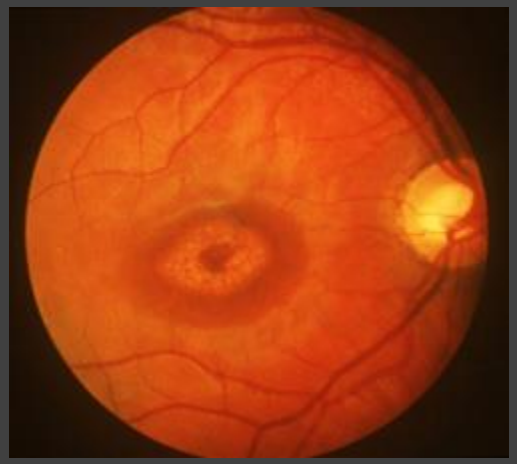
Table 2. Screening Frequency

Baseline Screening
Fundus examination within first year of use
Add visual fields and SD OCT if maculopathy is present
Annual Screening
Begin after 5 yrs of use
Sooner in the presence of major risk factors

SD OCT = spectral-domain optical coherence tomography.

Antimalarial agents: management of toxicity

- **No effective treatment**
- **Discontinue med in conjunction with patient's internist or rheumatologist**
- **Drug clears slowly from the body = ocular changes may continue after cessation of treatment**
- **F/u every 3 months until ocular findings stabilize, then annually**



http://www.silverspringeye.com/wp-content/themes/jonathans_lyons/images/eyecondition_bullseye.jpg

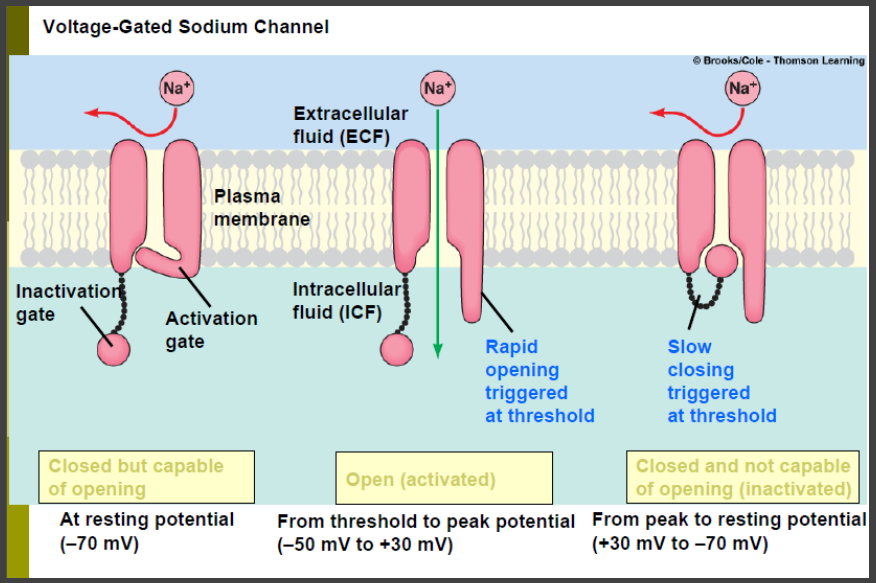
Topamax (topiramate)

Topamax (topiramate)

- Used to treat seizures and now for the prevention of headaches.
- Used off-label in weight reduction and for treating bipolar
- Anticonvulsant
- Adverse effect usually (85%) occurs in the first 2 weeks.

Topiramate mechanism of action

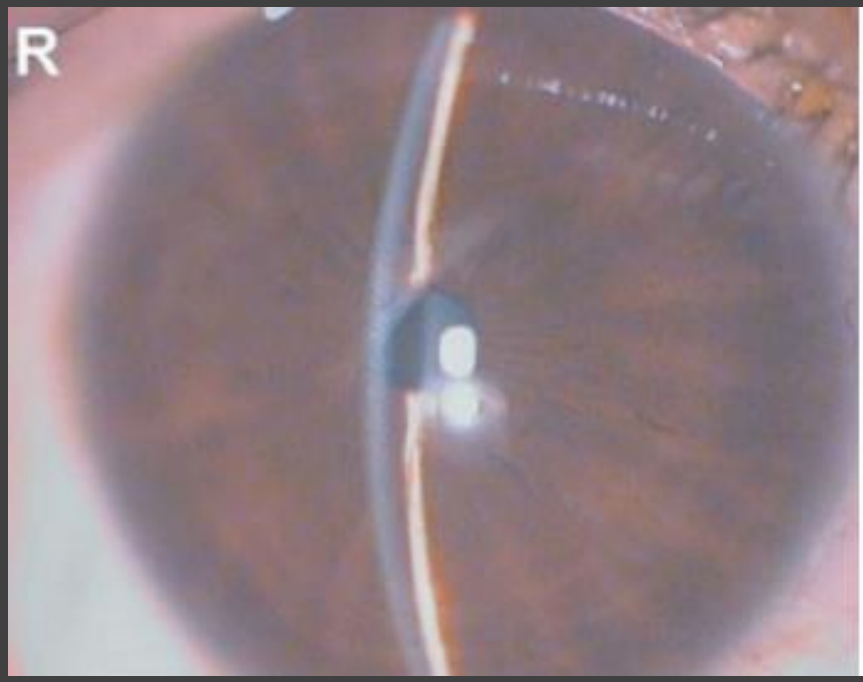
- Precise mechanism of action is unknown
- Inhibits voltage gated sodium channels and high voltage gated calcium channels.
- Also inhibits some subtypes of carbonic anhydrase.



https://s3.amazonaws.com/test.classconnection/11/flashcards/399011/png/na_channel.png

Topiramate ocular side effects

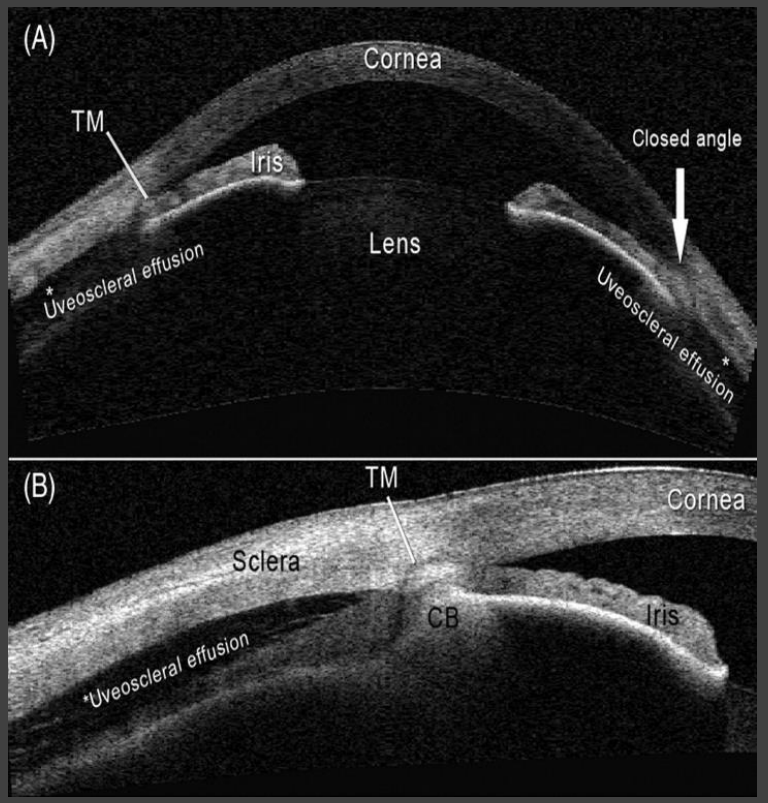
- **Manifests as an atypical angle closure glaucoma with a narrow anterior chamber, acute myopia and a quiet eye.**
- **LPI is ineffective in this condition.**



Levy J, Yag R, Petroca A, et al. Topiramate-induced bilateral angle-closure glaucoma. Can J. Ophthalmol 2006;41:221-5.

Topamax (topiramate) angle closure

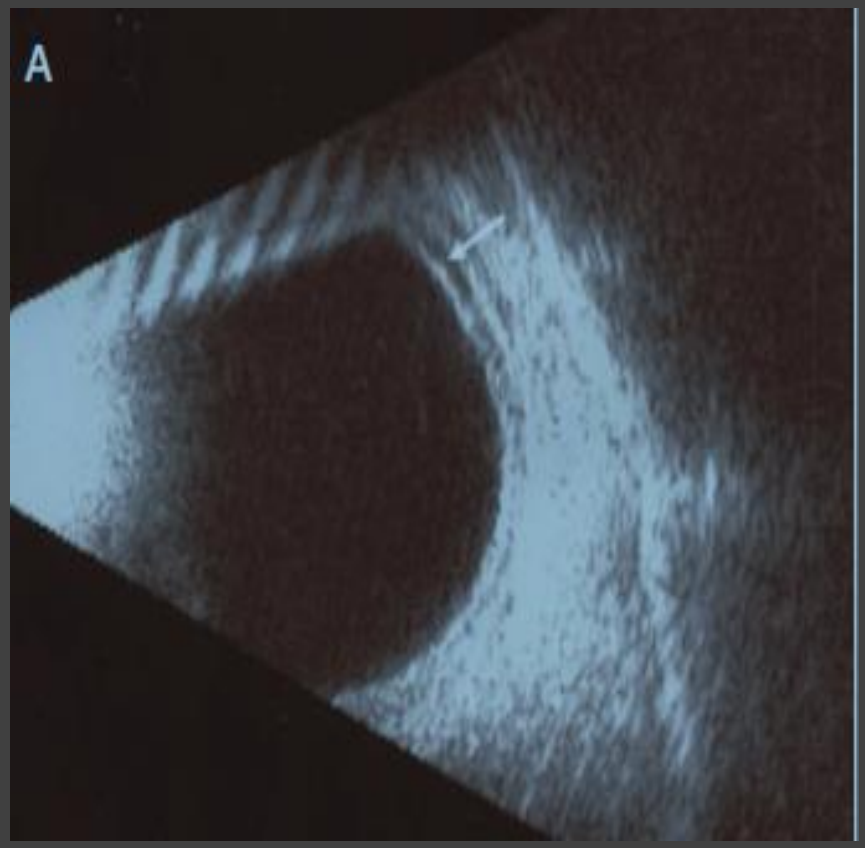
- **Bilateral presentation, (regular angle closure is very rarely bilateral).**
- **Mechanism: ciliochoroidal effusion causing a forward rotation of the lens-iris diaphragm. This causes a narrow anterior chamber and acutely elevated IOP**



Topamax (topiramate) angle closure

- **Acute myopia is presumably due to ciliary body edema, which causes relaxation of the zonules and induced myopic shift in refraction. There is also anterior movement of the entire lens.**

- **Treatment: d/c topiramate, anti-glaucoma meds, topical steroid, Atropine.**

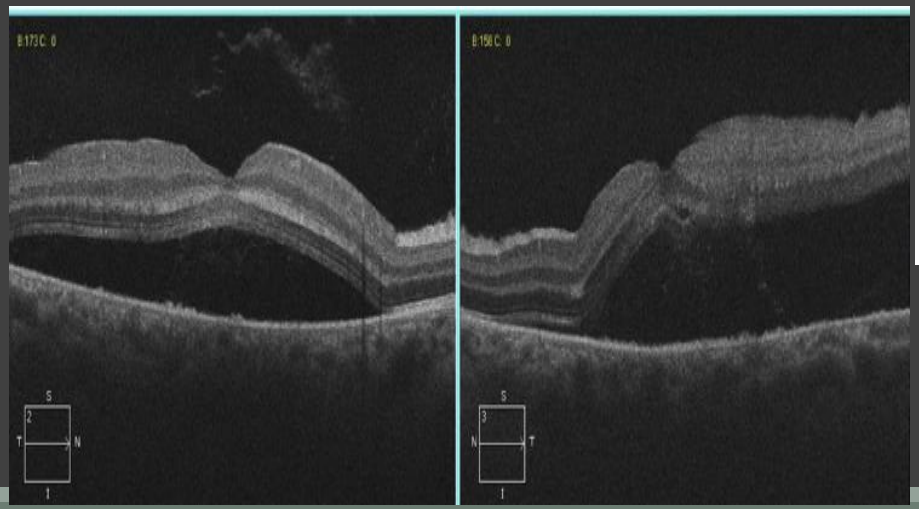


Levy J, Yag R, Petroca A, et al. Topiramate-induced bilateral angle-closure glaucoma. Can J. Ophthalmol 2006;41:221-5.

Other side effects associated with topiramate

Two cases of macular neurosensory retinal detachments.

Both cases resolved after discontinuing the medication.



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journal homepage: http://www.ajocasereports.com/

Case report

Topiramate-induced macular neurosensory retinal detachment

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ABSTRACT

Purpose: To present a previously unreported retinal side-effect from topiramate use in two cases.
Observations: Macular neurosensory retinal detachments were seen in two patients shortly after beginning oral topiramate. The macular detachments resolved shortly after discontinuing this medication.
Conclusions and importance: As these two cases represent the first reports of topiramate-induced macular neurosensory retinal detachment, clinicians should be aware of this potential ocular side effect when administering this medication.

Erectile dysfunction medications

Erectile dysfunction medications

- **Phosphodiesterase type 5 inhibitor (PDE5 inhibitor)**
- **Blocks PDE5 in the smooth muscle cells lining the blood vessels supplying the corpus cavernosum of the penis.**
- **Widely used medications in the US**

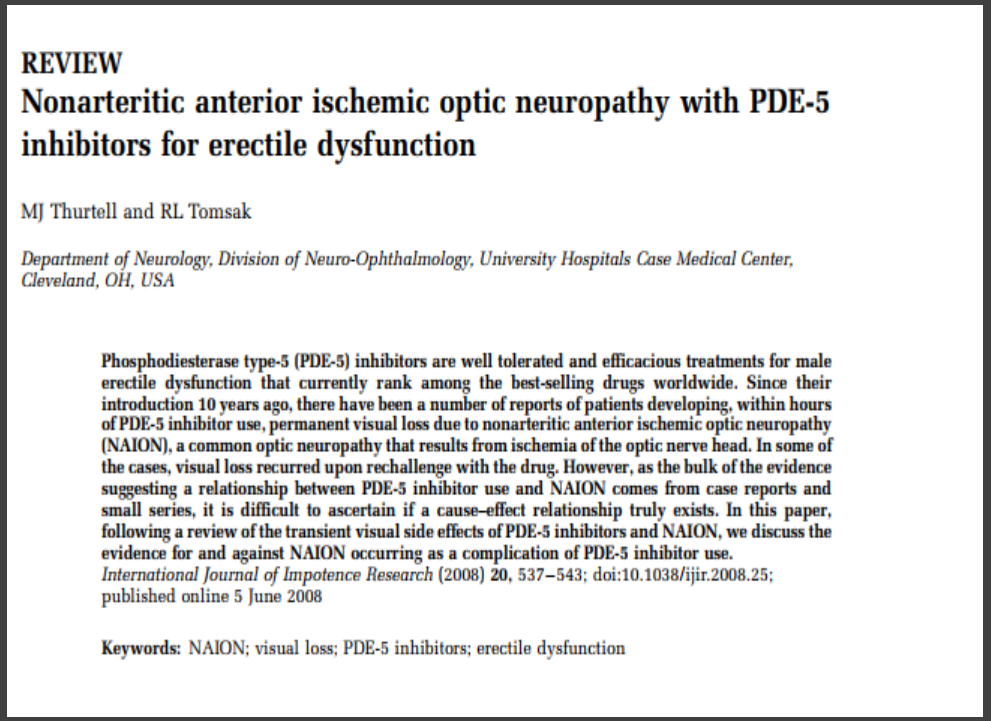
https://www.urologicalcare.com/upload/ed/viagra.jpg

Erectile dysfunction medication ocular side effects

- Vision can have a ‘blue hue’
- Sudden, painless loss of vision (NAION) has been found to be two- fold the risk in patients who take PDE5 inhibitors in some studies. Others show no link to NAION.

NAION?

- Possible mechanism is mildly reduced blood pressure in the evening after PDE-5 inhibitor use.
- This may exacerbate nocturnal hypotension in patients who are at risk for NAION:
  - "Disc at risk"
  - Atherosclerotic risk factors
  - Hypertension medications



REVIEW

Nonarteritic anterior ischemic optic neuropathy with PDE-5 inhibitors for erectile dysfunction

MJ Thurtell and RL Tomsak

Department of Neurology, Division of Neuro-Ophthalmology, University Hospitals Case Medical Center, Cleveland, OH, USA

Phosphodiesterase type-5 (PDE-5) inhibitors are well tolerated and efficacious treatments for male erectile dysfunction that currently rank among the best-selling drugs worldwide. Since their introduction 10 years ago, there have been a number of reports of patients developing, within hours of PDE-5 inhibitor use, permanent visual loss due to nonarteritic anterior ischemic optic neuropathy (NAION), a common optic neuropathy that results from ischemia of the optic nerve head. In some of the cases, visual loss recurred upon rechallenge with the drug. However, as the bulk of the evidence suggesting a relationship between PDE-5 inhibitor use and NAION comes from case reports and small series, it is difficult to ascertain if a cause–effect relationship truly exists. In this paper, following a review of the transient visual side effects of PDE-5 inhibitors and NAION, we discuss the evidence for and against NAION occurring as a complication of PDE-5 inhibitor use.

International Journal of Impotence Research (2008) **20**, 537–543; doi:10.1038/ijir.2008.25; published online 5 June 2008

Keywords: NAION; visual loss; PDE-5 inhibitors; erectile dysfunction

NAION?

- No definitive cause has been established to date
- If your patient has had an NAION and has significant risk factors (disc at risk, HTN, etc) then you should discuss the possibility of NAION with PDE-5 inhibitors.

REVIEW

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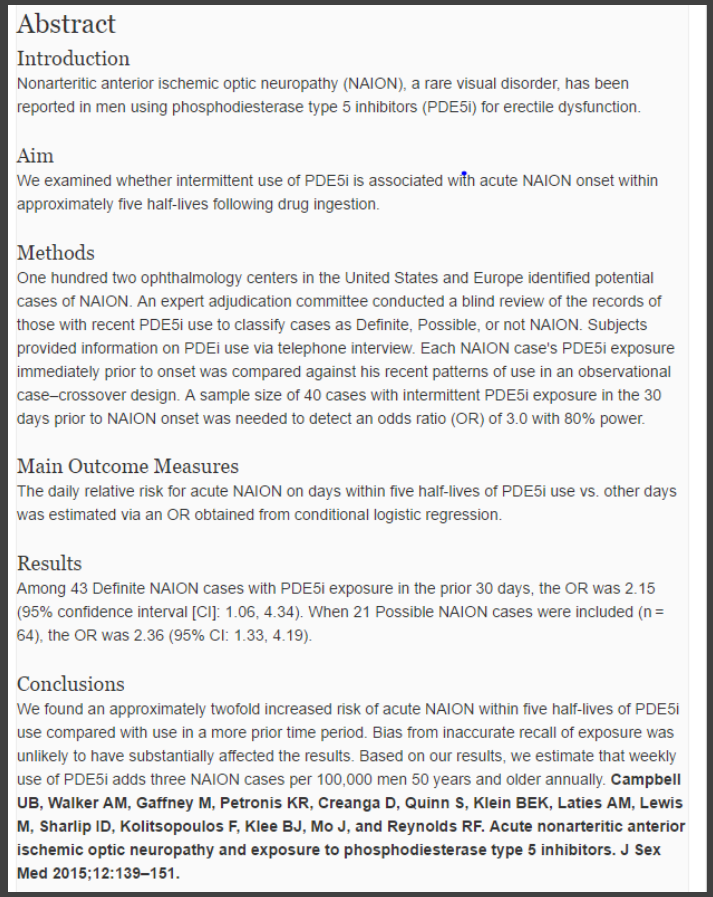
Keywords: NAION; visual loss; PDE-5 inhibitors; erectile dysfunction

My PDE-5 study experience

- I was site principal investigator for an NAION study sponsored by Bayer pharmaceuticals.
- Participants who had an NAION (confirmed not to be arteritic via blood work) were then asked to do a phone interview regarding their PDE-5 inhibitor use.
- Study found a two-fold risk in NAION in patients using PDE-5 inhibitors.



Abstract

Introduction

Nonarteritic anterior ischemic optic neuropathy (NAION), a rare visual disorder, has been reported in men using phosphodiesterase type 5 inhibitors (PDE5i) for erectile dysfunction.

Aim

We examined whether intermittent use of PDE5i is associated with acute NAION onset within approximately five half-lives following drug ingestion.

Methods

One hundred two ophthalmology centers in the United States and Europe identified potential cases of NAION. An expert adjudication committee conducted a blind review of the records of those with recent PDE5i use to classify cases as Definite, Possible, or not NAION. Subjects provided information on PDEi use via telephone interview. Each NAION case's PDE5i exposure immediately prior to onset was compared against his recent patterns of use in an observational case–crossover design. A sample size of 40 cases with intermittent PDE5i exposure in the 30 days prior to NAION onset was needed to detect an odds ratio (OR) of 3.0 with 80% power.

Main Outcome Measures

The daily relative risk for acute NAION on days within five half-lives of PDE5i use vs. other days was estimated via an OR obtained from conditional logistic regression.

Results

Among 43 Definite NAION cases with PDE5i exposure in the prior 30 days, the OR was 2.15 (95% confidence interval [CI]: 1.06, 4.34). When 21 Possible NAION cases were included (n = 64), the OR was 2.36 (95% CI: 1.33, 4.19).

Conclusions

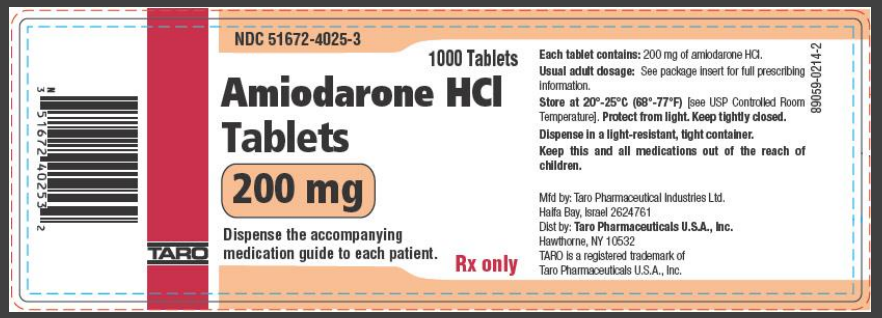
We found an approximately twofold increased risk of acute NAION within five half-lives of PDE5i use compared with use in a more prior time period. Bias from inaccurate recall of exposure was unlikely to have substantially affected the results. Based on our results, we estimate that weekly use of PDE5i adds three NAION cases per 100,000 men 50 years and older annually. **Campbell UB, Walker AM, Gaffney M, Petronis KR, Creanga D, Quinn S, Klein BEK, Laties AM, Lewis M, Sharlip ID, Kolitsopoulos F, Klee BJ, Mo J, and Reynolds RF. Acute nonarteritic anterior ischemic optic neuropathy and exposure to phosphodiesterase type 5 inhibitors. J Sex Med 2015;12:139–151.**

Anti-Arrhythmic medications

Anti-Arrhythmic medications

Amiodarone:

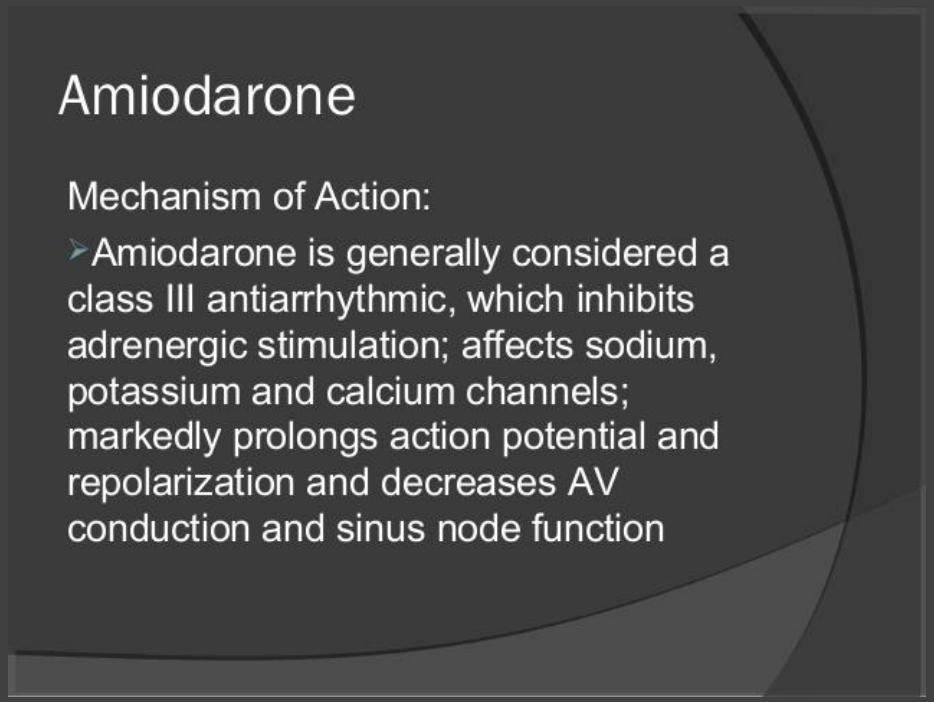
- benzofuran derivative
- Normal dose: 600-800 mg QD x 1 month, then 400 mg QD thereafter
- Used to treat ventricular arrhythmias and atrial fibrillation



https://dailymed.nlm.nih.gov/dailymed/archives/image.cfm?archiveid=229531&name=amiodarone-03.jpg

Amiodarone mechanism of action

- **Inhibits inward sodium and calcium channels.**
- **Results in suppression of excitability and conductivity of cardiac tissues**



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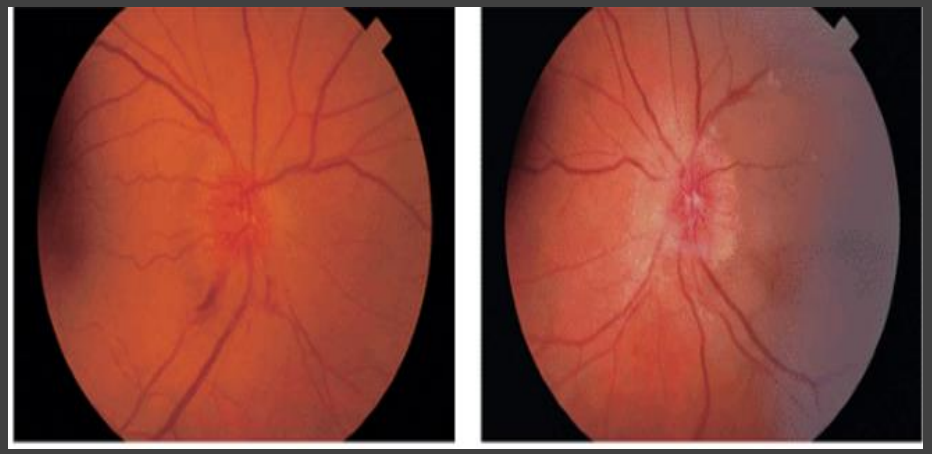
Amiodarone: potential side effects

- Superficial punctate opacities (69-100%)
- Corneal edema
- Whorl-like (vortex) keratopathy
  - Lipophilic drug attaches to the basal stem cells at the limbus and is carried to the center of the cornea until the cells differentiate and desquamate
- Photophobia (57%)

Amiodarone: potential side effects

- Anterior subcapsular yellow-white punctate opacities



Optic neuropathy (1.8%)

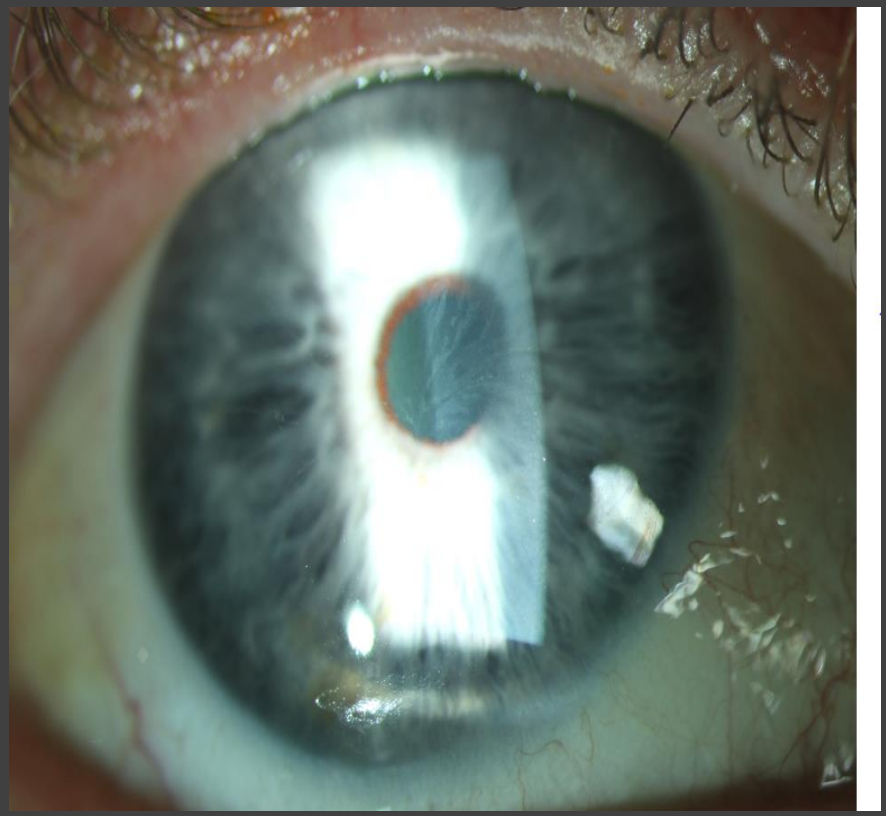
- Drug-induced lipid storage disease
- Accumulation of intracytoplasmic lamellar inclusions in the optic nerve axons; impairs axoplasmic flow and causes optic disc edema
- Predisposing risk factors: DM, HTN

Toxic Neuropathy vs NAION

	Amiodarone-induced Optic Neuropathy	NAION
Onset of visual loss	Insidious (months)	Rapid (days to weeks)
Degree of vision loss	20/20 to 20/200	20/20 to NLP
Ocular involvement	Usually simultaneous	Rarely simultanous

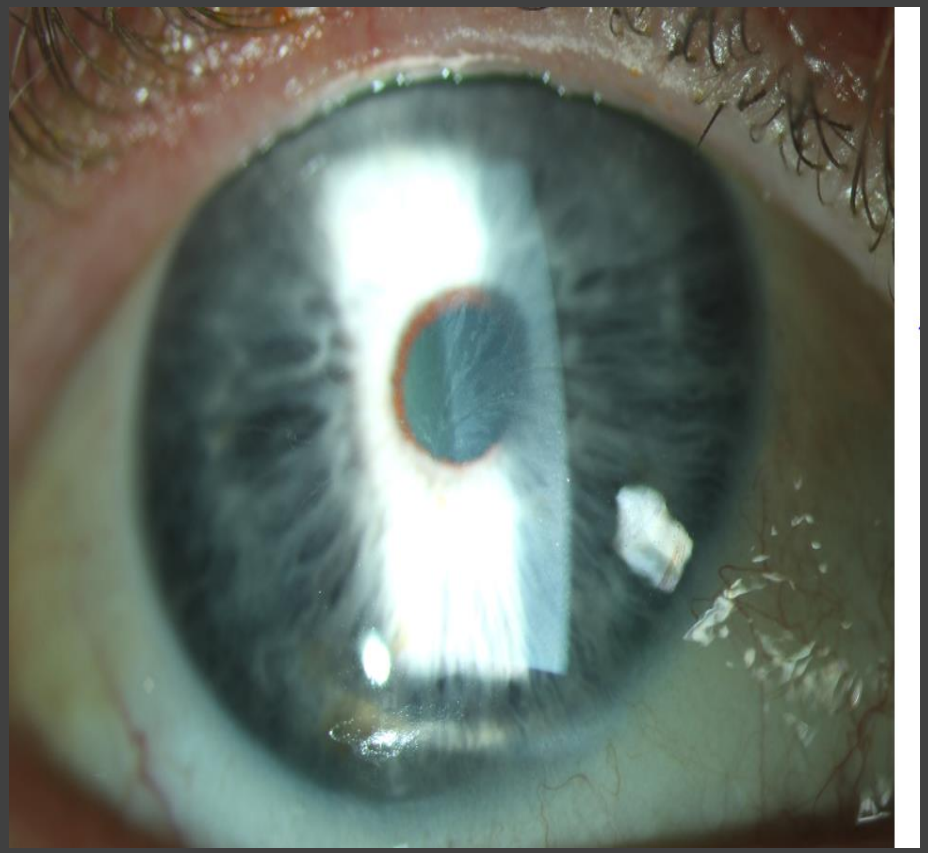
Amiodarone: baseline examination (AOA guideline)

- **Complete eye exam including DFE**
- **Screening visual field**
- **Amsler grid**
- **Color vision (red/green, blue/yellow)**



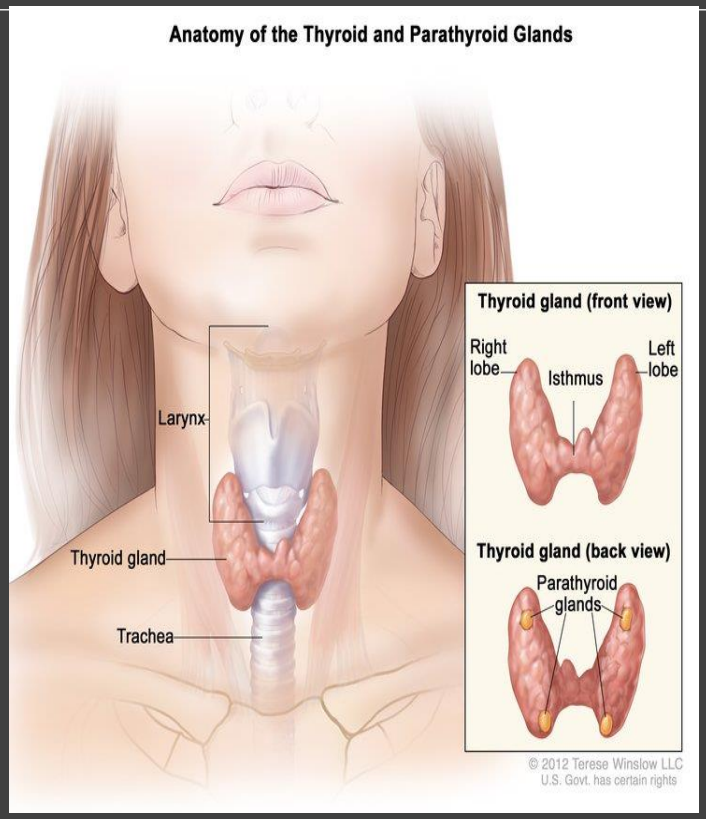
Amiodarone: management of ocular toxicity

- Report adverse side effects to cardiologist and/or PCP
- Protective sun wear for photophobia
- Discontinue medication in conjunction with the prescribing doctor if optic neuropathy develops



Amiodarone: one more thing…

- **Can cause thyroid dysfunction**
  - **Inhibits peripheral conversion of T4 to T3**
  - **Hypothyroidism or hyperthyroidism**
  - **Tx: decrease dosage**



https://www.womenshealth.gov/publications/our-publications/fact-sheet/images/thyroid-zoom.jpg

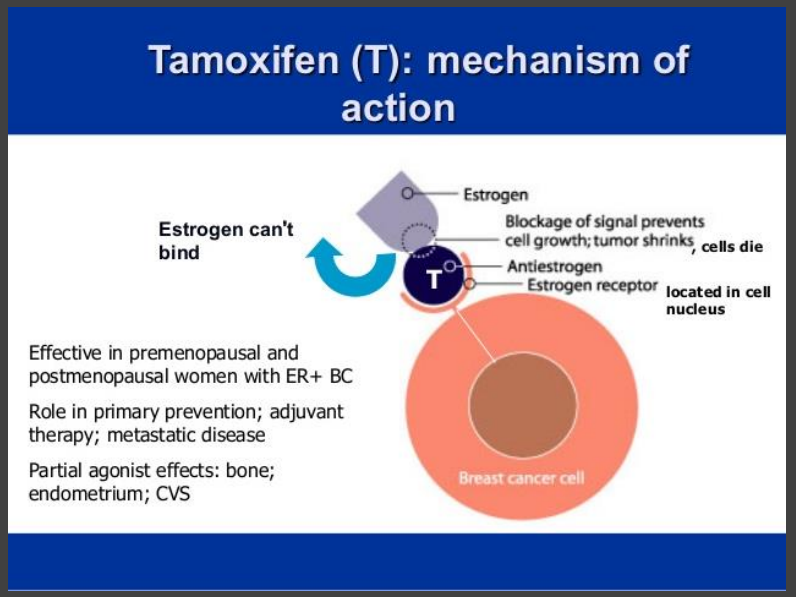
Tamoxifen (Nolvadex)

Tamoxifen (Nolvadex)

- **Nonsteroidal anti-estrogen agent used for long-term, preventative therapy after breast cancer surgery**
  - **Normal dosage: 20 – 40 mg QD**
  - **Retinal findings more common at dosages of 180 mg QD**

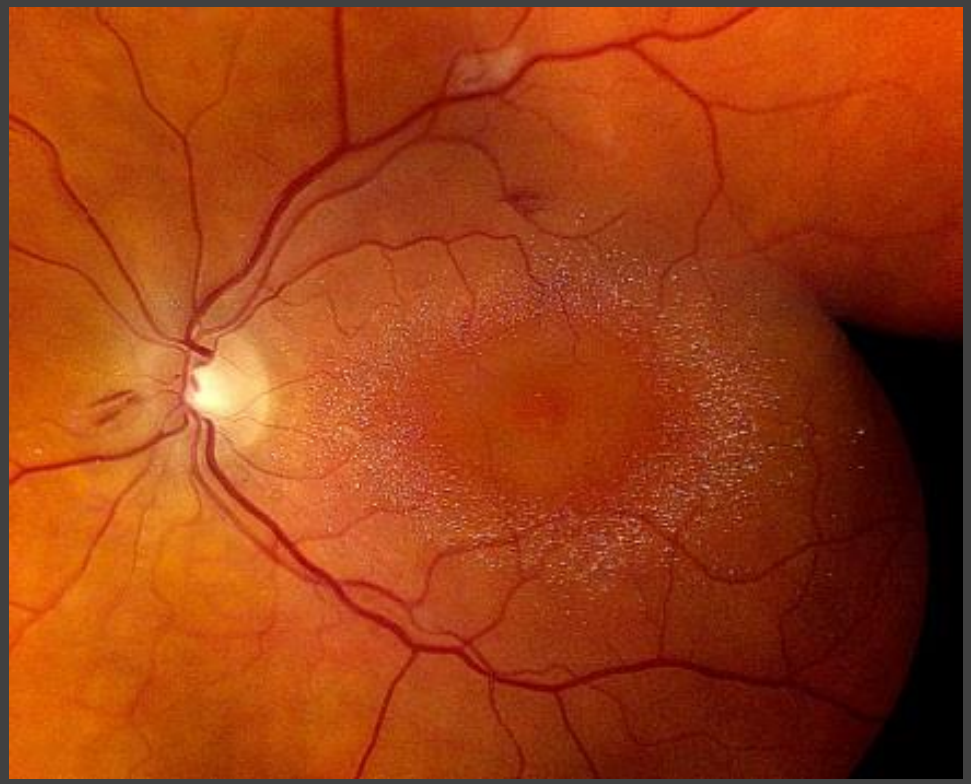
Tamoxifen: mechanism of action

- **Binds to the Estrogen receptor.**
- **Strongly anti-estrogenic on the mammillary epithelium**
- **Lowers the circulating levels of insulin-like growth factor (IGF-1) in breast cancer patients. IGF-1 may stimulate the growth of breast cancer cells.**



Tamoxifen ocular side effects

- **Crystalline retinopathy (incidence: 6%)**
  - **Refractile bodies in the inner retina; may be product of axonal degeneration**
- **Macular edema**
- **Optic neuritis**

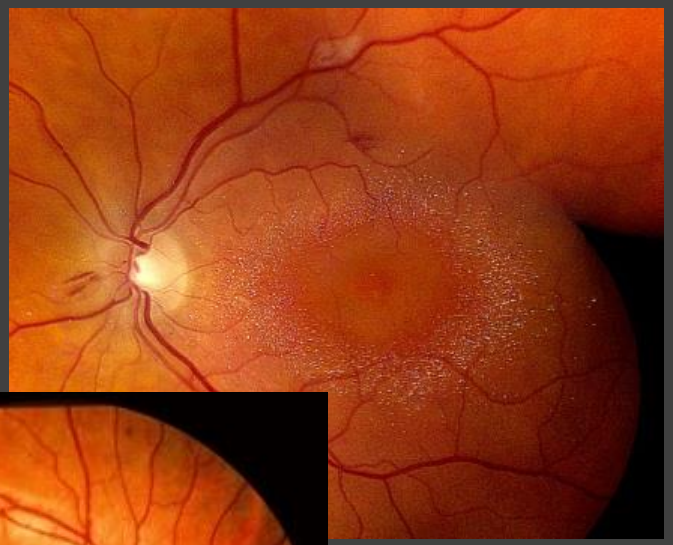


Tamoxifen ocular side effects

- **Keratopathy (subepithelial calcium map-dot changes)**
- **Cataracts**

<u>Management:</u>

- **d/c medication in conjunction with oncologist.**
- **Follow-up annually unless retinopathy noted, then q3 months**



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Case 3

Case

27 year old African American male presents with a complaint of blurry vision OD x 2 weeks. Started with fluctuating blur and progressed to constant blur the last 16 hours.

Occupation: Air traffic controller

Medications: 20 mg prednisone PO. On a taper for asthma.

Allergies: none

DVA: sc

- **20/40**
- **20/20**

EOMS: full and smooth OD/OS

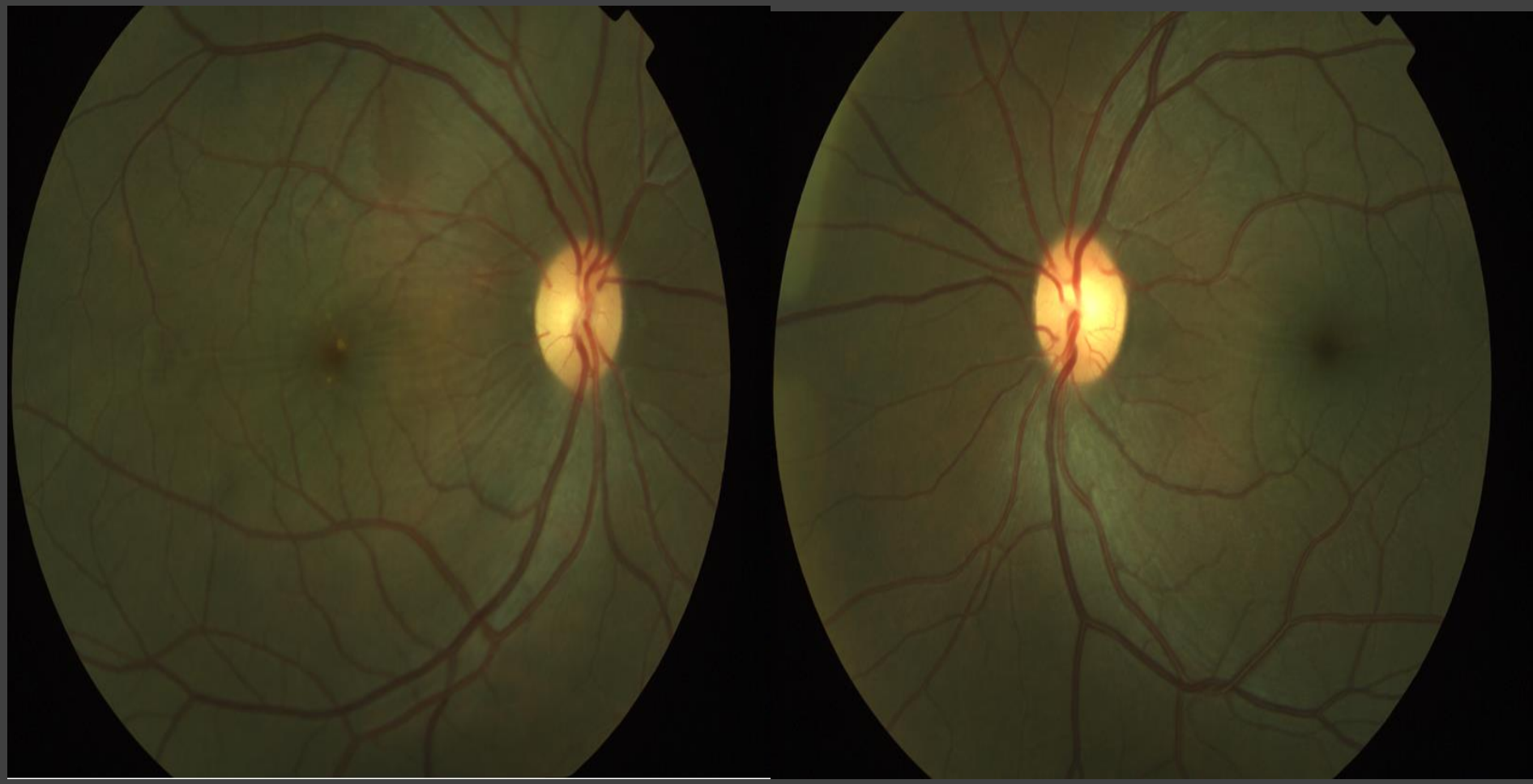
Pupils: ERRL (-) APD

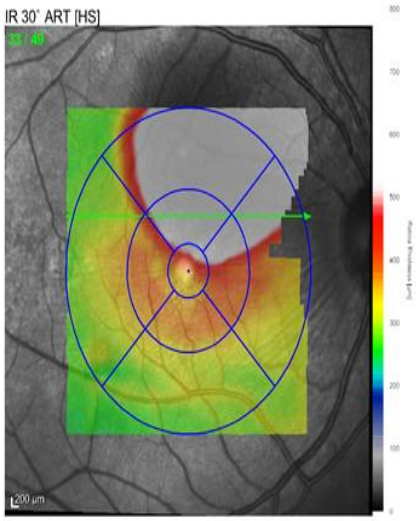
Manifest:

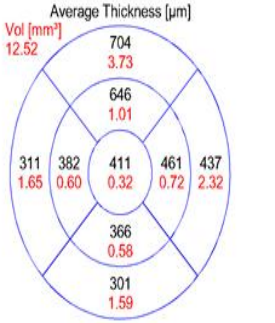
- **OD: -1.00 20/20**
- **OS: +0.25 20/20**

Anterior segment unremarkable.

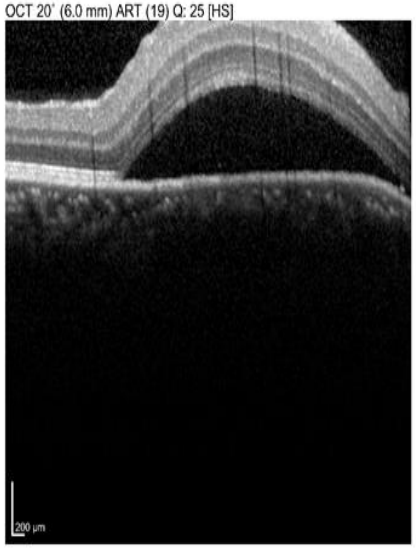
Pt dilated…..

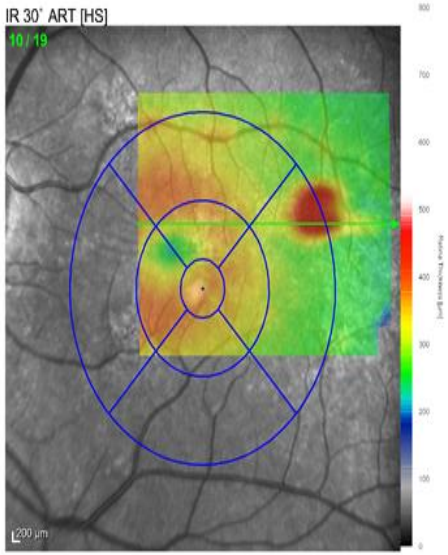


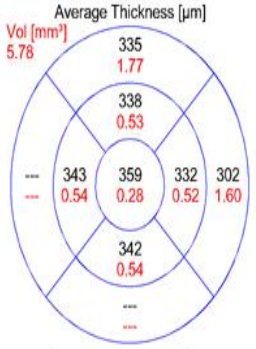




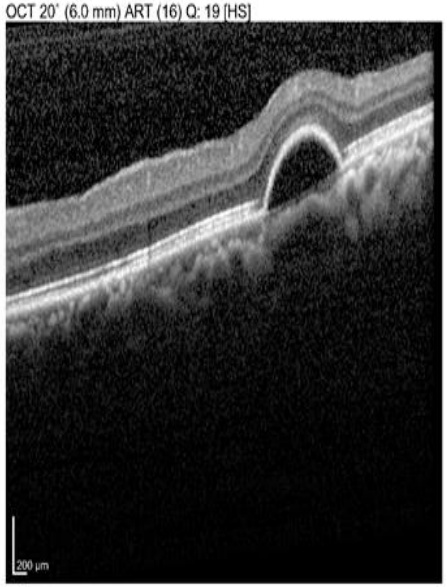
Center: 367 µm
Central Min: 340 µm
Central Max: 553 µm
Circle Diameters: 1, 3, 6 mm ETDRS

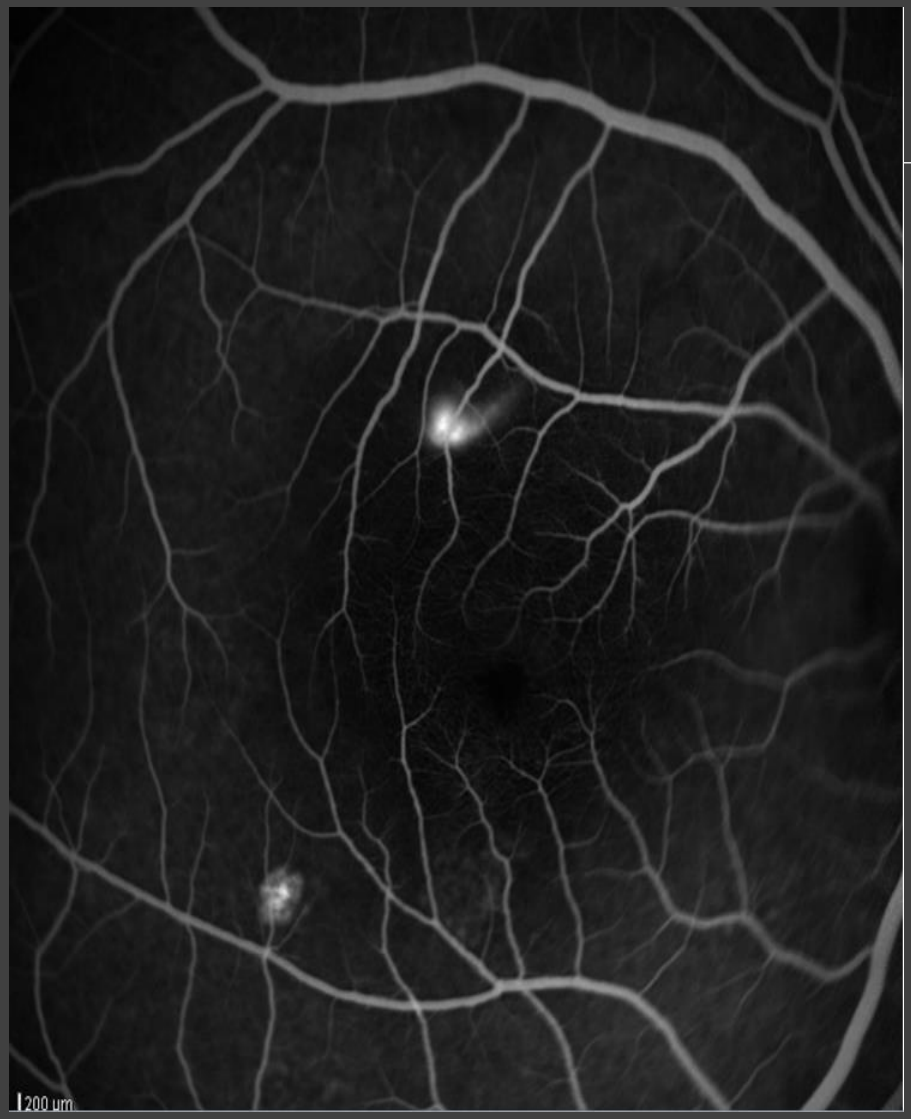


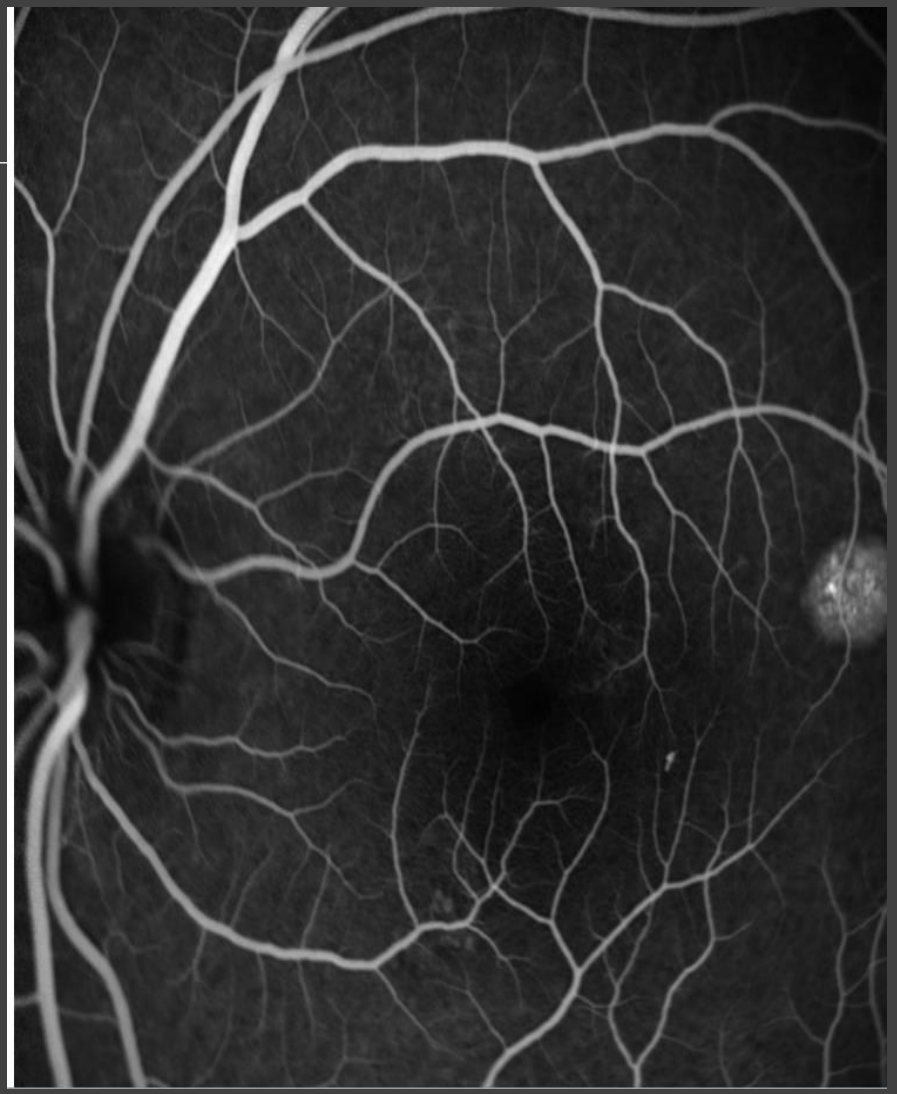




Center: 362 µm
Central Min: 308 µm
Central Max: 377 µm
Circle Diameters: 1, 3, 6 mm ETDRS

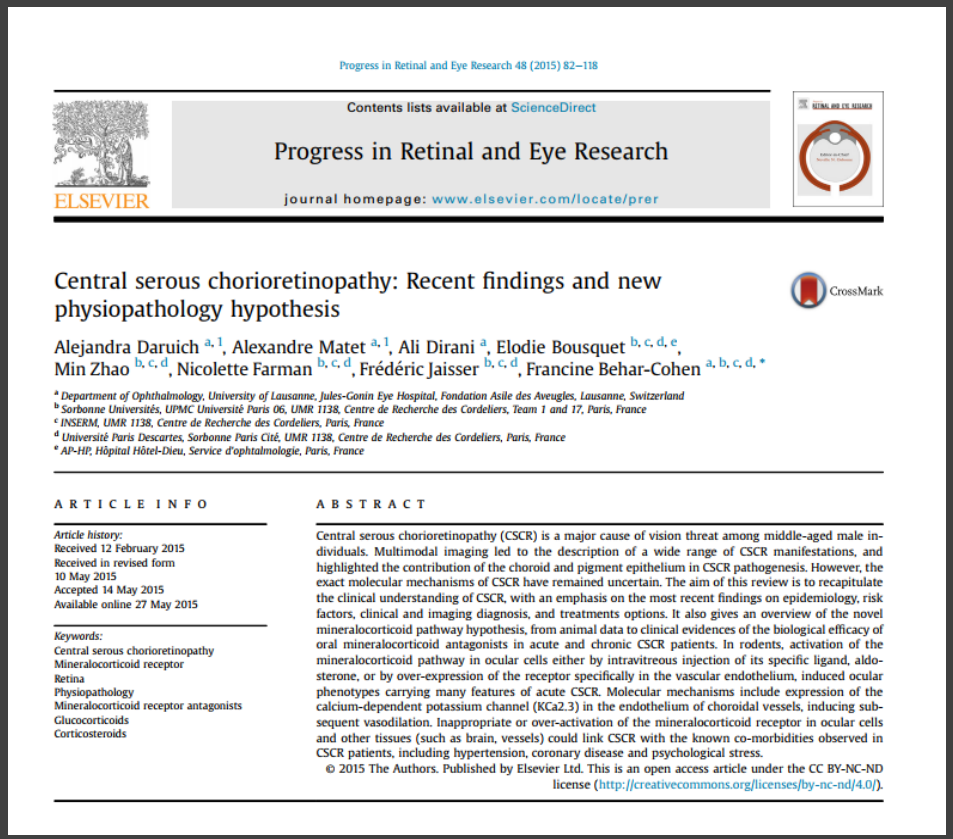



200 µm



Idiopathic central serous chorioretinopathy

- A posterior segment disease characterized by localized and limited serous detachments of the neurosensory retina, often associated with focal detachments of the RPE.
- In studies, 72-88% of cases occurred in male subjects
- Age range is ~ 39-51 years of age. The condition can occur in the elderly, but is rarely seen in children.



Progress in Retinal and Eye Research 48 (2015) 82–118

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Central serous chorioretinopathy: Recent findings and new physiopathology hypothesis

Alejandra Daruich [a, 1], Alexandre Matet [a, 1], Ali Dirani [a], Elodie Bousquet [b, c, d, e], Min Zhao [b, c, d], Nicolette Farman [b, c, d], Frédéric Jaisser [b, c, d], Francine Behar-Cohen [a, b, c, d, *]

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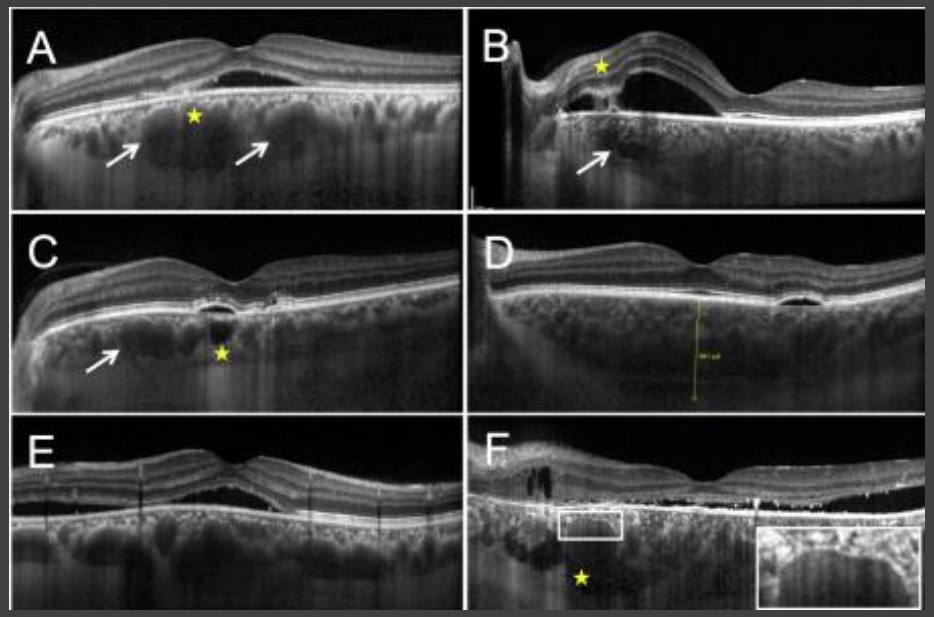
ABSTRACT

Central serous chorioretinopathy (CSCR) is a major cause of vision threat among middle-aged male individuals. Multimodal imaging led to the description of a wide range of CSCR manifestations, and highlighted the contribution of the choroid and pigment epithelium in CSCR pathogenesis. However, the exact molecular mechanisms of CSCR have remained uncertain. The aim of this review is to recapitulate the clinical understanding of CSCR, with an emphasis on the most recent findings on epidemiology, risk factors, clinical and imaging diagnosis, and treatments options. It also gives an overview of the novel mineralocorticoid pathway hypothesis, from animal data to clinical evidences of the biological efficacy of oral mineralocorticoid antagonists in acute and chronic CSCR patients. In rodents, activation of the mineralocorticoid pathway in ocular cells either by intravitreous injection of its specific ligand, aldosterone, or by over-expression of the receptor specifically in the vascular endothelium, induced ocular phenotypes carrying many features of acute CSCR. Molecular mechanisms include expression of the calcium-dependent potassium channel (KCa2.3) in the endothelium of choroidal vessels, inducing subsequent vasodilation. Inappropriate or over-activation of the mineralocorticoid receptor in ocular cells and other tissues (such as brain, vessels) could link CSCR with the known co-morbidities observed in CSCR patients, including hypertension, coronary disease and psychological stress.

Idiopathic central serous chorioretinopathy

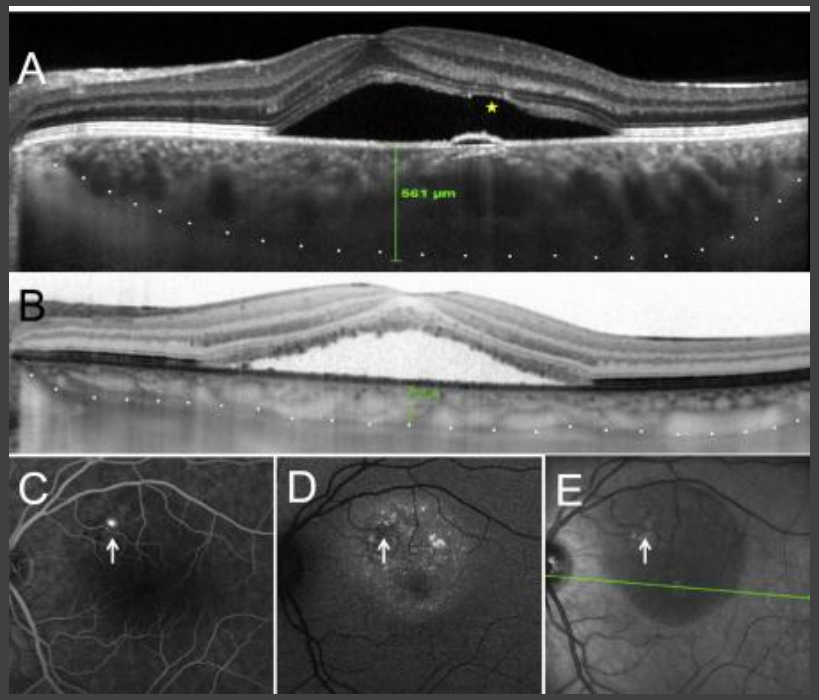
- **Pt's with hypertension have a higher risk of developing CSCR (OR 2.25-2.3)**
- **Males with CSCR have a slightly higher rate of coronary artery disease (OR 1.72), Ischemic stroke (HR:1.56) , erectile dysfunction (HR 2.14)**
- **CSCR patients often have a sympathetic-parasympathetic imbalance with over activation of the sympathetic system. This may lead to modulation of the choroidal blood flow and damage the RPE.**



Daruich A, Matet A, Dirani A et al. Central serous chorioretinopathy: recent findings and new physiopathology hypothesis. Progress in retinal and eye research 2015;48:82-118.

Oral steroids and central serous

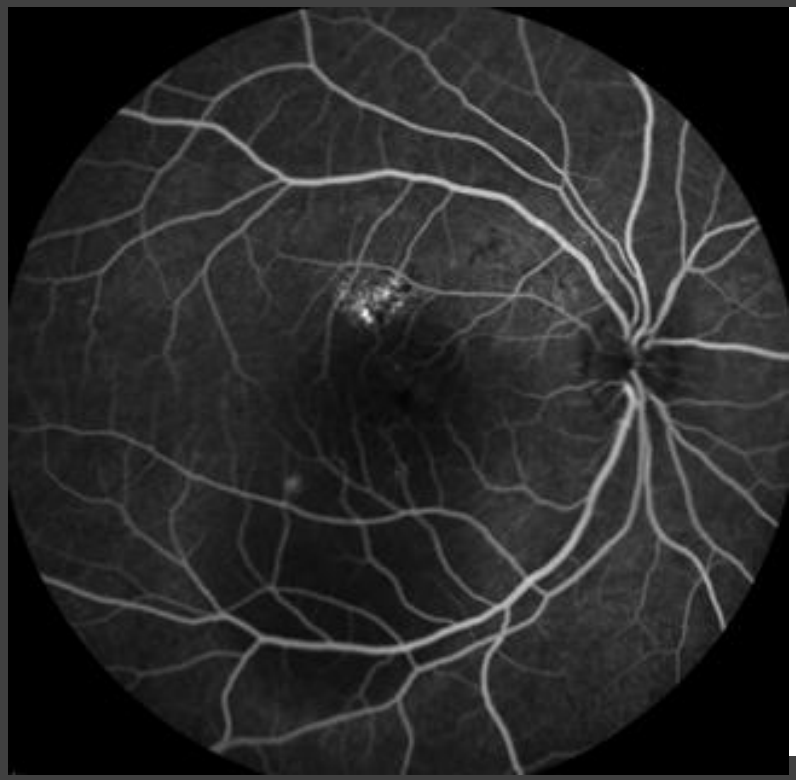
- **Corticosteroids have been associated with this condition, even in low dose concentrations.**
- **Steroid-induced CSCR has longer occurrences, increased recurrences and frequently has a bilateral presentation.**
- **Steroid-induced CSCR has less male predilection than idiopathic CSCR.**
- **Exact mechanism poorly understood.**

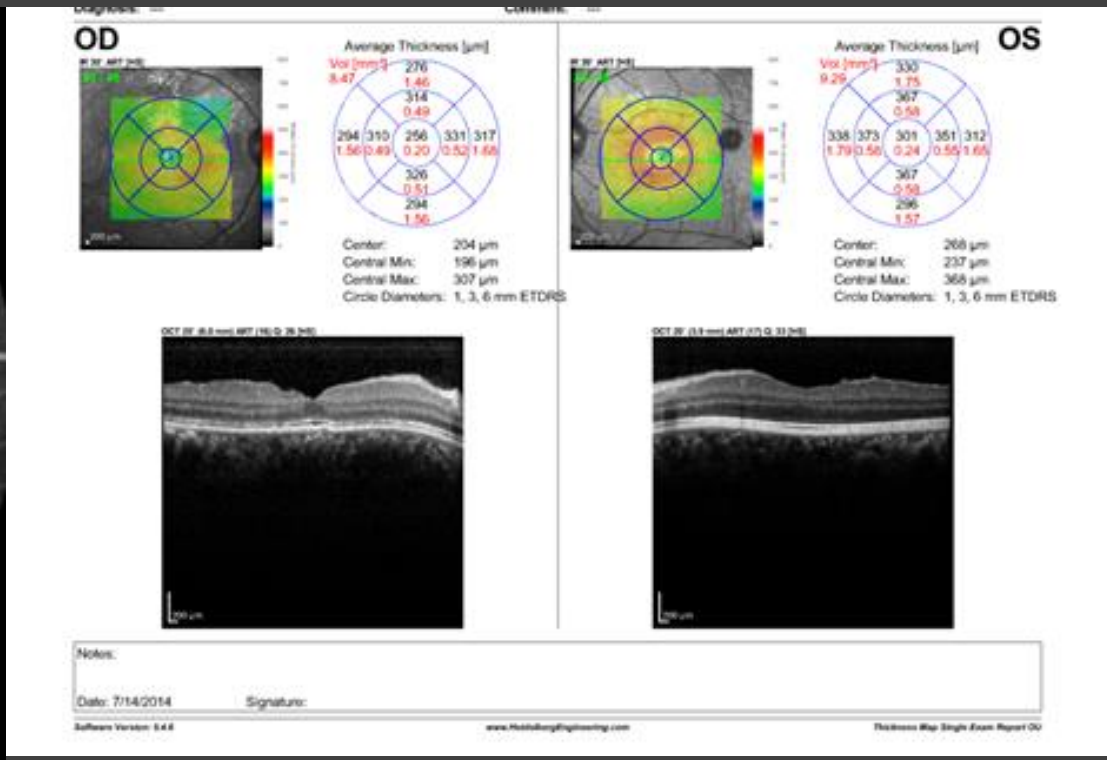


Daruich A, Matet A, Dirani A et al. Central serous chorioretinopathy: recent findings and new physiopathology hypothesis. Progress in retinal and eye research 2015;48:82-118.

Our patient

Underwent uncomplicated half-fluence PDT:





Our patient

Last visit:

- **2 months after PDT**

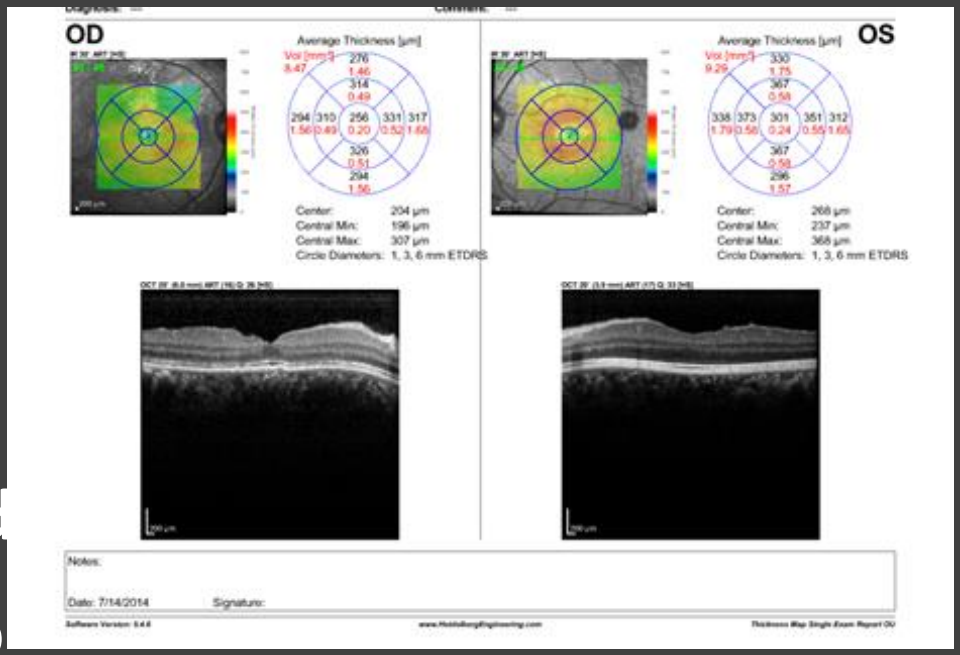
BCVA:

OD: 20/20-

OS: 20/20

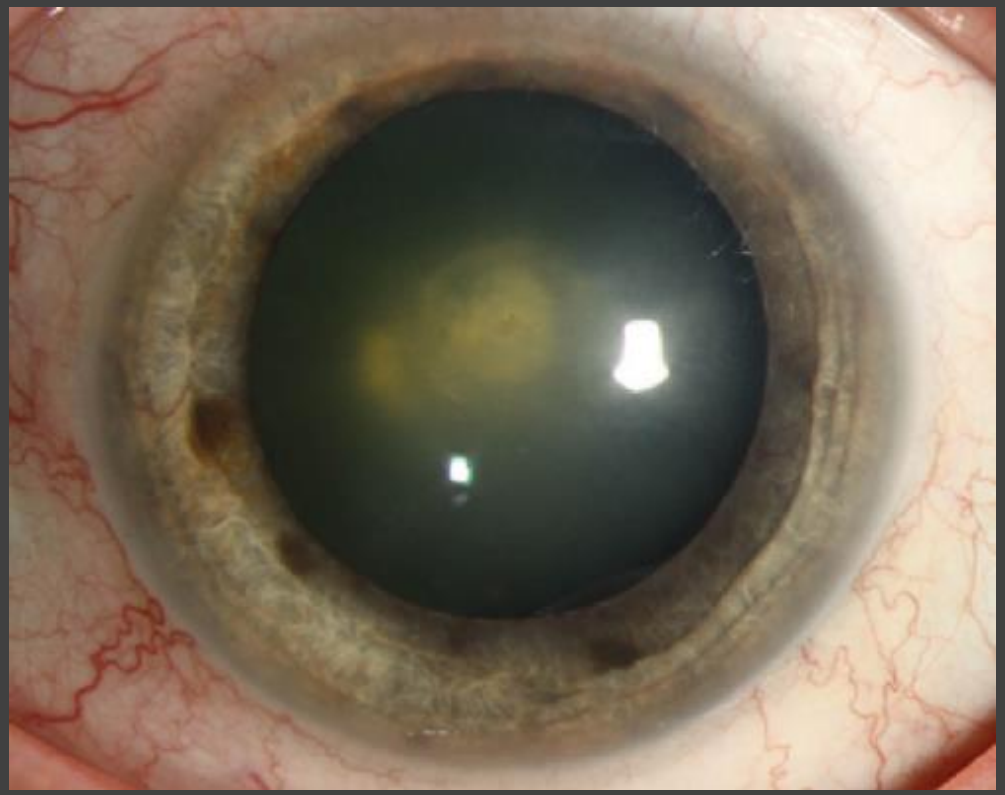
Resolution of subretinal fluid

Patient was able to return to work unrestricted.



Other ocular side effects of oral steroids

- **Cataracts**
- **Increased intraocular pressure.**
- **Papilledema**



http://www.reviewofcontactlenses.com/CMSImagesContent/2015/5/topical-steroid-use.jpg

Flomax (Tamsulosin)

Flomax (Tamsulosin)

- Alpha-adrenergic blocker.
- FDA approved to improve urination in men with benign prostatic hyperplasia
- Works by relaxing bladder muscles and the muscle fibers in the prostate.
- Very commonly prescribed medication, so many of your male patients (and some women) are taking tamsulosin

https://edc2.healthtap.com/ht-staging/user_answer/avatars/397595/large/stringio.jpeg?1386597180

Flomax (Tamsulosin)

Instructions for use:

- 0.4 mg capsule ½ an hour after the same meal each day

Side effects:

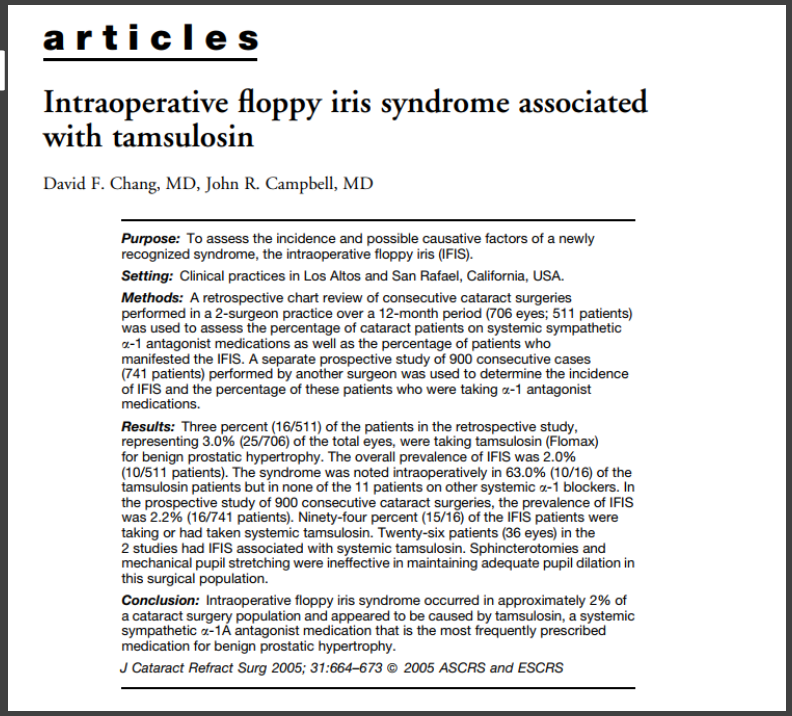
- Cough or hoarseness
- Lower back pain
- Dizziness and lightheadedness when suddenly getting up
- Hypotension
- Fainting

https://edc2.healthtap.com/ht-staging/user_answer/avatars/397595/large/stringio.jpeg?1386597180

Flomax (Tamsulosin) ocular side effects

Intraoperative Floppy Iris Syndrome:

- **Flaccid iris stroma that undulates and billows in response to intraocular fluid currents**
- **A propensity for the floppy iris stroma to prolapse toward the phaco and side-port incisions despite proper wound construction**
- **A progressive intraoperative pupil constriction despite standard pharmacologic measures to prevent this.**



articles

Intraoperative floppy iris syndrome associated with tamsulosin

David F. Chang, MD, John R. Campbell, MD

Purpose: To assess the incidence and possible causative factors of a newly recognized syndrome, the intraoperative floppy iris (IFIS).

Setting: Clinical practices in Los Altos and San Rafael, California, USA.

Methods: A retrospective chart review of consecutive cataract surgeries performed in a 2-surgeon practice over a 12-month period (706 eyes; 511 patients) was used to assess the percentage of cataract patients on systemic sympathetic α-1 antagonist medications as well as the percentage of patients who manifested the IFIS. A separate prospective study of 900 consecutive cases (741 patients) performed by another surgeon was used to determine the incidence of IFIS and the percentage of these patients who were taking α-1 antagonist medications.

Results: Three percent (16/511) of the patients in the retrospective study, representing 3.0% (25/706) of the total eyes, were taking tamsulosin (Flomax) for benign prostatic hypertrophy. The overall prevalence of IFIS was 2.0% (10/511 patients). The syndrome was noted intraoperatively in 63.0% (10/16) of the tamsulosin patients but in none of the 11 patients on other systemic α-1 blockers. In the prospective study of 900 consecutive cataract surgeries, the prevalence of IFIS was 2.2% (16/741 patients). Ninety-four percent (15/16) of the IFIS patients were taking or had taken systemic tamsulosin. Twenty-six patients (36 eyes) in the 2 studies had IFIS associated with systemic tamsulosin. Sphincterotomies and mechanical pupil stretching were ineffective in maintaining adequate pupil dilation in this surgical population.

Conclusion: Intraoperative floppy iris syndrome occurred in approximately 2% of a cataract surgery population and appeared to be caused by tamsulosin, a systemic sympathetic α-1A antagonist medication that is the most frequently prescribed medication for benign prostatic hypertrophy.

J Cataract Refract Surg 2005; 31:664–673 © 2005 ASCRS and ESCRS

Chang D, Campbell J. Intraoperative floppy iris syndrome associated with Tamsulosin. J cataract refract surg 2005;31:664-673.

Flomax (Tamsulosin)

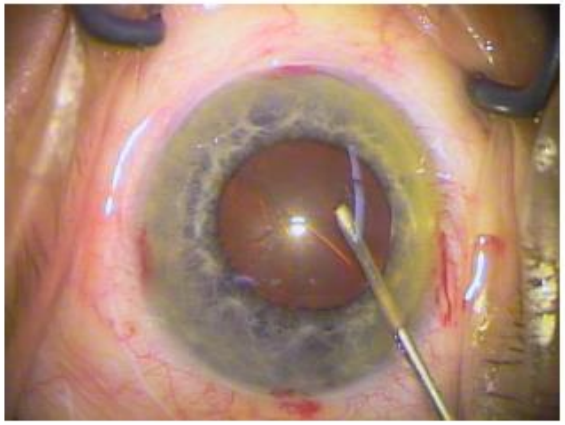


Figure 1. Moderate pupil dilation permits capsulorhexis in a tamsulosin patient.

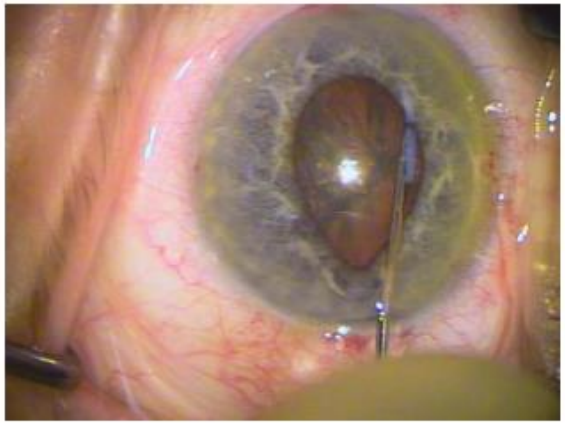
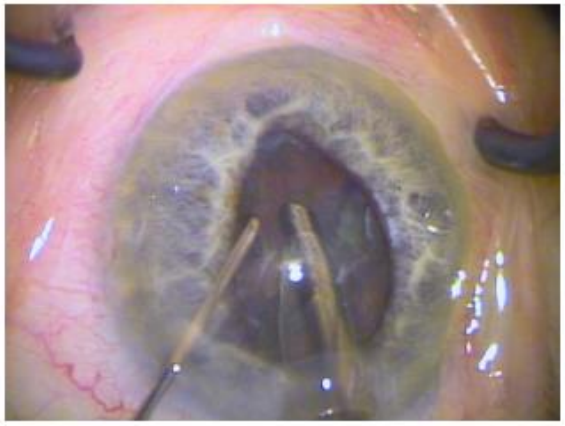


Figure 2. Iris immediately prolapses during initiation of hydrodissection.



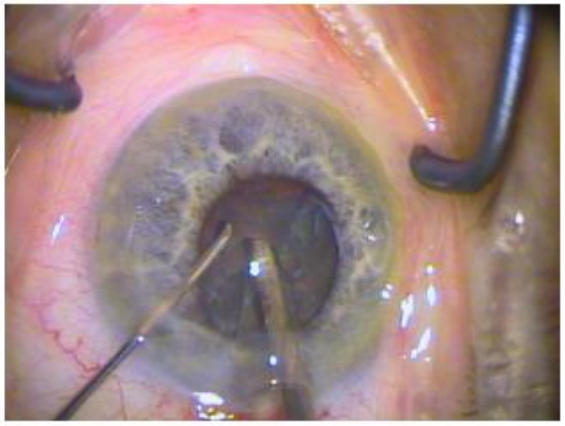
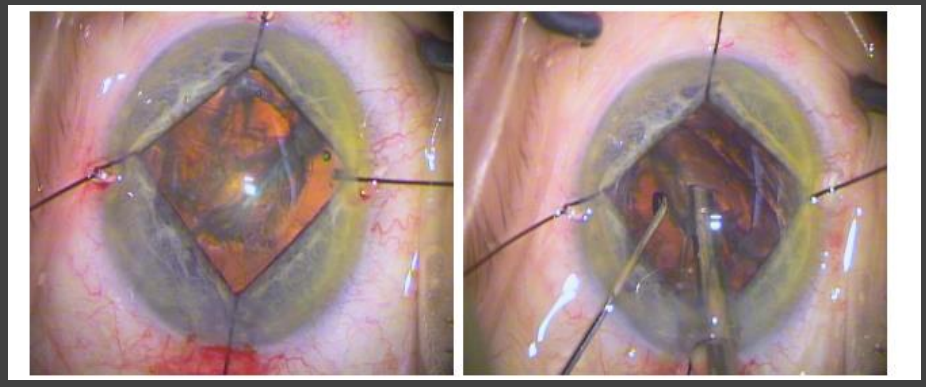
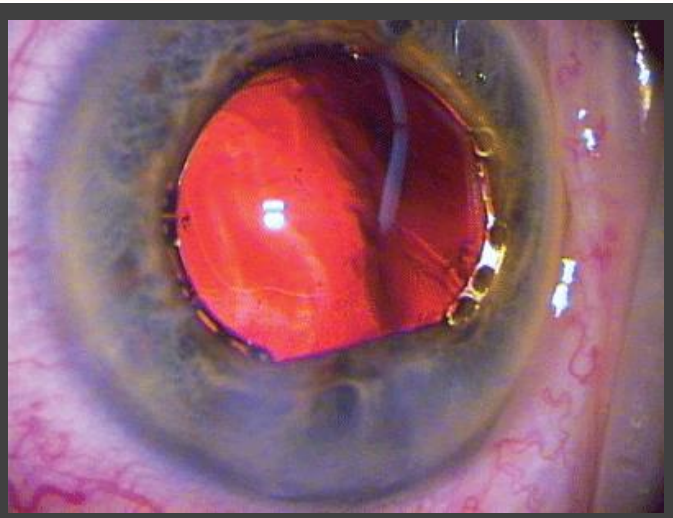


Figure 3. Iris billows, prolapses to both incisions, and the pupil constricts.

Intraoperative floppy iris syndrome

- Overall prevalence is 1.5-2.5%
- Surgeons modify technique by using gentle hydrodissection of the lens, lowering irrigation flow.
- Adding atropine 3 days prior to surgery is of some benefit.
- Iris retractors are used to prevent incarceration of the iris into the phaco wounds and to keep adequate pupil size for the surgery.
- Pupil expanders can be used to hold a pupil open during surgery.





http://www.changcataract.com/websites/Review_of_Ophthalmology.htm

Oral Contraceptives

Oral Contraceptives

Estrogen and/or progesterone

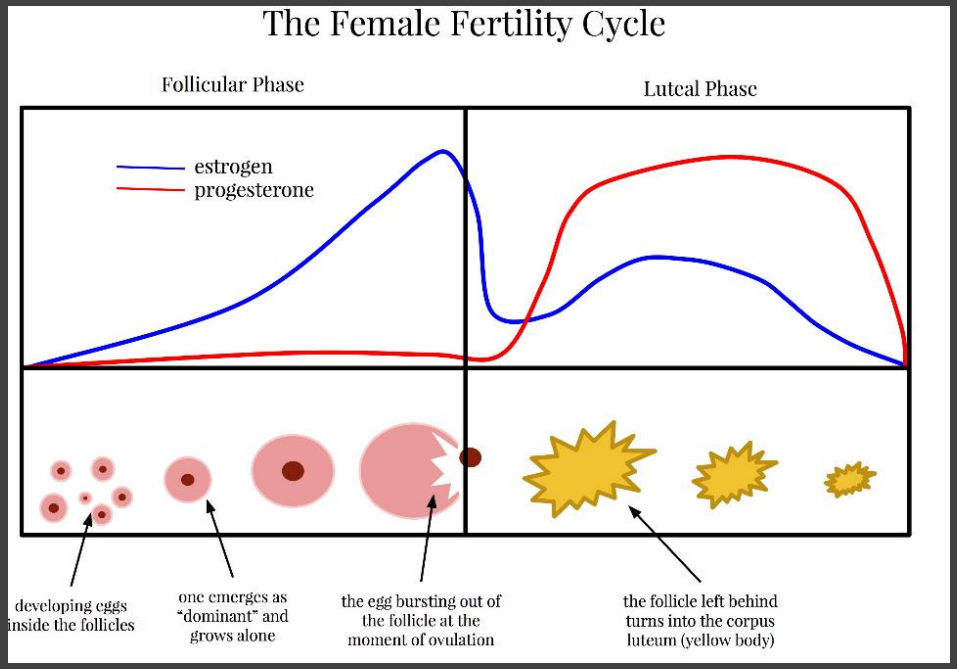
- **Two female sex hormones**
- **Work by preventing ovulation and change the lining of the uterus to prevent pregnancy.**

http://static.guim.co.uk/sys-images/Guardian/Pix/pictures/2013/1/27/1359301618438/Contraceptive-pills-004.jpg

Female Fertility cycle

Estrogen: Causes growth of the uterine lining, inhibits FSH. Stimulates LH and the release of the egg.

Progesterone: Maintains the lining of the uterus, inhibits LH after ovulation.

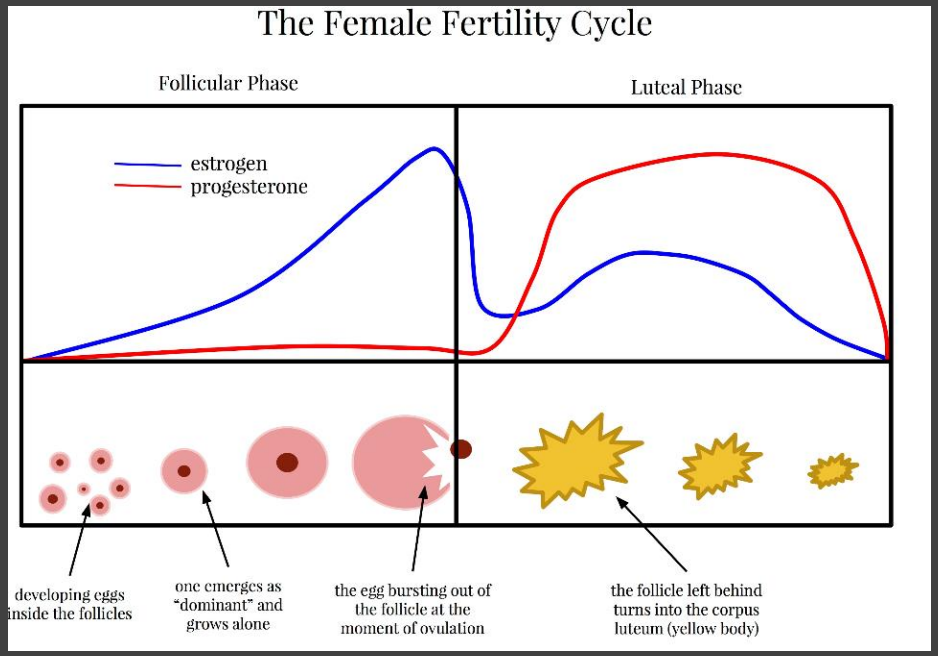


http://bumpintoreality.com/wp-content/uploads/2014/09/Menstrual-Cycle-Hormones-glad-rags-version.jpg

Female Fertility cycle

<u>Leutinizing Hormone (LH):</u> Stimulates the release of the egg (ovulation). Stimulates estrogen and progesterone production.

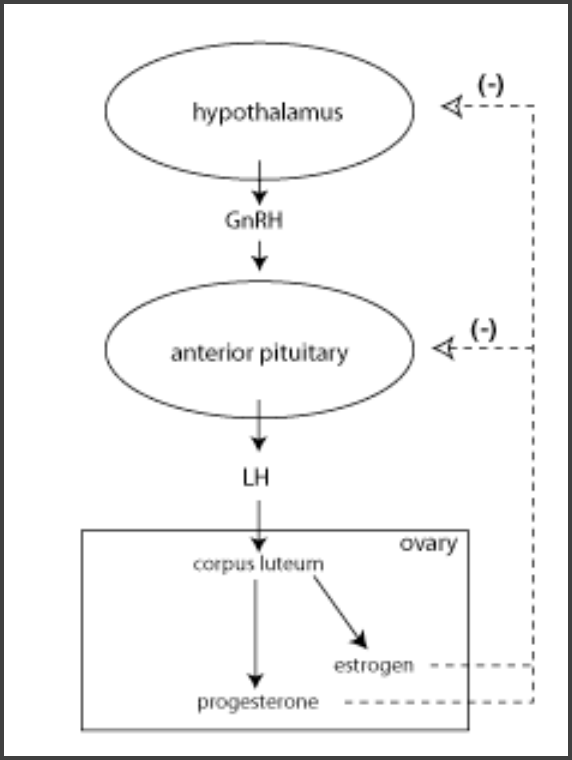
<u>Follicle Stimulating Hormone (FSH):</u> Stimulates egg development and release of estrogen.



http://bumpintoreality.com/wp-content/uploads/2014/09/Menstrual-Cycle-Hormones-glad-rags-version.jpg

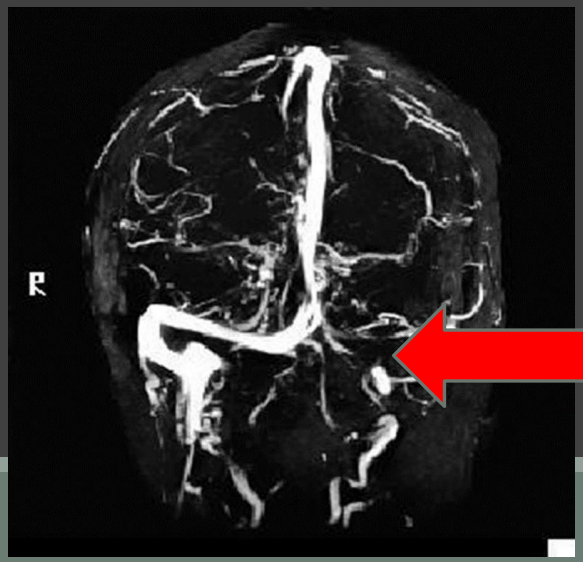
Contraception effect on fertility cycle

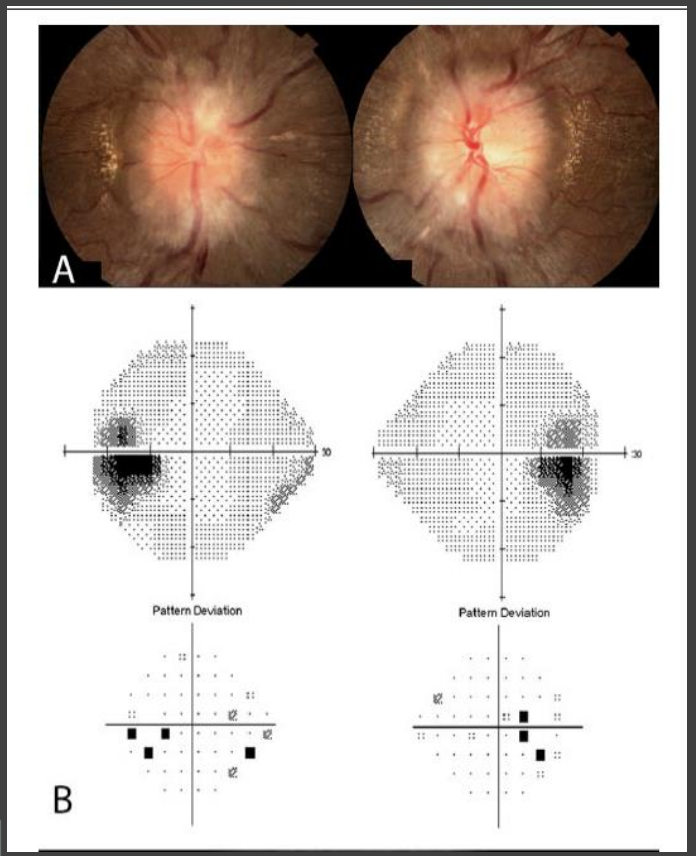
- **Estrogen inhibits secretion of FSH through negative feedback in the anterior pituitary.**
- **Progesterone inhibits secretion of LH and prevents ovulation.**
- **Estrogen and progesterone work together to alter the endometrium to discourage egg implantation.**



Oral Contraceptives effects on the eyes

- **Papilledema**
  - **Venous sinus thrombosis.**
  - **Idiopathic intracranial hypertension**
- **Retinal artery occlusions**



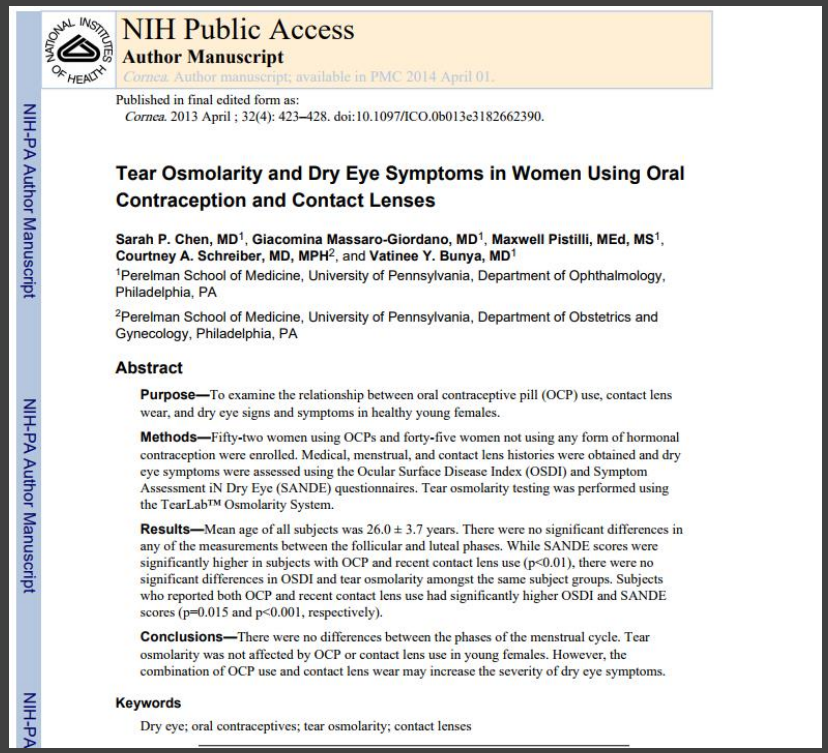


Dry eye and oral contraceptives?

Females age 18-40

- **52 took oral contraceptives**
- **45 had no oral contraceptives**

- **There was no significant difference in tear osmolarity or OSDI (ocular surface disease index) between groups taking oral contraceptives and those without**
- **Subjects with both oral contraceptives and contact lens wear had the highest median OSDI score.**
- **In other studies, oral contraceptive use is not necessarily tied to dry eye**



Published in final edited form as:
Cornea. 2013 April ; 32(4): 423–428. doi:10.1097/ICO.0b013e3182662390.

Tear Osmolarity and Dry Eye Symptoms in Women Using Oral Contraception and Contact Lenses

Sarah P. Chen, MD[1], **Giacomina Massaro-Giordano, MD**[1], **Maxwell Pistilli, MEd, MS**[1], **Courtney A. Schreiber, MD, MPH**[2], and **Vatinee Y. Bunya, MD**[1]

[1]Perelman School of Medicine, University of Pennsylvania, Department of Ophthalmology, Philadelphia, PA

[2]Perelman School of Medicine, University of Pennsylvania, Department of Obstetrics and Gynecology, Philadelphia, PA

Abstract

Purpose—To examine the relationship between oral contraceptive pill (OCP) use, contact lens wear, and dry eye signs and symptoms in healthy young females.

Methods—Fifty-two women using OCPs and forty-five women not using any form of hormonal contraception were enrolled. Medical, menstrual, and contact lens histories were obtained and dry eye symptoms were assessed using the Ocular Surface Disease Index (OSDI) and Symptom Assessment iN Dry Eye (SANDE) questionnaires. Tear osmolarity testing was performed using the TearLab™ Osmolarity System.

Results—Mean age of all subjects was 26.0 ± 3.7 years. There were no significant differences in any of the measurements between the follicular and luteal phases. While SANDE scores were significantly higher in subjects with OCP and recent contact lens use ($p<0.01$), there were no significant differences in OSDI and tear osmolarity amongst the same subject groups. Subjects who reported both OCP and recent contact lens use had significantly higher OSDI and SANDE scores ($p=0.015$ and $p<0.001$, respectively).

Conclusions—There were no differences between the phases of the menstrual cycle. Tear osmolarity was not affected by OCP or contact lens use in young females. However, the combination of OCP use and contact lens wear may increase the severity of dry eye symptoms.

Keywords

Dry eye; oral contraceptives; tear osmolarity; contact lenses

Lithium

Lithium

- Used for mental illness including bipolar, depression and schizophrenia.
- Used for eating disorders: anorexia and bulimia.
- It has been shown to reduce suicide rates in people with major depressive disorders.

http://www.bipolardisorderscenters.com/wp-content/uploads/lithium-and-bipolar-disorder-300x199.jpg

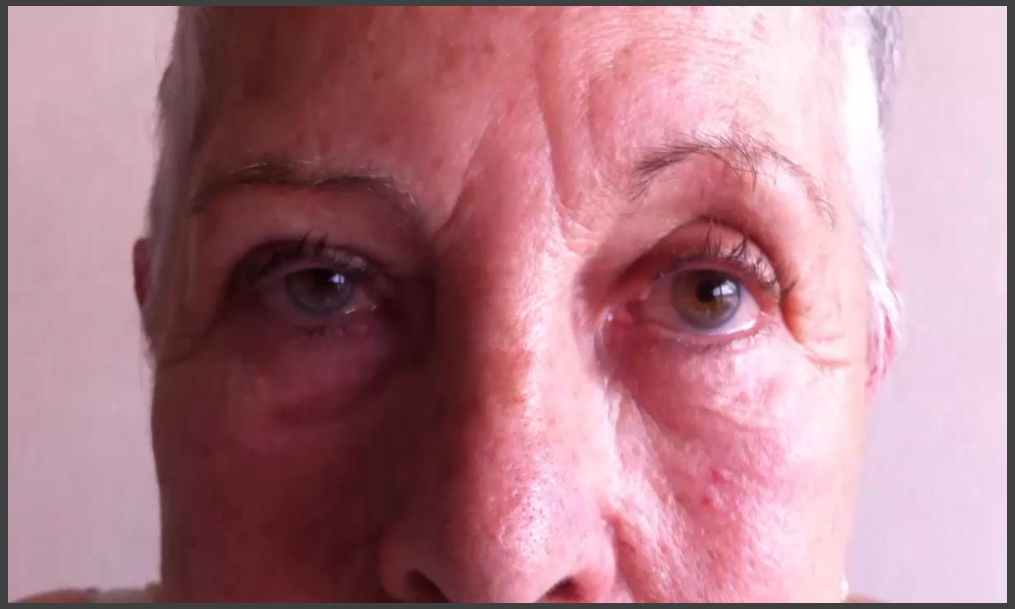
Systemic side effects with Lithium

- Increased urination
- Tremors in the hands
- Hypothyroidism
- Diarrhea
- Vomiting
- Poor coordination
- Tinnitus

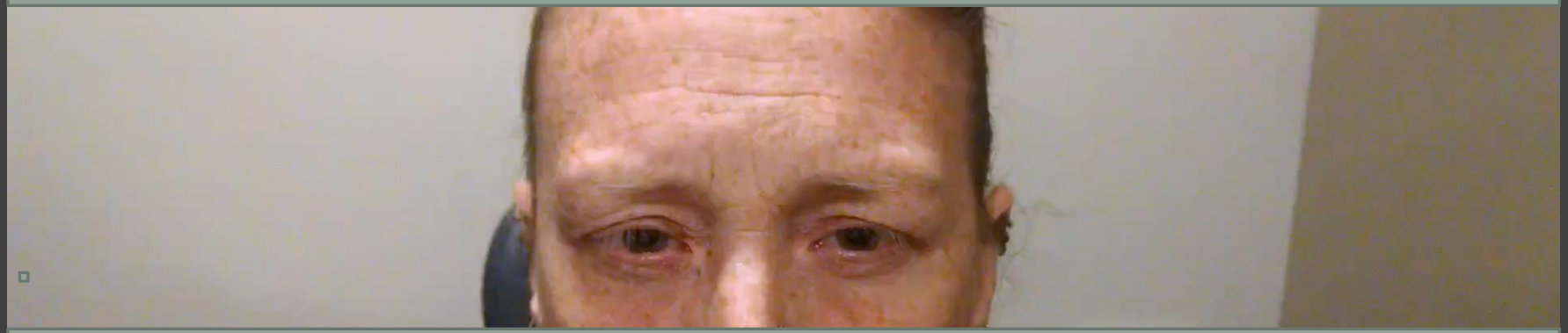
http://www.bipolardisorderscenters.com/wp-content/uploads/lithium-and-bipolar-disorder-300x199.jpg

Lithium side effects

- **Diplopia**
- **Keratitis Sicca**
- **Blurred vision**
- **Downbeat Nystagmus**



Schein F, Manoli P, Cathebras P. Lithium induced downbeat nystagmus. American journal of ophthalmology case reports 2017;7:74-75.

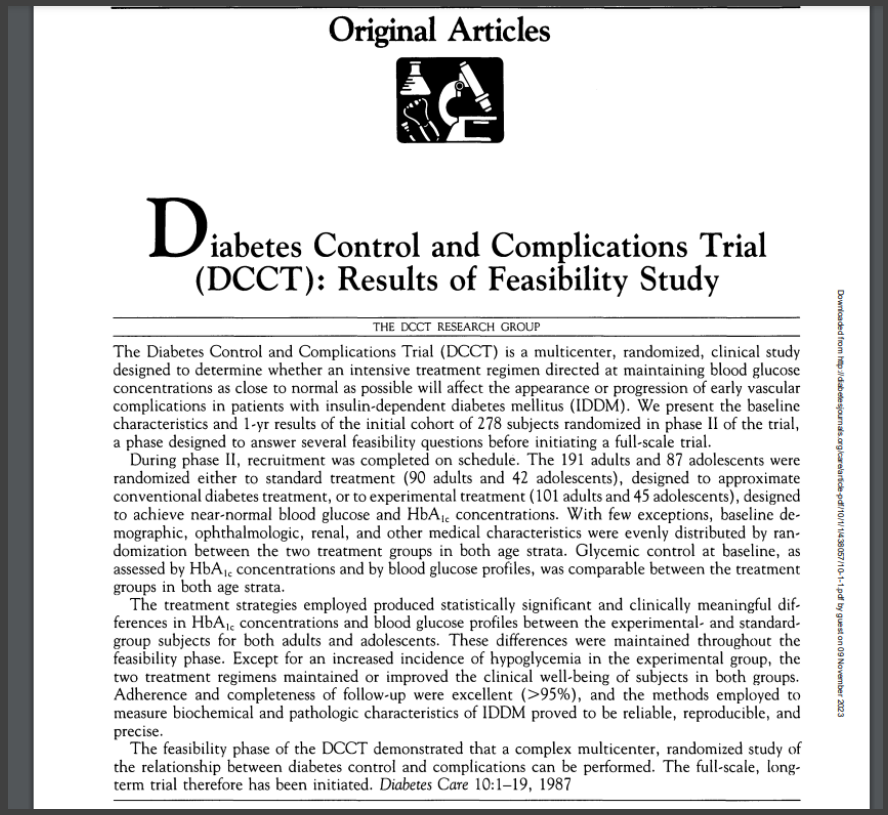


Ozempic (semaglutide)

Ozempic (semaglutide)

- A Glucagon-like peptide-1 agonist
- Slows gastric emptying and reduces glucose absorption
- Prompts the body to produce more insulin which lowers blood sugar.
- Has been shown to significantly improve blood sugar control and to assist in weight loss.

Ozempic (semaglutide)



Original Articles

Diabetes Control and Complications Trial (DCCT): Results of Feasibility Study

THE DCCT RESEARCH GROUP

The Diabetes Control and Complications Trial (DCCT) is a multicenter, randomized, clinical study designed to determine whether an intensive treatment regimen directed at maintaining blood glucose concentrations as close to normal as possible will affect the appearance or progression of early vascular complications in patients with insulin-dependent diabetes mellitus (IDDM). We present the baseline characteristics and 1-yr results of the initial cohort of 278 subjects randomized in phase II of the trial, a phase designed to answer several feasibility questions before initiating a full-scale trial.

During phase II, recruitment was completed on schedule. The 191 adults and 87 adolescents were randomized either to standard treatment (90 adults and 42 adolescents), designed to approximate conventional diabetes treatment, or to experimental treatment (101 adults and 45 adolescents), designed to achieve near-normal blood glucose and HbA_{1c} concentrations. With few exceptions, baseline demographic, ophthalmologic, renal, and other medical characteristics were evenly distributed by randomization between the two treatment groups in both age strata. Glycemic control at baseline, as assessed by HbA_{1c} concentrations and by blood glucose profiles, was comparable between the treatment groups in both age strata.

The treatment strategies employed produced statistically significant and clinically meaningful differences in HbA_{1c} concentrations and blood glucose profiles between the experimental- and standard-group subjects for both adults and adolescents. These differences were maintained throughout the feasibility phase. Except for an increased incidence of hypoglycemia in the experimental group, the two treatment regimens maintained or improved the clinical well-being of subjects in both groups. Adherence and completeness of follow-up were excellent (>95%), and the methods employed to measure biochemical and pathologic characteristics of IDDM proved to be reliable, reproducible, and precise.

The feasibility phase of the DCCT demonstrated that a complex multicenter, randomized study of the relationship between diabetes control and complications can be performed. The full-scale, long-term trial therefore has been initiated. *Diabetes Care* 10:1–19, 1987

- Remember the results of the DCCT:
  - Patients whose blood sugar was corrected to better levels quickly showed a worsening of retinopathy vs the control group.
- Similar effects have been reported with Ozempic. The A1C improves, but the patient's diabetic retinopathy worsens.

How does this affect Optometry/Ophthalmology?

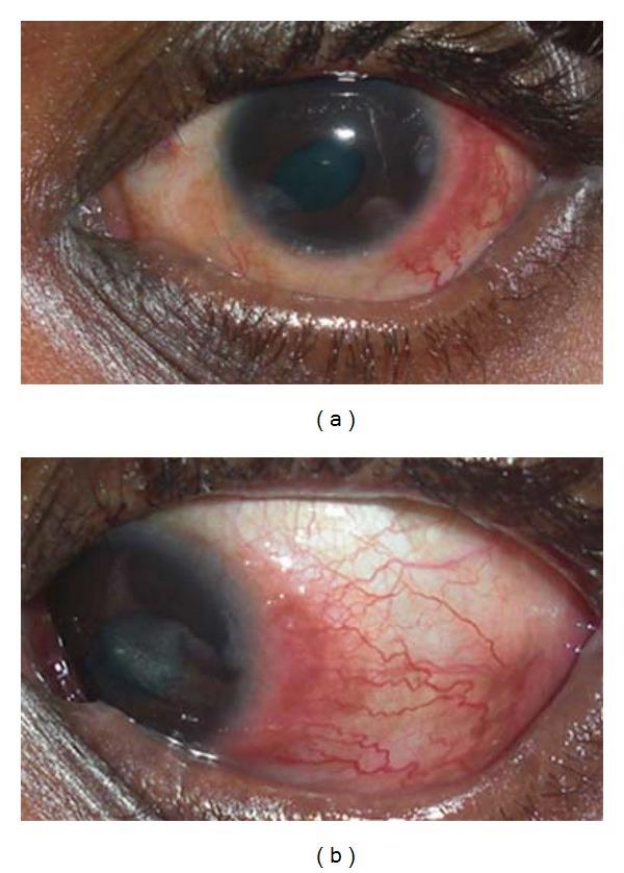
- I have a close relationship with the VAs Endocrinologist
- He will alert me when he is starting a diabetic on Ozempic. I will then tighten the follow-up on that patient.
- Remember we are only part of the patient's healthcare. If their retinopathy worsens, but they are managed appropriately and they lower their risk for cardiovascular events by 25% and lose weight, then this is likely an acceptable risk.

Dupixent (dupilumab)

Dupixent (dupilumab)

- A fully human monoclonal antibody that binds to the alpha subunit of the IL-4 receptor and blocks signaling of IL-4 and IL-13, Both key components of inflammation
- Indicated for:
  - Atopic dermatitis
    - **pt's with this condition can be predisposed for conjunctivitis or keratoconus **
  - Moderate to severe asthma
  - Chronic rhinosinusitis with nasal polyps.

Dupixent (dupilumab)



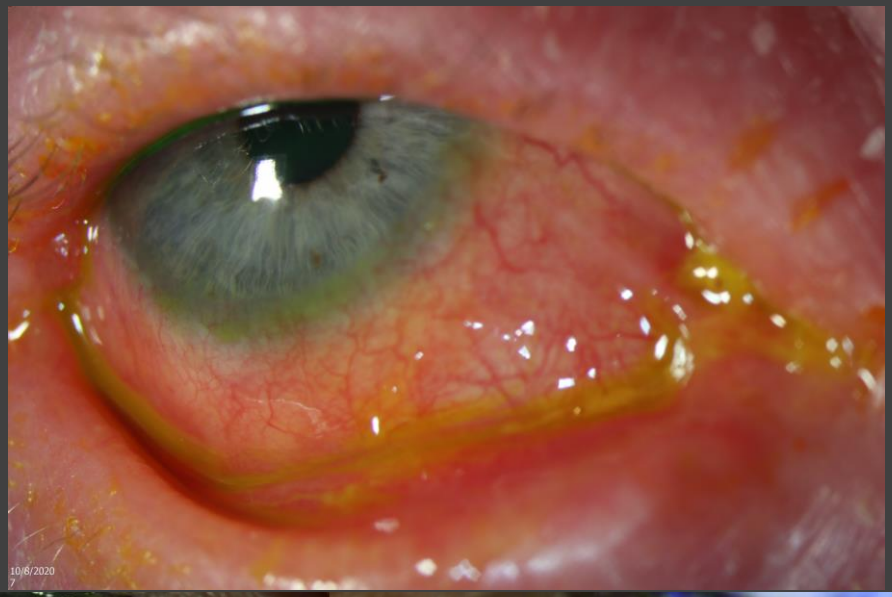
- The most common side effect is conjunctivitis, but keratitis and blepharitis have been observed
- Other observed side effects: limbitis, papillary reactions and blepharitis
- Corneal perforation has been noted in the literature, but this is rare.

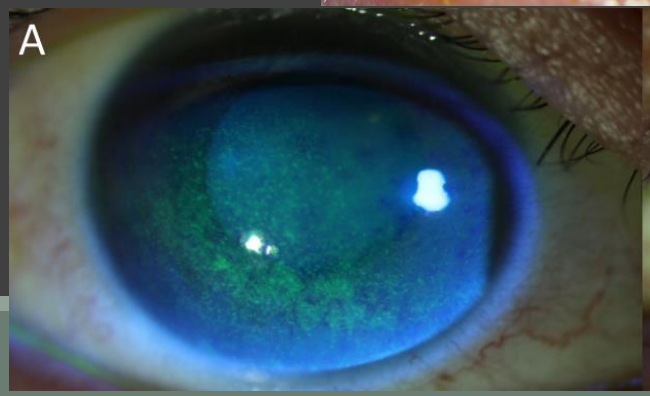
- Phylactou M, Jabbour S, Ahmad S, Vasquez-Perez A. Corneal Perforation in Patients Under Treatment With Dupilumab for Atopic Dermatitis. Cornea. 2022 Aug 1;41(8):981-985.

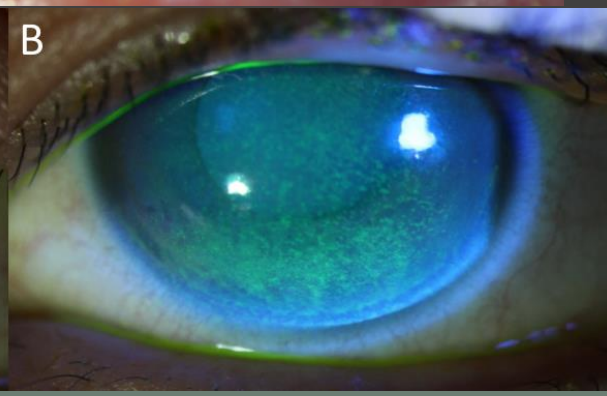
https://pubmed.ncbi.nlm.nih.gov/22606467/#&gid=article-figures&pid=figure-1-uid-0

Dupixent (dupilumab)

- Presentation is usually bilateral, but asymmetric.
- Management:
  - Where possible, discontinuation of dupilumab should be avoided.
  - Pts can be treated prophylactically with topical artificial tears
  - If more moderate to sever symptoms, patients can be managed with topical steroids, restasis, and topical artificial tears.







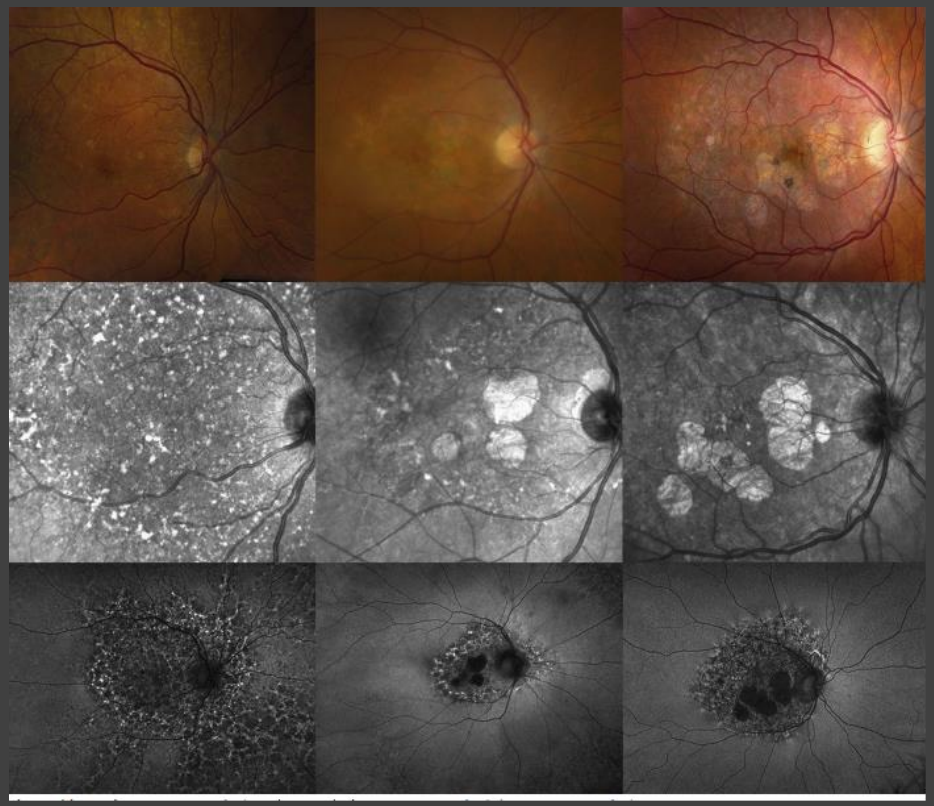
Elmiron (pentosan polysulfate sodium)

Elmiron (pentosan polysulfate sodium)

- A semisynthetic sulfated polysaccharide. The only FDA approved oral therapy for interstitial cystitis
- Approved and widely prescribed since 1996 in the United states
- Thought to protect the bladder lining from irritants by replacing glycoaminoglycans in the bladder urothelium.

Ocular side effects

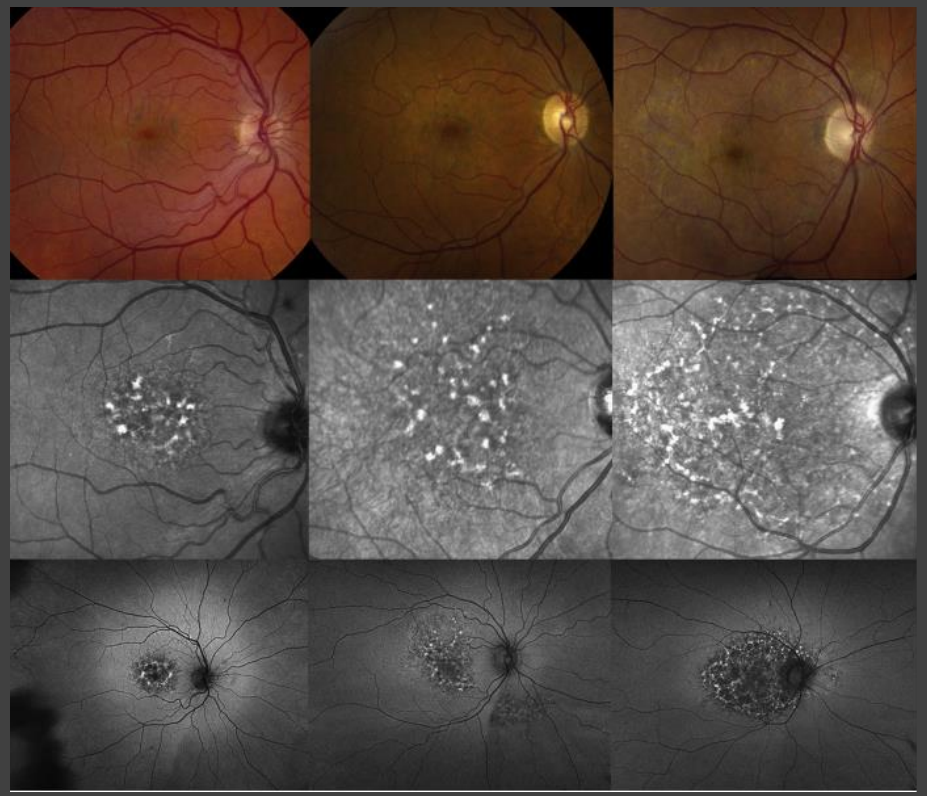
- Since 2018, reports have surfaced linking the medication to a pigment maculopathy that is tied to long-term use of the medication
- Appears to primarily affect the RPE and photoreceptors.
- May cause RPE atrophy, cystoid macular edema, vitelliform maculopathy and CNVM.
- Symptoms: difficulty reading, poor dark adaptation, loss of central vision



Pearce WA, Chen R, Jain N. Pigmentary Maculopathy Associated with Chronic Exposure to Pentosan Polysulfate Sodium. Ophthalmology. 2018;125(11):1793-1802. doi:10.1016/j.ophtha.2018.04.026

Ocular side effects

- The primary risk factor is the cumulative exposure to the medication.
- No clear pathophysiology for the ocular side effects is known at this time.
- Maculopathy has been shown to progress even after discontinuing the medication.



Pearce WA, Chen R, Jain N. Pigmentary Maculopathy Associated with Chronic Exposure to Pentosan Polysulfate Sodium. Ophthalmology. 2018;125(11):1793-1802. doi:10.1016/j.ophtha.2018.04.026

Recommendations for these patients.

- No official guidelines yet
- Some suggest baseline examination at the start of treatment to include fundus photos, OCT and FAF.
- Annual examinations with fundus imaging starting 5 years after the initiation of therapy.

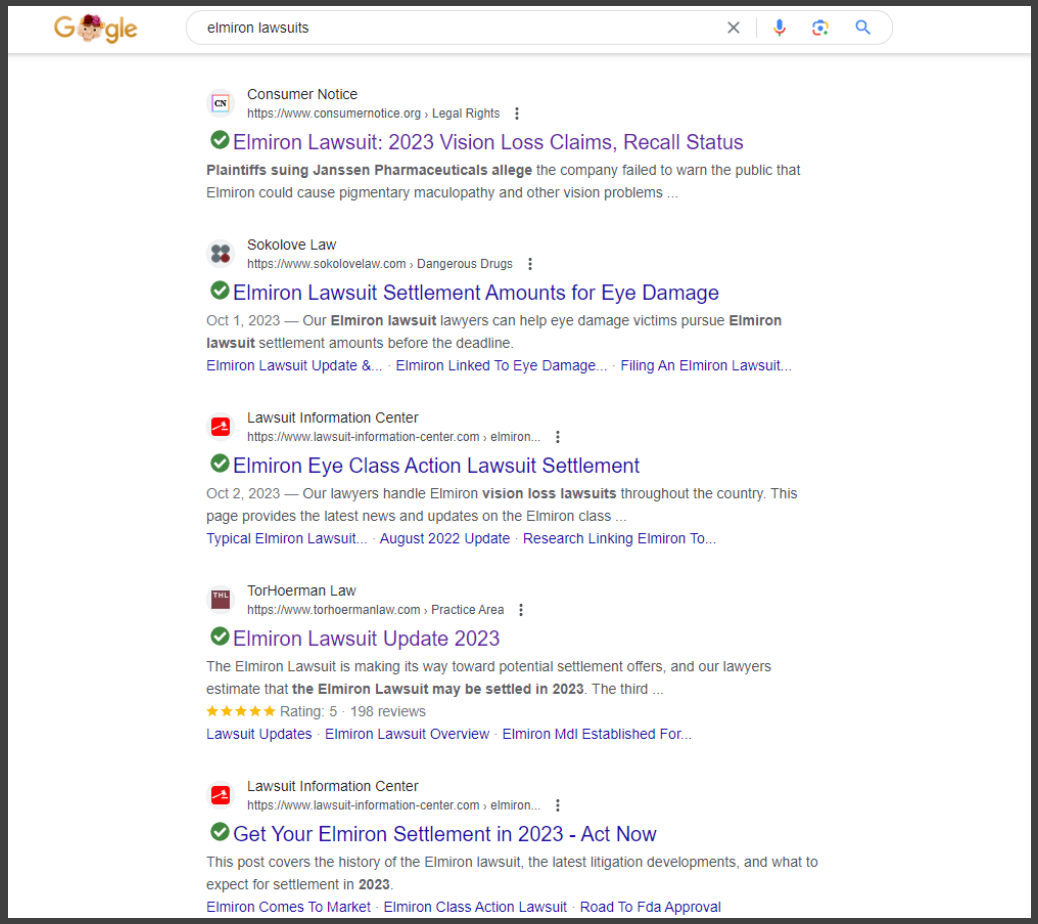
Median Age:	60 years (range: 37 to 79 years)
Median Duration of PPS Intake:	14.5 years (range: 3 to 22 years)
Common Presenting Symptoms:	Blurred vision while reading (48.6 percent) Prolonged dark adaptation (48.6 percent) Metamorphopsia (11.4 percent)
Median Duration of Visual Symptoms:	4 years (range: 1 to 9 years)
Median Visual Acuity:	OU: 20/25 OD Range: 20/20 to 20/300 OS Range: 20/15 to 20/400

Data documented in a series of 35 confirmed cases of PPS-associated maculopathy.[12]

https://www.reviewofophthalmology.com/article/clinical-pearls-for-a-new-condition

Li AL, Jain N, Yu Y, VanderBeek BL. Association of macular disease with long-term use of pentosan polysulfate sodium: findings from a large U.S. national insurance database. May 1, 2019. Association for Research in Vision and Ophthalmology. Vancouver, BC.

Elmiron lawsuits



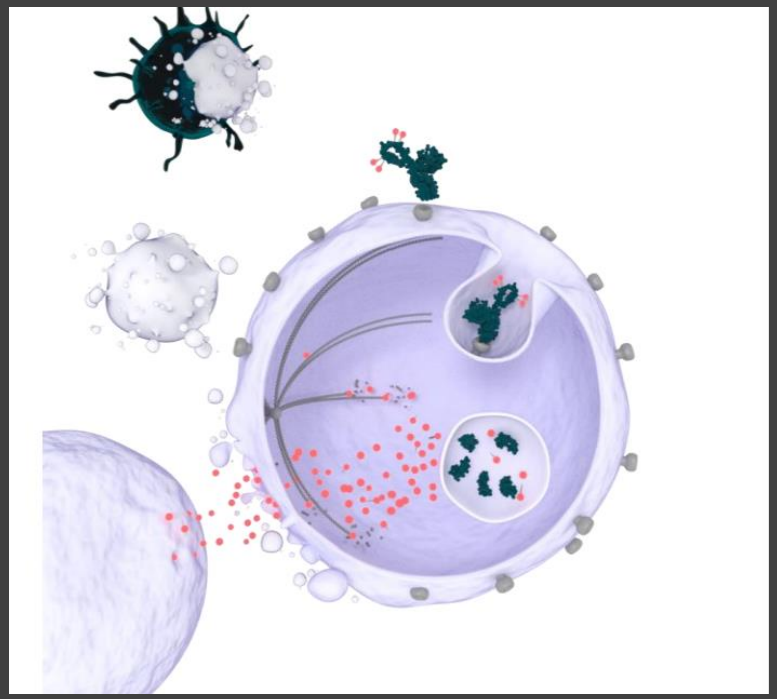
Elahere (Mirvetuximab Soravtansine)

Elahere (Mirvetuximab Soravtansine)

- An antibody drug conjugate (ADC) comprising a folate receptor alpha (FRα)-binding antibody, cleavable linker, and the maytansinoid payload DM4, a potent tubulin-targeting agent to kill the targeted cancer cells.

- Used in patients with FRα- positive plantinum-resistant Ovarian cancer.

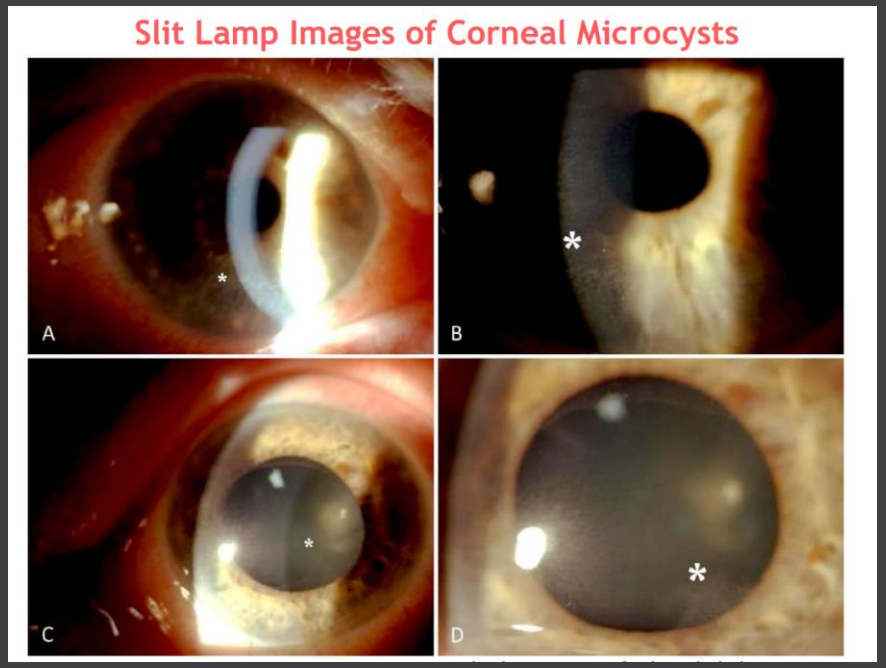
- Platinum-resistant ovarian cancer has a median survival of 9–12 months and less than 15% respond to subsequent chemotherapy



https://erc.bioscientifica.com/view/journals/erc/25/5/ERC-17-0336.xml

Ocular side effects of Elahere

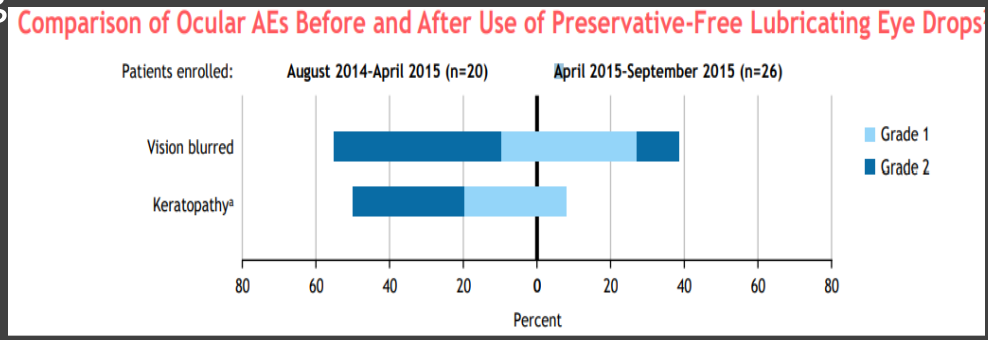
- A dose-dependent toxicity of the corneal epithelium.
- Microcystic lesions were present in the perilimbal cornea and were less severe in lower doses of the medication



Corbelli E, et al. Cornea. 2019;38(2):229-232

Ocular side effects of Elahere

Management: The daily use of lubricating eye drops, avoiding contact lens wear, using warm compresses and hygiene, and wearing sunglasses during the daytime significantly reduces advrse effects from the medications.



- Prophylactic use of steroid eye drops appeared to reduce the frequency and severity of ocular events, thereby reducing the number of patients requiring dose reductions

What does this mean for you?

- Ocular adverse events happened in ~50% of patients on the medication
- >90% of blurry vision and corneal events were minor
- Ocular side effects typically developed at 1.3 months.
- With topical steroids and lubrication, most patients did not need a dose reduction of the medication.
- Monitor these patients at baseline and every 6 weeks of therapy to catch these ocular side effects as soon as possible.