INTRO 2

MED REC / PLAQUENIL / PVD / NEVI

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MEDICATION RECONCILIATION

- WHY DONE?
  - MAKING SURE ALL OF US KNOW WHAT MEDS OUR PATIENTS TAKE
  - THEORETICALLY
    - TO AVOID INTERACTIONS WITH DRUGS WE ARE USING DURING OUR EYE EXAM THAT MAY INTERFERE WITH THOSE THAT A PATIENT IS CURRENTLY TAKING
      - THIS IS NOT REALLY AN ISSUE WITH WHAT WE USE (FLURESS/CAINES, M1, N2.5)

MEDICATION RECONCILIATION

- WHY ELSE IS IT DONE?
  - MAKING SURE WE KNOW WHAT MEDICATIONS A PATIENT IS TAKING
    - A DOUBLE CHECK OF THEIR SYSTEMIC DISEASE +/-
  - TO SEE IF ANY (RX OR OTC) MAY CAUSE EYE PROBLEMS
  - ALWAYS LOOK FOR
    - MEDICATIONS THAT MAY CAUSE OCULAR SIDE EFFECTS / VISION LOSS, ETC
- NEED TO KNOW IF MEDS (RX OR OTC) MAY CAUSE EYE PROBLEMS
  - LOOK FOR: SEMAGLUTIDE (OZEMPIC), AMIODARONE, PLAQUENIL (HYDROXYCHLOROQUINE), ETHAMBUTOL, INTERFERON, ED MEDS, FLOMAX, BLOOD THINNERS, STEROIDS, GILENYA, TAMOXIFEN, TOPAMAX, ANTIDEPRESSANTS, ANTIPSYCHOTICS, ETC.

MEDICATION RECONCILIATION

- PATIENT
  - IS SUPPOSED TO BE GIVEN A LIST OF KNOWN VA / PRIVATE MEDICATIONS
    - UNFORTUNATELY, THAT IS NOT BEING DONE
  - HOWEVER, PATIENT IS SUPPOSED TO KNOW THEIR OWN LIST PRIOR TO SEEING DOCTOR
    - NOT ALWAYS
    - SOMETIMES THEY JUST HAND YOU THEIR OWN WRITTEN/TYPED LIST
    - DO NOT WASTE TIME (CAN DO THIS DURING DILATION)

WHAT DOES THE MED REC TEMPLATE SAY?

MEDICATION RECONCILIATION
1. MEDICATION RECONCILIATION: Medication reconciliation was done. Written medication list was given and reviewed with patient/family/caregiver. The complete Medications list including current prescribed medications, current Non-VA, OTC, herbals, supplements and remote list was reviewed.

It was stated the list was accurate; no discrepancies found. Importance of managing medication was discussed with patient/family/caregiver.

2. MEDICATION RECONCILIATION: Medication reconciliation was done. Medication list was reviewed with patient/family/caregiver. The complete Medications list including current prescribed medications, current Non-VA, OTC, herbals, supplements and remote list was reviewed.

Discrepancies were found and/or new medications ordered and list updated. Written list given to patient. Importance of managing medication was discussed with patient/family/caregiver.

3. MEDICATION RECONCILIATION: Medication Reconciliation was attempted but could not be successfully completed. The complete medication list including current prescribed medications, current Non-VA, OTC, herbals, supplements and remote list was reviewed.

The reason the list could not be successfully completed is:
__Patient/caregiver unable to confirm all the medicaions being taken. Reconciliation done with available information.
__A criticual clinical situtation occurred preventing med reconciliation. Reconciliation done with available information.
__Patient refused to provide information on non-VA medications.
Reason:

4. MEDICATION RECONCILIATION: Reviewed. Mo medications were administered, ordered or changed.

THE VA FULL EYE EXAM TEMPLATE

CHIEF COMPLAINT:

OCULAR PAIN: /10 by / per

ARE YOU HAVING ANY OTHER PAIN TODAY? Y / N
Where and on a scale of 0-10, how bad is it?
List:
Pain level >4? Y / N
Is the pain being managed by someone? Y / N
If not, patient advised to see primary care provider ASAP. Y / N
VA Primary care provider to be alerted by addendum to this note. Y / N

OCULAR HISTORY:
LAST EYE EXAM:

OCULAR MEDS:

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MEDICAL HISTORY: LAST UPDATED |TODAY'S DATE|
-dm -insulin -htn -heart -chol -stroke -copd -sleep apnea -cancer -thyroid -migraines -MS

last a1c |HEMOGLOBIN A1C 2/2YR|
last bp |BLOOD PRESSURE| pulse |PULSE|
|ACTIVE PROBLEM LIST|

ALLERGIES: |ALLERGIES/ADR|

FAM HISTORY: -dm -glaucoma -blind -amd

CURRENT SOC HISTORY: -etoh -tobacco

OTHER RELEVANT MEDICAL DATA (IMAGING, ETC.):

VA OD RX: cc
VA OS RX: cc

	WNL ou (x)
PUPILS:	x
CON FIELDS:	x
EOMS:	x
HIRSCH:	x
OTHER:	

|TODAY'S DATE|
MRX OD:
MRX OS:

	WNL ou (x)
ADNEXA:	x
LIDS/LASHES:	x
CONJ/SCLERA:	x
CORNEA:	x
ANT CHAMBER:	x
IRIS:	x
OTHER:	

IOP:

Patient educated |TODAY'S DATE| about need to be dilated and agreed to have it done. Patient advised of blurred near vision, to use caution when driving and to wear sunglasses home which were provided to patient.

M1N2.5 x WNL ou (x) 78d/20d LAST DONE |TODAY'S DATE|
LENS:
C/D RATIO:
ONH DESCRIP:
MACULA:
POST POLE:
VESSELS:
VITREOUS:
PERIPHERY:
OTHER:

IMPRESSION:

PLAN:

ASSESSED TODAY:

MEDICATION RECONCILIATION

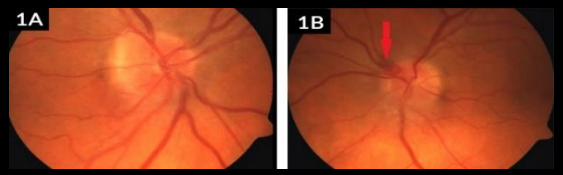
- WE ASK
  - IS YOUR LIST OF MEDICATIONS UP TO DATE?
    - IF YES = NO CHANGES, LEAVE #1 AND DELETE 2,3,4
    - IF PATIENT UNSURE, LEAVE #3 AND DELETE 1,2,4
  - IF YES (AND PATIENT KNOWS THEM), WHAT ARE THE CHANGES?
    - RECORD THEM UNDER #2 MED REC
      - ODS AND RESIDENTS MUST ADD NAME ONLY TO NON-VA LIST
      - EVEN ARTIFICIAL TEARS AND VISINE, ETC. SHOULD BE LISTED HERE
      - IF PATIENT SAYS NO LONGER TAKING EYE MED, YOU CAN REMOVE IT
      - IF PATIENT SAYS NO LONGER TAKING VA SYSTEMIC MED, DOCUMENT BUT DO NOT REMOVE IT
    - STUDENT RECORDS THEM UNDER #2 MED REC AND TELLS OD
  - KEEP IN MIND
    - IF NO NONVA MEDICATIONS ARE LISTED AND PATIENT DOES NOT TAKE ANY…
      - ODS / RESIDENTS ARE TO ADD "NO NONVA MEDS" TO FILL IN THE BLANK SPACE
      - STUDENT TELLS THE OD SO WE CAN ADD "NO NONVA MEDS"
  - WE CAN DELETE THINGS FROM NONVA MEDS BUT CANNOT FROM VA MED LIST
  - FYI OTC ARTIFICIAL TEARS, VISINE, ETC. SHOULD BE ON NONVA LIST

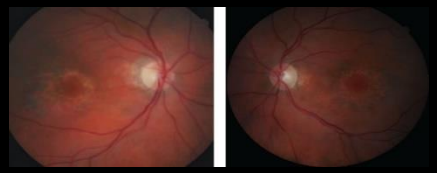
MEDICATION RECONCILIATION

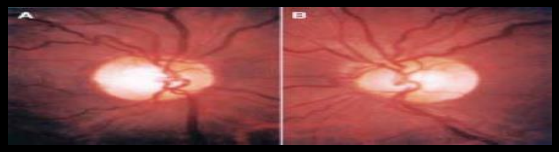
- IF STARTING A NEW OPHTHALMIC MEDICATION
  - SEND TO PHARMACY TO PICK UP
    - NEW MEDICATION WILL BE ADDED AND PRINTED ON NEW SHEET AT PHARMACY
  - SENDING HOME AND WILL BE MAILED
    - NEW MEDICATION SHOULD BE WRITTEN ON PRINTED SHEET BY STUDENT, RESIDENT, STAFF OD
  - IF STARTING A 2ND OR 3RD GLAUCOMA MEDICATION
    - FILL OUT GLAUCOMA EYE MED INSTRUCTION SHEET AND GIVE TO PATIENT AND REVIEW

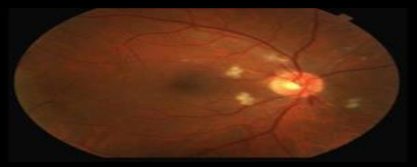
MEDICATIONS THAT MAY CAUSE OCULAR SIDE EFECTS

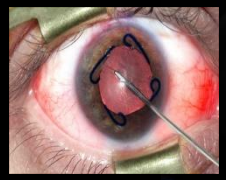
- SEMAGLUTIDE (OZEMPIC)
- AMIODARONE
- HYDROXYCHLOROQUINE (PLAQUENIL)
- ETHAMBUTOL
- INTERFERON
- ED MEDS
- FLOMAX
- BLOOD THINNERS
- STEROIDS
- GILENYA
- TAMOXIFEN
- TOPAMAX
- ANTIDEPRESSANTS
- ANTIPSYCHOTICS
- ETC.

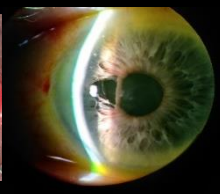


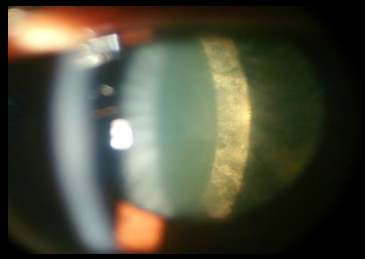


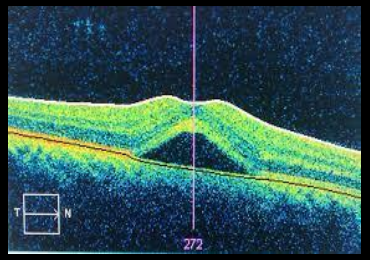


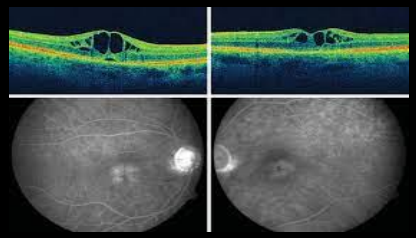


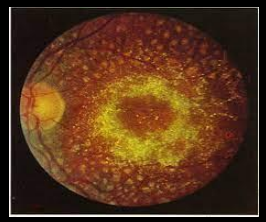


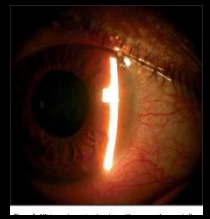


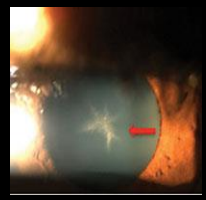












MEDICATIONS THAT MAY CAUSE OCULAR SIDE EFECTS

- SEMAGLUTIDE (OZEMPIC)
- AMIODARONE
- HYDROXYCHLOROQUINE (PLAQUENIL)
- ETHAMBUTOL
- INTERFERON
- ED MEDS
- FLOMAX
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- STEROIDS
- GILENYA
- TAMOXIFEN
- TOPAMAX
- ANTIDEPRESSANTS
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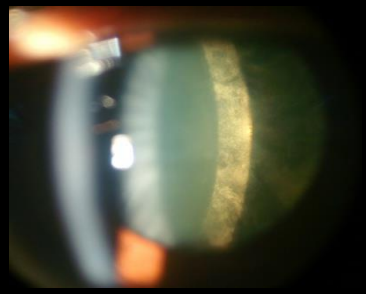
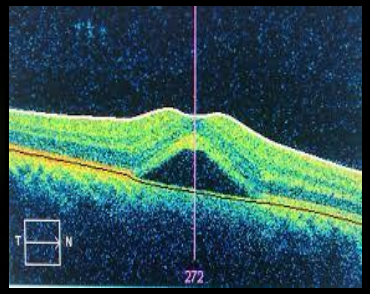
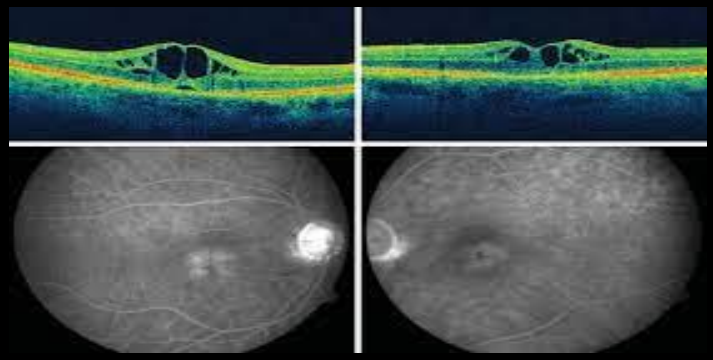
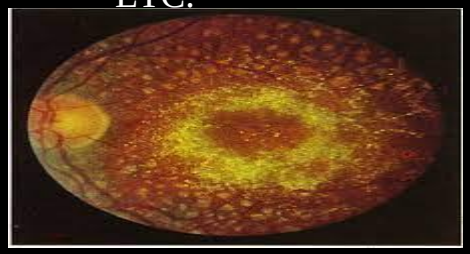
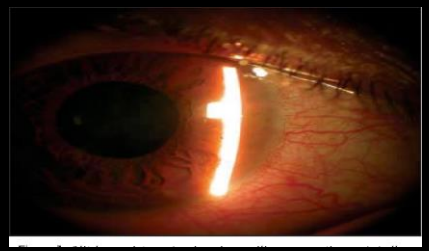
- ETC.









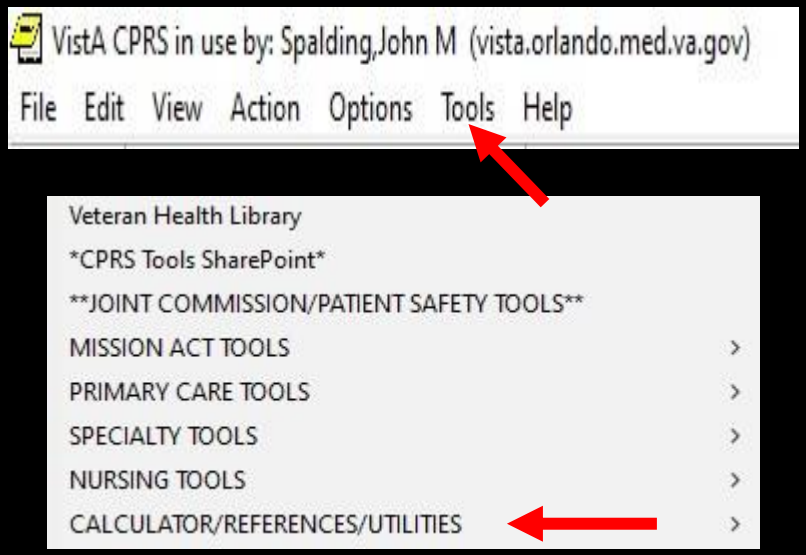


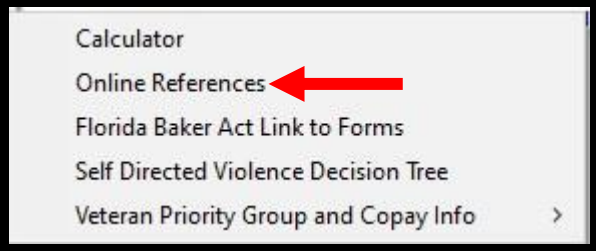
ALWAYS TRY TO LEARN ABOUT MEDS

- REVIEW PATIENT LISTS
- LISTEN TO WHAT PATIENTS TELL YOU
- LISTEN TO ADVERTISEMENTS
- LOOK UP MEDS YOU ARE NOT FAMILIAR WITH
- LOOK CAREFULLY AT MEDS LIST IF CANNOT IMPROVE VISION
    - GO LOOKING FOR VISION RELATED SIDE EFECTS
        - DOCUMENT IN CHART IF ANY FOUND

MEDICATION INFORMATION

- WHILE AT THE VA
  - USE UPTODATE





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Back All Adult Pediatric Patient Graphics

Showing results for **Plaquenil** *(Hydroxychloroquine)*

Cutaneous dermatomyositis in adults: Overview and initial management

...therapy with **hydroxychloroquine** and quinacrine or **hydroxychloroquine** and methotrexate, we typically attempt to discontinue quinacrine or methotrexate prior to tapering **hydroxychloroquine**. Quinacrine can ...

Selection of systemic therapy

Summary and recommendations

Alternatives to methotrexate for the initial treatment of rheumatoid arthritis in adults

...depending upon comorbidities, prognostic features, and other factors, include sulfasalazine (SSZ), **hydroxychloroquine** (HCQ), and other much less frequently used agents. The use of HCQ monotherapy is typically ...

Hydroxychloroquine

Summary and recommendations

Safety of rheumatic disease medication use during pregnancy and lactation

...generally considered safe. The following medications are viewed as relatively safe in pregnancy: **Hydroxychloroquine** (HCQ) Sulfasalazine (SSZ) Low-dose aspirin Azathioprine (AZA) and 6-mercaptopurine (6-MP) ...

Hydroxychloroquine

Summary and recommendations

See images of reactions to Hydroxychloroquine in VisualDx

Hydroxychloroquine

General Pediatric Patient

View Full Topic

Hydroxychloroquine: Drug information

Dosing

Adult

Renal Impairment (Adult)

Hepatic Impairment (Adult)

Pediatric See Pediatric tab above for full pediatric topic

Geriatric

Obesity (Adult)

Adverse Reactions

Brand Names

Administration

Dosage Forms

Mechanism of Action

Pharmacologic Category

Alerts Special Alerts

Drug Interactions

Launch drug interactions program

Adverse Reactions

The following adverse drug reactions and incidences are derived from product labeling unless otherwise specified.

1% to 10%: Ophthalmic: Retinopathy (4%; serum concentration dependent [Petri 2020b]; early changes reversible [may progress despite discontinuation if advanced])

<1%: Hematologic & oncologic: Hemolysis (rare; primarily a theoretical concern in patients with glucose-6-phosphate deficiency; data do not support withholding therapy in these patients [Luzzato 2016; Mohammad 2018])

Frequency not defined:

Cardiovascular: Sick sinus syndrome

Dermatologic: Alopecia (Sharma 2020), erythema multiforme, exacerbation of psoriasis, exfoliative dermatitis, hair discoloration, pruritus, skin photosensitivity (Sharma 2020), skin rash (Borik 2019), urticaria

Endocrine & metabolic: Exacerbation of porphyria, weight loss

Gastrointestinal: Abdominal pain, anorexia

Hematologic & oncologic: Agranulocytosis (rare) (Andrès 2017), anemia, aplastic anemia, bone marrow failure, leukopenia, thrombocytopenia

Hepatic: Abnormal hepatic function tests, acute hepatic failure

Hypersensitivity: Angioedema

Nervous system: Ataxia, dizziness, emotional lability, fatigue, headache, irritability, nervousness, nightmares, psychosis (Das 2014), seizure, sensorineural hearing loss, vertigo

Neuromuscular & skeletal: Asthenia, myopathy (including paralysis or neuromyopathy, leading to progressive weakness and atrophy of proximal muscle groups; may be associated with mild sensory changes and loss of deep tendon reflexes; Casado 2006)

Ophthalmic: Corneal changes (corneal edema, corneal opacity, corneal sensitivity, corneal deposits, visual disturbance, blurred vision, photophobia), decreased visual acuity, macular degeneration, maculopathy, nystagmus disorder, retinal pigment changes, retinitis pigmentosa, scotoma, vision color changes, visual field defect

Otic: Tinnitus

Respiratory: Bronchospasm

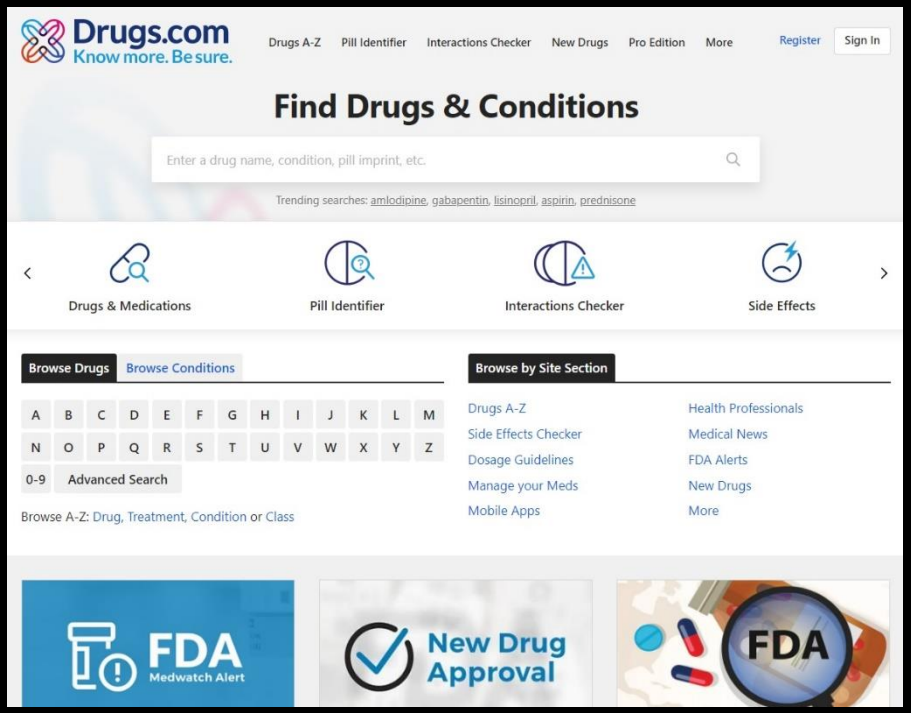
MEDICATION INFORMATION

- WHEN NOT AT THE VA
  - CAN USE NOVA'S LIBRARY AND ALSO USE UPTODATE

  OR
  - DRUGS.COM

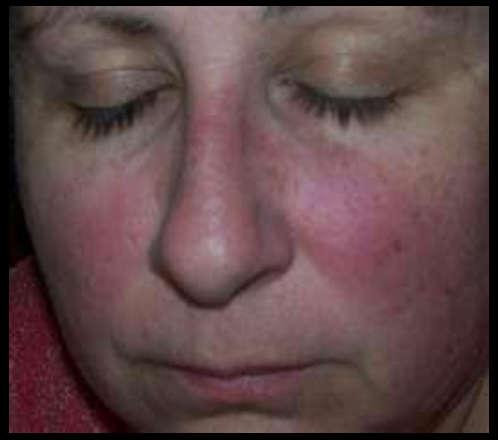
  OR
  - GOOGLE THE DRUG

  OR
  - PHONE APPS



PLAQUENIL

- GENERIC
  - HYDROXYCHLOROQUINE SULFATE
    - A CHLOROQUINE DERIVATIVE
- USES
  - DISCOID AND SYSTEMIC LUPUS ERYTHEMATOSIS
  - RHEUMATOID ARTHRITIS
  - MALARIA
  - SJOGREN'S SYNDROME
  - DERMATOLOGIC DISORDERS

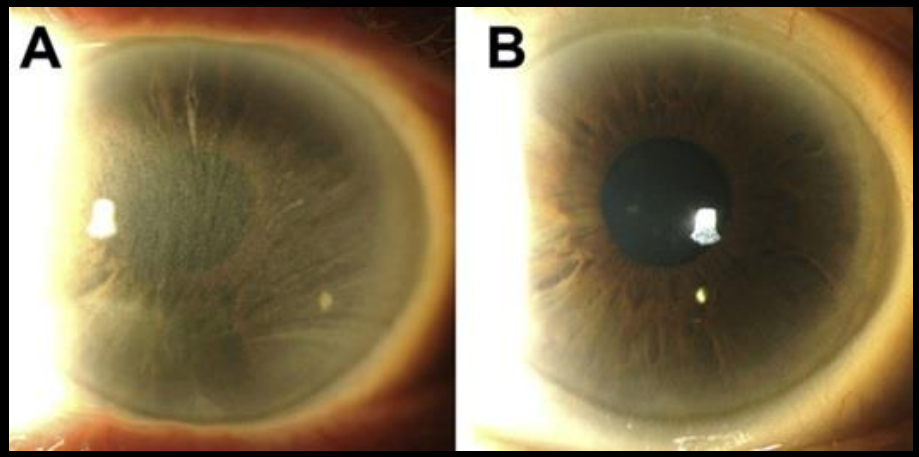


PLAQUENIL

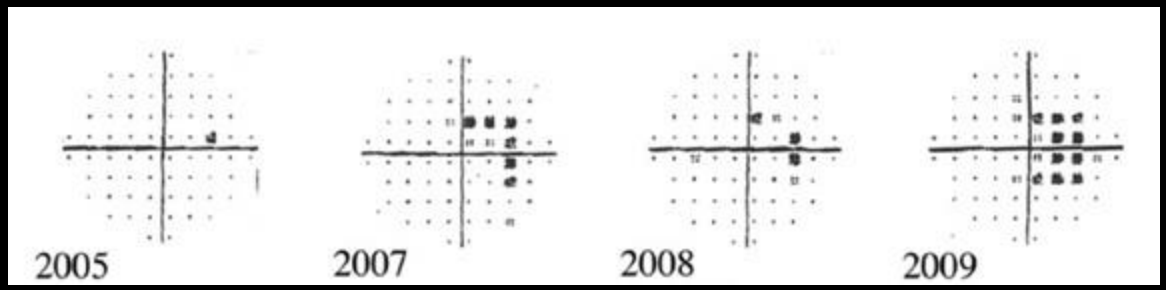
- DOSAGE
  - 400mg QD OR BID FOR WEEKS / MONTHS
  - 200-400 mg/day FOR PROLONGED THERAPY
- MECHANISM
  - CLASSIFIED AS A DISEASE MODIFYING ANTIRHEUMATIC DRUG
  - EXACT MECHANISM IS UNKNOWN
  - THOUGHT TO WORK BY BLOCKING RECEPTORS IN BODY INVOLVED IN INFLAMMATION AND ANTIGEN PRESENTATION
  - SUPPRESSES CYTOKINE CELL SIGNALING AND LYMPHOCYTE PROLIFERATION

PLAQUENIL

- ADVERSE REACTIONS
  - OTHER
    - CARDIOVASCULAR, CNS, DERMATOLOGIC, GI, HEMATOLOGIC, HEPATIC, NEUROMUSCULAR / SKELETAL, OTIC, RESPIRATORY, OTHERS
  - OCULAR
    - Corneal changes
      - edema, opacity, sensitivity
      - Deposits (vortex = Fabry, amiodarone, rhokinase inhibitors)
      - visual disturbance, blurred vision, photophobia
    - Decreased visual acuity
    - Macular degeneration, Maculopathy
    - Nystagmus disorder
    - Retinal pigment changes, RP
    - Scotoma
    - Vision color changes
    - Visual field defect



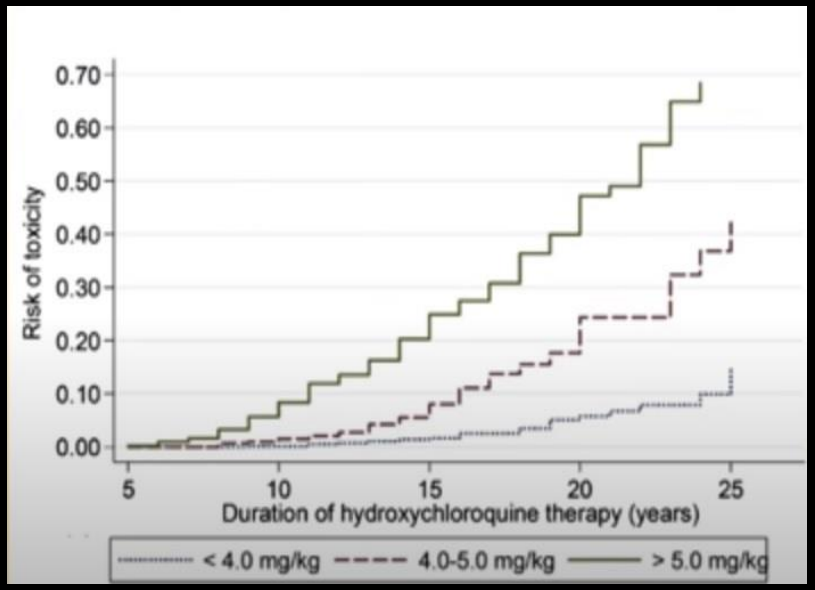
CLINICIAN'S PERSPECTIVE



RISK FACTORS

- DOSAGE
  - HISTORICALLY
    - DAILY DOSE > 400 mg (6.5 mg/kg) REGARDLESS OF WEIGHT
  - NOW
    - AAO RECOMMENDATIONS ≤ 5.0 mg/kg REAL WEIGHT

- DURATION
  - MOST CASES OF TOXICITY OCCUR AFTER ~ 5 YRS OF USE
  - 6.5 MG / KG / D FOR 8.7 YEARS
    - TOXICITY IN 0.05% OF PTS
    - 1% WITH > 5 YEARS OR > 1000 G
      - 400 mg DAILY X 365 DAYS X 7 YEARS = 1022 GRAMS
    - 2% AT 10 YEARS
    - 20% AT 20 YEARS
  - SUGGESTION
    - RECORD DATE STARTED ON PLAQUENIL



OTHER MAJOR RISK FACTORS

- RENAL DISEASE
- TAMOXIFEN USE
- RETINAL AND MACULAR DISEASE

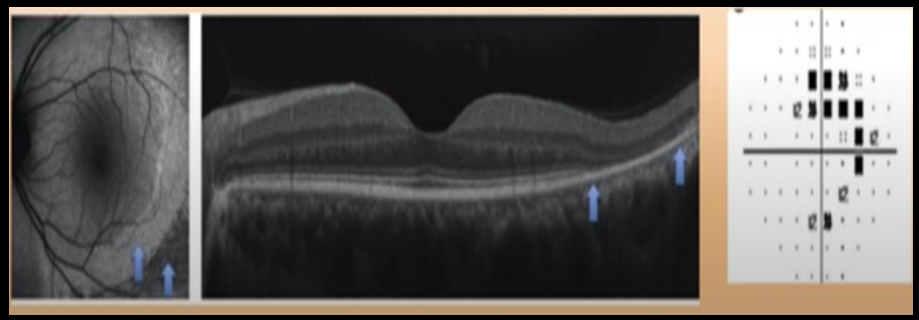
Table 1. Major Risk Factors for Toxic Retinopathy

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.

OTHER RISK FACTORS

- ASIANS
  - INFREQUENT BULL'S EYE
  - MORE COMMON PERIPHERAL OR EXTRAMACULAR DISTRIBUTION NEAR ARCADES
  - DO VF 24-2 OR 30-2



LESSER RISK FACTORS

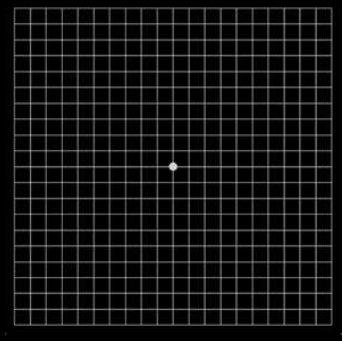
- AGE
  - ELDERLY MAY BE AT HIGHER RISK
    - POSSIBLY DUE TO DRUG CLEARANCE ISSUES
- LIVER DISEASE
  - LOWER DOSES DUE TO LIMITED DRUG CLEARANCE
- GENETIC FACTORS
- SHORT STATURE
  - LOWER DOSES SHOULD BE USED BASED ON IDEAL BODY WEIGHT
- OBESE
  - BASE ON HEIGHT DUE TO RISK OF OVERDOSE IF DONE ON WEIGHT
- RETINAL / MACULAR DISEASE
  - A CONTRAINDICATION TO STARTING / CONTINUING THE MEDICATION?
    - HARDER TO RECOGNIZE SIGNS OF EARLY TOXICITY
    - CONSIDER GETTING RETINA SPECIALIST'S OPINION

WHAT SHOULD OPTOMETRISTS DO?

- KNOW WHAT MEDICATIONS PATIENTS ARE ON
- BE AWARE OF THE POTENTIAL FOR DAMAGE
- KNOW WHAT TESTS INVOLVED IN SCREENING FOR PLAQUENIL DAMAGE
- DETECT DAMAGE EARLY!

PRIOR TO 2011
SCREENING FOR DAMAGE

- HISTORICALLY
  - COMPREHENSIVE EYE EXAM
  - COLOR VISION
    - RED-GREEN COLOR DEFECTS
  - AMSLER GRID
  - DILATED FUNDUS EXAM
  - PHOTOS
    - BASELINE
  - VISUAL FIELD
    - WHITE 10-2 OR RED 10-2?
      - RED THOUGHT TO BE MORE SENSITIVE FOR EARLY TOXICITY
      - HOWEVER, NO NORMATIVE DATABASE, HIGH FALSE POSITIVES



2011 / 2016 UPDATES

American Academy of Ophthalmology Update

Revised Recommendations on Screening for Chloroquine and Hydroxychloroquine Retinopathy

Michael F. Marmor, MD,[1] Ulrich Kellner, MD,[2] Timothy Y. Y. Lai, MD,[3] Jonathan S. Lyons, MD,[4] William F. Mieler, MD,[5] for the American Academy of Ophthalmology

Background: The American Academy of Ophthalmology recommendations for screening of chloroquine (CQ) and hydroxychloroquine (HCQ) retinopathy were published in 2002, but improved screening tools and new knowledge about the prevalence of toxicity have appeared in the ensuing years. No treatment exists as yet for this disorder, so it is imperative that patients and their physicians be aware of the best practices for minimizing toxic damage.

Risk of Toxicity: New data have shown that the risk of toxicity increases sharply toward 1% after 5 to 7 years of use, or a cumulative dose of 1000 g, of HCQ. The risk increases further with continued use of the drug.

Dosage: The prior recommendation emphasized dosing by weight. However, most patients are routinely given 400 mg of HCQ daily (or 250 mg CQ). This dose is now considered acceptable, except for individuals of short stature, for whom the dose should be determined on the basis of ideal body weight to avoid overdosage.

Screening Schedule: A baseline examination is advised for patients starting these drugs to serve as a reference point and to rule out maculopathy, which might be a contraindication to their use. Annual screening should begin after 5 years (or sooner if there are unusual risk factors).

Screening Tests: Newer objective tests, such as multifocal electroretinogram (mfERG), spectral domain optical coherence tomography (SD-OCT), and fundus autofluorescence (FAF), can be more sensitive than visual fields. It is now recommended that along with 10-2 automated fields, at least one of these procedures be used for routine screening where available. When fields are performed independently, even the most subtle 10-2 field changes should be taken seriously and are an indication for evaluation by objective testing. Because mfERG testing is an objective test that evaluates function, it may be used in place of visual fields. Amsler grid testing is no longer recommended. Fundus examinations are advised for documentation, but visible bull's-eye maculopathy is a late change, and the goal of screening is to recognize toxicity at an earlier stage.

Counseling: Patients should be aware of the risk of toxicity and the rationale for screening (to detect early changes and minimize visual loss, not necessarily to prevent it). The drugs should be stopped if possible when toxicity is recognized or strongly suspected, but this is a decision to be made in conjunction with patients and their medical physicians.

Financial Disclosure(s): Proprietary or commercial disclosure may be found after the references.

Ophthalmology 2011;118:415–422

AMERICAN ACADEMY™ OF OPHTHALMOLOGY

American Academy of Ophthalmology Statement

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

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

Background: The American Academy of Ophthalmology recommendations on screening for chloroquine (CQ) and hydroxychloroquine (HCQ) retinopathy are revised in light of new information about the prevalence of toxicity, risk factors, fundus distribution, and effectiveness of screening tools.

Pattern of Retinopathy: Although the locus of toxic damage is parafoveal in many eyes, 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.

Risk of Toxicity: 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.

Major Risk Factors: High dose and long duration of use are the most significant risks. Other major factors are concomitant renal disease, or use of tamoxifen.

Screening Schedule: 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.

Screening Tests: The primary screening tests are automated visual fields plus spectral-domain optical coherence tomography (SD OCT). These should look beyond the central macula in Asian patients. The multifocal electroretinogram (mfERG) can provide objective corroboration for visual fields, and fundus autofluorescence (FAF) can show damage topographically. Modern screening should detect retinopathy before it is visible in the fundus.

Toxicity: 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.

Counseling: Patients (and prescribing physicians) should be informed about risk of toxicity, proper dose levels, and the importance of regular annual screening. *Ophthalmology 2016;123:1386-1394*

SINCE 2016
SCREENING FOR DAMAGE

Table 3. Clinical Examination Techniques

Recommended Screening Tests
Primary tests: ideally do both
Automated visual fields (appropriate to race)
SD OCT
Other objective tests (as needed or available):
mfERG
FAF
Newer tests of possible value in future
Microperimetry
Adaptive optics retinal imaging
Not Recommended for Screening
Fundus examination
Time-domain OCT
Fluorescein angiography
Full-field ERG
Amsler grid
Color testing
EOG

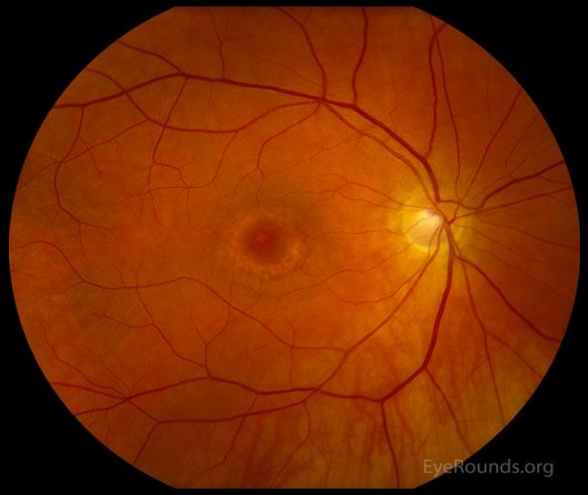
EOG = electro-oculogram; ERG = electroretinogram; FAF = fundus autofluorescence; mfERG = multifocal electroretinogram; SD OCT = spectral-domain optical coherence tomography.

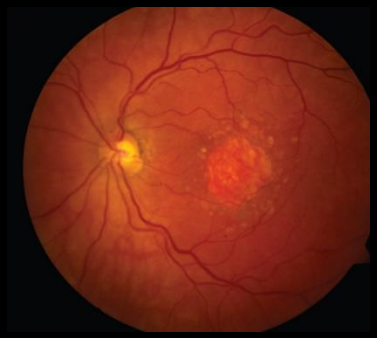
FUNDUS EVALUATION

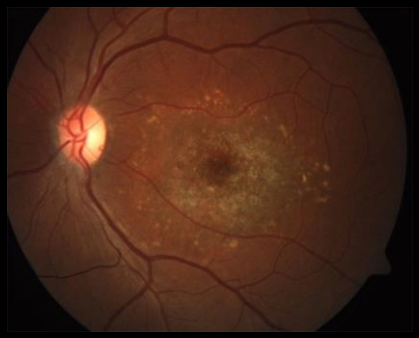
- WHY “NECESSARY”?
  - GUIDELINE SAYS IT IS NOT
  - HOWEVER….LOOK FOR RETINAL CHANGES CAN CAUSE DECREASED VISION, SCOTOMA, ETC., OTHER RETINAL DISEASES
- WHAT TEST?
  - DFE
- WHAT TO LOOK FOR?
  - EARLY
    - SUBTLE RPE STIPPLING, LOSS OF FOVEAL LIGHT REFLEX
  - LATE
    - RPE CHANGES , BULL’S EYE PATTERN (RING OF HYPER / HYPO PIGMENTATION)
  - ADVANCED
    - PERIPHERAL RETINA MAY BE AFFECTED
      - RPE PROLIFERATION, VASCULAR ATTENUATION
    - OPTIC ATROPHY
- IS IT NORMAL / ABNORMAL?
  - PRIOR OR SUBSEQUENT MACULAR DISEASE MAY BE A CONTRAINDICATION TO USING PLAQUENIL

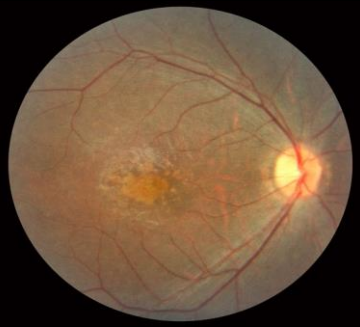
PLAQUENIL RELATED MACULOPATHY

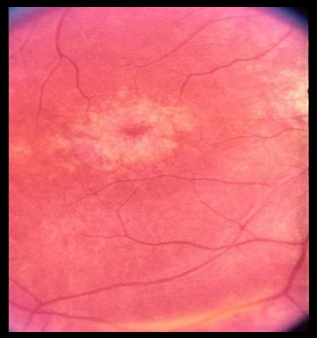
- DIFFERENTIAL DIAGNOSIS
  - PLAQUENIL MACULOPATHY
  - AGE-RELATED MACULAR DEGENERATION
  - CENTRAL AREOLAR CHOROIDAL DYSTROPHY
  - STARGARDT'S DISEASE
  - CONE-ROD DYSTROPHY
  - BENIGN CONCENTRIC ANNULAR DYSTROPHY



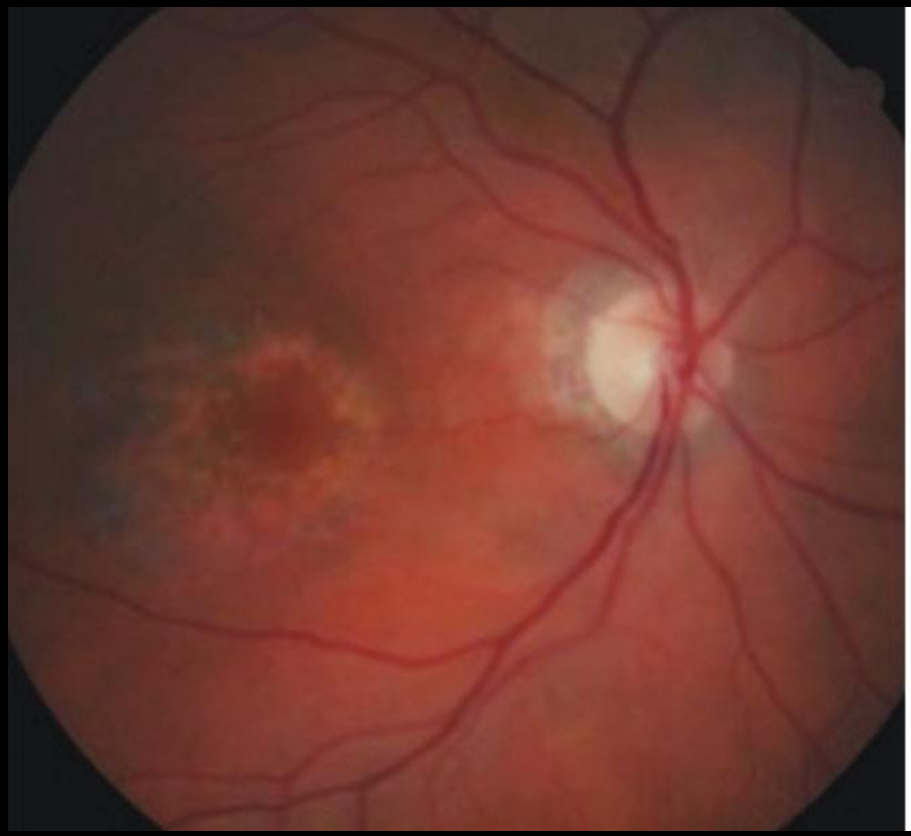


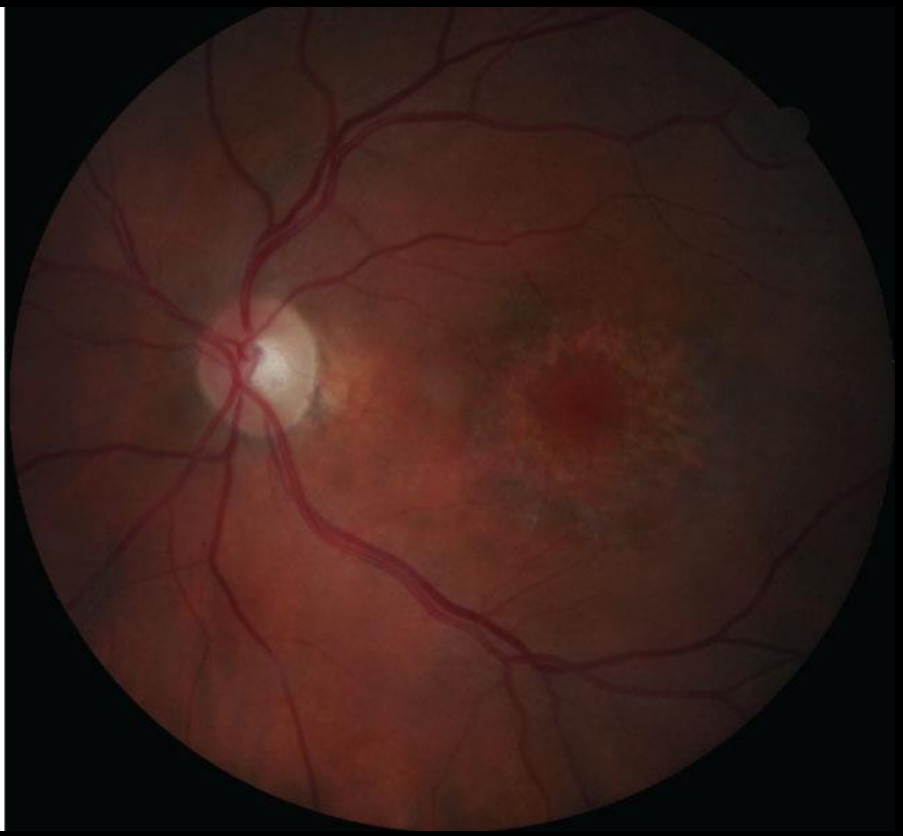




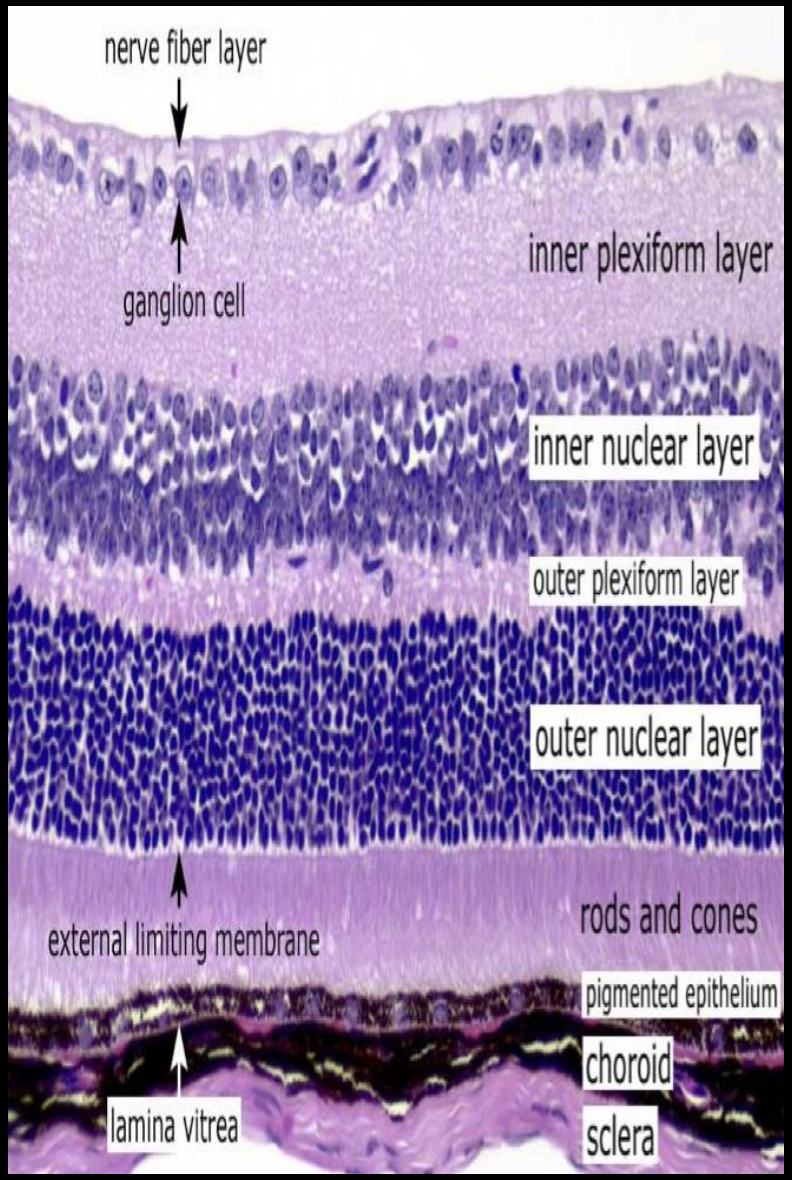


BULL'S EYE MACULOPATHY





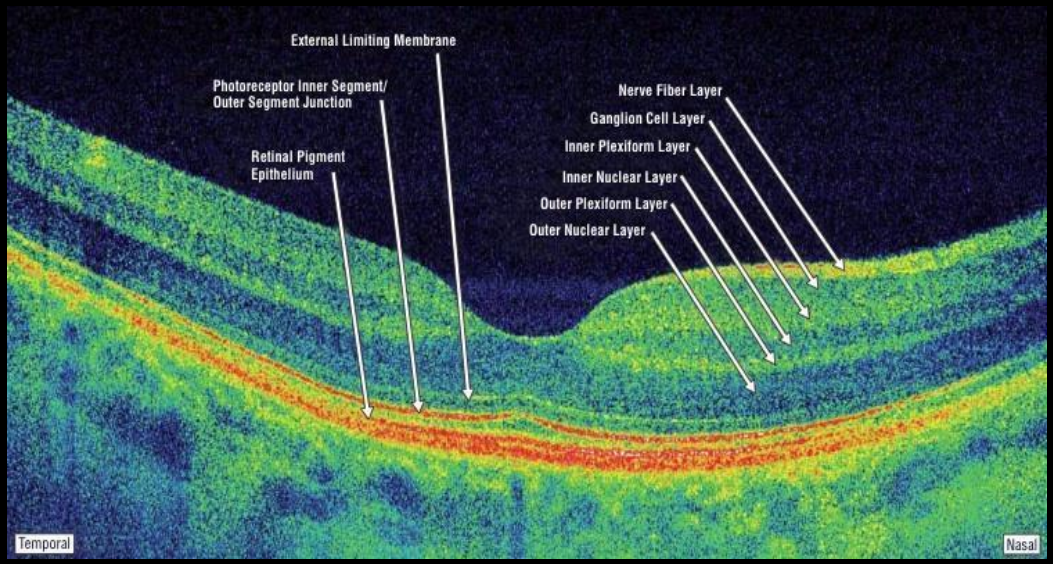
KNOW YOUR ANATOMY

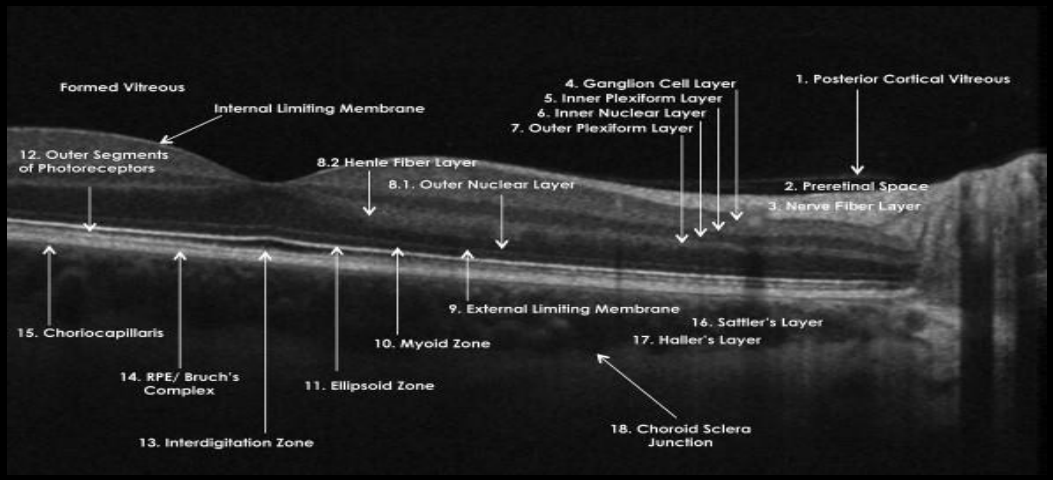


- INTERNAL LIMITING MEMBRANE
- NERVE FIBER LAYER
- GANGLION CELL LAYER
- INNER PLEXIFORM LAYER
- INNER NUCLEAR LAYER
- OUTER PLEXIFORM LAYER
- OUTER NUCLEAR LAYER
- EXTERNAL LIMITING MEMBRANE
- INNER / OUTER PHOTORECEPTOR SEGMENT
- RETINAL PIGMENT EPITHELIUM
- BRUCH'S MEMBRANE
- CHOROID
- SCLERA

OCT EVALUATION

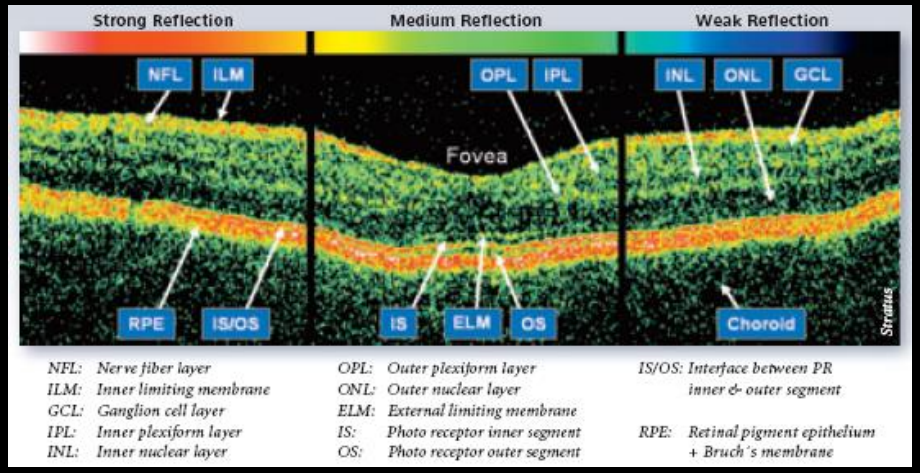
- WHY NECESSARY?
  - OBJECTIVE
- WHAT TEST?
  - SPECTRAL DOMAIN OCT
    - TIME DOMAIN NOT AS DETAILED

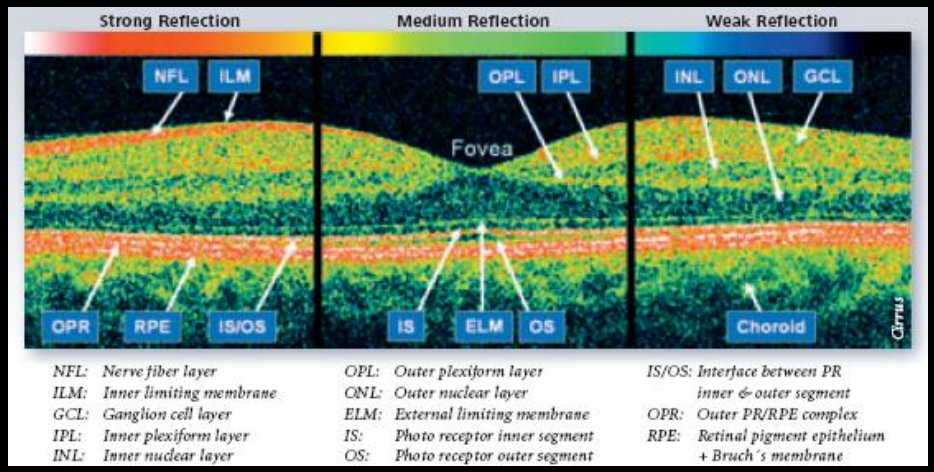




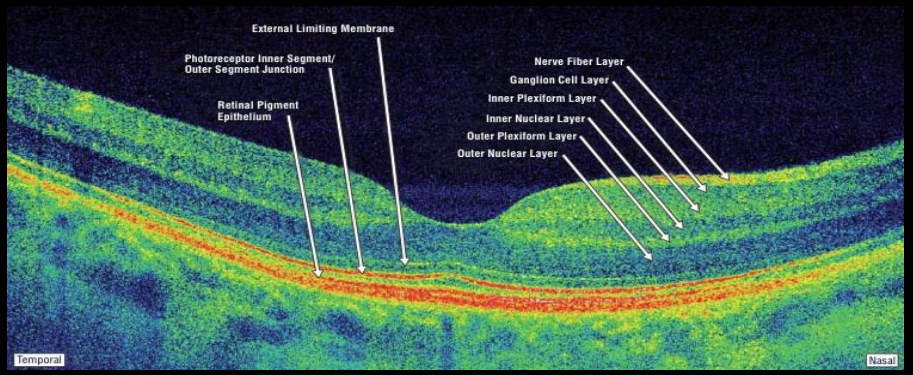
OCT EVALUATION

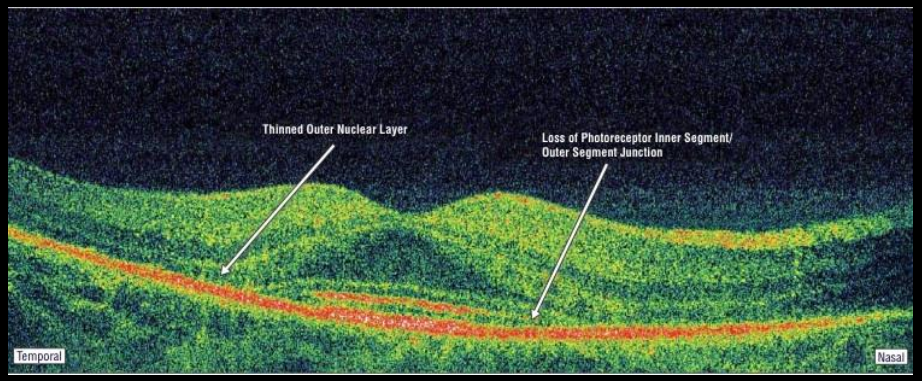
- WHAT TO LOOK FOR?
  - LOCALIZED THINNING OF RETINAL LAYERS IN PARAFOVEAL REGION
- IS IT NORMAL / ABNORMAL?
  - MILD
    - LOSS OF OR DISRUPTION OF PARAFOVEAL INNER / OUTER SEGMENT JUNCTION (IS-OS)
    - THINNING OF OUTER NUCLEAR LAYER
  - LATE
    - COMPLETE LOSS OF IS-OS JUNCTION THROUGHOUT THE FOVEA
  - FLYING SAUCER PATTERN

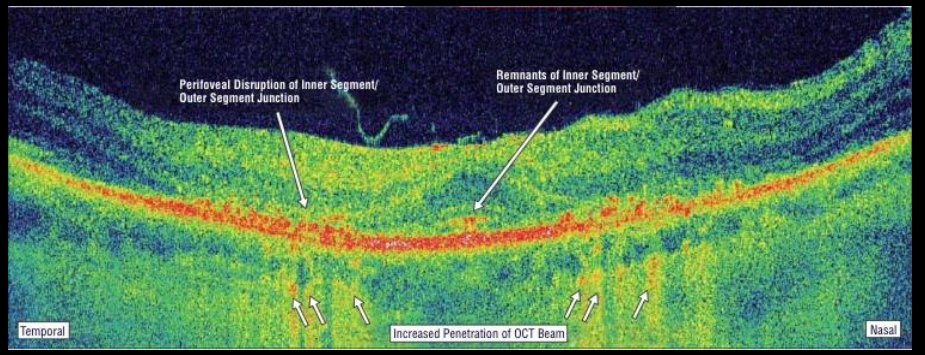




PLAQUENIL OCT CHANGES



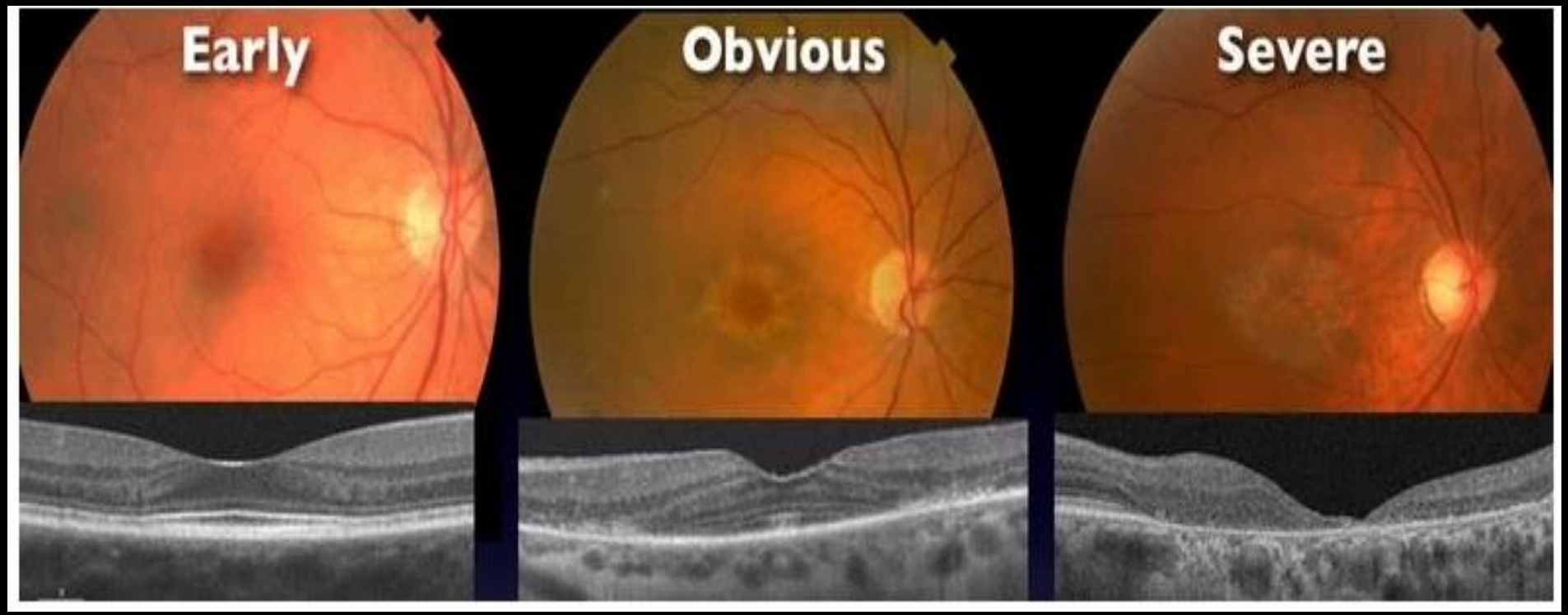




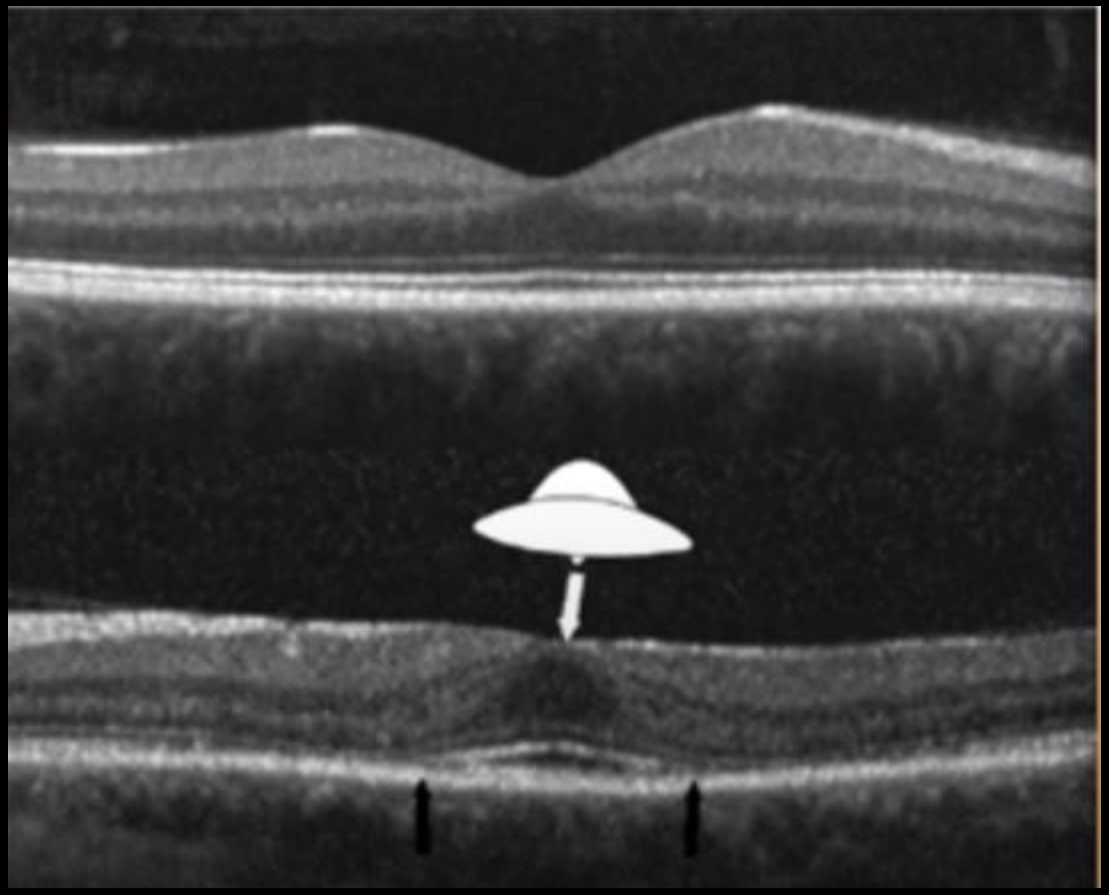
- LOSS OF OR DISRUPTION OF PARAFOVEAL INNER / OUTER SEGMENT JUNCTION (IS-OS)
- THINNING OF OUTER NUCLEAR LAYER

- COMPLETE LOSS OF IS-OS JUNCTION THROUGHOUT FOVEA

PLAQUENIL MACULOPATHY



THE “FLYING SAUCER SIGN”



NORMAL

PLAQUENIL TOXICITY

LOSS / THINNING OF PARAFOVEAL AREA

THE “FLYING SAUCER SIGN”

Spectralis

Cirrus

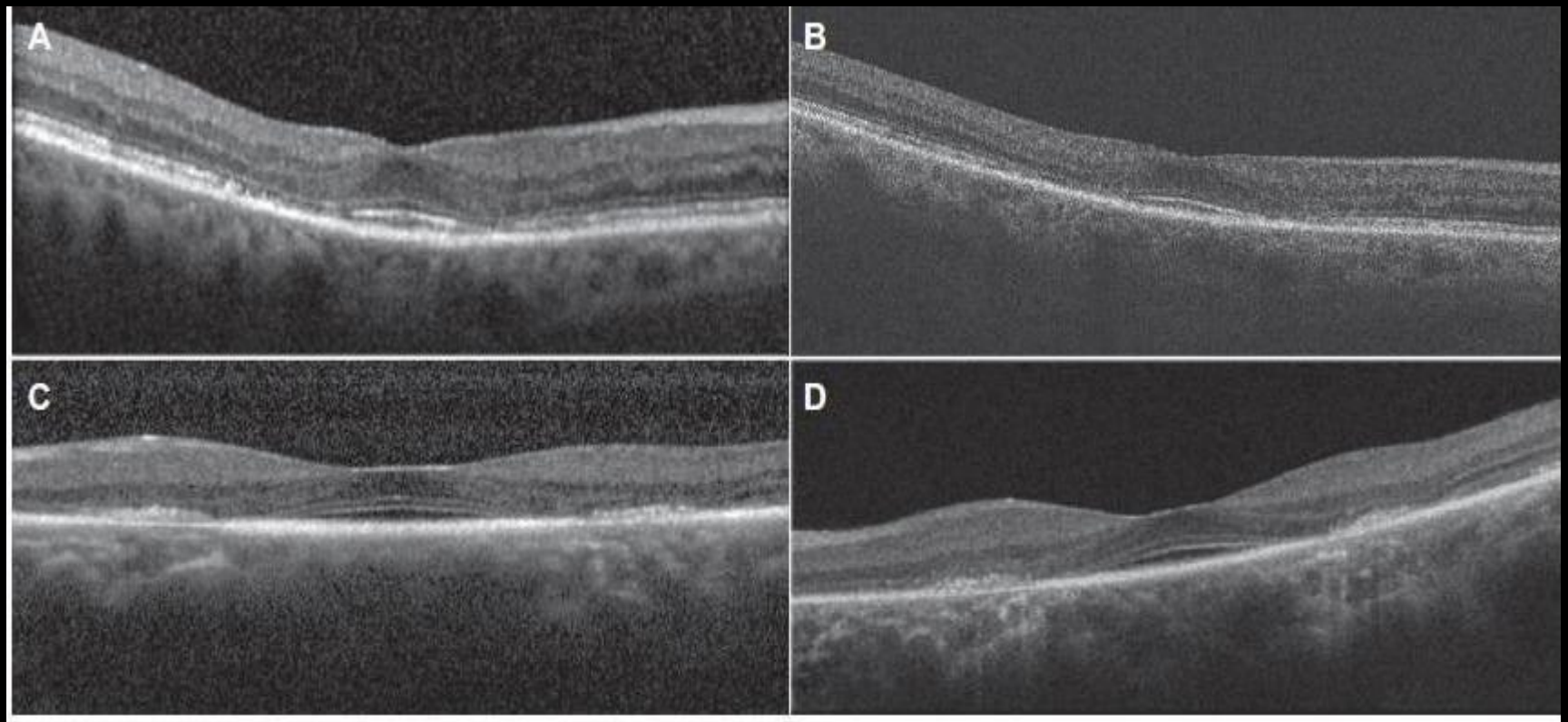


Figure 2 Spectral domain optical coherence tomography (SD OCT) images taken with different commercially available SD OCT machines demonstrate the “flying saucer” sign is consistent in different individuals with hydroxychloroquine retinopathy. **A**) Heidelberg Spectralis SD OCT in patient 9, OD. **B**) Zeiss Cirrus SD OCT in patient 9, OD. **C**) Heidelberg Spectralis SD OCT in patient 4, OS. **D**) Zeiss Cirrus SD OCT in patient 4, OS.

OCT PATTERNS

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Use of OCT Retinal Thickness Deviation Map for Hydroxychloroquine Retinopathy Screening

Ko Eun Kim, MD, PhD,[1,] Seong Joon Ahn, MD, PhD,[2,*] Se Joon Woo, MD, PhD,[3] Kyu Hyung Park, MD, PhD,[3] Byung Ro Lee, MD, PhD,[2] Yeon-Kyung Lee, MD,[4] Yoon-Kyoung Sung, MD, PhD[4]*

Purpose: To investigate the use of a retinal thickness deviation map generated from swept-source (SS) OCT images for hydroxychloroquine retinopathy screening.

Design: Retrospective cohort study.

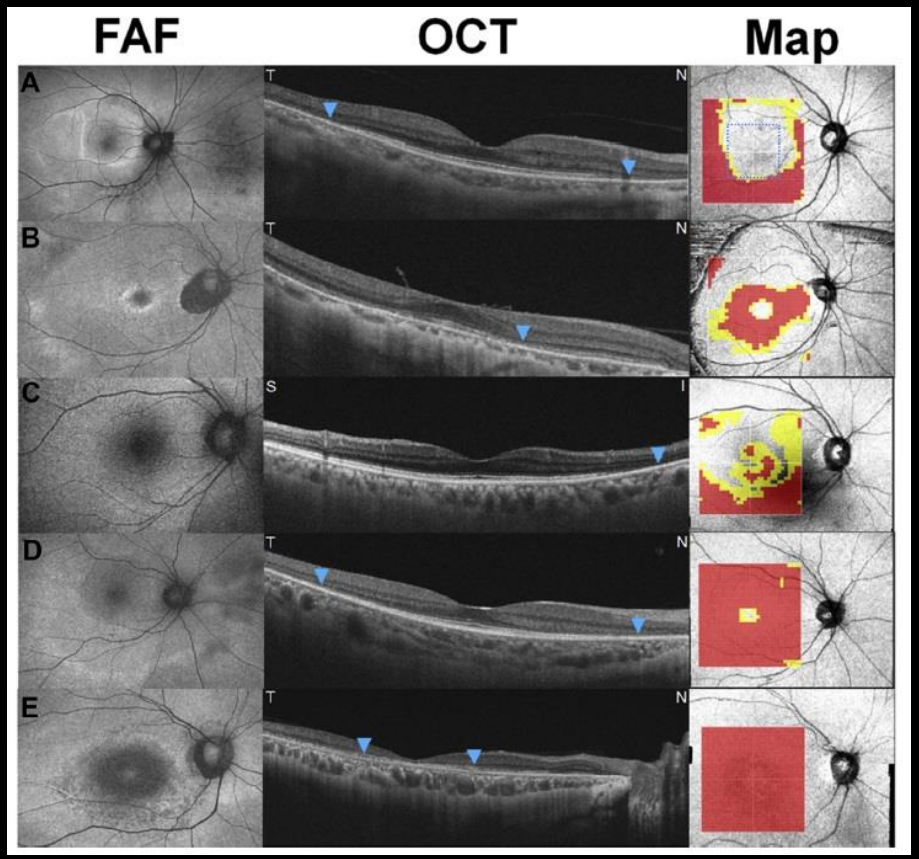
Participants: This study included 1192 Korean patients with a history of hydroxychloroquine treatment: 881 patients (1723 eyes) in the discovery set and 311 patients (591 eyes) in the validation set. Patients were screened for retinal toxicity using SS OCT, fundus autofluorescence, and standard automated perimetry.

Methods: According to the 2016 American Academy of Ophthalmology guidelines, hydroxychloroquine retinopathy was diagnosed by the presence of abnormalities on ≥1 objective structural tests alongside corresponding visual field defects. The 12 × 9-mm^2 macular volume SS OCT scan was performed, and the retinal thickness deviation map was generated automatically using the built-in software. On this map, yellow (retinal thickness, <5% of the normative level) or red (<1% of the normative level) pixels were defined as abnormal. Abnormal findings were evaluated, and diagnostic criteria were developed based on the discovery set data; criteria were validated using the validation set data.

Main Outcome Measures: The rate and patterns of abnormalities on the retinal thickness deviation map and sensitivity and specificity of the diagnostic criteria.

Results: The retinal thickness deviation map showed the following abnormal patterns in eyes with hydroxychloroquine retinopathy: pericentral (36.0%) or parafoveal (6.1%) ring, mixed-ring (34.2%), central island (13.2%), and whole macular thinning (10.5%). The criterion of ≥5 contiguous red pixels showing 1 of the 5 characteristic patterns in both eyes yielded the greatest diagnostic performance (sensitivity and specificity of 98.2% and 89.1% and of 100% and 87.5% in the discovery and validation set data, respectively). Moreover, the area of abnormal pixels on the map was correlated significantly with the mean deviation ($P < 0.001$) and pattern standard deviation ($P < 0.001$) on the Humphrey 30-2 test in eyes with hydroxychloroquine retinopathy.

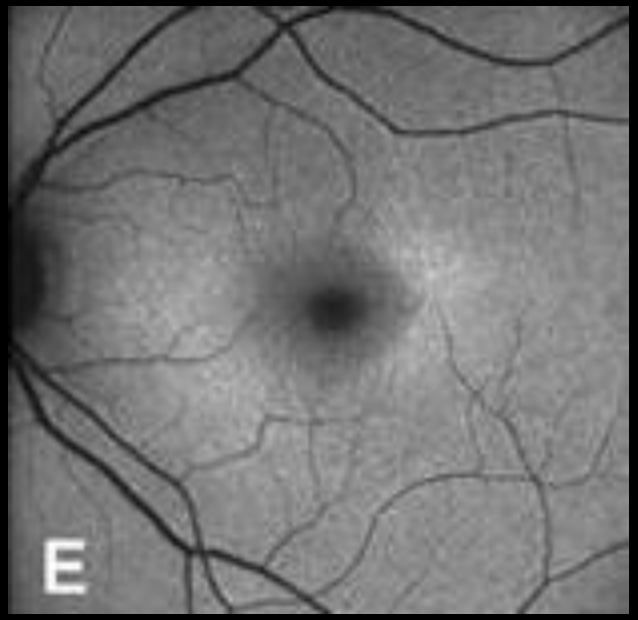
Conclusions: The retinal thickness deviation map may facilitate the objective evaluation of hydroxychloroquine retinopathy because it does not require subjective, morphologic evaluation of the outer retinal layers. The map has the potential to enhance hydroxychloroquine retinopathy screening when used in conjunction with conventional screening methods. *Ophthalmology 2021;128:110-119*



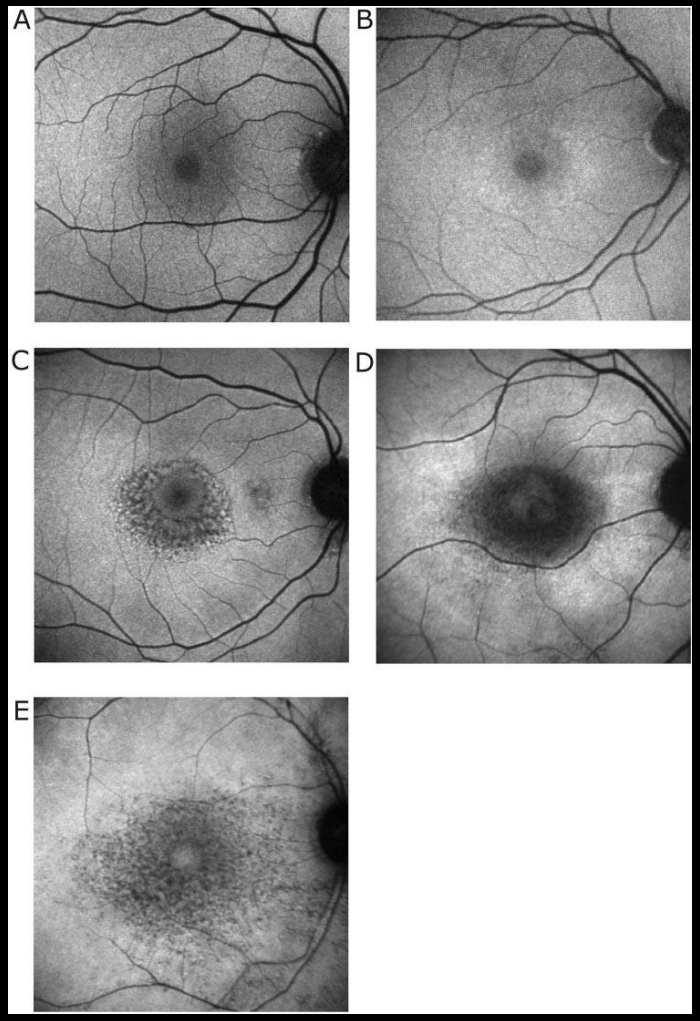
FUNDUS AUTOFLUORESCENCE

- INCREASED FAF
  - INDICATES ACCUMULATION OF LIPOFUSCIN (COMMON IN MANY RETINAL DISEASES)
  - ABNORMAL METABOLISM WITH INCREASED PHAGOCYTOSIS OF PHOTORECEPTOR OUTER SEGMENT

  OR
  - INHERITED / ACQUIRED DEFECT OF PHAGOCYTIC PROCESS OF RPE
- DECREASED FAF
  - INDICATES PHOTORECEPTOR OR RPE CELL LOSS

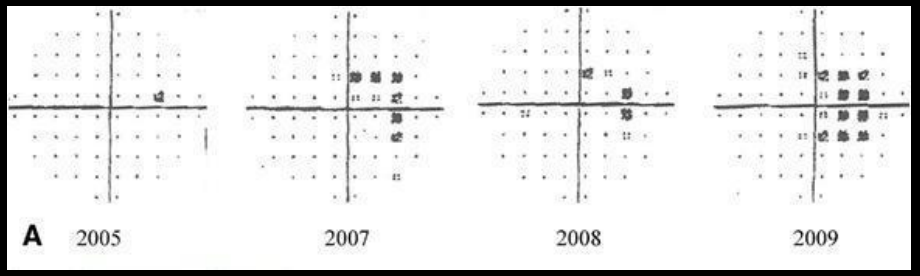


FUNDUS AUTOFLUORESCENCE



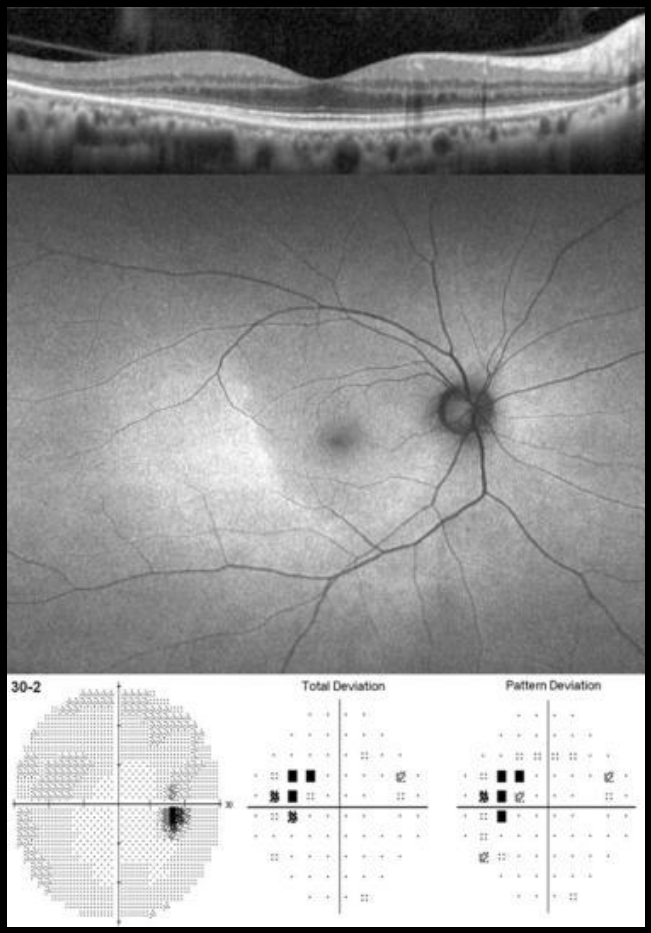
VISUAL FIELD EVALUATION

- WHY NECESSARY?
  - PARAFOVEAL LOSS OF RETINAL SENSITIVITY MAY APPEAR BEFORE FUNDUS CHANGES
- WHAT TEST?
  - 10-2 WHITE
- WHAT TO LOOK FOR?
  - RELIABILITY (FL / FN / FP < 33%)
  - INTERPRET PATTERN DEVIATION
- IS IT NORMAL / ABNORMAL?
  - "INTERPRET WITH LOW THRESHOLD OF SUSPICION"
  - P VALUE < 5% (4 DOTS) INDICATES HIGH PROBABILITY OF ABNORMALITY
  - REPEAT TO CONFIRM
  - ANY REPRODUCIBLE CENTRAL OR PARAFOVEAL SPOTS MAY INDICATE EARLY TOXICITY



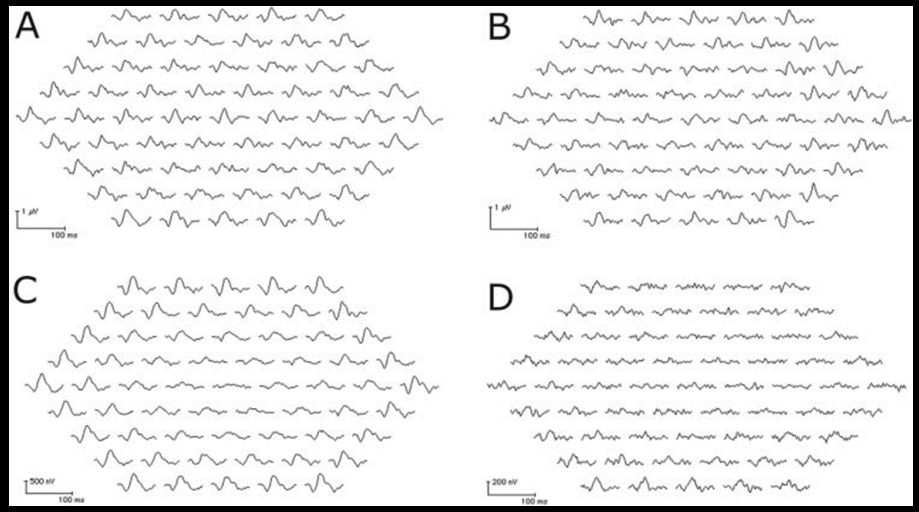
ASIAN PATIENTS

- SKIP THE 10-2
- DO 24-2 OR 30-2
- RARE BULL'S EYE
- MORE COMMON PERIPHERAL OR EXTRAMACULAR DISTRIBUTION NEAR ARCADES

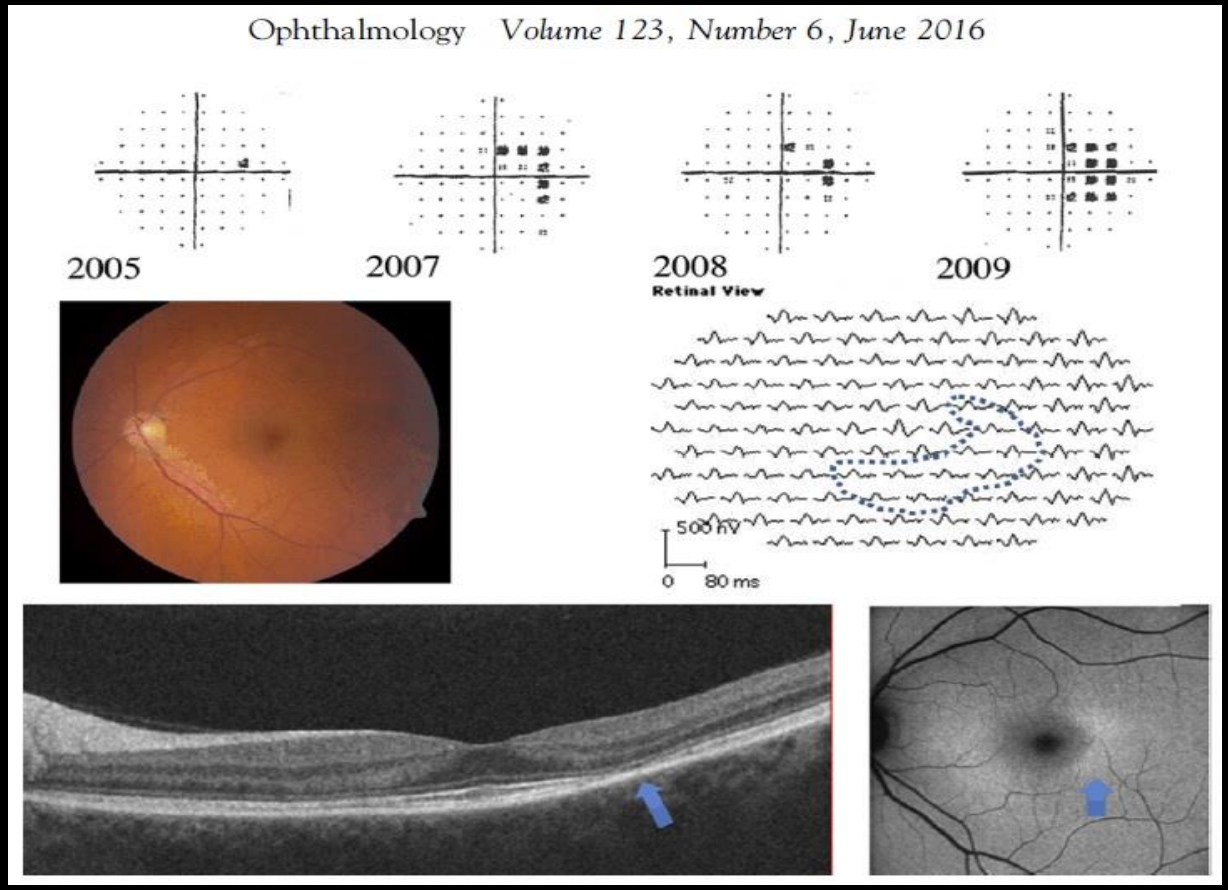


MULTIFOCAL ELECTRORETINOGRAM

- WHY NECESSARY?
  - OBJECTIVE
- WHAT TO LOOK FOR?
  - LOCALIZED PARACENTRAL DEPRESSION IN EARLY TOXICITY
  - POSSIBLY MORE SENSITIVE THAN VF 10-2 WHITE



TO DETECT TOXICTY EARLY…

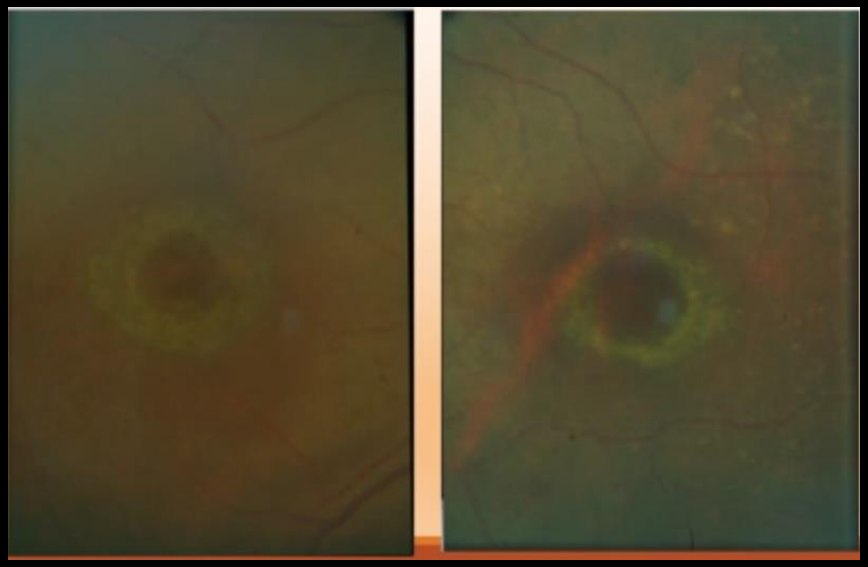


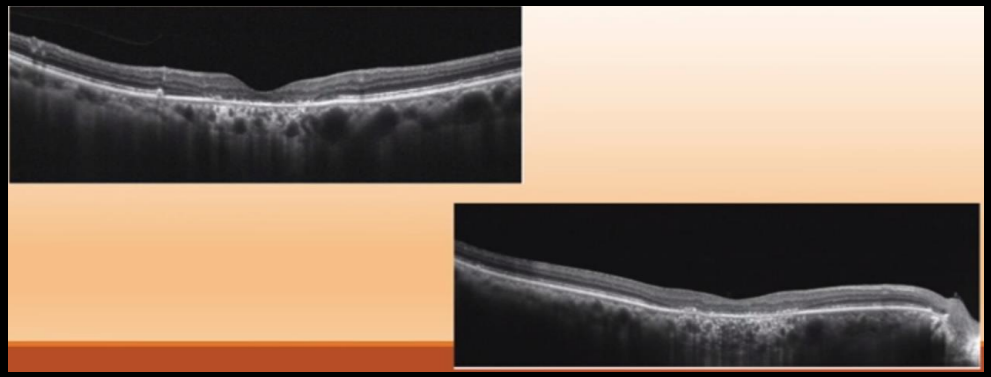
DO AS MUCH AS YOU CAN!

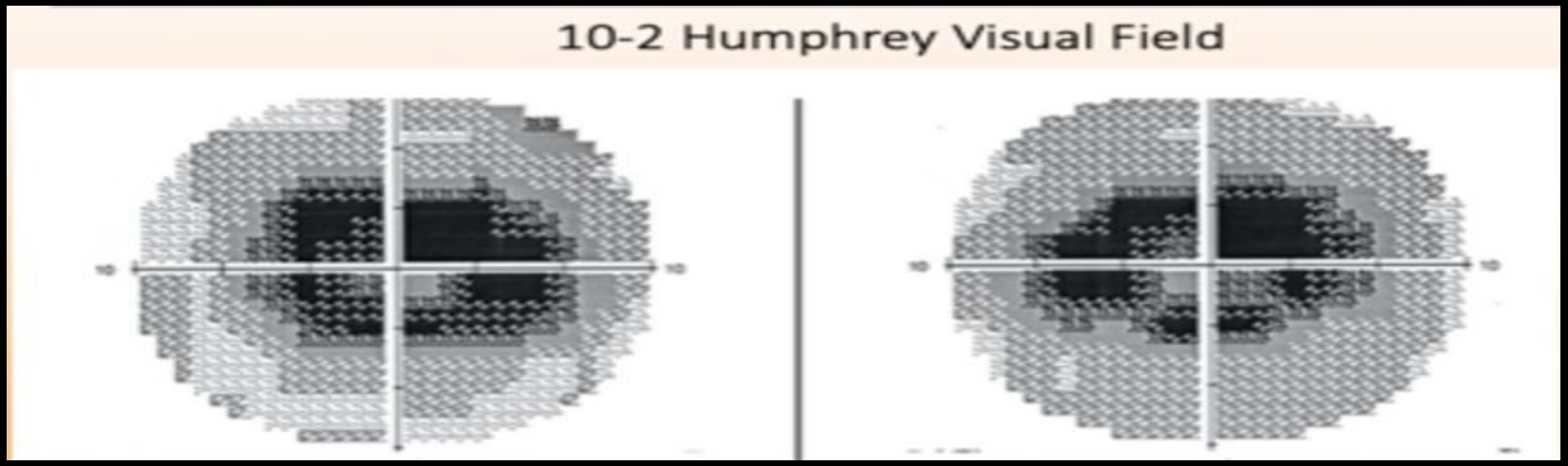
EXAMPLE 1

20/40 OD, 20/40 OS

5.84 mg/kg x 20 years



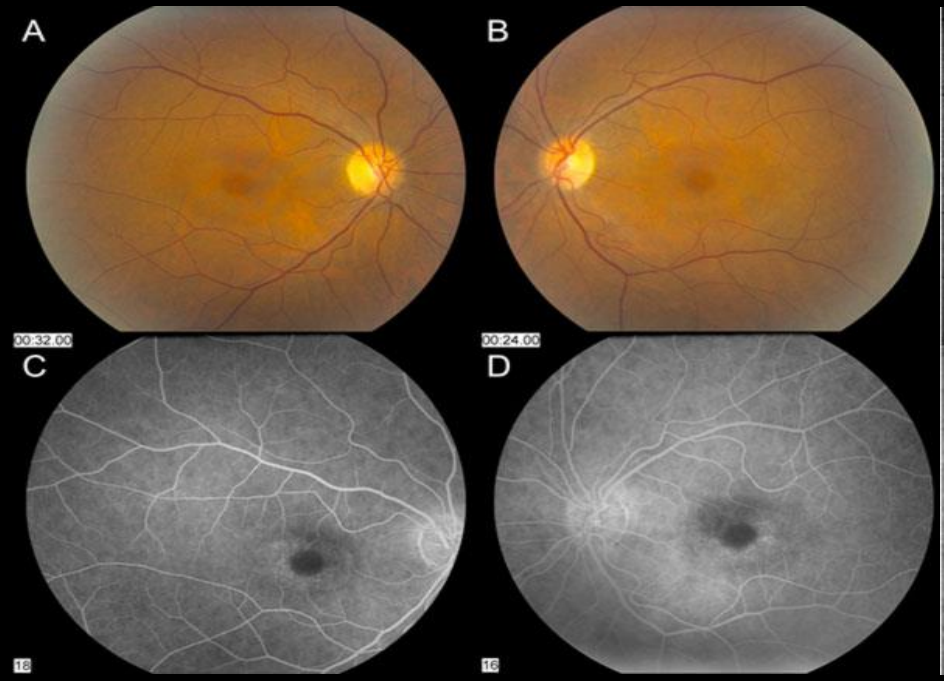


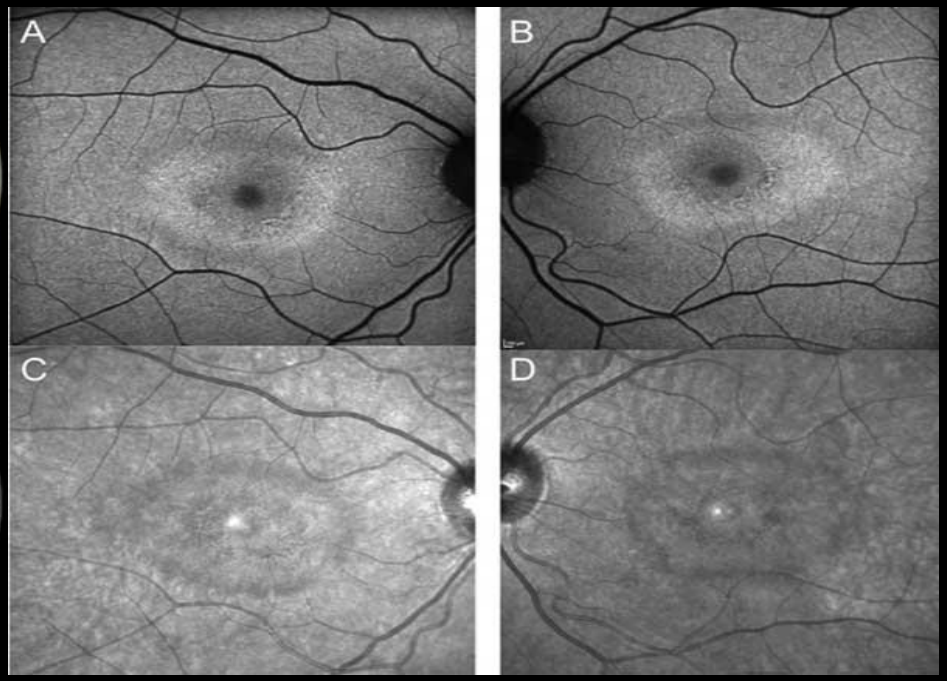


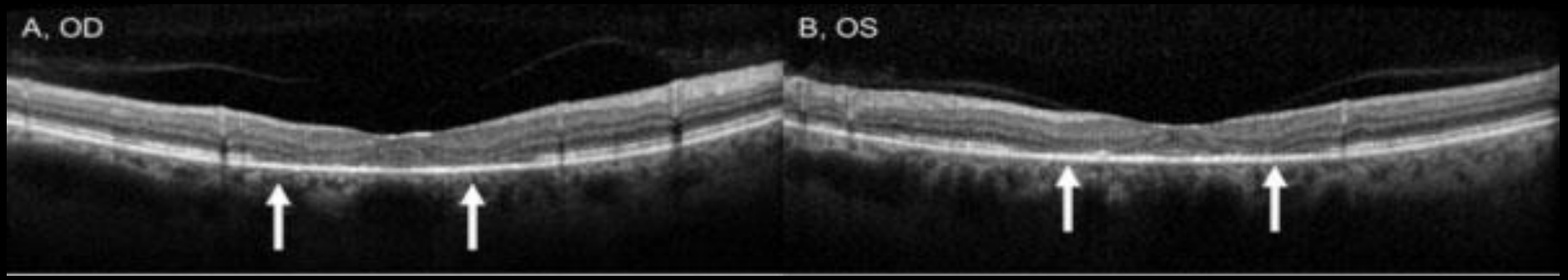
EXAMPLE 2

20/30, 20/25

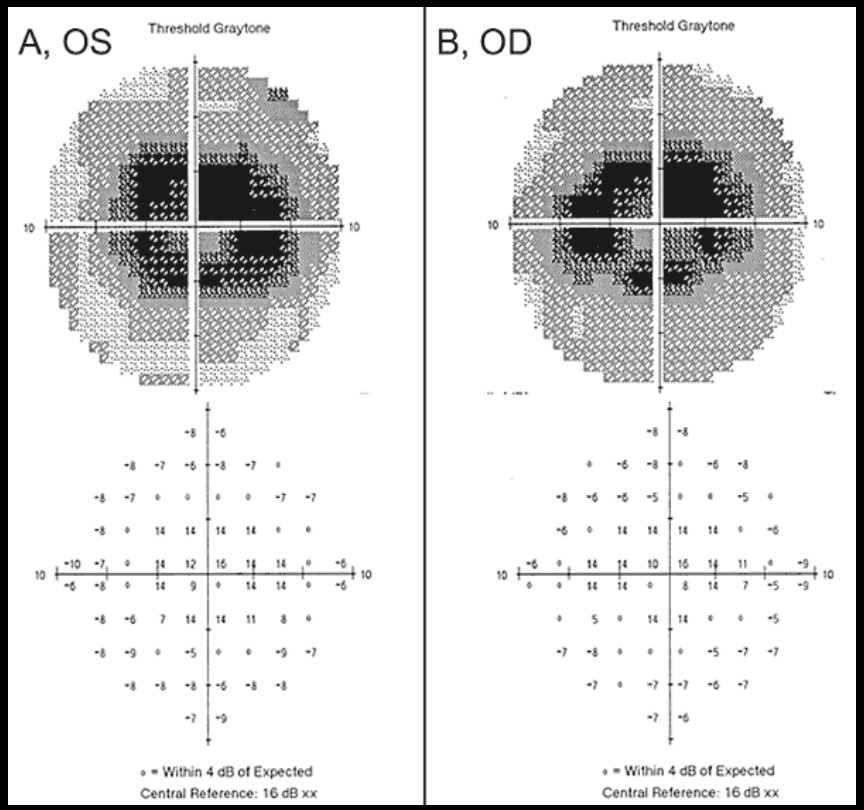
6.5 mg/kg x 10 yrs

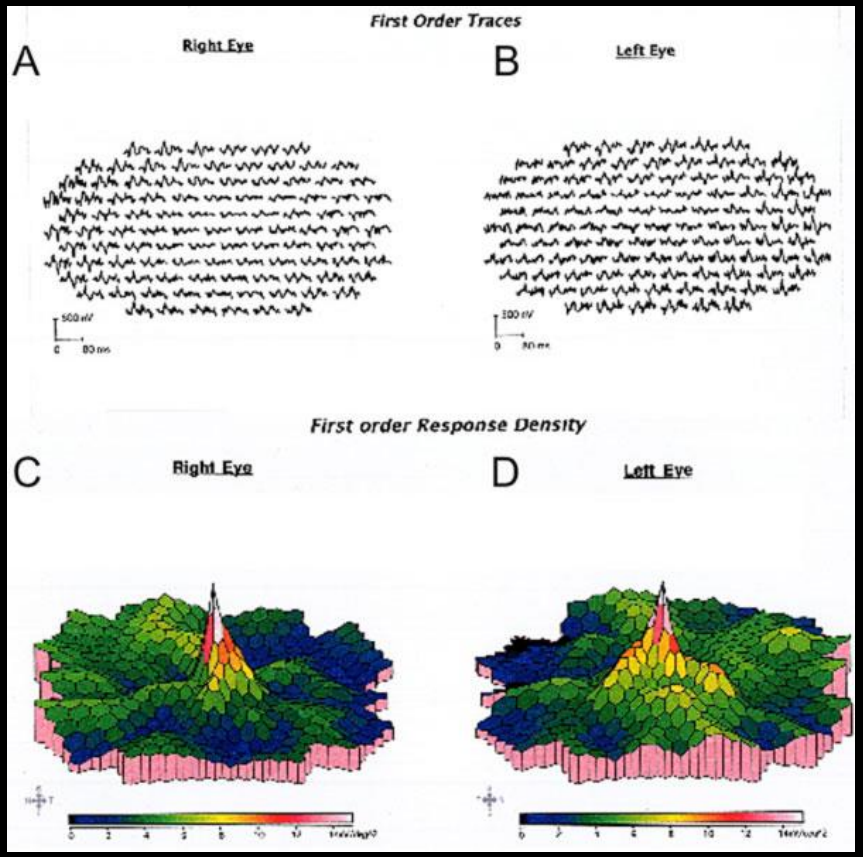






EXAMPLE 2


A, OS
Threshold Graytone
B, OD
Threshold Graytone
◦ = Within 4 dB of Expected
Central Reference: 16 dB xx
◦ = Within 4 dB of Expected
Central Reference: 16 dB xx


First Order Traces
A
Right Eye
B
Left Eye
First order Response Density
C
Right Eye
D
Left Eye

EXAMPLE 3 ASIAN PATIENT

8 mg/kg x 8 yrs, 4 mg/kg x 2yr

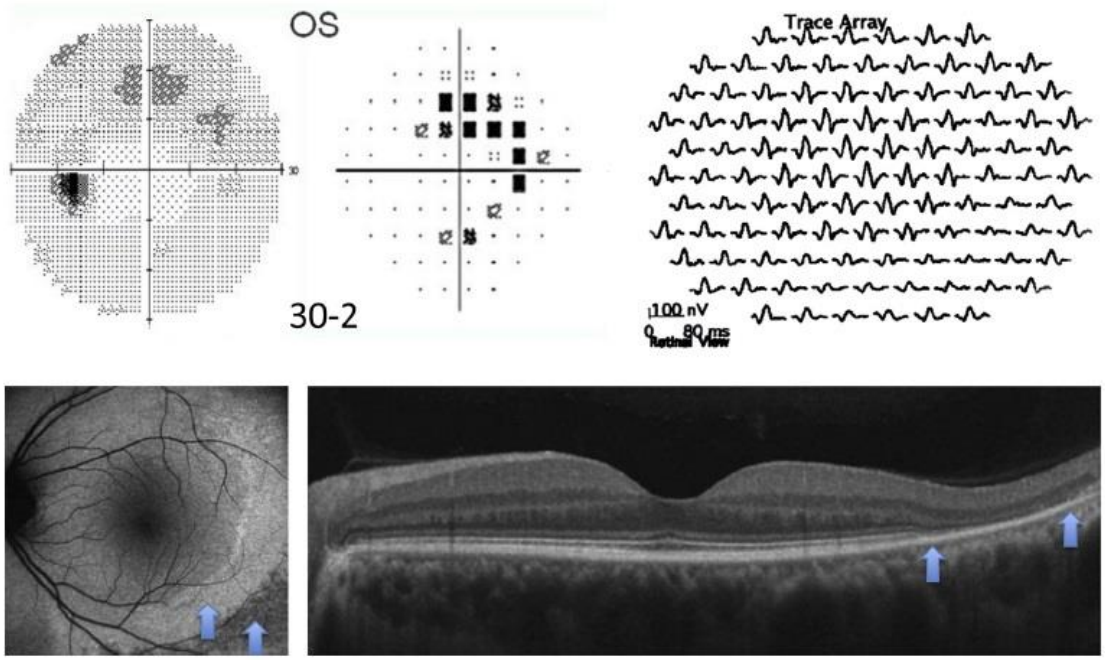


Figure 2. Findings in the left eye of a 42-year-old Chinese woman showing extramacular retinopathy. She had used 8 mg/kg hydroxychloroquine (HCQ) for 8 years and 4 mg/kg for another 2 years. **Top**: 30-2 fields in grey scale and pattern deviation, showing partial ring scotoma outside the parafoveal region; multifocal electroretinogram (mfERG) showing signal weakness most strikingly in an inferotemporal arc of extramacular responses (traces extend to 20° eccentricity). **Bottom**: Autofluorescence image showing increased autofluorescence near the arcades (*left arrow*) and decreased autofluorescence that signals early RPE loss more peripherally (*right arrow*); Spectral-domain optical coherence tomography (SD OCT) cross-section showing marked loss of outer nuclear layer and ellipsoid zone corresponding to the increased autofluorescence (*left arrow*), and beginning retinal pigment epithelium (RPE) disruption at the outer edge of the scan (*right arrow*). There is no parafoveal damage. Modified with permission from Melles RB, Marmor MF. Pericentral retinopathy and racial differences in hydroxychloroquine toxicity. Ophthalmology 2015;122:110–6.[3] OS = left eye.

EXAMPLE 4
PROGRESSIVE CHANGE

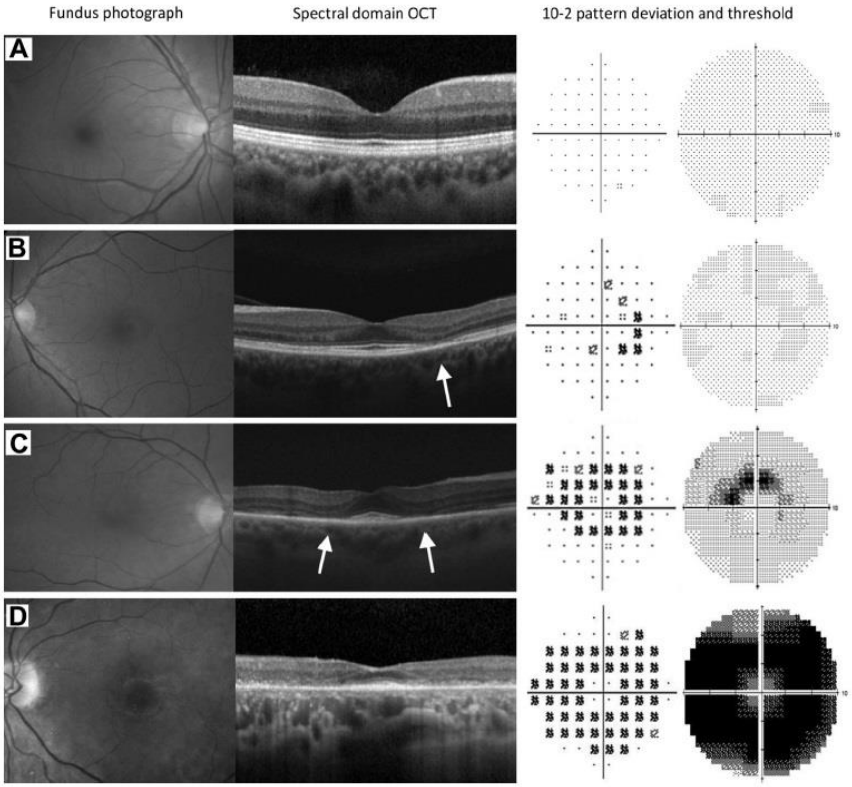


Figure 3. Illustration of progressive changes in hydroxychloroquine (HCQ) retinopathy for European patients. **Left to right**: fundus appearance, spectral-domain optical coherence tomography (SD OCT), 10-2 field pattern deviation, and grey scale. **Top to bottom**: (**A**) normal eye; (**B**) early damage with temporal SD OCT thinning (*arrow*) and mild field loss; (**C**) moderate damage with no fundus changes or retinal pigment epithelium (RPE) loss, but more severe SD OCT (*arrows*) and field changes; (**D**) severe retinopathy with a prominent bull's-eye macular lesion, RPE damage on SD OCT, and a dense ring scotoma. 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] OCT = optical coherence tomography.

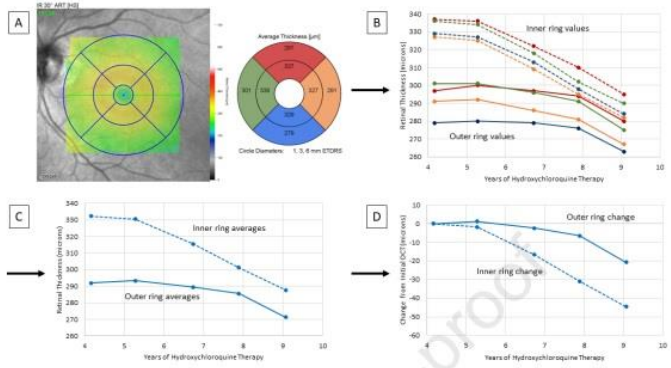
WHAT'S THE LATEST?

- Retinal thickness remains stable for many years in most patients on long-term HCQ 36 therapy, but after a critical point the retina may begin to thin rapidly.
- Sequential plots of inner and outer 37 ETDRS ring macular thickness provide objective evidence of this early structural change several years 38 before conventional signs appear.
- This approach can alert patients and prescribing physicians to 39 potential retinal damage and uses readily available OCT measurements that could be automated by 40 manufacturers for use in comprehensive eyecare settings

› Ophthalmology. 2022 May 11;S0161-6420(22)00335-9. doi: 10.1016/j.ophtha.2022.05.002.
Online ahead of print.

Rapid Macular Thinning is an Early Indicator of Hydroxychloroquine Retinal Toxicity

Ronald B Melles [1], Michael F Marmor [2]



HOW OFTEN TO SEE PATIENT?

- HISTORICALLY
  - 1993
    - PLAQUENIL PRODUCT INSERT
      - BASELINE
      - REGULAR OPHTHALMIC ASSESSMENTS EVERY 3 MOS
  - 1994
    - 79% OF OPHTHALMOLOGISTS RECOMMEND EVERY 6 MOS
  - 1996
    - BASELINE AND THEN ANNUALLY

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.

- NOW
  - BASELINE
    - IF CONCOMITANT RISK FACTOR… YEARLY
    - IF NO OTHER RISK FACTORS… 5 YEARS
  - AT 5 YEARS
    - THEN YEARLY
  - AT VA
    - WE TEND TO FOLLOW YEARLY

PLAQUENIL ALTERNATIVES

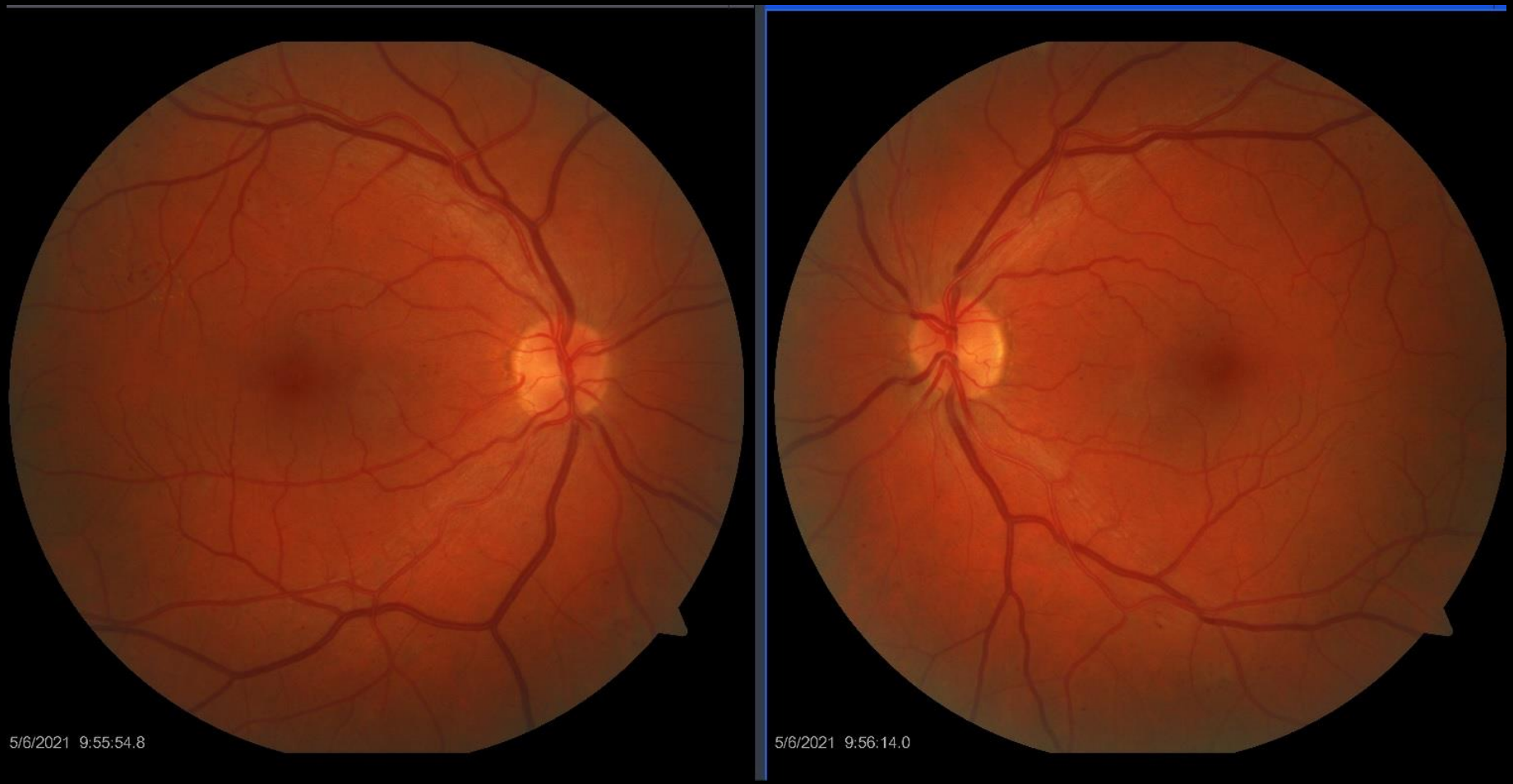
- DISEASE MODIFYING ANTI-RHEUMATIC DRUGS
  - OPTIONS
    - LEFLUNOMIDE (ARAVA)
    - CYCLOSPORINE (NEORAL)
    - SULFASALZINE (AZULFIDINE)
    - GOLD (RIDAURA, SOLGANAL, MYOCHRISINE)
    - METHOTREXATE (RHEUMATREX, TREXALL)
    - CYCLOPHOSPHAMIDE (CYTOXAN)
    - AZATHIOPRINE (IMURAN)
    - BIOLOGICS (ACETMRA, CIMZIA, ENBREL, HUMIRA, KINERET, ORENCIA, REMICADE, RITUXAN, SIMPONI)
  - ALL HAVE THEIR OWN POTENTIAL SIDE EFFECTS

REAL WORLD DILEMMA

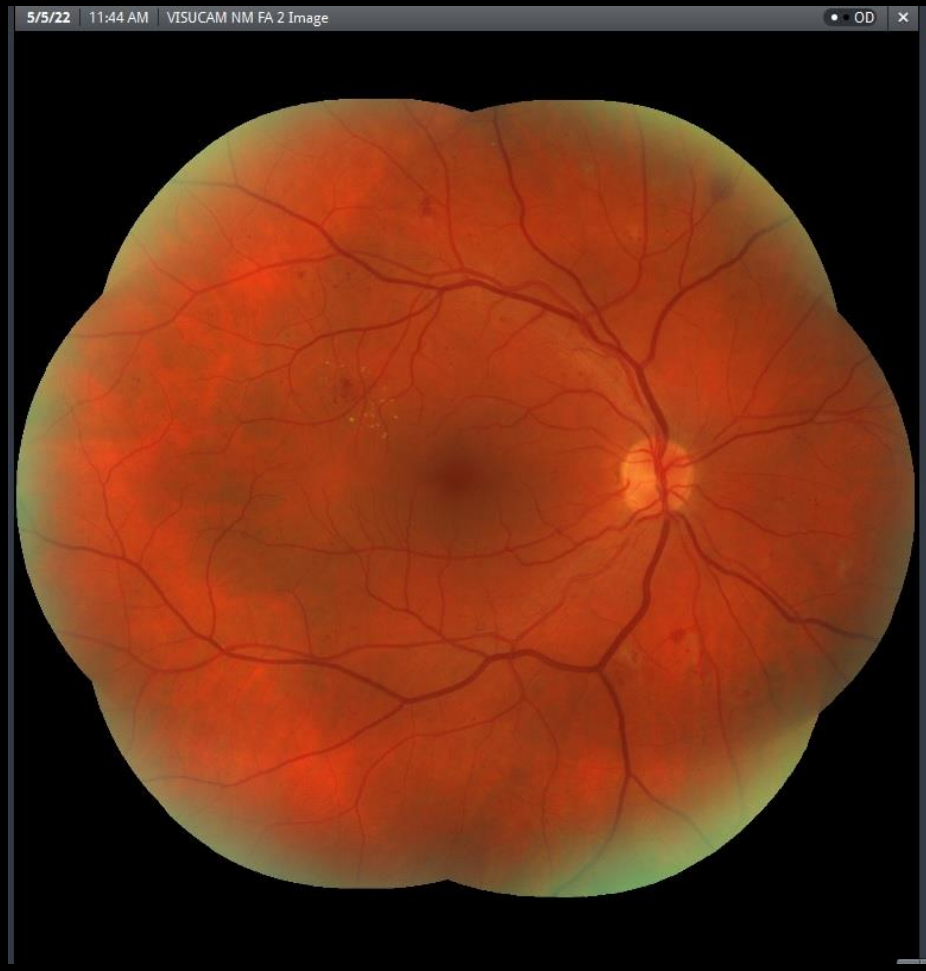
- WHAT IF YOU ARE WORKING AT A LOCATION WITHOUT THE NECESSARY EQUIPMENT?
  - AS SOON AS YOU HEAR THE PATIENT IS ON PLAQUENIL
    - EXPLAIN SITUATION TO PATIENT
    - PRESENT OPTIONS
      1. REFER COMPLETELY TO SOMEONE WITH THE EQUIPMENT
         - » SUGGESTION
           - » DO IT BEFORE YOU CHARGE THE PATIENT. THEY APPRECIATE IT.
         - » UNFORTUNATELY YOU WILL LOSE THE PATIENT MAYBE FAMILY TOO
      2. REFER TO COLLEAGUE WITH EQUIPMENT AND YOU INTERPRET THE RESULTS
         - » YOU MAY END UP KEEPING THE PATIENT AND FAMILY TOO
           - » MAY BE BEST FOR CONTACT LENS PATIENTS, ETC.

ANOTHER REASON FOR MEDICATION RECONCILIATION

2021



2022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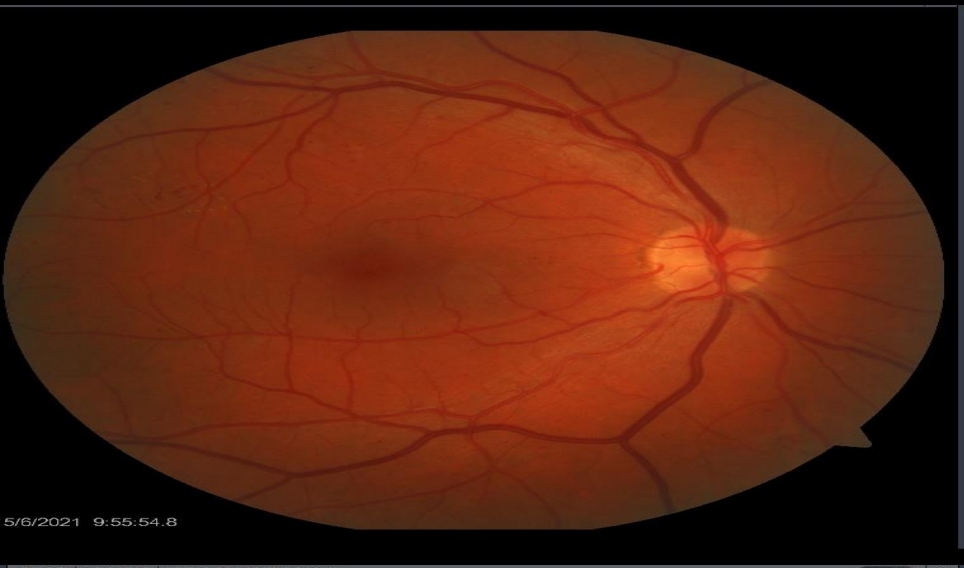
OD


5/5/22 | 11:46 AM | VISUCAM NM FA 2 Image
OS

TREND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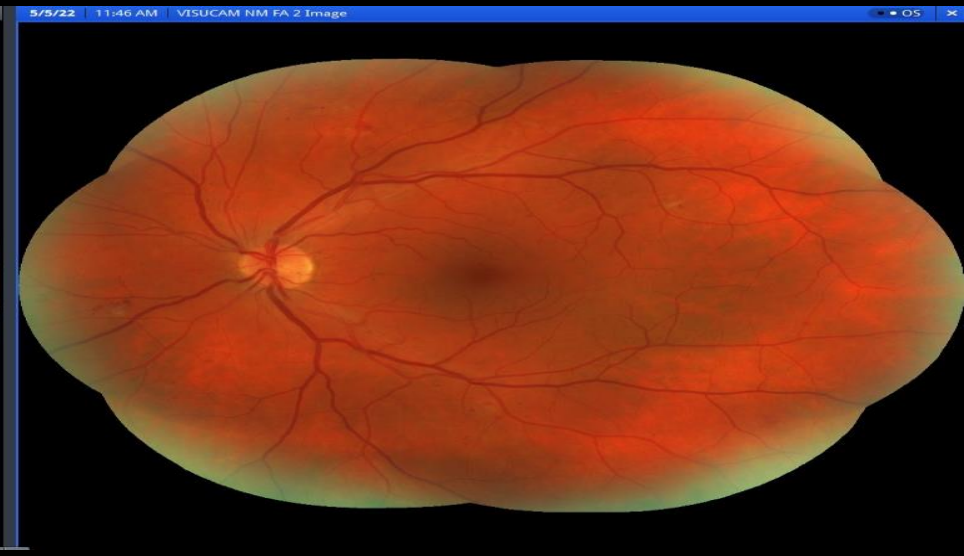

5/5/22 11:46 AM VISUCAM NM FA 2 Image OS

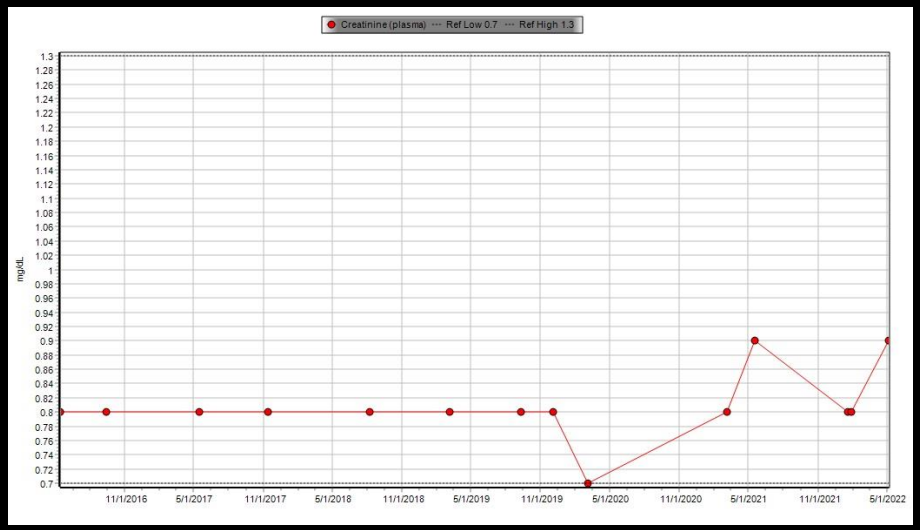
WHY DID THE RETINOPATHY GET WORSE?

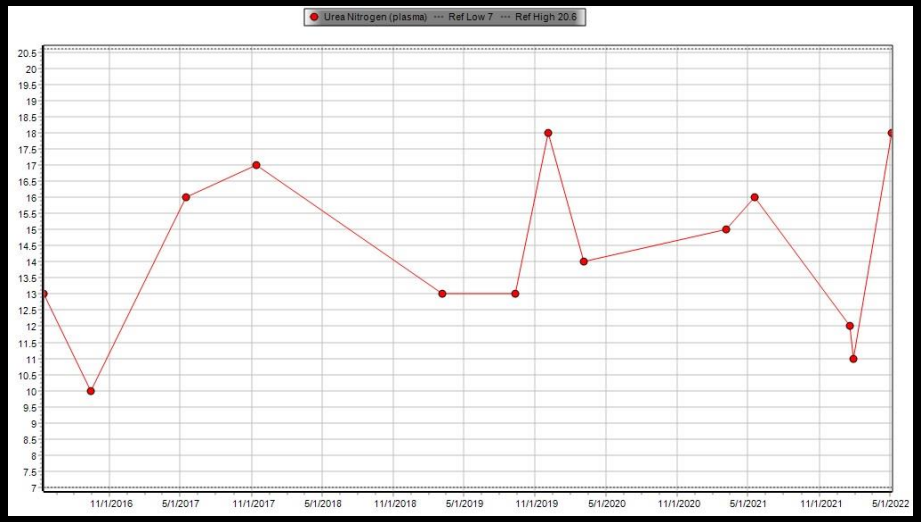
BP DATA


Sys.
Dias.
164
160
156
152
148
144
140
136
132
128
124
120
116
112
108
104
100
96
92
88
84
80
76
72
68
05-16-16 09:39:42
09-14-16 09:14:03
02-07-17 12:40:08
07-10-17 07:32:46
11-14-17 08:11:02
07-09-18 08:03:29
03-11-19 08:01:24
12-04-19 09:05:00
03-09-21 07:45:44
05-04-22 07:58:07

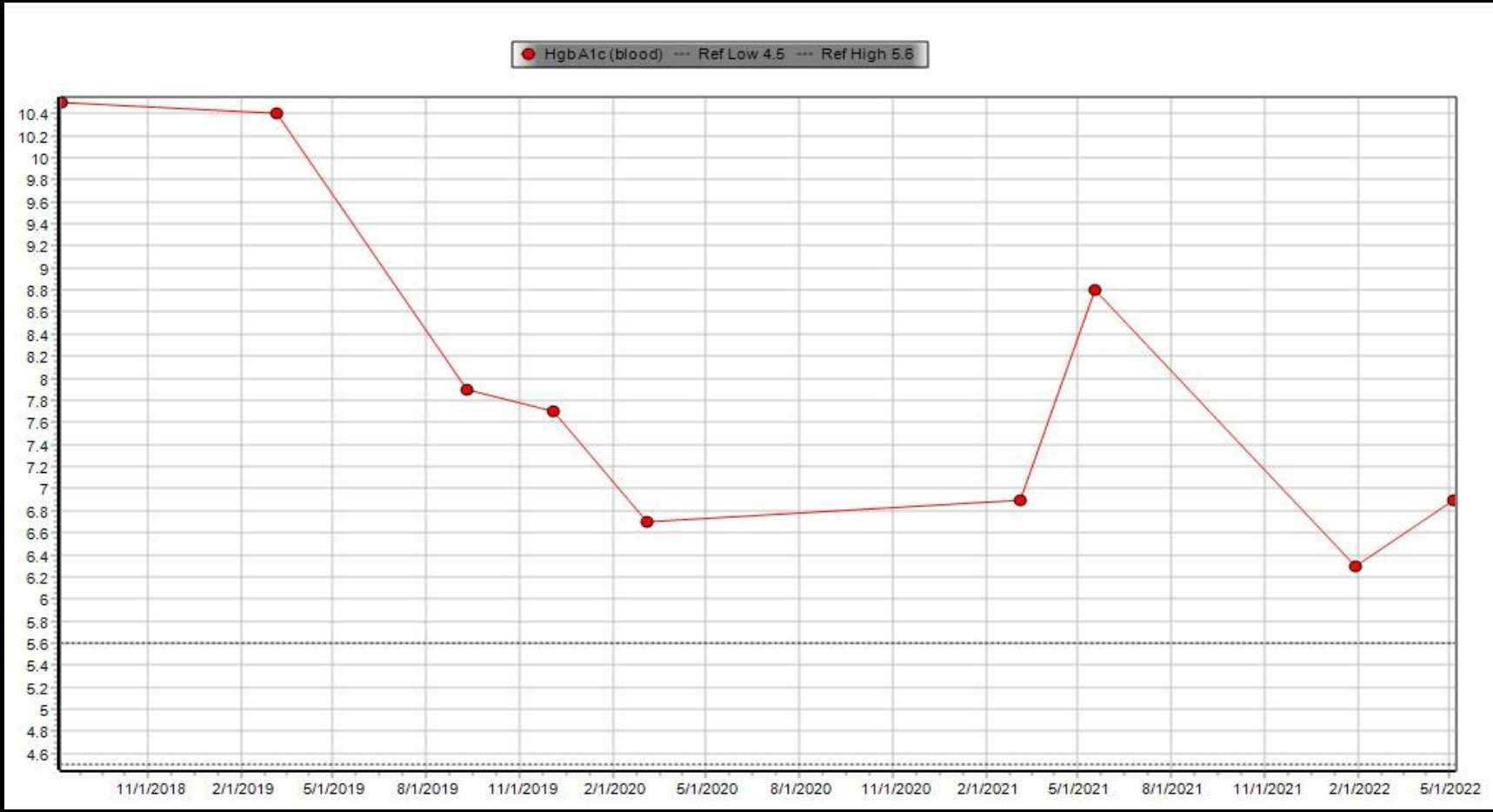
LAB DATA

CREATININE / UREA NITROGEN / GFR



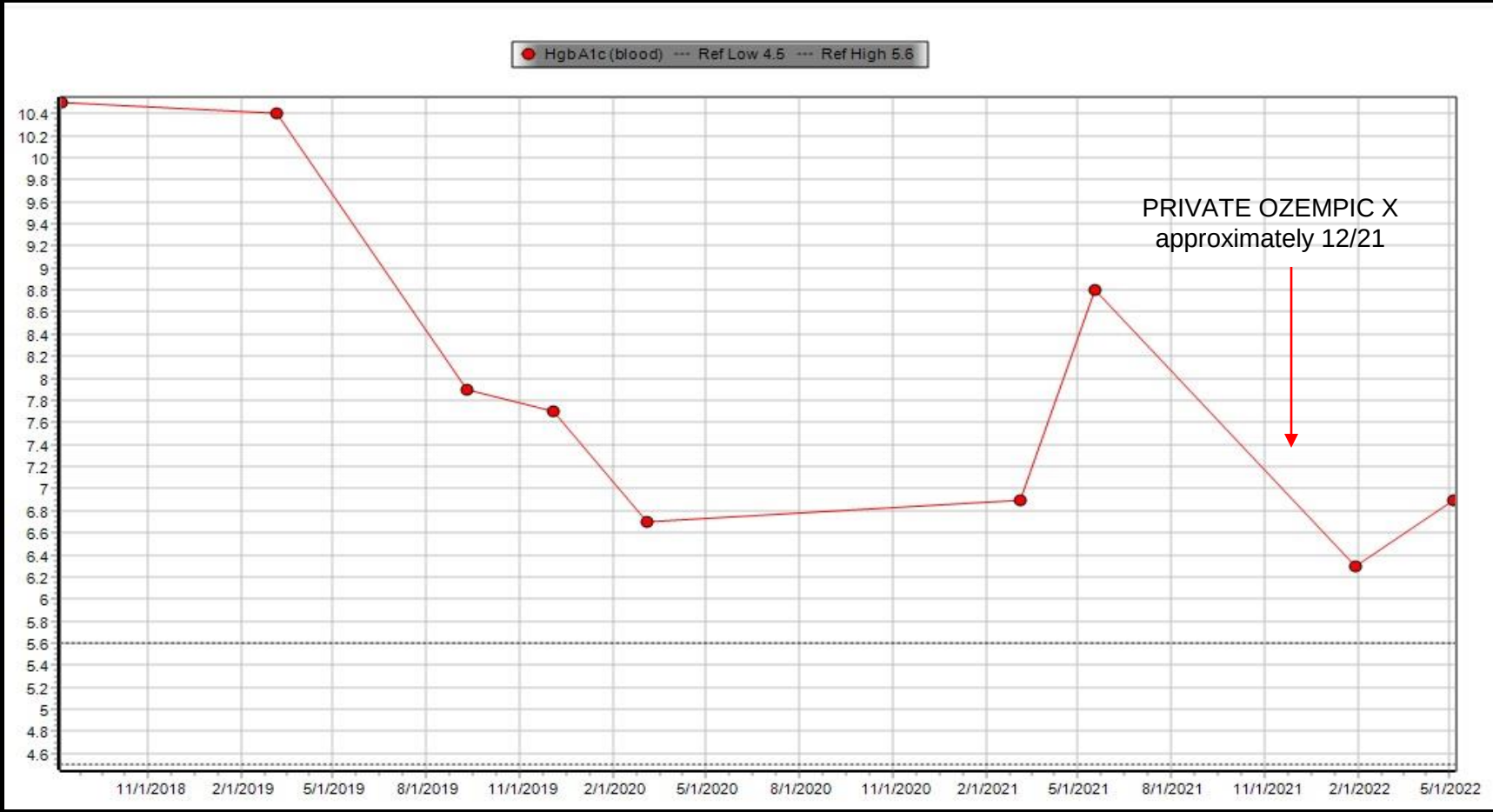


A1C REVIEW



HIS A1c HAS IMPROVED, WHY IS HE GETTING WORSE?

A1C REVIEW



IS IT POSSIBLY RELATED TO RAPID A1c REDUCTION AND/OR OZEMPIC?

FROM THE LITERATURE

- …INCREASE IN DIABETIC RETINOPATHY COMPLICATIONS WITH SEMAGLUTIDE VS PLACEBO MAY RELATED WITH THE LARGE AND RAPID DECLINE IN HbA1c DURING THE FIRST 16 WEEKS OF TREATMENT
- EARLY WORSENING OF DIABETIC RETINOPATHY IS A KNOWN PHENOMENON ASSOCIATED WITH THE RAPIDITY AND MAGNITUDE OF IMPROVEMENT IN GLYCEMIC CONTROL WITH INSULIN

- BOTTOMLINE…
  - RAPID REDUCTION IN A1c FROM ANY METHOD IS A RISK FACTOR FOR RETINOPATHY PROGRESSION
  - THIS IS NOT NEW
    - KNOWN SINCE 1998

Received: 22 August 2017 | Revised: 2 November 2017 | Accepted: 21 November 2017

DOI: 10.1111/dom.13172

WILEY

ORIGINAL ARTICLE

Semaglutide, reduction in glycated haemoglobin and the risk of diabetic retinopathy

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Funding information
Novo Nordisk A/S

Aims: To evaluate diabetic retinopathy (DR) data from across the SUSTAIN clinical trial programme.

Materials and methods: The SUSTAIN clinical trial programme evaluated the efficacy and safety of semaglutide, a glucagon-like peptide-1 analogue, for the treatment of type 2 diabetes (T2D). In SUSTAIN 6, a 2-year, pre-approval cardiovascular outcomes trial, semaglutide was associated with a significant increase in the risk of DR complications (DRC) vs placebo. DR data from across the SUSTAIN trials were evaluated, and post hoc analyses of the SUSTAIN 6 data were conducted. These included subgroup analyses to identify at-risk patients and a mediation analysis with initial change in glycated haemoglobin (HbA1c; percentage-points at week 16) as a covariate, to examine the role of the magnitude of reduction in HbA1c as an intermediate factor affecting risk of DRC.

Results: There was no imbalance in DR adverse events across the SUSTAIN 1 to 5 and Japanese trials. The majority of the effect with semaglutide vs placebo in SUSTAIN 6 may be attributed to the magnitude and rapidity of HbA1c reduction during the first 16 weeks of treatment in patients who had pre-existing DR and poor glycaemic control at baseline, and who were treated with insulin.

Conclusions: Early worsening of DR is a known phenomenon associated with the rapidity and magnitude of improvement in glycaemic control with insulin; the DRC findings in SUSTAIN 6 are consistent with this. Guidance regarding the early worsening of DR is recommended with insulin. Similar recommendations may be appropriate for semaglutide.

KEYWORDS
antidiabetic drug, diabetic retinopathy, GLP-1 analogue

OZEMPIC

- GENERIC
  - SEMAGLUTIDE
- USES
  - DM TYPE 2
  - WEIGHT MANAGEMENT
- DOSAGE
  - ORAL
  - SUBCUTANEOUS
- MECHANISM
  - Glucagon-Like Peptide-1 (GLP-1) Receptor Agonist
    - bind and activate the GLP-1 receptor
    - enhancing insulin secretion and slowing gastric emptying.
    - GLP-1 receptor agonists are generally recommended as second and third-line therapy for type 2 diabetes mellitus (T2DM).

OZEMPIC

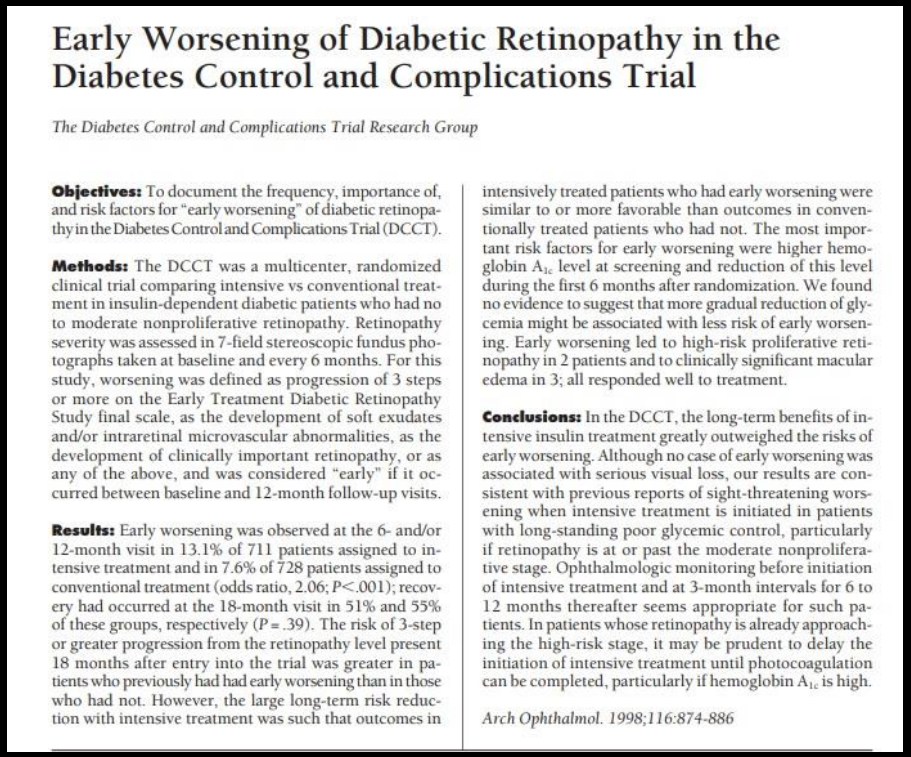
- MECHANISM
  - Glucagon-Like Peptide-1 (GLP-1) Receptor Agonist
    - bind and activate the GLP-1 receptor
    - enhancing insulin secretion and slowing gastric emptying.
    - GLP-1 receptor agonists are generally recommended as second and third-line therapy for type 2 diabetes mellitus (T2DM).
  - GLP-1 RAs exert both neuroprotective and microvascular protective effects via several pathways, leading to the prevention of vascular leakage, which is an early event in the pathogenesis of DR
- OTHER GLP-1 ANALOGS
  - LIRAGLUTIDE (SAXENDA, VICTOZA)
  - ALBIGLUTIDE
  - DULAGLUTIDE
  - EXENATIDE

OZEMPIC

- ADVERSE REACTIONS
  - OCULAR
    - An increased incidence of diabetic retinopathy complications (DRC) was noted during the SUSTAIN-6 study, a clinical trial evaluating the impact of SUBQ semaglutide on cardiovascular outcomes in patients with type 2 diabetes
      - complications included vitreous hemorrhage, onset of diabetes-related blindness, and the need for treatment with an intravitreal agent or retinal photocoagulation
    - In a separate analysis of SUSTAIN clinical trial data, the effect was reported to be mainly observed in patients with preexisting diabetic retinopathy (DR) and primarily attributable to the magnitude and rapidity of reduction in HbA1c during the first 16 weeks of the trial
    - Clinicians should note that this effect has been observed with SUBQ semaglutide, exenatide, and dulaglutide but not other glucagon-like peptide-1 receptor agonists
      - trials are underway to better understand the long-term effects of semaglutide on diabetic eye disease.
    - Oral semaglutide has not been associated with an increased incidence of DRC
  - Mechanism:
    - Unknown; in general, worsening of preexisting DR is a known consequence of rapid improvement of hyperglycemia, especially in patients with uncontrolled diabetes
    - Although unlikely, a direct toxic effect or potential angiogenic action of semaglutide has not been ruled out
    - Onset: Varied; the increased incidence of DRC during the SUSTAIN-6 study may be attributed to the reduction in HbA1c at week 16 however, clinicians should note that DR is a progressive condition and the onset of DRCs may vary.
  - Risk factors:
    - Preexisting diabetic retinopathy
    - Large (>1.5%) and rapid (≤16 weeks) decline in HbA1c

WHY DOES RETINOPATHY WORSEN?

- EXACT MECHANISM IS NOT CLEAR
- THEORIES
  - SUSTAIN-6 TRIAL POSSIBLE REASONS
    - PATIENTS WERE OLDER
    - STARTED FROM HIGHER BASELINE A1c
    - WERE DIABETICS FOR LONGER
  - 1998 DCCT POSSIBLE REASONS
    - DECREASE IN NUTRIENT SUBSTRATE
    - DECREASED ABILITY OF THE RETINAL CIRCULATION TO AUTOREGULATE
    - INCREASE IN GROWTH FACTORS
  - OTHER
    - OSMOTIC THEORY
      - RAPID CHANGES IN GLUCOSE RESULTS IN EXUDATION OF FLUID FROM BLOOD VESSELS
    - IMPACT ON
      - VEGF (SEE DCCT)
      - OXYGEN-FREE RADICALS



Early Worsening of Diabetic Retinopathy in the Diabetes Control and Complications Trial

The Diabetes Control and Complications Trial Research Group

Objectives: To document the frequency, importance of, and risk factors for "early worsening" of diabetic retinopathy in the Diabetes Control and Complications Trial (DCCT).

Methods: The DCCT was a multicenter, randomized clinical trial comparing intensive vs conventional treatment in insulin-dependent diabetic patients who had no to moderate nonproliferative retinopathy. Retinopathy severity was assessed in 7-field stereoscopic fundus photographs taken at baseline and every 6 months. For this study, worsening was defined as progression of 3 steps or more on the Early Treatment Diabetic Retinopathy Study final scale, as the development of soft exudates and/or intraretinal microvascular abnormalities, as the development of clinically important retinopathy, or as any of the above, and was considered "early" if it occurred between baseline and 12-month follow-up visits.

Results: Early worsening was observed at the 6- and/or 12-month visit in 13.1% of 711 patients assigned to intensive treatment and in 7.6% of 728 patients assigned to conventional treatment (odds ratio, 2.06; $P<.001$); recovery had occurred at the 18-month visit in 51% and 55% of these groups, respectively ($P=.39$). The risk of 3-step or greater progression from the retinopathy level present 18 months after entry into the trial was greater in patients who previously had had early worsening than in those who had not. However, the large long-term risk reduction with intensive treatment was such that outcomes in intensively treated patients who had early worsening were similar to or more favorable than outcomes in conventionally treated patients who had not. The most important risk factors for early worsening were higher hemoglobin A_{1c} level at screening and reduction of this level during the first 6 months after randomization. We found no evidence to suggest that more gradual reduction of glycemia might be associated with less risk of early worsening. Early worsening led to high-risk proliferative retinopathy in 2 patients and to clinically significant macular edema in 3; all responded well to treatment.

Conclusions: In the DCCT, the long-term benefits of intensive insulin treatment greatly outweighed the risks of early worsening. Although no case of early worsening was associated with serious visual loss, our results are consistent with previous reports of sight-threatening worsening when intensive treatment is initiated in patients with long-standing poor glycemic control, particularly if retinopathy is at or past the moderate nonproliferative stage. Ophthalmologic monitoring before initiation of intensive treatment and at 3-month intervals for 6 to 12 months thereafter seems appropriate for such patients. In patients whose retinopathy is already approaching the high-risk stage, it may be prudent to delay the initiation of intensive treatment until photocoagulation can be completed, particularly if hemoglobin A_{1c} is high.

Arch Ophthalmol. 1998;116:874-886

AAO RECOMMENDATIONS

- "The presence of semaglutide in a medical profile should alert the ophthalmologist to a potential risk"
- "The whole point with these drugs is that you're trying to reduce mortality from cardiovascular risks"
- "Whether patients progress in diabetic retinopathy or not, I would rather we potentially ameliorate their macrovascular risk of cardiovascular and cerebrovascular diseases, instead of worrying about microvascular, eye-related risks that we can manage appropriately with current modalities."
- FOLLOW-UP
  - MILD
    - 6 MOS
  - MODERATE
    - EVERY 3 MOS
  - SEVERE
    - 4-6 WEEKS
  - THINGS STABILIZE AFTER 12-18 MOS
- FOCUS TRIAL
  - ENROLLING 1500 PATIENTS
  - RANDOMIZED TO PLACEBO OR SEMAGLUTIDE + CURRENT DM MEDS
  - OUTCOME MEASURES
    - PROGRESISON OF DM RETINOPATHY
    - INCIDED OF TREATMENT WITH ANTI-VEGF, LASER OR VITRECTOMY.
    - CONCLUDES 2027

COMPREHENSIVE
CLINICAL UPDATE

Update on Semaglutide Risks

The diabetes drug semaglutide is back in the spotlight, thanks to its FDA approval this summer as a weight loss aid. As many ophthalmologists know, the drug has been associated with early worsening of diabetic retinopathy (DR). Given this expanded indication for treatment of obesity, do the benefits of semaglutide still outweigh the risks—and what should ophthalmologists expect?

Risk of DR Progession

Semaglutide is a glucagon-like peptide-1 (GLP-1) agonist, a metabolic hormone released by intestinal cells. It slows gastric emptying and reduces glucose absorption.[1] "Semaglutide produces an impressive drop in blood sugar and hemoglobin A1c, so in patients for whom other medications cannot achieve control, it's an important drug, because controlling blood sugar helps patients in the long run," said JoAnn A. Giaconi, MD, at the Greater Los Angeles Veterans Administration and the Stein Eye Institute at the University of California, Los Angeles (UCLA).

A treatment paradox. However, the drug's effectiveness presents clinicians with a challenge. As Dr. Giaconi said, "The VA in Los Angeles recently made a GLP-1 formulary switch to semaglutide, which is great for glycemic control, but it worsens existing diabetic retinopathy. I have clinicians asking me whether to switch patients back to their old diabetes drugs."

This paradoxical worsening of DR after a sudden drop in blood glucose is a well-documented phenomenon. For instance, in a study of early worsening of DR after intensive insulin treatment, pancreas transplant, or bariatric surgery,[2] 10% to 20% of patients had worsening of DR within three to six months—with twice that many for patients who already had advanced DR at baseline.

And well-known trials such as the DCCT (Diabetes Control and Complications Trial) found an association between better blood glucose control and risk of early worsening of DR.

"It's not uncommon to see this progression of DR if we improve glucose control," said Rishi P. Singh, MD, at the Cole Eye Institute in Cleveland. "This happened back in the era of the DCCT, when patients had an intermittent worsening of retinopathy for the first year or two, but then had far better control of the retinopathy long-term."

A question of heart versus eye. The global SUSTAIN trials (Semaglutide Unabated Sustainability in Treatment of Type 2 Diabetes) demonstrated the drug's gains in both A1c and weight loss.[3] In SUSTAIN 6, a preapproval cardiovascular outcomes study, semaglutide showed an impressive 26% drop in cardiovascular events compared to placebo at two years.[3] The study's secondary endpoint, microvascular complications, turned up a lower risk of renal complications—but higher risk of retinal complications, such as early worsening of DR.

"They found DR progression in only the SUSTAIN 6 data," said Ashish Sharma, MD, at Lotus Eye Hospital and Institute in Coimbatore, India. "SUSTAIN 1-5 excluded patients with known proliferative diabetic retinopathy, and the upper limit of A1c was 10 or 10.5, while SUSTAIN 6 had no exclusion criteria related to diabetic retinopathy and no upper limit of A1c."

"The whole point with these drugs is that you're trying to reduce mortal-

KEY QUESTION. *Do the benefits of semaglutide still outweigh the risk of worsening of DR?*

BY REBECCA TAYLOR, CONTRIBUTING WRITER, INTERVIEWING JOANN A. GIACONI, MD, ASHISH SHARMA, MD, AND RISHI P. SINGH, MD.

NOVEMBER 2021
https://www.aao.org/eyenet/article/update-on-semaglutide-risks

SO WHAT SHOULD WE DO?

- FOR OZEMPIC PATIENTS…
  - PER ORLANDO VAMC RETINA
    - If no diabetic retinopathy
      - 6 months.
    - Mild NPDR without DME
      - then monitor every 3-4 months initially
      - if stable for two visits can extend to 6 months.
    - Moderate and severe NPDR without DME
      - every 3 months.
    - Severe NPDR with concern for possible PDR
      - refer to retina.
    - PDR
      - referred to retina.
    - Any NPDR with clinically significant DME
      - start ketorolac QID and refer to retina.

- I THINK SHOULD DOCUMENT
  - +DM x (START YEAR OF ANY TREATMENT)
  - +/- INSULIN
  - +/- OZEMPIC (START DATE)