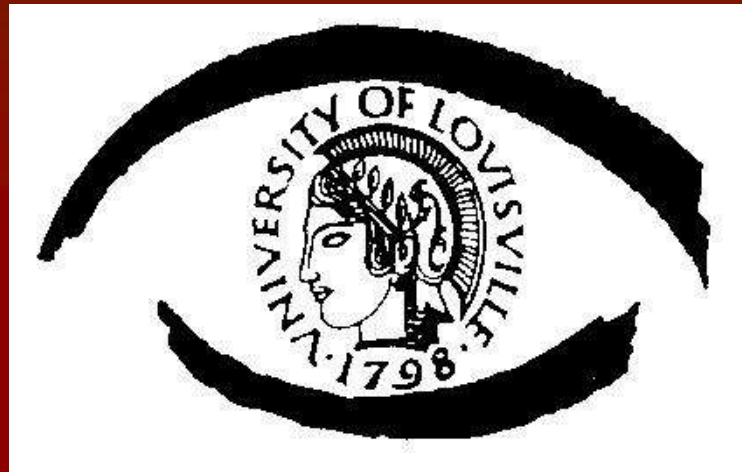


# Retina Conference



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**Department of Ophthalmology and Visual Sciences**

**12/09/10**

# Presentation

CC: “decrease in peripheral vision”

HPI: 30 yo WF c/o gradual worsening of her vision, particularly her peripheral vision. She says when she looks at someone’s face she cannot see the whole face. She is also having trouble with night vision

POH: - Plaquenil (Hydroxychloroquine)  
maculopathy (2000)

- Cataract extraction OU (2005)

- Refractive error

PMH: Systemic Lupus Erythematosus (SLE)

(treated with Plaquenil for extended period of time and taken off in 2000, exact dosage and duration unknown) with nephritis, HTN, Thrombophlebitis, Thyroid disease

Meds: Prednisone, Cellcept (Mycophenolate), Levothyroxin, Warfarin, Enalapril, Omeprazole

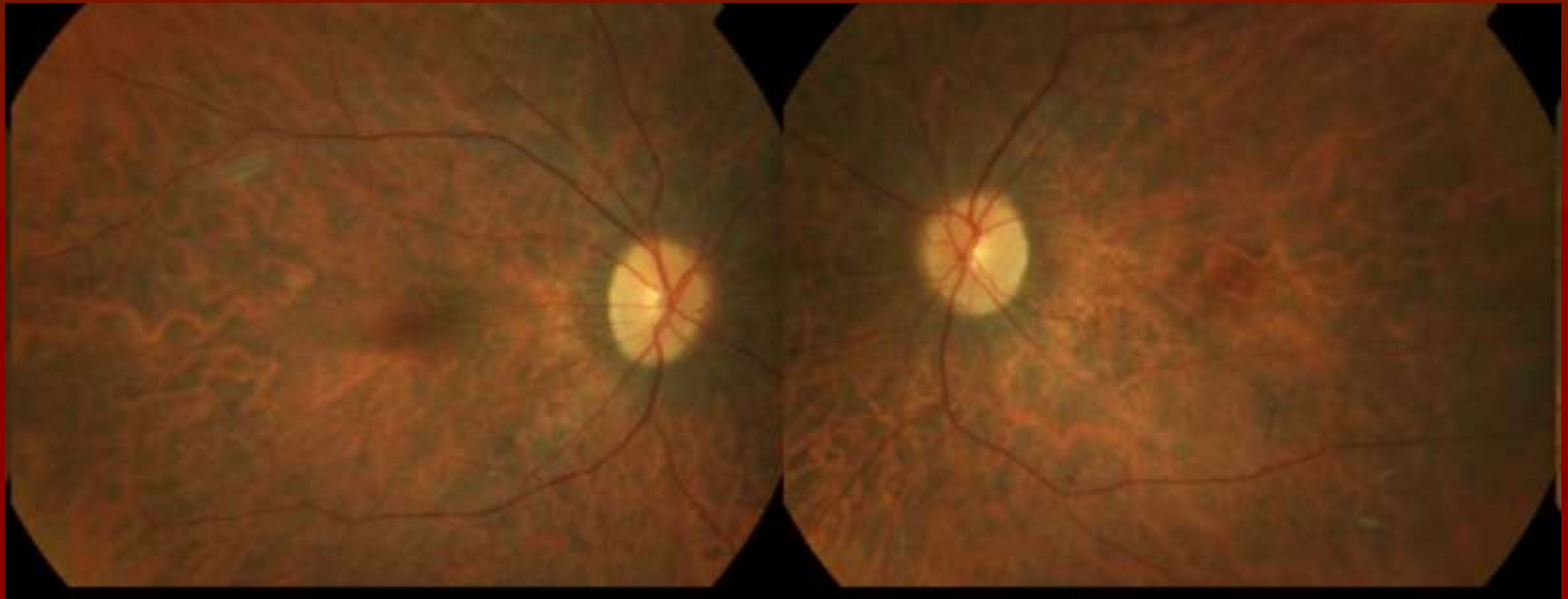
Allergy: Phenergan

Family History: non contributory

# Physical Examination

	OD	OS
<u>BCVA:</u>	20/60	20/70
<u>IOP:</u>	14	15
<u>Pupils:</u>	4 → 2mm OU no RAPD	
<u>EOM:</u>	full OU	
<u>Anterior segment:</u>	PCIOL OU	

# Color Fundus Photo

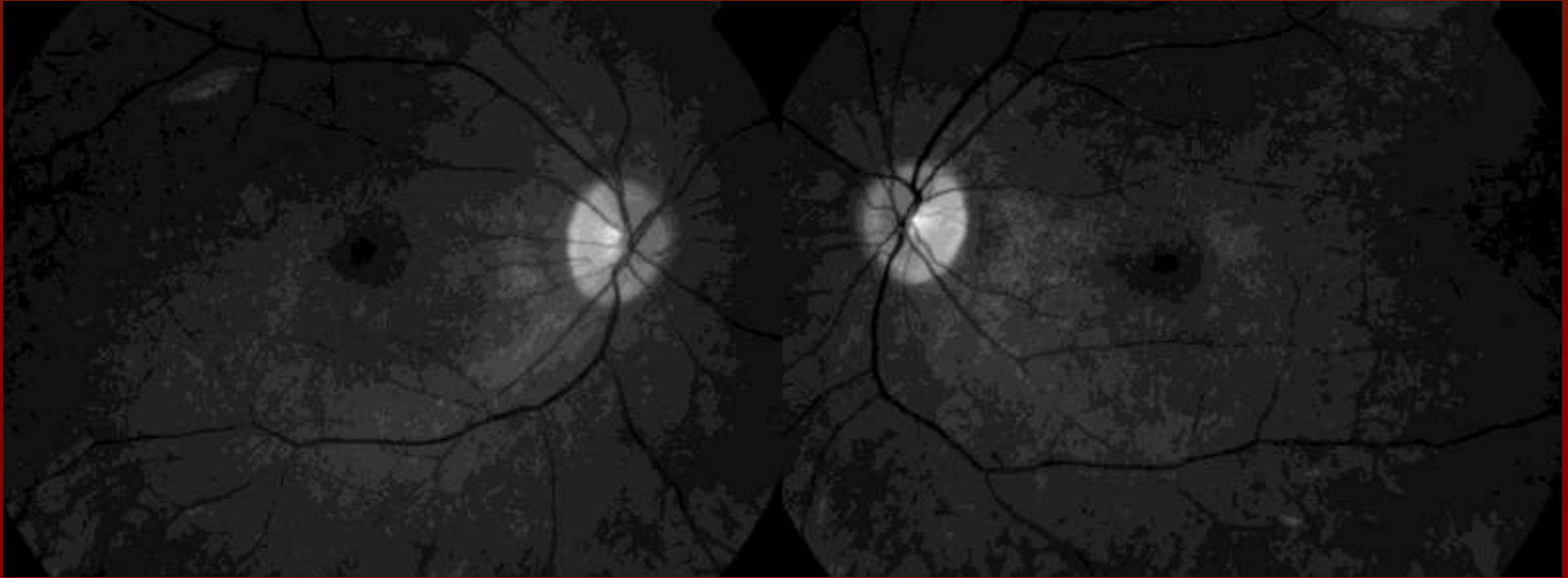


OD

OS

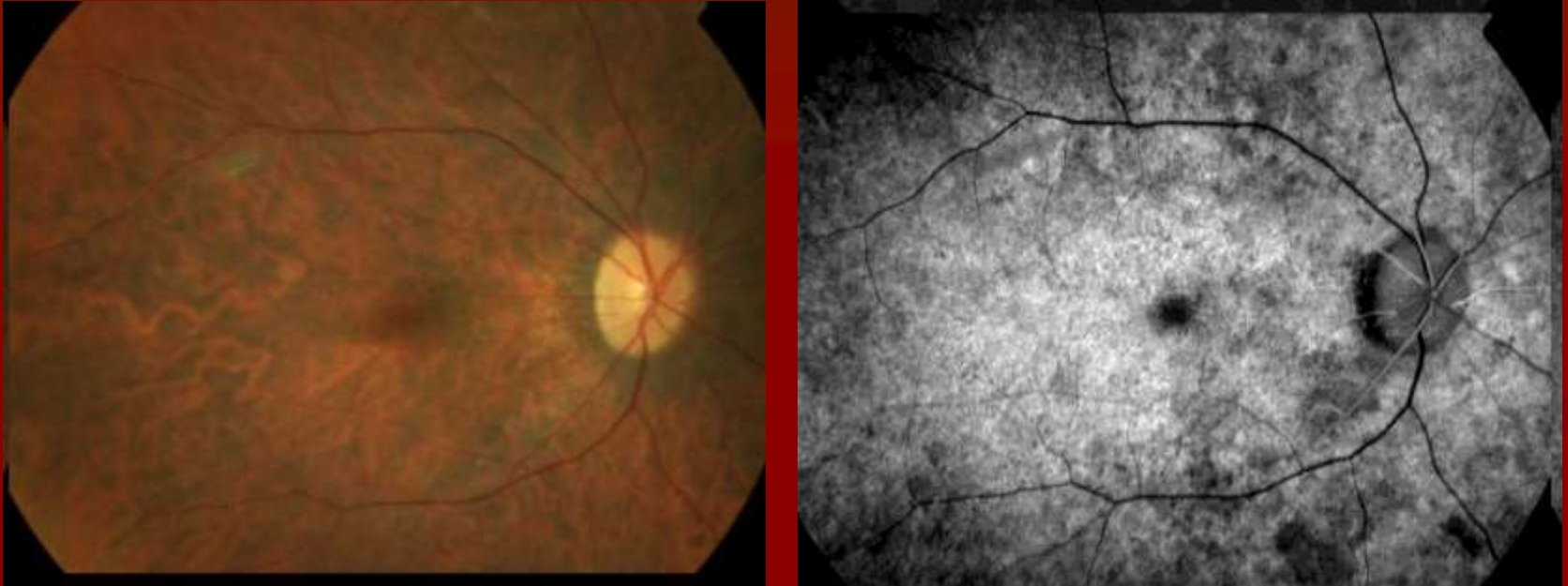
Color fundus photograph : optic disk WNL, severe vascular attenuation, and widespread irregular hypopigmentation

# Red free photos



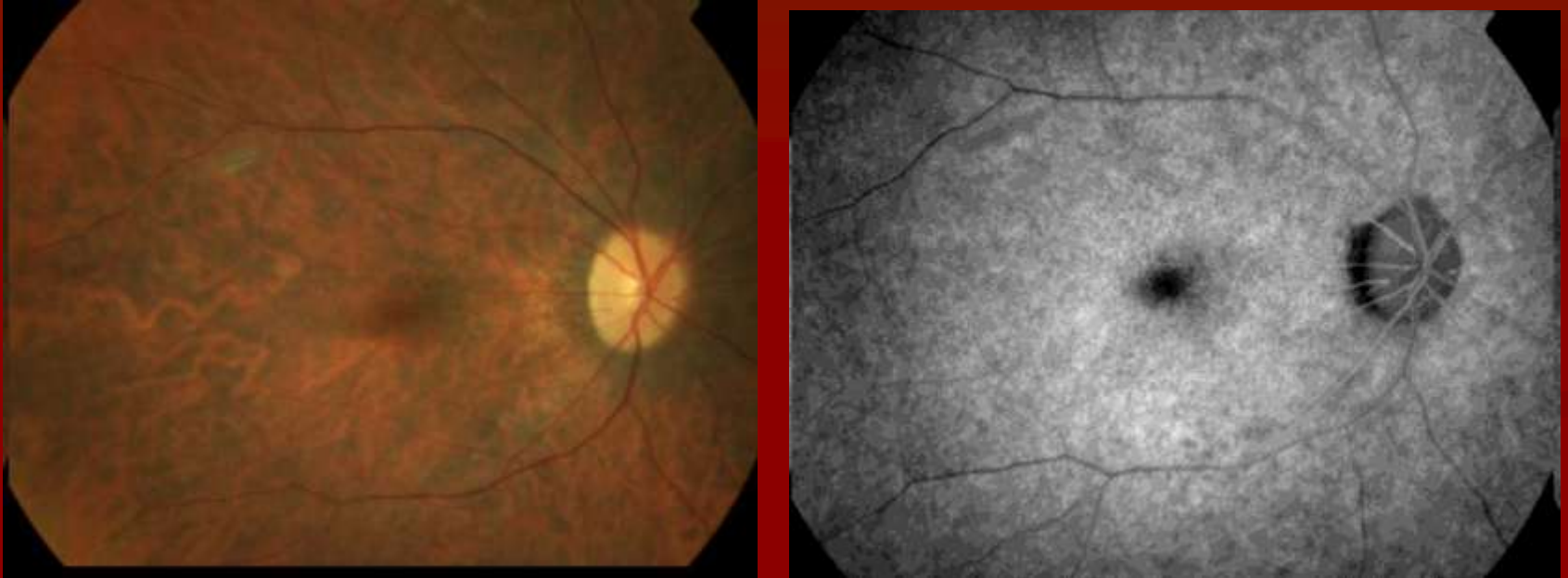
Red free photo showing the hypopigmentation surrounding the fovea as well as vascular attenuation OU

# Fluorescein Angiography



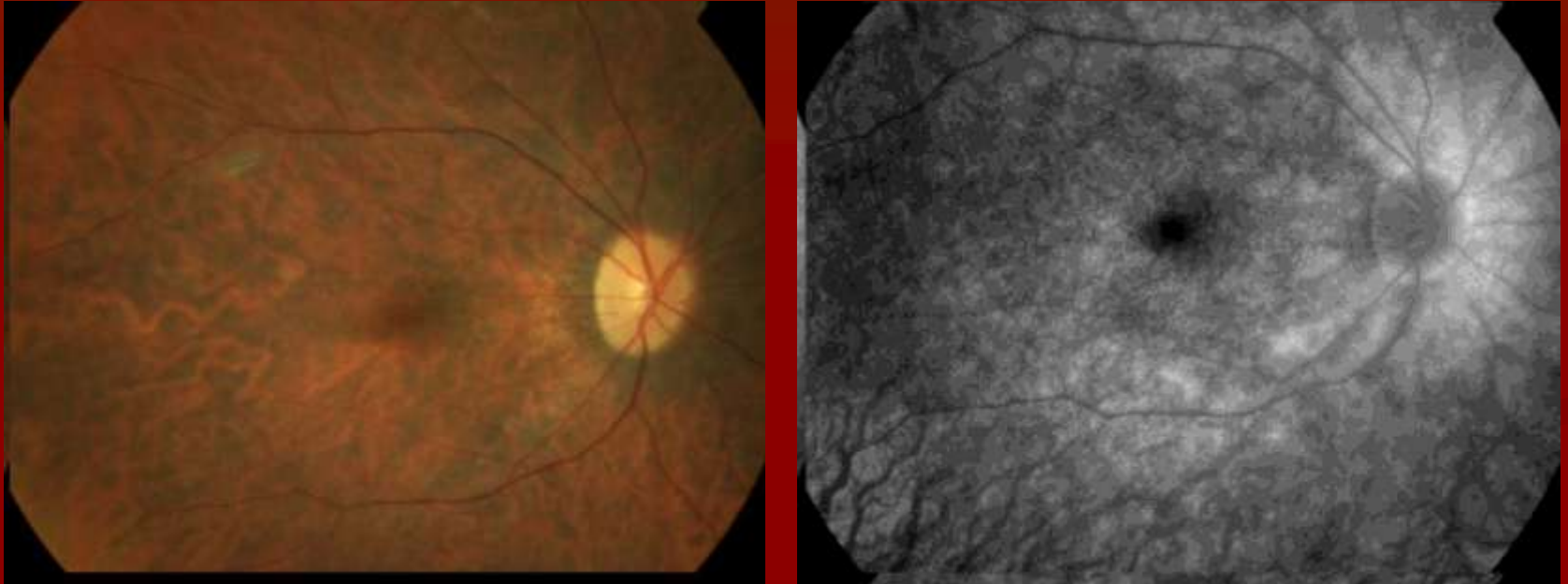
Arterial phase – OD showing vascular attenuation, diffuse hyperfluorescence in the macula with hypofluorescence of the fovea, and patchy choroidal filling

# Fluorescein Angiography



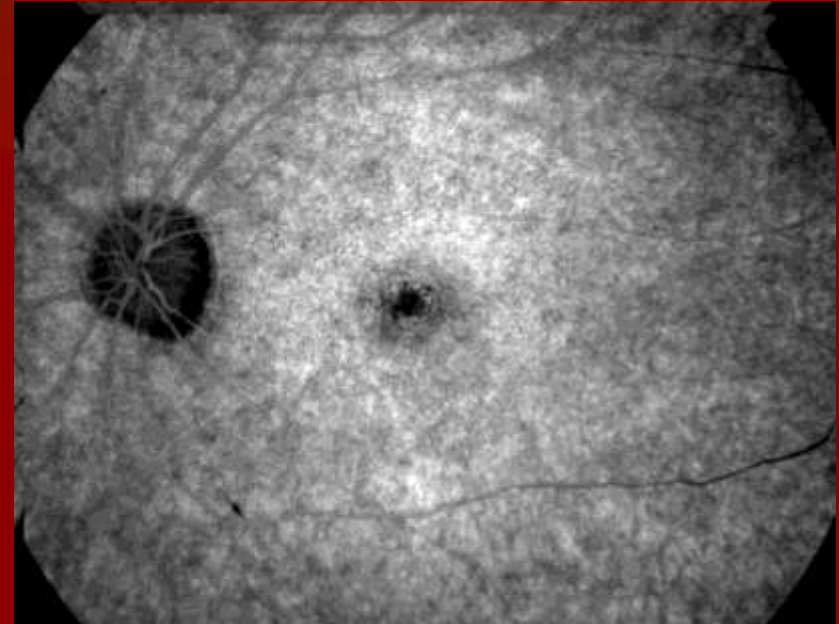
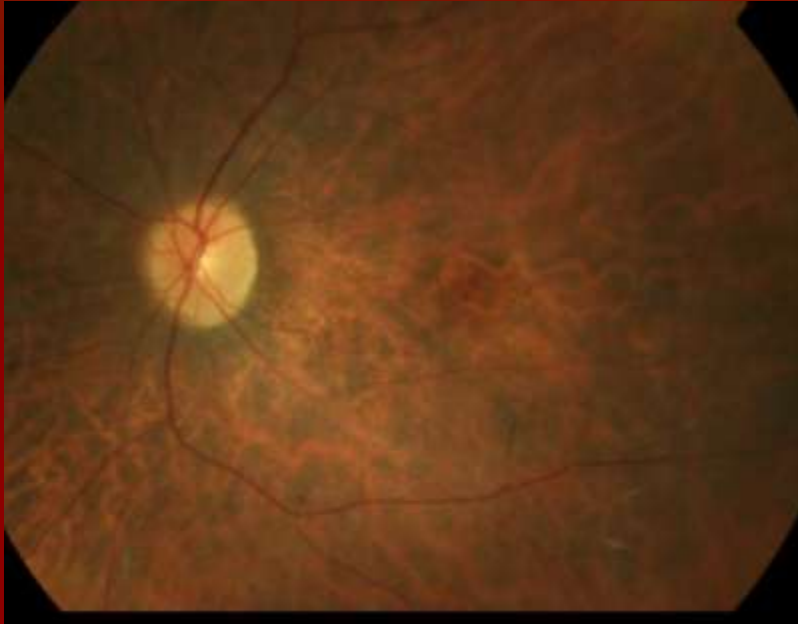
Mid AV phase – OD showing vascular attenuation, persistent hyperfluorescence in the macula, and more homogenous choroidal filling

# Fluorescein Angiography



Recirculation phase – OD showing vascular attenuation and fading hyperfluorescence in the macula

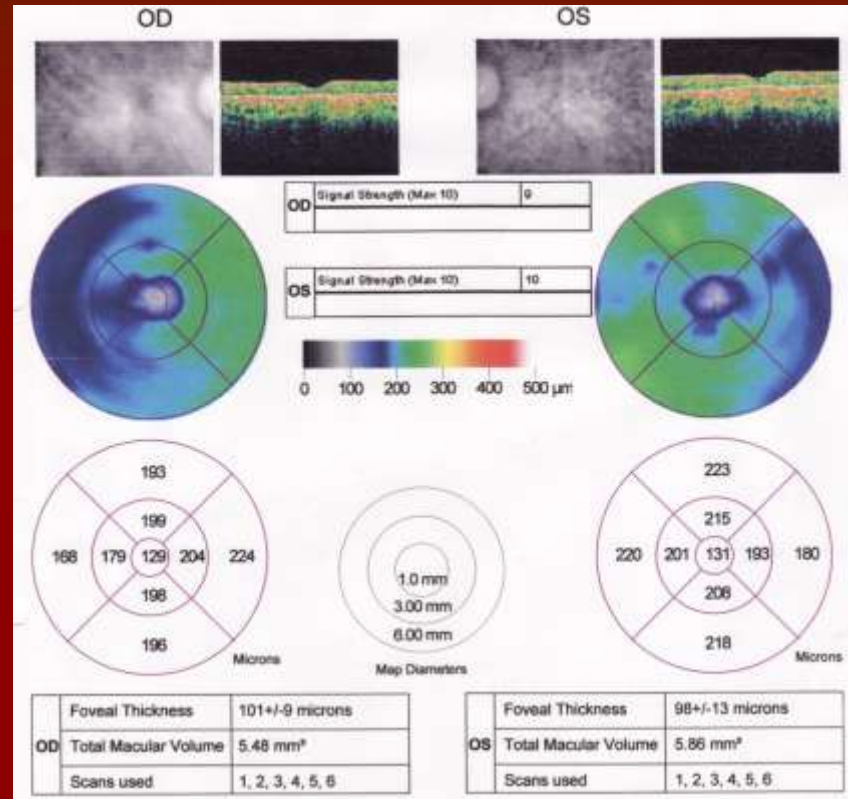
# Fluorescein Angiography



Symmetric changes were found in the left eye.

AV phase OS showing vascular attenuation, hyperfluorescence in the macula surrounding a hypofluorescent fovea.

# OCT



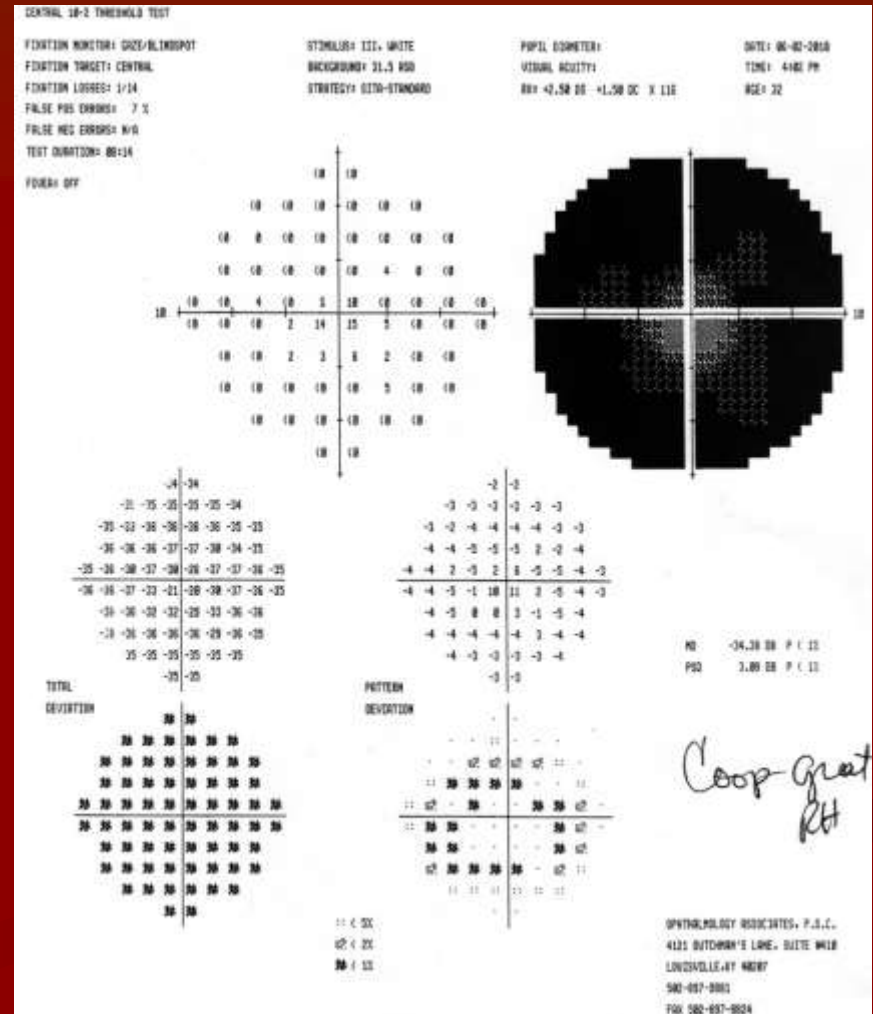
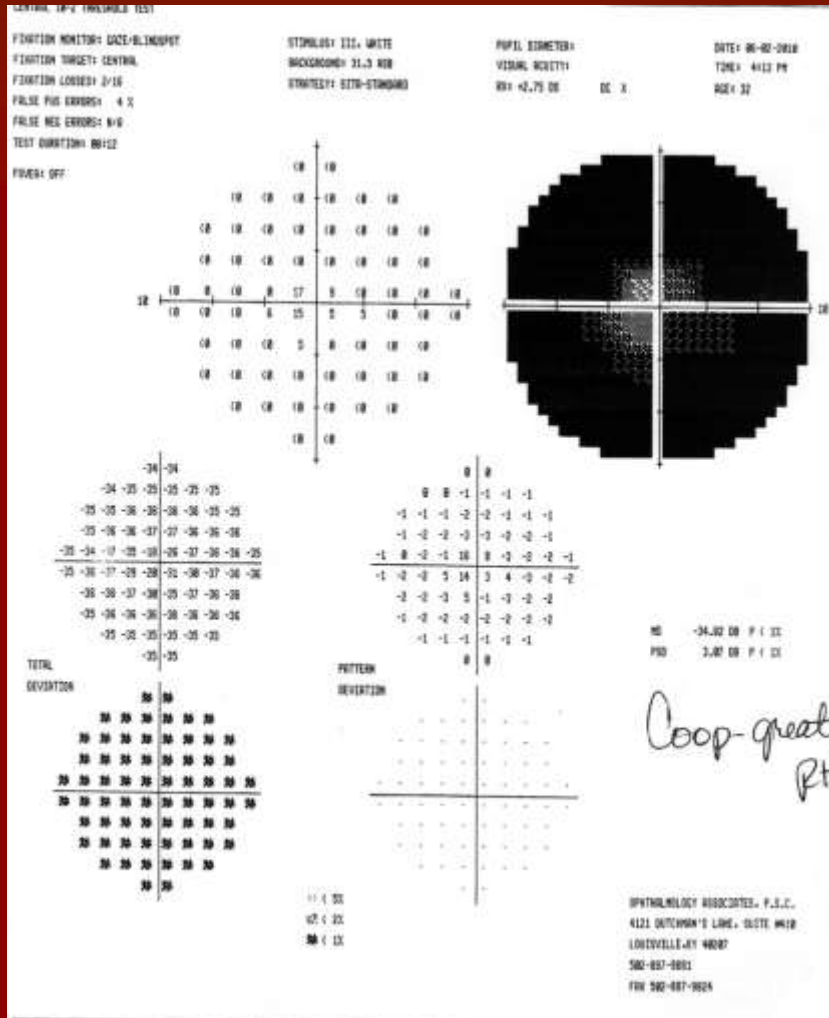
Stratus OCT retinal thickness analysis report showing decreased central macular thickness OU

# Visual Fields

- 10-2 Humphrey visual field: severe constriction of visual field OU with preserved central island of vision

OS

OD



# Electroretinogram ERG

- Light adapted single flash: flat
- Dark adapted single flash: flat
- Light adapted white flicker: small response

# Assessment

30 yo WF with SLE and h/o hydroxychloroquine maculopathy presenting bilateral severe vascular attenuation and pigmentary changes in her retina with constriction of visual fields

## Differential Diagnosis

- **Advanced hydroxychloroquine toxicity**
- Lupus retinopathy
- Retinitis pigmentosa

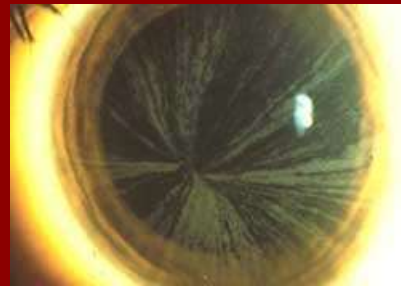
# Chloroquine/Hydroxychloroquine toxicity

## ■ Chloroquine/Hydroxychloroquine

- used for treatment of amebiasis, malaria prophylaxis, rheumatoid arthritis, SLE, and other connective tissue disease.
- interfere with phospholipids breakdown, probably by damaging lysosomes → affect metabolism of retinal cells with damage to photoreceptors, ganglion cells and RPE.
- have a selective affinity to melanin in RPE → may serve to concentrate the drugs or prolong their adverse effect
- very slow excretion rate. Small amounts of chloroquine are detectable in blood and urine as long as 5 years after the drug is discontinued

# Ocular signs

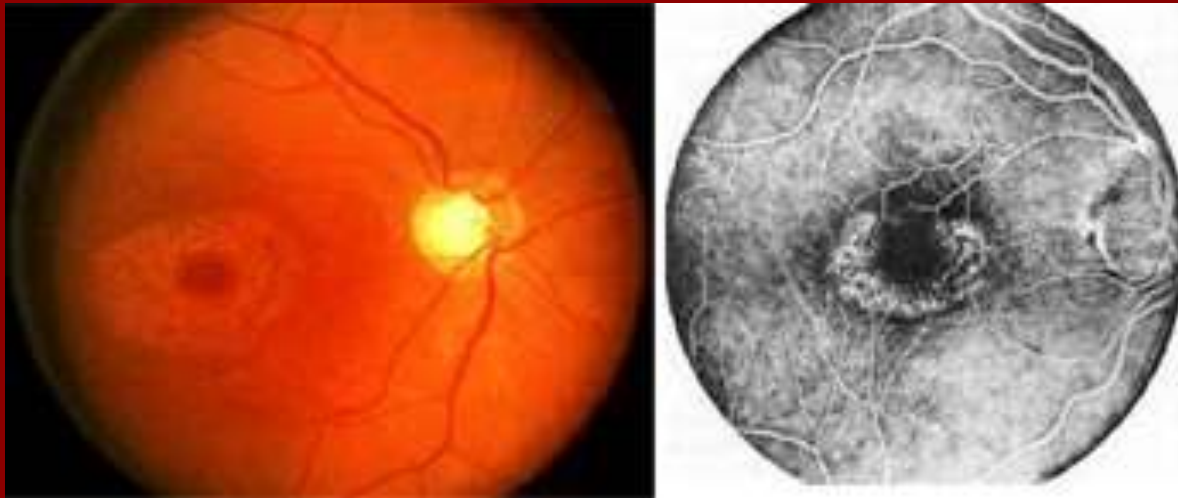
- Corneal whorl deposition (verticillata), usually reversible with discontinuation of the drug



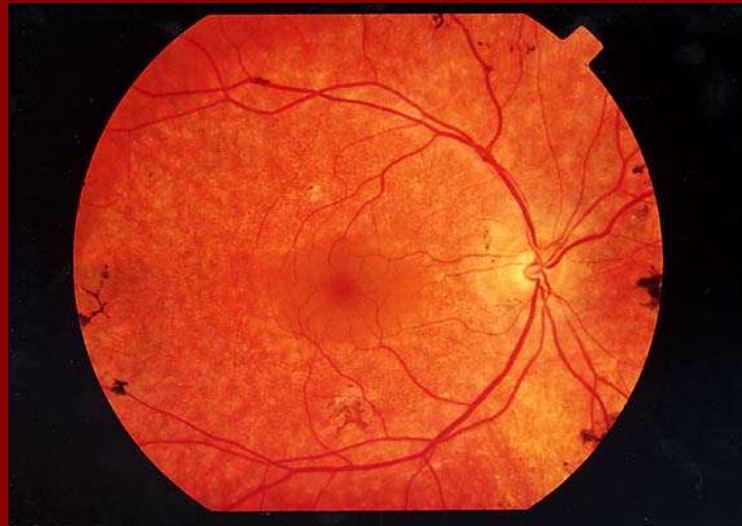
■ Maculopathy:

- loss of foveal reflex, pigment stippling
- pericentral ring of depigmentation:

Bull's eye maculopathy



- widespread pigment epithelial and retinal atrophy, vascular narrowing, optic disc pallor, bony spicules → mimic retinitis pigmentosa



# Chloroquine / Hydroxychloroquine Maculopathy

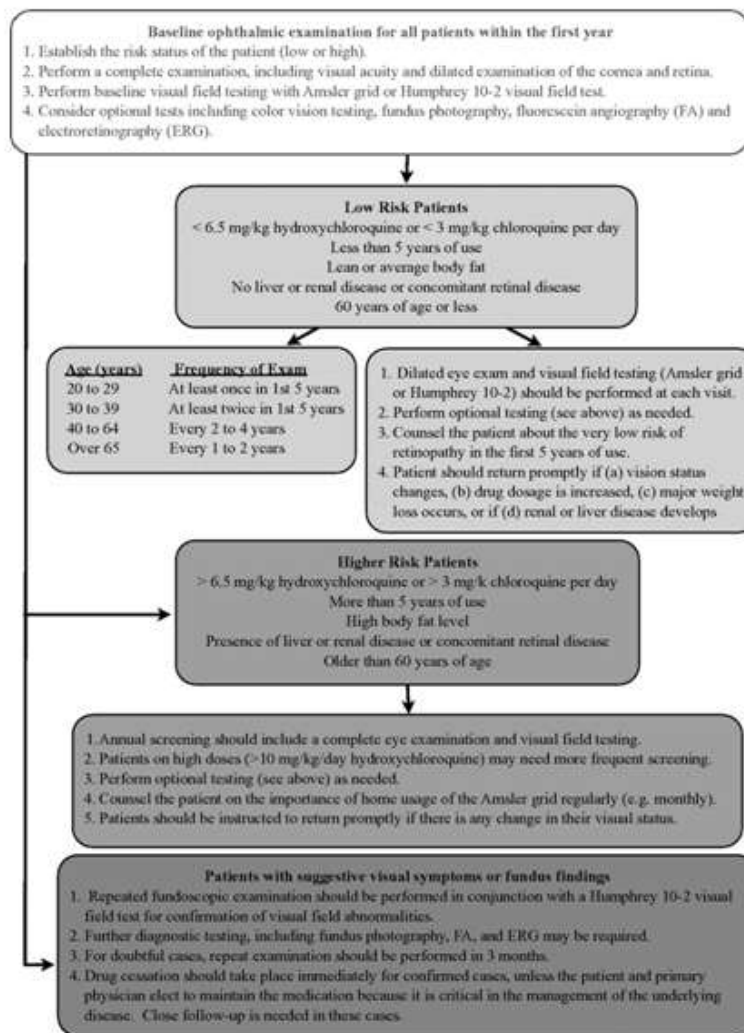
- usually irreversible
- rarely subtle changes can revert to normal after cessation of therapy
- it may progress despite discontinuation of the drug. Case report of deterioration after more than 18 y after cessation of the drug.<sup>1</sup>

# Risk Factors

- Low incidence of retinopathy (0.5%) when hydroxychloroquine is used at recommended daily dose (<6.5 mg/kg/d)

	Higher Risk
<b>Dosage</b>	> 6.5mg/kg hydroxychloroquine > 3 mg/kg chloroquine
<b>Duration of use</b>	> 5 years
<b>Habitus</b>	high fat level (unless dosage is appropriately low)
<b>Renal/liver disease</b>	present
<b>Concomitant retinal disease</b>	present
<b>Age</b>	> 60 years

# Overview of the American Academy of Ophthalmology screening recommendations for chloroquine and hydroxychloroquine retinopathy.



Payne J F et al. Br J Ophthalmol  
doi:10.1136/bjo.2009.172148

# Limitations

- Screening is aimed primarily at the early detection and minimization of toxicity, rather than at prevention
- Arthritis Care Res (Hoboken). 2010 Jun;62(6):775-84.

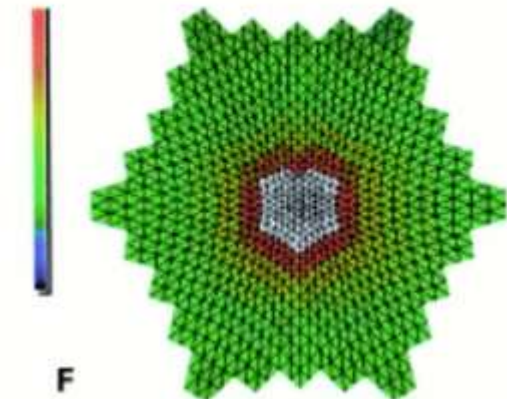
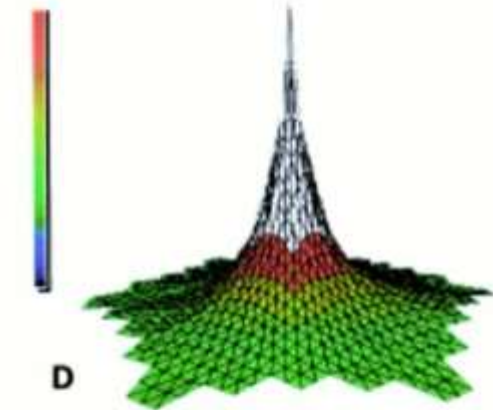
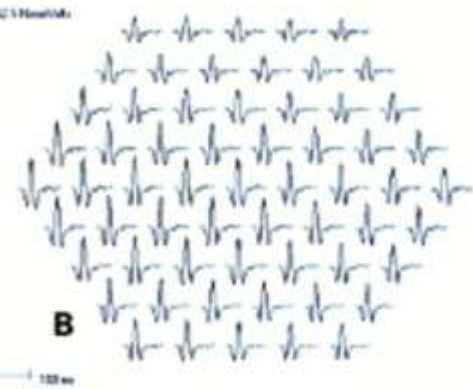
**Rates and predictors of hydroxychloroquine retinal toxicity in patients with rheumatoid arthritis and systemic lupus erythematosus. Wolfe F, Marmor MF.**

- The risk of toxicity was low in the initial 7 years of exposure, and was approximately 5 times greater after 7 years of usage (or 1,000 gm total exposure).
- Toxicity was unrelated to age, weight, or daily dosage.

# New Screening Tools

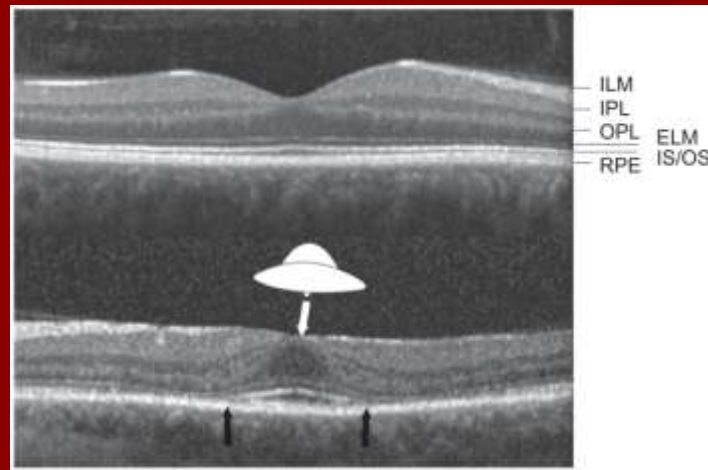
## Multifocal ERG:

- may detect decreased retinal function in hydroxychloroquine patients with normal clinical examinations
- more reliable detection of retinal damage
- can document reversal of toxicity<sup>2</sup>



- Spectral domain OCT:

Can identify loss of the perifoveal photoreceptor inner segment/outer segment junction with intact outer retina under the fovea (“flying saucer”) in early toxicity and even before ophthalmoscopic fundus changes<sup>3</sup>



Thank You!

# References

1. Normalization of generalized retinal function and progression of maculopathy after cessation of therapy in a case of severe hydroxychloroquine retinopathy with 19 years follow-up. Salu P, Uvijls A, van den Brande P, Leroy BP. *Doc Ophthalmol*. 2010 Jun;120(3):251-64. Epub 2010 Apr 16. PubMed PMID: 20397038.
2. A novel method for screening the multifocal electroretinogram in patients using hydroxychloroquine. Chang WH, Katz BJ, Warner JE, Vitale AT, Creel D, Digre KB. *Retina*. 2008 Nov-Dec;28(10):1478-86.
3. Spectral domain optical coherence tomography as an effective screening test for hydroxychloroquine retinopathy (the "flying saucer" sign). Chen E, Brown DM, Benz MS, Fish RH, Wong TP, Kim RY, Major JC. *Clin Ophthalmol*. 2010 Oct 21;4:1151-8.