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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*

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R3 Guilherme Rozza
Oftalmologia (Hospital das Clinicas de Ribeirao Preto)

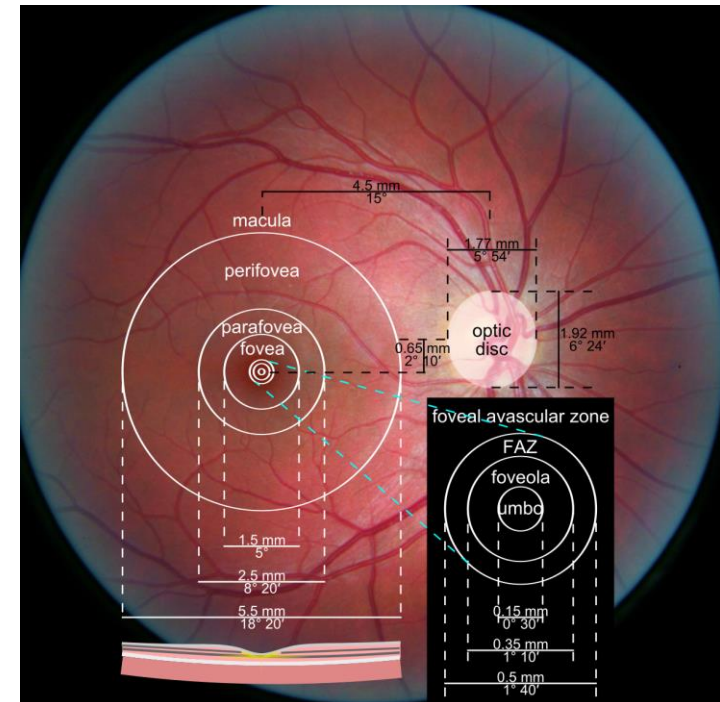
Hidroxicloroquina (HCQ) e Cloroquina(CQ)

- Tóxico para o EPR (mecanismo não elucidado)
- Também afeta camadas externas da retina
- Culmina em Atrofia das Camadas mais Externas da retina e EPR (Afinamento Retiniano)
- Parafoveal x Extramacular (Asiáticos)
- Leva a PERDA VISUAL IRREVERSIVEL

OBJETIVO



Detectar, precocemente, achados que precedam a perda visual



Hidroxicloroquina (HCQ) e Cloroquina(CQ)

- Usos....
- Dose x Tempo de exposição
- Estabilização da droga no sangue após semanas de administração
- Pool de droga após cessar o uso.
 - Pode lesar, ainda que levemente, a retina.
 - Mas o decréscimo visual após cessar uso não foi relatado no estudo
- Lesões estruturais não necessariamente implicam em redução da AV

Achados

- Campo visual (10:2 vs 24:2)
 - ERG
 - AF (precoce vs tardio)
 - OCT
-
- Fundo de Olho
 - Biomicroscopia (Córnea: Verticilata)

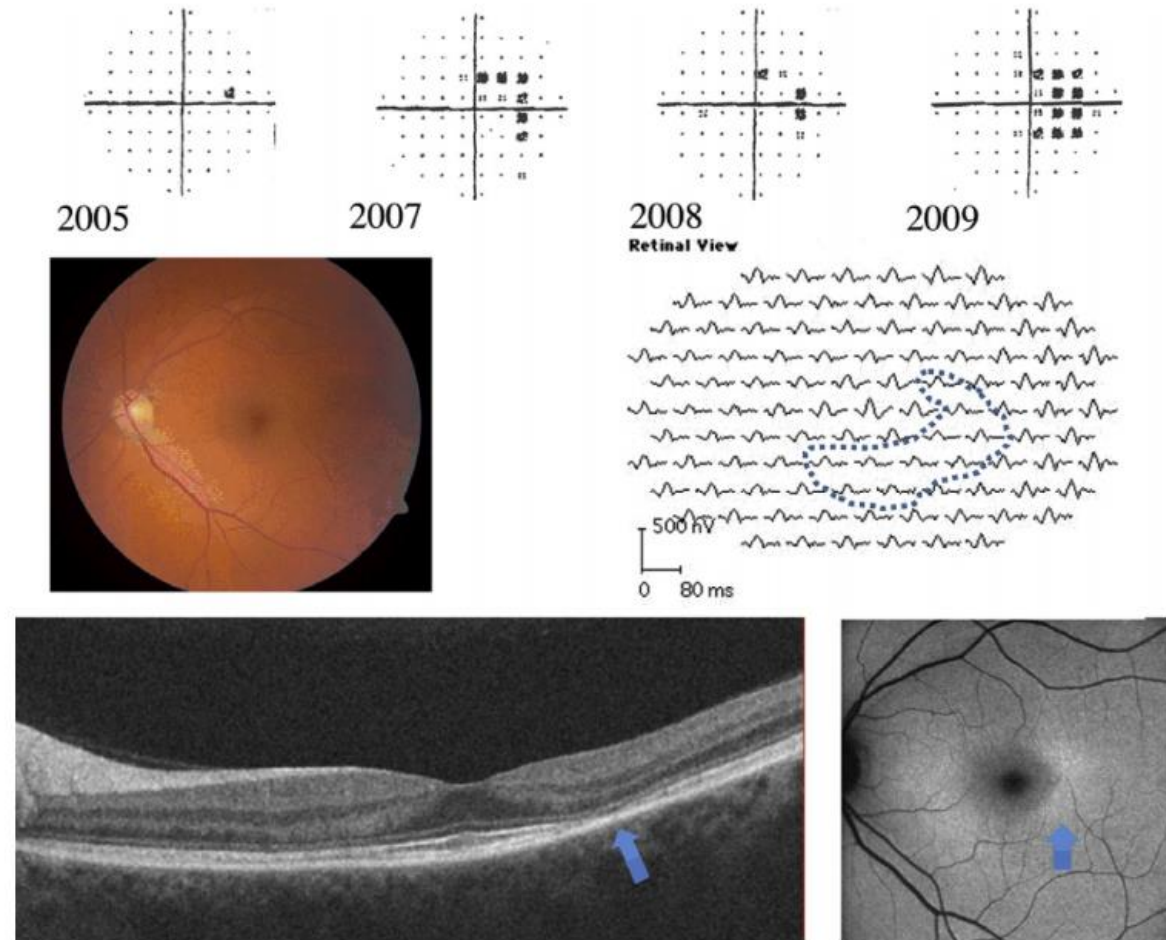


Figure 1. Findings in the left eye of a 48-year-old woman of European descent using hydroxychloroquine (HCQ) at 8 mg/kg for 25 years, showing early parafoveal maculopathy from HCQ. **Top:** 10-2 visual fields over a 4-year period showing changes that were deemed inconsequential until 2009, when she was finally referred for more comprehensive testing. These could have triggered specialty examination sooner. **Middle:** The fundus appears normal, but the multifocal electroretinogram (mfERG) shows weak responses in the parafoveal region (especially in the third ring about center: dotted region). **Bottom:** Spectral-domain optical coherence tomography (SD OCT) showing temporal parafoveal thinning and loss of outer segment structural lines (arrow), and fundus autofluorescence (FAF) showing increased fluorescence paracentrally (arrow). Modified with permission from Marmor MF, Kellner U, Lai TY, et al. Revised recommendations on screening for chloroquine and hydroxychloroquine retinopathy. *Ophthalmology* 2011;118:415–22.¹

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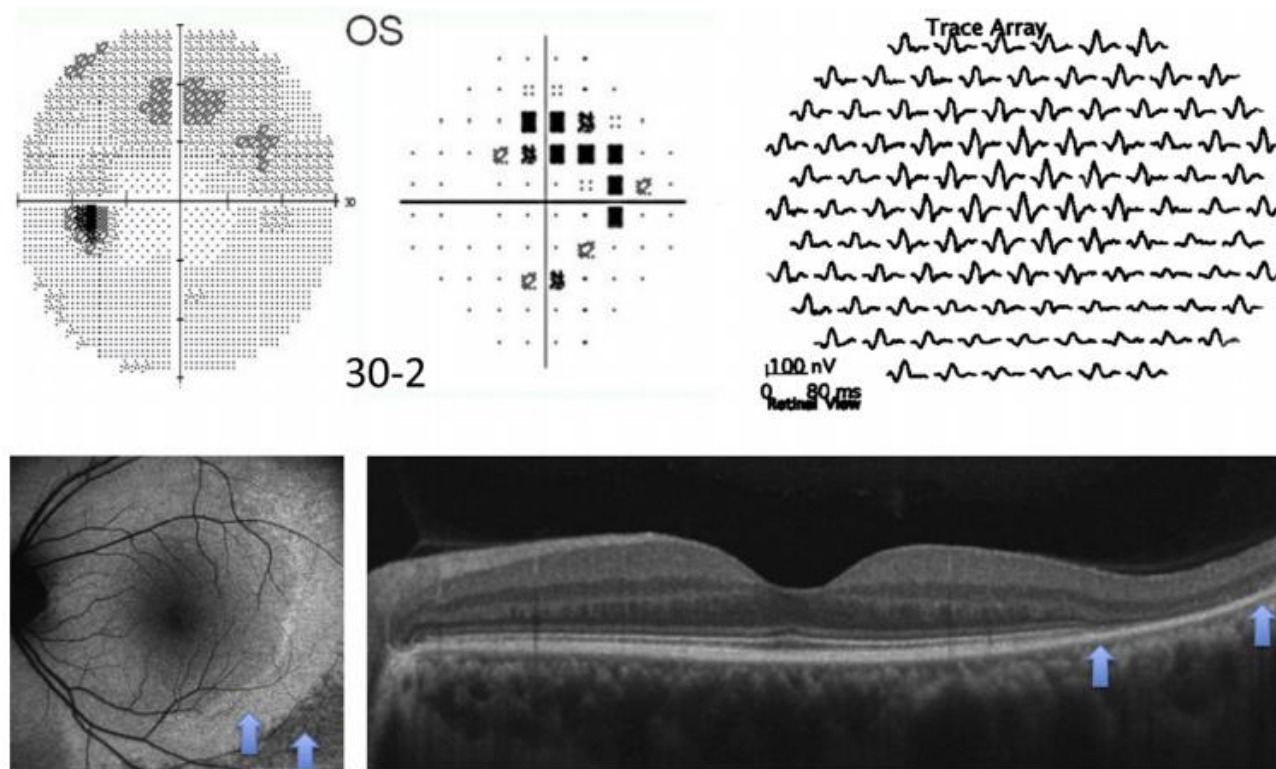


Figure 2. Findings in the left eye of a 42-year-old Chinese woman showing extramacular retinopathy. She had used 8 mg/kg hydroxychloroquine (HCQ) for 8 years and 4 mg/kg for another 2 years. **Top:** 30-2 fields in grey scale and pattern deviation, showing partial ring scotoma outside the parafoveal 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.

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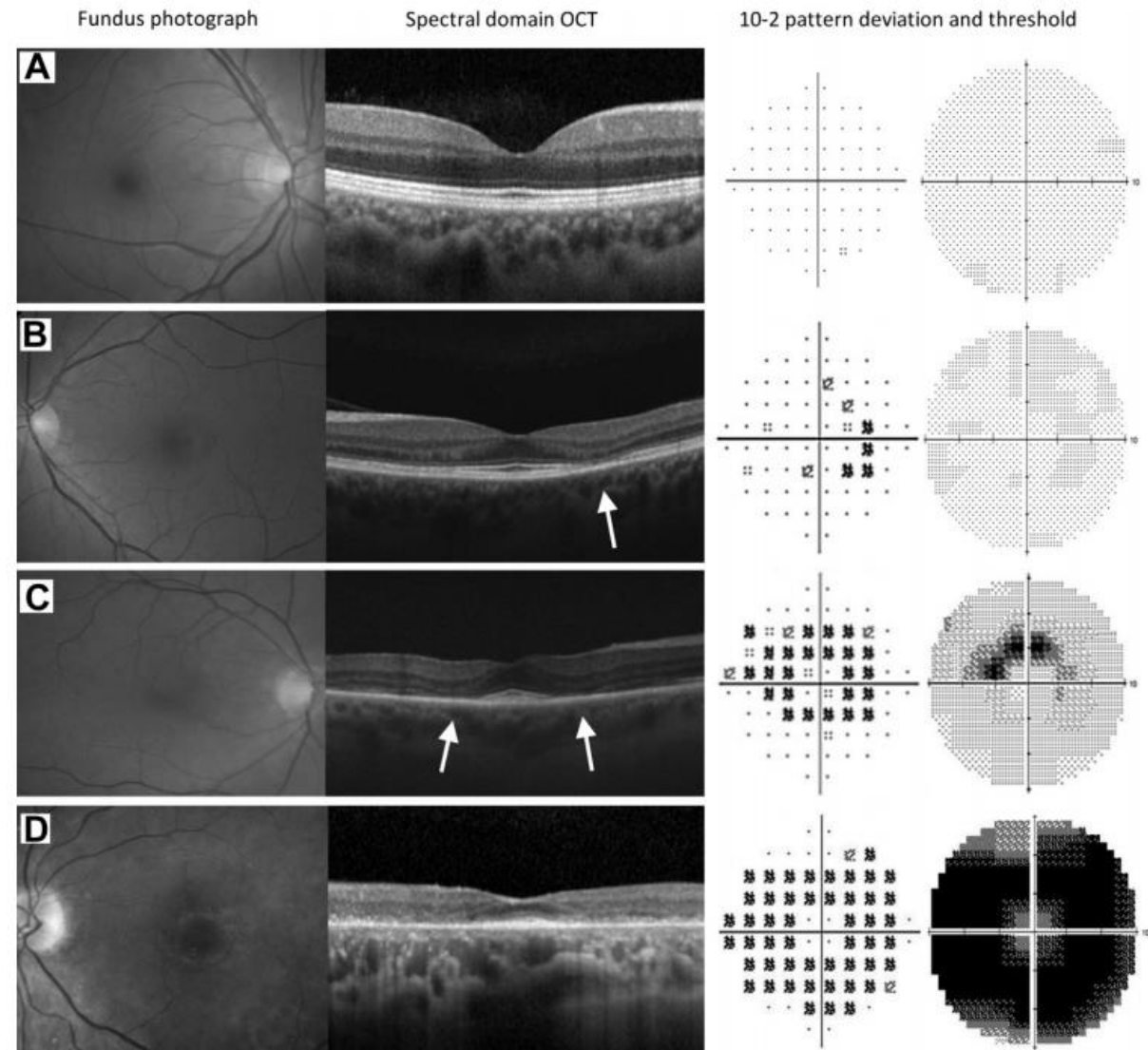
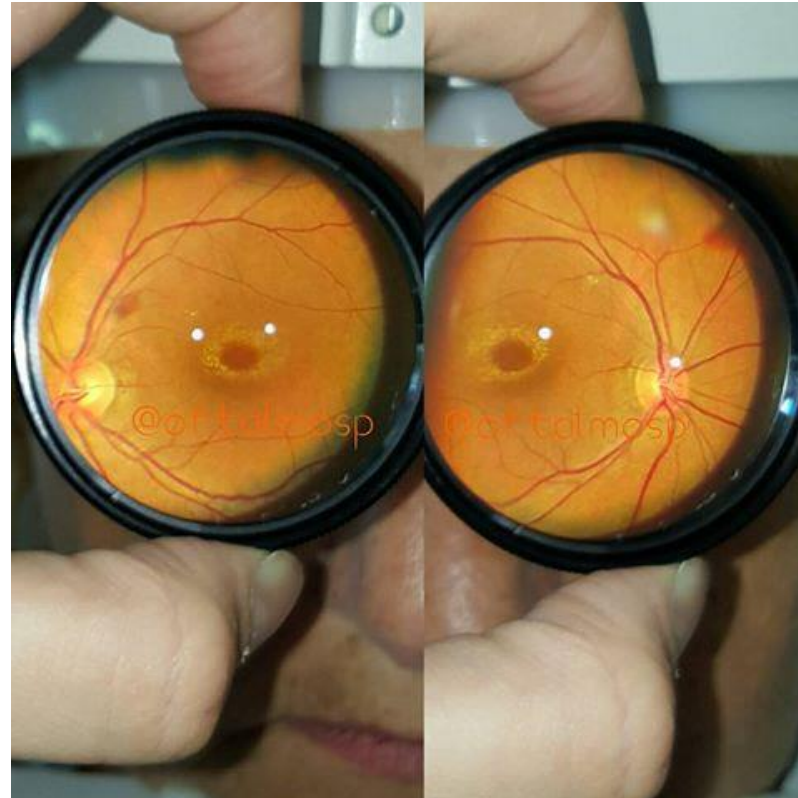


Figure 3. Illustration of progressive changes in hydroxychloroquine (HCQ) retinopathy for European patients. **Left to right:** fundus appearance, spectral-domain optical coherence tomography (SD OCT), 10-2 field pattern deviation, and grey scale. **Top to bottom:** (A) normal eye; (B) early damage with 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.

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Outras considerações sobre HCQ e CQ

- Vias de Eliminação
 - Renal
 - Hepática (citocromo P450)
- Sinergismo de lesões
 - Outras drogas: Tamoxifeno
 - Doenças retinianas e maculares (razoabilidade, sem dados)
- Embora baixa, [HCQ ou CQ] também se dá em tecidos gordurosos

Até então...

- Estudo AAO 2011
- HCQ < 6,5mg/kg (P ideal)
- CQ < 3 mg/kg (P ideal)

Alguns Pacientes com Longos Períodos de Exposição
Considerava lesões severas (Bull's Eye)



Novo Estudo AAO 2016

- 2361 pacientes
- HCQ por mais de 5 anos
- Usando OCT e CV
- Peso Real

Resultados extrapolados para CQ

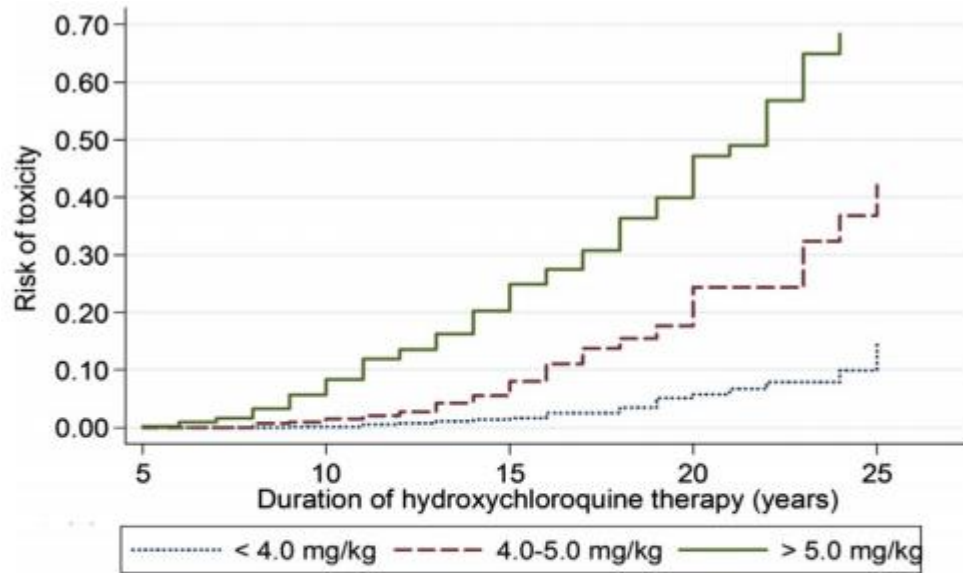


Figure 4. Kaplan–Meier curves showing the cumulative risk of retinopathy over time, with different levels of hydroxychloroquine (HCQ) use. When use is between 4.0 and 5.0 mg/kg, the risk is very low within the first 5 to 10 years, but it increases markedly thereafter. Reprinted with permission from Melles RB, Marmor MF. The risk of toxic retinopathy in patients on long-term hydroxychloroquine therapy. *JAMA Ophthalmol* 2014;132:1453–60.²

Risco com HCQ

- < 5mg/kg por 5 anos – 1%
- Por mais de 10 anos – 2%
- Por mais de 20 anos – 20 %



Extrapolando dados de 2011 para CQ

* Mesmas estáticas mas com Dose < 2,3mg/kg

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

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- * 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.

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.

Demais exames e Frequência de reavaliações:

Conforme a necessidade de cada caso

-Asiático

-Doenças Progressivas (Retina, Rins, Fígado, outras medicações)

-Doses mais altas



Se alterações

-Discutir conjuntamente com outra Clinica assistente a possibilidade de suspender a droga, conforme a relação risco x beneficio quando comparada a outras drogas para controle da doença de base

Obrigado !!!

