# Royal College of Ophthalmologists guidelines: Ocular toxicity and hydroxychloroquine

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## Guidelines for screening (replacing RCOphth Guidelines, 1993)

### *Background*

Chloroquine and hydroxychloroquine (quinolones) are used primarily by rheumatologists for rheumatoid arthritis and systemic lupus erythematosus, and by dermatologists for cutaneous lupus. They bind to melanin and interact with nucleic acids. Although irreversible retinopathy has been described with the use of these drugs, this has occurred at total doses in excess of those currently recommended. The literature[1,2] and contemporary practice[3,4] favour the use of low-dose hydroxychloroquine which confers minimal risk, or the unrelated antimalarial mepacrine (which has negligible ocular toxicity[5]). Chloroquine base should only be considered if these agents have failed, as there are inadequate data to advise on a safe maximum dose. In six case series with a total of some 1500 patients treated with hydroxychloroquine, only one case of retinopathy with visual loss was observed.[6–11] In the largest single series one patient out of 1207 developed retinopathy after 7 years.[12] Where doses of hydroxychloroquine were kept below 6.5 mg/kg/day lean body weight, no cases of toxicity were found in 973 patients followed.[9,13] However, 2 cases of retinopathy have been reported when the drug was used for > 6 years.[14]

### *Clinical features*

*Reversible*

- Corneal epithelial changes (verticillata): these do not often cause symptoms.
- Loss of normal foveal reflex.

*Irreversible*

- Fine granular appearance to macula.
- 'Bull's eye' maculopathy – only this sign is associated with impaired visual acuity and central visual field disturbance.

### *Is there a case for screening for quinolone toxicity?*

Despite two recent editorials[15,16] that recommend baseline ophthalmological examination, the working party believes that were quinolones to be introduced now, no evidence-based case for the cost-effectiveness of a screening programme would be justified.[1,2] A recent audit confirmed that screening where offered was patchy and adhered poorly to best practice.[3,4,17] Screening programmes are costly and may generate needless anxiety, work for clinicians and unnecessary appointments. More importantly, screening may not enable ophthalmologists to pick up reversible toxicity as (a) there is no reliable screening test which will identify this before ophthalmoscopic changes develop and (b) it is difficult to distinguish toxicity from age-related macular degeneration.[18]

## Recommendations for good practice in rheumatology and dermatology clinics

### *Baseline assessment*

- Establish renal and liver function.
- Ask about visual impairment (which is not corrected by spectacles).
- Record near visual acuity of each eye (with spectacles where appropriate) using a test type* or the reading chart in Fig. 1.

If no abnormality is detected, treatment with hydroxychloroquine can be commenced.

### *Maximum daily dosage recommendations*

Hydroxychloroquine 6.5 mg/kg lean body weight (usually 400 mg) daily. If the patient is overweight check lean body weight with body mass index calculator available in endocrine clinics.

*Available from: Keeler Limited, Clewer Hill Road, Windsor, Berkshire SL4 4AA, UK. Tel: +44 (0)1753 857177. Fax: +44 (0)1743 857817.

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**TEST TYPES**

Use the texts below to test each eye separately with glasses when appropriate. Record the smallest text that can be read at a distance most comfortable to the patient

**N.5**

He moved forward a few steps: the house was so dark behind him, the world so dim and uncertain in front of him, that for a moment his heart failed him. He might have to search the whole garden for the dog.

**N.6**

The camp stood where, until quite lately, had been pasture and ploughland; the farm house still stood in fold of the hill and had served us for battalion offices; ivy still supported part of what had once been the walls of a fruit garden;

**N.8**

And another image came to me of an arctic hut and a trapper alone with his furs and oil lamp and log fire; the remains of supper on the table, a few books.

**Fig.1.** *Test types.*

If visual impairment is present an assessment by an optician is advised. Any relevant abnormality detected would be referred to an opthalmologist in the usual way.

### *Annual evaluation*

Patients should be monitored yearly, enquiring about visual symptomatology, rechecking acuity and assessing for blurred vision using the reading chart. (Amsler Charts have not yet been validated beyond their use in ophthalmology clinics.[19])

### *Referral to the ophthalmologist*

Referral to the ophthalmologist is appropriate if any patient:

- Has visual impairment or eye disease detected at baseline assessment. It should be noted that in elderly patients there is often coincidental ocular morbidity from cataract, glaucoma and age-related maculopathy.
- Develops change in acuity or blurred vision (as assessed by reading chart) whilst on treatment. Patients should be warned to stop treatment and seek advice from the prescribing doctor.
- Although quinolones are not officially licensed for children, the drug (often chloroquine for convenient dosage) is used in specialist units particularly in the management of juvenile chronic arthritis and systemic lupus erythematosus. These children are already attending the ophthalmologist for slit-lamp examination to check for the development of uveitis.

### *Examination by the ophthalmologist*

Examination should include assessment of:

- distance and near acuity;
- colour vision;
- visual field – use of a red pin and red Amsler grid is helpful;
- examination of the cornea by slit-lamp;
- the retina.

Examination may need to be extended according to signs and symptoms.

Subsequent examinations should be at the discretion of the ophthalmologist, but indefinite follow-up is not likely to be required. For the patient who ultimately requires long-term treatment (> 5 years) an individual arrangement should be agreed with the local ophthalmologist.

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