Hydroxychloroquine (Plaquenil) and Chloroquine (Resochin)

- **Indications**
  - Malaria
  - Autoimmune disease
    - Systemic lupus erythematosus
    - Rheumatoid arthritis
  - Other
- **Retinal toxicity**
  - 0.33% @<5 years, 1% @5-7 years, 2.1% @15 years
- **Mechanism**
  - Poorly understood
  - Binds to retinal pigment epithelium
  - Affects photoreceptor metabolism

**Manifestations of Toxicity**

- No visible changes
- “Bull’s-eye” maculopathy
- Subfoveal RPE atrophy
- Diffuse RPE atrophy
- Decreased visual acuity
- Peripheral field defects

**Risk Factors for Toxicity**

- Duration of use > 5 years
- Cumulative dose
  - HCQ > 1000 g
  - CQ > 460 g
- Daily dose
  - HCQ > 400 mg/day (>6.5 mg/kg ibw/day)
  - CQ > 250 mg/day
- Age
  - Elderly
- Systemic disease
  - Kidney or liver dysfunction
- Ocular disease
  - Retinal disease or maculopathy

**Recommendations**

American Academy of Ophthalmology Update

Revised Recommendations on Screening for Chloroquine and Hydroxychloroquine Retinopathy

Michael P. Mercurio, MD; Michael Klotz, MD; Timothy F. Lai, MD; Jonathan S. Lyons, MD; William F. Marler, MD (for the American Academy of Ophthalmology)
Baseline Visit

- **History**
  - Duration
  - Dose
  - Height
  - Age
  - Renal/hepatic disease

- **Calculations**
  - Ideal body weight
  - Dose (mg/kg ibw/day)
  - Cumulative dose

- **Physical Exam**
  - Ophthalmic Exam
  - 10-2 visual field (red stim.)
  - Color photograph*
  - SD-OCT* and/or
  - mf-ERG* and/or
  - Fundus autofluorescence*
  (* = if available)

- **Patient discussion**
  - Risk of irreversible vision loss
  - Even with screening
  - Importance of exams
  - Report new visual changes

Calculations

**Ideal body weight (kg)**

- **Method #1**
  - ♂: 50 kg + 2.3 kg/inch
  - Start at 5 feet
  - ♀: 45.5 kg + 2.3 kg/inch
  - Start at 5 feet

- **Method #2**
  - ♂: (height (cm) - 100) - 10%
  - ♀: (height (cm) - 100) - 15%

Cumulative dose

- **“Magic height”**
  - ♂: ~5 feet, 6 inches
  - ♀: ~5 feet, 7 inches

Follow-up visits

- **Standard recommendation**
  - No later than 5 years after starting medication
  - Yearly thereafter
  - Includes all measures of baseline visit except color photographs

- **Special considerations**
  - Closer follow-up and more objective measures in higher risk patients

*The balance of frequency and extent of screening, relative to cost and legal considerations, is a judgment that individual physicians and health plans must make in light of the risk status of individual patients.*

Diagnosing Toxicity

10-2 HVF (threshold, red stimulus)
Management

- Cessation of drug is the only intervention known to minimize the risk of further toxicity
  - Risk of blinding ocular toxicity must be weighed against the risk of worsening systemic disease and side effects of alternative treatments
  - Decision must be made in conjunction with the internist or rheumatologist and the patient
- Re-evaluation at 3 months and then yearly until findings stabilize
Unanswered Questions

- Marmor et al. did not:
  - Define “short in stature,” “elderly,” “kidney or liver dysfunction,” or “retinal disease”
  - Specify how frequently “high risk” patients should be seen
  - Clearly state when SD-OCT, FAF, or mf-ERG should be done
  - Recommend red stimulus on 10-2 HVF
  - Clearly support or refute the importance of 6.5 mg/kg/day dosing limit

What would you do?

Is this Plaquenil toxicity?

Should this patient continue to receive Plaquenil?

Which SD-OCT is superior?

Additional Questions?