Preface

This book provides a single source from which an interested ophthalmologist or optometrist can learn most of what is known in 2014 about the cause, prevention, and detection of hydroxychloroquine and chloroquine retinopathy.

The book is oriented to the needs of the practitioner. In real life, acquisition of ancillary studies is often done at a simpler level than in an academic environment. Whereas avoiding artifacts in ancillary tests is a goal everywhere, the clinician must often make interpretations in spite of them, and real cases are presented in which this has been done.

No monograph can be completely self-contained, but this one aspires to that goal. The intended reader is the ophthalmologist or optometrist who sees patients taking 4-aminoquinolines. Often far removed from their training, these clinicians may not remember the precise meanings of prevalence, odds ratio, pretest probability, sensitivity, epitope, decibels, visual field threshold, and coefficient of variance. Therefore, a refresher is included here. Thus, in addition to the main subject of clinical ophthalmology, the book is a platypus with sections on pathology, physiology, pharmacokinetics, toxicology, and statistics. Along the way, sidebars guide the reader on interesting tangents.

Unfortunately, the literature on 4-aminoquinoline retinopathy is large and dispersed. Even using the Internet, it is difficult to access and synthesize the sources. The aim of this book is to accomplish just that. With this text as your guide, you can become the local expert on this iatrogenic and largely preventable condition.

Nomenclature is important, but confusing. Although the book focuses on chloroquine and hydroxychloroquine, much of it applies to other related drugs (e.g., quinacrine). These drugs were formerly termed antimalarials, as they were first used against malaria. However, their main use currently is in the treatment of autoimmune diseases. Because both chloroquine and hydroxychloroquine are 4-aminoquinolines, a timeless chemical descriptor, this is the preferred usage when writing about both drugs. When only one of the two is referred to, the particular compound is named. When quinacrine is also implied, it is mentioned specifically.

Evidence-based medicine is the benchmark for clinicians in 2014, yet in the field of hydroxychloroquine and chloroquine retinopathy there are no level-1 studies. Instead, we have eminence-based medicine, in the phrase of Graham Hughes, relying on case series and personal experience. In this context, the recognized authorities over the last 50 years were Bernstein and Mackenzie, followed by Easterbrook, and latterly Marmor.

Some have despaired that a higher quality of evidence cannot be achieved. Perhaps the best that can be done is to analyze the literature, identify flaws, and develop a contemporary perspective. Yet the development of a network of ophthalmologists linked by the Internet to a hub with expertise in clinical trials (along the lines of the Diabetic Retinopathy Clinical Research Network) makes one hopeful that questions may eventually be answered in a rigorous manner. In particular, answers are needed to these:

- Why is the perifoveal retina preferentially affected by the toxicity?
- What is the prevalence of 4-aminoquinoline retinopathy?
- What is the relative importance of adjusted daily dose and cumulative dose?
- What are the relative sensitivity and specificity of 10–2 visual fields, multifocal electroretinography, spectral domain optical coherence tomography, and fundus autofluorescence for the detection of 4-aminoquinoline retinopathy?
- Does screening for 4-aminoquinoline retinopathy in properly dosed patients make economic sense?

The field of study is dynamic; some might say volatile. In 1993, 10–2 visual fields were considered optional as screening aids. By 2002, they were recommended in all cases. By 2011, the additional use of multifocal electroretinography, spectral domain optical coherence tomography, and fundus autofluorescence imaging was recommended. By 2013, experts were backing away from these expanded recommendations. The reader can expect even more changes in the future, especially as economic constraints pressure proponents of tests to prove their value.

Elmore Leonard's tenth rule for writing well was to leave out the part that no one reads, which is good advice for writing novels, but not textbooks. For example, a clinician may occasionally want to know how hydroxychloroquine affects the binding of the invariant chain to MHC class II molecules. This, and other recondite facts, are found in this book, which aims to be a resource both for daily practice and for in-depth study.

Finally, although I have attempted to fairly lay out the evidence in support of all sides in controversies surrounding 4-aminoquinoline retinopathy, the facts have led me to a point of view that has not been hidden. The evidence suggests that too many people lose vision from 4-aminoquinoline retinopathy because of insufficient attention paid to dosing. Moreover, the recommendation favoring universal ancillary testing of those taking 4-aminoquinolines seems wasteful, when the emphasis should be on detecting toxic dosing with selective use of tests based on clinically assessed risk. Paracelsus told us 500 years ago, "It is the dose that makes the poison." What follows is an elaboration on the truth of that adage.

Charlotte, NC, USA David J. Browning

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Browning, D.J.

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