ELECTRODIAGNOSTIC FINDINGS IN QUININE AMBLYOPIA*†

BY

JOAN BEHRMAN AND ALAN MUSHIN

Electrodiagnostic Clinic, Moorfields Eye Hospital, City Road Branch, London

SINCE von Graefe first described blindness as a result of quinine intoxication, the symptomatology, pathology, and progress of quinine amblyopia have been well documented (Auvert, Dollfus, and Moncade, 1965). The changes in the electroretinogram during the course of the amblyopia have been described by Vainio-Mattila and Zewi (1954), Berggren and Rendahl (1955), Le Grand, Dehaze, and Lecomte (1960), Bard and Gills (1964), Bonnet, Ravault, and Istré (1964), and Auvert and others (1965).

Electroretinographic studies have not so far been wholly successful in resolving the controversy which exists over the mechanism by which the quinine causes blindness.

In this report, the electro-oculogram (EOG) was recorded in addition to the electroretinogram (ERG) in a patient with quinine poisoning in order to obtain a more complete assessment of the nature of the retinal dysfunction.

Case Report

A 40-year-old married woman had been under treatment for paranoid schizophrenia for 2 years. She had had several periods of hospital admission and had been treated on different occasions with chlorpromazine (50 mg. three times a day), imipramine (50 mg. three times a day), and haloperidol (1.5 mg. three times a day). The above dosages were not exceeded. More recently she had undergone a course of electroconvulsive therapy.

On September 22, 1966, she obtained and swallowed 75 tablets of quinine (total dose 24 g.). The following day she was discovered unconscious in a field and later, on arousal, was found to be deaf and blind. She was admitted to hospital on September 24, and bilateral stellate ganglion block was performed (McLenachan, 1963) with no apparent effect.

Examination.—When she was first seen by one of us on September 29, the visual acuity was reduced to doubtful perception of light in both eyes, and the pupils were semi-dilated and fixed. Ophthalmoscopy showed the disc edges to be blurred and swollen; the retinal vessels were normal.

She first attended the Electrodiagnostic Clinic at Moorfields Eye Hospital on October 3, 1966, 10 days after taking the tablets. The visual acuity had improved slightly, the optic discs were observed to be pale, and the arteries had become narrow. She was seen subsequently 5, 10, 20, and 40 weeks after the acute attack. Her pupils remained semi-dilated and non-reactive. The characteristic fundus picture of atrophic discs and narrow retinal vessels with peripapillary sheathing gradually appeared. The visual acuity improved over the weeks to 6/9 in each eye.

Electrodiagnostic Tests

Method.—The EOG technique used at Moorfields Eye Hospital is identical to that described by Arden, Barrada, and Kelsey (1962).

The ERG procedure is similar to that first introduced by Karpe (1945). The response is elicited by a Xenon flash from a commercial $\frac{1}{4}$ Joule stroboscope and recorded on a direct writing instru-

*Received for publication January 9, 1968.

† Address for reprints: Moorfields Eye Hospital, City Road, London, E.C.1.

ment, the Schwarzer P.E.E.4, with a time constant of 2 seconds. Records were taken after 8 minutes' dark adaptation.

Results.—The EOG and ERG results are summarized in Fig. 1.

The ERG first recorded, 10 days after intoxication, shows a normal a-wave followed by a slow rounded b-wave of 160 μ V. At this point the EOG was abnormal and no light-induced rise in potential occurred. The level of the corneo-fundal potential, however, appeared normal. A month later, the b-wave had disappeared and a negative ERG was recorded; this became progressively smaller during the following months. The EOG on the other hand, improved and a normal light rise was recorded 10 months after the acute period.

FIG. 1.—Changes in visual acuity, EOG, and ERG in the right and left eyes, showing time after intoxication.

Subjective Tests

The visual fields were first plotted on the Goldmann perimeter, when the visual acuity had improved to appreciation of hand movements, and were re-examined on subsequent visits. They were found to be grossly constricted to all targets and little change occurred with time, as shown in Fig. 2 (see p. 927).

Dark-adaptation curves were plotted, using the Goldmann-Weekers dark adaptometer, on her last two visits. Both the "rod" and "cone" final threshold intensity levels were above normal as seen in Fig. 3 (see p. 927).

Discussion

In most of the recent reports of quinine amblyopia, the amaurosis has been explained in terms of the direct action of the quinine on the retina, with narrowing of the arteries occurring as a secondary effect (Traquair, 1949; Vainio-Mattila and Zewi, 1954; Drance, 1955; Berggren and Rendahl, 1955; Turtz, 1957; Bard and Gills, 1964). The arguments have been based on the fact that in the acute initial stage the retinal arteries are of normal calibre and the ERG is normal. The presence of a normal ERG indicates that the loss of vision is not due to generalized retinal ischaemia and the cause must therefore lie in the

FIG. 2.—Visual fields plotted 5 weeks and 10 months after intoxication.

FIG. 3.—Dark-adaptation curve plotted 10 months after intoxication.

third order neurones or more centrally. Since the only ophthalmoscopic abnormality at this time is retinal oedema, it seems likely that the visual loss is due to damage to the elements of the nerve fibre layer.

The partial progressive return of central vision which occurs in most patients indicates that some at least of the nerve fibres recover function with time. However, some impairment of vision invariably remains, as evidenced by the contraction of the visual fields. In addition, it has been consistently shown that, as the vision recovers, the ERG becomes more abnormal. In our case, within 5 weeks of intoxication, P II, the component arising in the inner nuclear layer (Granit, 1947) had disappeared and the ERG consisted of P III, the negative receptor potential only. This receptor potential appeared to decrease in size during the succeeding months, but it has been reported (Auvert and others, 1965) that even after 16 or 17 years some response remains.

It therefore appears that a considerable proportion of the nerve fibres is permanently damaged and this will be associated with death of the ganglion cells. At this point the ERG is normal, but a subsequent transynaptic degeneration involving the bipolar cell layer could explain the negative waveform of the ERG recorded a few weeks later.

The EOG during the acute stage is grossly abnormal and there is no light rise. This implies loss of function of the receptors or the pigment epithelium (Arden and Kelsey, 1962), caused either by the direct toxic action of the quinine on these layers or by a disturbance of the choroidal circulation. The EOG light rise gradually returns to normal after 10 months, suggesting that these effects are transient. It is known, however, that a normal EOG light rise indicates normally-functioning receptors and this, considered with the fact that the receptor potential component of the ERG is decreasing, suggests that two separate processes may be occurring within the receptors (Arden and Kelsey, 1962).

Summary

In quinine poisoning the ERG is initially relatively unaffected, but later becomes grossly abnormal. The EOG, on the other hand, parallels the visual acuity, at first showing no "light rise" but gradually returning to normal. The significance of these findings is discussed.

We should like to thank Dr. Denis Martin and Dr. Elizabeth Schoenberg of Claybury Hospital for allowing us to follow their patient.

REFERENCES

- ARDEN, G. B., BARRADA, A., and KELSEY, J. H. (1962). *Brit. J. Ophthalmol.*, **46**, 449.
 ——— and KELSEY, J. H. (1962). *J. Physiol. (Lond.)*, **161**, 189.
 AUVERT, B., SAMSON-DOLLFUS, D., and MONCADE, J. (1965). *Bull. Soc. Ophtal. Fr.*, **65**, 559.
 BARD, L. A., and GILLS, J. P. (1964). *Arch. Ophthalm. (Chicago)*, **72**, 328.
 BERGGREN, L., and RENDAHL, I. (1955). *Acta ophthalm. (Kbh.)*, **33**, 217.
 BONNET, J.-L., RAVAUULT, M. P., and ISTRE, M. (1964). *Bull. Soc. Ophtal. Fr.*, **64**, 829.
 DRANCE, S. M. (1955). *Brit. J. Ophthalmol.*, **39**, 178.
 LE GRAND, P., DEHAZE, and LECOMTE (1960). *Bull. Soc. belge Ophtal.*, No. 125, p. 965.
 GRANIT, R. (1947). "Sensory Mechanisms of the Retina". Oxford University Press, London.
 KARPE, G. (1945). *Acta ophthalm. (Kbh.)*, Suppl. 24.
 MCLENACHAN, J. (1963). *Brit. J. Ophthalmol.*, **47**, 62.
 TRAQUAIR, H. M. (1949). "An Introduction to Clinical Perimetry", 6th ed. Kimpton, London.
 TURTZ, C. A. (1957). *Amer. J. Ophthalmol.*, **44**, 110.
 VAINIO-MATTILA, B., and ZEWEI, M. (1954). *Acta ophthalm. (Kbh.)*, **32**, 451.