test will not only reassure the reader, but also be found of service in busy clinics.

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QUININE AMBLYOPIA

BY

A. BISHAY

EGYPT

THE two last years which I spent in Kom-Ombo of Upper Egypt, a district infected with a severe epidemic of malignant malaria, had given me one of the most wonderful chances to study the subject of quinine amblyopia, and it would have been very difficult under normal circumstances to give such an account in such a short time. During this period I had seen in my hospital and private practice, seven cases of quinine amblyopia, which is relatively a large number of such cases for an ophthalmologist to see in two years. Dealing with these seven cases, I have observed some very interesting points in examination, diagnosis and treatment, which I am glad to state to my colleagues.

Symptomatology

From the accompanying table we can conclude :—

- (1) The age of the patient does not matter in the case.
- (2) The amount of the drug (quinine) must not necessarily be big as said by de Schweinitz, because out of my seven cases only two took a large dose of the drug, while the other five developed their amblyopia by taking ordinary doses ; but the outstanding feature is that all of them took the quinine on an empty stomach. Thus in my opinion due to these observations, it is not only large doses of quinine that lead to amblyopia, but it is some kind of sensitiveness

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to quinine which leads to it, and when I reach the discussion about the theories of explanation of quinine amblyopia, I will discuss my point of view in detail.

(3) We can also see from the attached table that all of the seven cases, those who took large doses as well as those who took normal pharmacopoeial doses have developed vomiting after taking the quinine.

(4) Vomiting was followed in every case by loss of consciousness as an outstanding fact, and the patient after regaining his consciousness found himself blind. The period from taking the drug until the patient develops the amblyopia varies between a few minutes and one hour.

(5) Other symptoms mentioned by Foster Moore as tinnitus and deafness are not always the rule.

Clinical Features

From thorough examination of my seven cases, I put the main clinical features of quinine amblyopia as follows:—

- (I) Anaemic blanched conjunctiva,
 - (II) Partial anaesthesia of cornea which is not always a constant sign.
 - (III) Dilated pupil.
 - (IV) Immobile iris "the limitation of immobility depends on the amount of defective vision and is complete if the vision is 'no P.L.'"
 - (V) Pallor of optic discs.
 - (VI) Marked contraction of retinal blood vessels.
 - (VII) Marked contraction of field of vision which is observed in cases which do not develop complete amblyopia as well as in cases which recover. In these last cases (recovering cases) the contraction persists to a certain extent even after complete recovery. When a patient first regains vision he gets some sort of tubal vision with very contracted field (see charts).
 - (VIII) Diminution of colour sense, specially red and green.
- Other signs such as oedema of retina, haziness of optic discs, venous engorgement, etc., as described by Berens to be the earliest signs, I could not see in any of my seven cases.

Differential diagnosis

Other drugs which lead to a similar amblyopia as that of quinine are salicylic acid and salicylates, optochin, felix mass, organic compounds of arsenic ost atoxyl, etc., their amblyopia differs in details from that of quinine, e.g., that of salicylic acid and salicylates is relatively shorter than that of quinine, that of organic compounds of arsenic is always of grave prognosis, and leads to blindness in many

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CASE No. 1, 25th day, $V = 6/24$.

CASE No. 2, after three months, $V = 6/18$.

CASE No. 6, after five days, $V = 6/24$.

CASE NO. 7, 25th day, V. = 6/12.

cases; but the most important thing usually in diagnosis is the history of the patient "that he took quinine" and the analysis of the drug if the patient does not admit the drug he had taken.

Theories of explanation of quinine amblyopia

Pharmacology.—Quinine as described by all pharmacologists (Cushing, Gunn, Dixon and others) is a protoplasmic poison, and in certain concentration it paralyzes the protoplasm of living cells, then kills after a certain time. Its effect on the small blood vessels was found to be tetanic-like contraction, which ends in their thready appearance. The vessels of the retina behave like all other vessels of the body and become constricted to some degree, depending on the amount of concentration of quinine as de Schweinitz said, and on the sensitiveness of the patient to quinine as I would say, because as it is clear from the table herewith, most patients have got their amblyopia from ordinary pharmacological doses.

This leads us to discuss the theories of quinine amblyopia. There are two theories which are predominant and most supported:—

- I. Direct toxic effect on retinal cells.
- II. Anaemia of retina caused by extreme constriction of retinal blood vessels due to quinine.

The supporters of the first theory, *i.e.*, toxic effect of quinine on the retinal cells, depends on experiments done on dogs by Holden, who showed that after giving dogs large doses of quinine there was marked degeneration in the retinal ganglion cells on the third day and consequently the degeneration took place in the optic nerve fibres extending to the brain. This theory has also been confirmed by Drault, Birch-Hirschfeld and many other observers depending

on the experimental results on animals and microscopical examinations afterwards. Another experiment has been done by de Schweinitz, who had found in his experimental work that there was no sign of disease in the vessels of the uveal tract in serial section alone in eyes of quinine amblyopia, which deprivation of blood causes the degeneration of the nerve cells. He also found that the organic lesions of vessels occur as a secondary element in the process. These experiments emphasise the theory that the drug has a selective effect on the retina.

On the other hand the vasomotor theory has its supporters, but there are several objections to it, *i.e.*, the blindness is not always absolute, and after a certain time recovery begins; thus if vascular closure be the cause of amblyopia one would expect absolute blindness without recovery if the blindness persists two or three hours, but in fact blindness remains even for days and recovery occurs. There are many other objections to this theory which make the idea that quinine acts directly on the visual nerve elements more believable.

Elliot and some other observers do not accept either views, and I myself join them in their belief as I will shortly state:—

Holden, de Schweinitz and other observers had based their theory of the toxic effect of quinine on retinal cells after experimental work on animals to which they had given large doses of quinine, but this theory will never explain how a patient who has taken one dose of quinine of 0.30 gms. developed quinine amblyopia. Moreover, he had vomited directly after taking the quinine which made the doses absorbed even less than 0.30 gms. as it had happened with five of the cases I had seen? Even if the vomiting had not rejected any of the quinine taken and all the dose (*i.e.*, 0.30 gms.) has been absorbed which is practically impossible, the concentration of quinine in the blood will not exceed 1/15,000, and I believe that such concentration can never be toxic to any kind of cells however delicate they may be.

From the above discussion I have come to the conclusion that *quinine amblyopia is some sort of sensitiveness of certain people to quinine*, but how the quinine acts I leave it for the present to further discussion and experimental work.

Treatment

All ophthalmological writers have agreed upon the use of strychnine, pushing it to its full limit, and upon the use of vaso dilators as amyl nitrite, etc. Some use in addition salicylates, iodide, tonics, etc., but they are not of extreme importance. Also other ophthalmologists advise large amounts of fluids to wash off excessive quinine from the body, in cases where large quantities had been absorbed.

Name of patient	Age years	Amount and manner of taking quinine	Symptoms	Examination	Treatment	Result	Notes
1. Mahfouz Mohamed	50	250 c.c. of 1 per cent. quinine solution on an empty stomach	Giddiness, severe vomiting, unconsciousness, regained consciousness after 20 minutes; found himself blind	In all seven cases I have found nearly the same signs with some difference in severity:— I. Anaemia of conjunctiva II. Partial anaesthesia of cornea III. Dilated pupils IV. Immobile iris V. Pallor of optic discs VI. Marked contraction of retinal blood vessels VII. Marked contraction of field of vision if blindness is not complete VII. Diminution of colour vision	Strychnine pushed to its full level, retro-bulbar and by mouth	Regained H.M. 3rd day and 6/24 on 25th day. Field of vision contracted as in charts. After three months 6/18 c slight improvement of field	Cornea clear. Patient says his original vision was 6/9 and 6/6 (see charts)
2. Mohamed Eid ...	25	0.30 gms. of quinine on an empty stomach	Severe vomiting, felt unconscious; after half-an-hour regained consciousness but felt completely blind	I. Anaemia of conjunctiva II. Partial anaesthesia of cornea III. Dilated pupils IV. Immobile iris V. Pallor of optic discs VI. Marked contraction of retinal blood vessels VII. Marked contraction of field of vision if blindness is not complete VII. Diminution of colour vision	ditto	Regained H.M. on 5th day, 6/24 after one month. No more improvement	Cornea clear
3. Nefissa Ali Ibrahim	30	Three coffee cupsful of 1 per cent. quinine solution on an empty stomach	Severe vomiting, felt unconscious for few minutes, then right eye blind, and left H.M.	I. Anaemia of conjunctiva II. Partial anaesthesia of cornea III. Dilated pupils IV. Immobile iris V. Pallor of optic discs VI. Marked contraction of retinal blood vessels VII. Marked contraction of field of vision if blindness is not complete VII. Diminution of colour vision	ditto	2nd day L. 50 cms. 10th day R. 1/60, L. 2/60. 30th day R. 5/60, L. 6/36	Both cornea are nebulous
4. Sayed Mohamed El-Selwawy	18	0.30 gms. quinine on an empty stomach	Severe vomiting, felt unconscious and became totally blind after he regained consciousness five minutes later	I. Anaemia of conjunctiva II. Partial anaesthesia of cornea III. Dilated pupils IV. Immobile iris V. Pallor of optic discs VI. Marked contraction of retinal blood vessels VII. Marked contraction of field of vision if blindness is not complete VII. Diminution of colour vision	ditto	4th day regained H.M. 15th day regained 6/36. 30 day regained R. 6/18, L. 6/24	Left cornea pannus
5. Sayedah Hussein Ibs Omar	25	Coffee cupful of 1 per cent. quinine solution on an empty stomach	Severe vomiting for a long period, then felt unconscious; after half-an-hour awakened blind	I. Anaemia of conjunctiva II. Partial anaesthesia of cornea III. Dilated pupils IV. Immobile iris V. Pallor of optic discs VI. Marked contraction of retinal blood vessels VII. Marked contraction of field of vision if blindness is not complete VII. Diminution of colour vision	ditto	6th day regained H.M. 30th day regained 6/60 and 6/24	Cornea nebulous
6. Danyal Eff Moun	42	Ordinary dose of 0.3 gm. quinine on an empty stomach	Vomited, felt unconscious, after few minutes awakened totally blind	I. Anaemia of conjunctiva II. Partial anaesthesia of cornea III. Dilated pupils IV. Immobile iris V. Pallor of optic discs VI. Marked contraction of retinal blood vessels VII. Marked contraction of field of vision if blindness is not complete VII. Diminution of colour vision	Paracentesis at once, then strychnine pushed to its full level	Regained P.L. on table. Regained 50 cms. 2nd day. Regained 6/24 5th day, field little contracted	Pt. is myope 6-30 (see charts)
7. Ibrahim El Suny El Keyfy	50	Ordinary dose of 0.30 gm. quinine on an empty stomach	Much vomiting, exhausted, felt semi-unconscious and observed his vision diminishing little by little until he became blind	I. Anaemia of conjunctiva II. Partial anaesthesia of cornea III. Dilated pupils IV. Immobile iris V. Pallor of optic discs VI. Marked contraction of retinal blood vessels VII. Marked contraction of field of vision if blindness is not complete VII. Diminution of colour vision	ditto	Regained P.L. on table. Regained H.M. and 1/10 2nd day. Regained 6/18 and 6/12 25th day; field little contracted	Pt. (see charts)

A. BISHAY

I have tried some other sort of treatment which helped me a lot to get better results as well as in shortening the period of treatment. Having tried it on my last two patients only, no full account can be given. These last two patients when I first saw and examined them to be sure of the diagnosis, I immediately performed paracentesis, and I was astonished to find out that they perceived the light of the operation lamp while they were still on the operation table, taking in consideration that they were completely blind with no P.L. On the second day one of them counted fingers at a distance of 50 cms.; and the other had only hand movements. Examining the fundi of these two patients on the second day, I found that the vaso-constriction was much less, so was the pallor of the disc. Moreover, they both took much shorter time to be cured and their fields are much less contracted than is usual after cure compared with the other cases treated with ordinary means of strychnine, etc. How does the paracentesis act in these cases? Is it only due to diminution of intra-ocular pressure and subsequent dilatation of vessels; or due to change of intra-ocular fluids (aqueous)? or a combined action of both? It is still a problem that needs further investigation.

Conclusion

It is obvious from what I have mentioned above that three important new facts were reached from dealing with my seven cases:—

(I) The amount of quinine that the patient takes need not be essentially large as described by all other writers.

(II) Neither vascular nor toxic theories explain all cases, and I believe there is another element in the subject, *i.e.*, sensitiveness of patient to quinine.

(III) In treatment, paracentesis immediately done to the patient, produces better and quicker results.

I hope that these points will be of interest to my colleagues to know and to deal with for further investigations.

NECESSITY OF AN INTERNATIONAL STUDY CENTRE OF TRACHOMA*

BY

DR. L. POLEFF

RABAT, MOROCCO

In connection with the general tendency for international co-operation in various matters of economic and cultural life of the different

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