

QUININE IN THE THERAPEUTICS OF MALARIA

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To most of us with tropical experience, the symptoms and treatment of malaria, as described of late from temperate zones, have been most bewildering, and in fact we have felt that, were all that has been published to be confirmed, we must in the past have been most unobservant and allowed our patients to suffer very unnecessarily. Conclusions have been stated dogmatically and it has appeared to be thought that what applied in Camberwell must also apply in Cathay. The latest *Report of the Malaria Commission of the League of Nations* has, however, cleared the air considerably by the statement that 'the therapeutics of malaria, like every other aspect of the disease, is much more a local and individual problem than has hitherto been thought'.

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choice in the large majority of patients, but parenteral routes should be adopted when this is not practicable. In view of the injury likely to result to the blood vessels, muscles, nerves, etc., by parenteral injections there is no justification for the routine use of this method in the treatment of malaria.

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For many years it has been obvious, from the literature and the contradictory descriptions of the disease, that neither the human host nor the parasite are fixed quantities. There are probably many factors concerned, race, environment, present and past treatment, and heredity, which may affect the relations of the human host to the parasite, and the latter may consist of various strains, or it may be influenced by the insect species or the length of the period elapsing between transmission from host to host. These complications make the problem and generalizations on it difficult, and it has to be realized that findings under certain conditions or in certain climates may not be applicable elsewhere.

It is, therefore, not so extraordinary that opinion regarding the treatment and cure of malaria with quinine even after so long a trial is still unsettled. Some pin their faith to treatment by large doses, such as forty grains daily, others are satisfied with twenty, and it has even been stated that a grain or two for a couple of days is sufficient. Statements affirming a cure require to be accepted very cautiously, for in the first place there is no certainty as to how long periods of latency may be, or for how long after infection relapses may be possible, and in this matter also observations made in England quite possibly do not apply to the tropics. A change to the hills or a more temperate zone is a powerful adjunct to the body winning in the fight against the parasite, so that results of experiments in more salubrious climes may not help with the management of the disease locally. Then, if the environment is not changed, the possibility of re-infections cannot be excluded, and these cannot be differentiated from relapses.

The standard course given

In an effort to effect a cure I have for many years prescribed a three months' course of quinine, ten grains daily, to suitable patients, including all my few European patients. Only the latter are here considered, as, on account of the precautions they take, they are not so liable to re-infections, and also they can be kept better under observation. Cases which have been free of fever for at least one year are counted as cures; it is not likely that in the enervating climate of Sylhet latent periods would exceed a year. Those getting fever with parasites within the year count as relapses, with the exception of a few cases where on the second occasion a different species of parasite was found. Patients who left the district before the elapse of one year are classed as unknown.

The average period between attacks is probably between two and three years, e.g., one patient had attacks in April 1928, September 1929 and October 1933, the first and last being benign and the intermediate attack malignant tertian; another patient had attacks of benign tertian in 1923, 1925 and 1932, each time in

June; and the writer has had three attacks in 1920, in 1923, and in 1931, the second one malignant tertian and the others benign, complete freedom being enjoyed in the intervening periods.

With these criteria the results of treatment in 110 cases have been:—

Cured	80
Relapsed	20
Results unknown	10

It is doubtful if there were any genuine relapses, as some were possibly re-infections and some patients certainly did not carry out the full treatment; a number confessed to not having done so, but unfortunately no note of this fact was made.

Courses limited to about six weeks appear to fail. The impression is that children require bigger proportionate doses, or possibly they are more exposed to re-infections.

Although the number of cases is small I feel that they have a definite value in that the patients were followed up in a way that is not usually possible in practice. Quite short courses have been reported as giving a big proportion of cures, but such are certainly not effective here. It may be that, if, instead of returning to work when their temperature has been normal for forty-eight hours, as patients do here, they rest for two or three weeks, they would do better on short treatments.

A few days quinine followed by three days atabrin appears to be useless as a cure, but two weeks quinine followed by nine days atabrin, three tablets daily, is promising and worthy of further trial.

In the treatment of the attack of fever twenty grains of quinine daily appear to be quite as efficacious as the larger doses, which only aggravate the discomfort of the patient. When quinine cannot be taken orally, intramuscular injections are effective, and these, given into the gluteus muscles, appear to have no untoward consequences. I used to give these injections very freely, but since I have used adrenalin to control vomiting they are hardly ever called for. The bilious remittent type of fever with its severe vomiting is unusual here, or they might be more often required. My assistants still continue to give a large number of injections and have an unshakable belief in them. They generally give them when the patient has had fever for about three days with quinine orally. The temperature comes down shortly after, as would be expected in any case, and doctor and patient are quite satisfied.

Only a few out of the many can be given a three months' treatment, and some even of the few will fail to stay the course, but the individual who can and does will, I believe, not be disappointed.

Discussion

The Malaria Commission say 'During the primary attack it may not be safe to abstain

for a day or two from giving a specific drug, but it is quite safe to do so in the first and any subsequent relapse'. This is a very sweeping statement, and, in my opinion, questionable. My own observation is that relapses may on occasion be more severe than the primary attack. A common history in a coolie child is two or three days fever treated with quinine; after ten days to three weeks the child has more fever, for which he is not brought for treatment, and he dies with convulsions on the second to the fourth day of the presumed relapse. Neither is the infection necessarily malignant tertian for that to occur. It is true that in the case of malignant tertian to some extent the Commission's advice is qualified, but the doctrine is an exceedingly dangerous one to preach to the laity, for blackwater fever most frequently occurs in just those patients who have been unadvisedly taking quinine on the lines recommended by the Commission. Moreover, a permitted relapse may take the cerebral form with disastrous consequences.

The ideal of the Commission appears to be Lagos and similar places, where nearly all the children and half the adults harbour parasites, and yet appear healthy. But has the toll taken in the process of acquiring this clinical immunity been considered, or that the scales are weighted against the patient in the case of intercurrent disease, accident, or maternity?

Not at least to attempt, as far as drugs and circumstances permit, a thorough treatment and cure would appear to be a policy of retrogression, more especially with the newer synthetic preparations at our command. The much-sought specific has yet to appear, but will probably be not long delayed. Recently an advertisement of a proprietary preparation announced the cure of numerous cases with one powder. Let us hope this flight of fancy will soon really materialize.

[Note.—The writer of the paper has just retired after many years of practice in Assam; during these years he has acquired a reputation as an astute clinical observer; we therefore welcome this summary of certain aspects of his clinical experience in the treatment of malaria. The figures he gives are not large, but, as he says, they make up in quality what they lack in quantity for he has had exceptional opportunities of following up his cases.

We note that he gives, as one of the reasons for the occurrence of relapses, failure to take the full course, some of his patients admitting their delinquency. His observation that 'courses limited to about six weeks appear to fail', seems to be dependent on the admissions of these delinquents, but is he certain that all of his 'successes' completed the full course of treatment? It seems possible that he did not question these patients nearly so closely.

Whilst we heartily agree with the writer that experience gained in Epsom is not necessarily applicable in Luskerpore, we must point out that, though he has shown that his three months' course will effect a reasonably good cure rate, he has produced no evidence to show that a shorter one would not have been equally effective.—EDITOR, *I.M.G.J.*