

CHLOROQUINE-RESISTANT FALCIPARUM MALARIA

IN SOUTH-EAST ASIA, WITH A REPORT OF A CASE FROM THAILAND

Colonel R. MONTGOMERY

M.B., M.R.C.P., F.R.F.P.S.(Glas.), late R.A.M.C.

Consultant in Medicine, British Military Hospital, Kinrara

Introduction

THE presence of chloroquine-resistant strains of *Plasmodium falciparum* in South-East Asia is now fully established.

At a UNESCO symposium on tropical parasitology, held in Singapore in November 1962, Dr. (Mrs.) Harinasuta described clinical cases from Thailand in which chloroquine resistance was probable. Young *et al.* (1963) have also reported on a chloroquine-resistant strain of *P. falciparum* from Thailand.

Montgomery and Eyles (1963a) encountered chloroquine-resistant malaria in Commonwealth troops who were operating in North-West Malaya from August to October 1962, and this finding was confirmed by the same authors when they studied cases of falciparum malaria from another unit which operated in the same region of Malaya from October to December 1962 (Montgomery and Eyles, 1963b).

Eyles *et al.* (1963) reported on similar chloroquine-resistant cases from Cambodia and the findings of both the Malayan and Cambodian series were confirmed when strains from these cases were inoculated into prison volunteers in the U.S.A. (Con-tacos *et al.*, 1963). In early 1963, Sandosham *et al.* carried out a survey of the indigenous population in the area of Malaya in which the Commonwealth troops had been deployed and found a high incidence of chloroquine resistance in falciparum infections.

Chloroquine resistance is also present in South Vietnam, as Powell *et al.* (1963) have reported on a resistant strain acquired by an American marine corps officer from that area.

In general it is found that the chloroquine-resistant strains of *P. falciparum* are also resistant to other antimalarial chemotherapeutic drugs (amodiaquine, mepacrine, pyrimethamine and proguanil), with only slight variation according to locality of origin.

There is little doubt that this poses a problem in South-East Asia in military medicine as it is certain that the indigenous peoples provide a large reservoir of falciparum infection, a high percentage of which may be chloroquine resistant (Sandosham *et al.*, 1963). The following case history indicates the type of problem which is being encountered.

Case History

Cpl. L., a soldier in a Commonwealth unit, returned to Singapore on 27th June, 1963, after a period of three weeks in Thailand on exercise.

He moved back to his base camp near Malacca on 2nd July, 1963, and was well until 9th July, 1963, when he complained of fever and headache. During the period of the exercise and since his return he had been taking 200 mg. proguanil daily and did not admit any lapse in this regime. He was an intelligent N.C.O. and was regarded as a reliable witness. He was admitted to the Medical Reception Station at his camp on 11th July and transferred to the British Military Hospital at Kinrara on 16th July, 1963. He was febrile on admission (102°F.) and blood slides showed a moderately heavy infection with *P. falciparum*—Hb. 79 per cent, W.B.C. 5,800. The spleen was not palpable. Chloroquine was given orally commencing p.m. 16th July, 1963, and the parasite count on 17th July, 1963, was 19,255 per c.mm. On this day he was given 200 mg. chloroquine base intramuscularly on two occasions and the oral chloroquine was continued until 20th July, 1963, when he had received a total dose of 2.8 Gm. chloroquine base. He became afebrile on 19th July, 1963, but fever recurred on 21st July, although he had no specific complaints. The parasitaemia did not clear.

Date	Asexual Parasites per c.mm.	Highest Fever °F.
17/7/63	19,255	102
18/7/63	3,774	99 ⁴
20/7/63	555	98 ²
21/7/63	132	99 ²
22/7/63	143	98 ⁸
23/7/63	413	99 ⁶
24/7/63	1,582	100 ⁴
25/7/63	3,345	99 ⁸
26/7/63	701	99
27/7/63	8	98 ⁶
29/7/63	Neg.	97 ⁸

Quinine hydrochloride 2 Gm. daily was given from 25th July for ten days. The patient became afebrile on 28th July and asexual parasites had cleared by 29th July. A gametocytaemia persisted until 12th August, 1963. The plasma chloroquine level on 22nd July was 349µg. litre.

Discussion

The present case of chloroquine-resistant *P. falciparum* malaria acquired in Thailand represents a more resistant strain than that occurring in previously reported Service patients who acquired their infection in North Malaya (Montgomery and Eyles, 1963b). The infections of North Malaya all showed some response to chloroquine in that the standard regime of 2.4 Gm. usually produced a temporary clearance of parasites for periods of 14 days and upwards.

Not only did this patient's blood fail to be cleared of parasites, but the dose of chloroquine (2.8 Gm. base), which included intramuscular doses, was greater than the usual regimen employed in the treatment of malaria. A satisfactory blood level was obtained as is shown by the plasma chloroquine level of 349µg. litre 48 hours after the last dose of the drug.

The problem is a serious one as Commonwealth troops may be widely deployed in South-East Asia and with the advent of air-trooping possible infected cases may be widely dispersed. It is also possible that such cases may return to the United Kingdom and, if the possibility of chloroquine resistance is not considered, a grave danger to the patient may arise.

To date quinine has been a very effective drug in clearing the chloroquine-resistant falciparum infections, usually employed in a ten-day course of approx. 2 Gm. quinine hydrochloride daily (10 gr. t.d.s.). However, this situation must also be watched closely as Powell *et al.* (1963) have reported failure of a seven-day course (1,620 mg. daily) to clear the parasitæmia in two out of four cases of a South Vietnam strain infection.

Summary

A brief note on the presence of chloroquine-resistant *P. falciparum malaria* in South-East Asia is given and a case of chloroquine-resistant falciparum malaria acquired in Thailand is described.

The inherent dangers of the present situation are also pointed out, especially those connected with troop movements.

Acknowledgments

I am indebted to my colleague, Dr. D. E. Eyles, and his staff at the Institute for Medical Research, Kuala Lumpur, not only for the parasite counts but for ever-ready help and advice.

The plasma chloroquine levels were performed at the Laboratory of Parasite Chemotherapy, Bethesda, Maryland, through the courtesy of Dr. Coatney.

Editor's Note. Since this article was prepared for publication we regret the sudden death of Dr. D. E. Eyles in October, 1963, just before his departure to the United States on retirement.

REFERENCES

- CONTACOS, P. G., LUNN, J. S., and COATNEY, G. R. (1963). *Drug-resistant falciparum malaria from Cambodia and Malaya. Trans. roy. Soc. trop. Med. Hyg.*, **57**, 417.
- EYLES, D. E., HOO, C. C., WARREN, MCW., and SANDOSHAM, A. A. (1963). *Plasmodium Falciparum resistant to chloroquine in Cambodia. Amer. J. trop. Med. Hyg. (in the press)*.
- HARINASUTA, M. (1963). *Chloroquine-resistant falciparum malaria in Thailand. Proc. UNESCO Symposium on Tropical Parasitology, Singapore (in the press)*.
- MONTGOMERY, R., and EYLES, D. E. (1963a). *Chloroquine-resistant falciparum malaria in Malaya. Trans. roy. Soc. trop. Med. Hyg.*, **57**, 409.
- MONTGOMERY, R., and EYLES, D. E. (1963b). *A further study of chloroquine-resistant falciparum malaria in Malaya with observation on cross-resistance and response to other drugs. Bull. Wld. Hlth. Org. (in the press)*.
- POWELL, R. D., BREWER, G. J., and ALVING, A. S. (1963). *Chloroquine-resistant Plasmodium Falciparum from Vietnam (in the press)*.
- SANDOSHAM, A. A., EYLES, D. E., PULL, J. H., and LING DING SEND (1963). *Chloroquine-resistant falciparum malaria in a semi-immune indigenous population in North Malaya. Bull. Wld. Hlth. Org. (in the press)*.
- YOUNG, M. D., CONTACOS, P. G., STITCHER, J. E., and MILLAR, J. W. (1963). *Drug resistance in Plasmodium Falciparum from Thailand. Amer. J. trop. Med. Hyg.*, **12**, 305.