Research Note

## A Study on Chloroquine Resistance of *Plasmodium falciparum* in Tanga, Tanzania 1989-1991

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(Accepted for publication; September 9, 1992)

Key words: Chloroquine resistance, Plasmodium falciparum, Tanzania

The Tanzania/Japan Urban Malaria Control Project was started in the City of Dar es Salaam and the Municipality of Tanga in August 1988 and epidemiological monitoring was initiated in March 1989. The present study was undertaken in Tanga in 1989, 1990 and 1991 as one of the Urban Malaria Control Project activities. *In vivo* assessment of the sensitivity of *Plasmodium falciparum* to chloroquine was carried out.

Chloroquine resistance was first recorded in the Africa continent in 1978 when non-immune visitors who had acquired their infections in Kenya or Tanzania failed to respond to a full regimen of chloroquine (Centre for Disease Control 1978). Since then Chloroquine resistant *P.falciparum* strains have been observed in various parts of the United Republic of Tanzania (Schwants *et al.*, 1983, Draper *et al.*, 1988, Kilimali and Mkufya, 1985, Kilimali, 1989).

Studies carried out in 1970 on asymptomatic school children in different localities in north-eastern Tanzania, showed that 5 mg of chloroquine base per kg of body weight produced a complete *P.falciparum* trophozoite clearance

within 72 hours of administration of the drug (Lelijveld and Mzoo, 1970). This situation changed in the studies carried out in 1975 which showed that 10 mg chloroquine base per kg of body weight could not achieve a complete clearance of asexual parasitaemia of *P. falciparum* in the same areas as those studied in 1970 (Goosen, 1975).

By 1983, the situation had changed significantly and a standard therapeutic regimen of 25 mg chloroquine base per kg of body weight could not produce a complete clearance of asexual parasites in 13–40% of the cases studied in different areas (Kilimali, 1989). In Dar es Salaam 17% resistance has recently been reported by Nishimura (1991).

Among those data, the highest degree of resistance was observed in the Tanga region which exactly coincides with the epicentre of the pyrimethamine resistance reported by Clyde in 1967.

This study was conducted in May to June 1989, November 1990 and October 1991 in the following schools; Kana, Mapirani, Kwanjeka, Mwakidila, Mabokweni and Kiomoni primary schools. All asymptomatic school children were chosen from standard I to IV (7–14 years'old) and blood samples were taken for the preparation of thin and thick films. These smears were stained with 10% Giemsa solution in pH 7.2 buffered distilled water for 30 minutes. The slides were examined for malaria parasites.

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The WHO standard field test (WHO 1973) was used to measure the *in vivo* response to chloroquine. This involved the administration of 25 mg chloroquine base per kg of body weight in divided doses over a period of three days (10 mg/kg body weight on the first and second days and 5 mg/kg body weight on the third day). The children who had taken chloroquine as prescribed for 3 days were given a repeat blood examination on the 5th, 6th or 7th day.

The results obtained from this study are shown in Table 1. Clearance of parasitaemia was not achieved in 23 (13%) out of 173 subjects studied in 1989, 22 (18%) out of 120 subjects studied in 1990 and in 10 (22%) out of 46 subjects studied in 1991. The degree and frequency of chloroquine resistance varied from place to place in Tanga region.

The resistance percentage was observed to increase slightly from 1989 to 1991 but difference was not statistically significant ( $\chi^2 = 2.424$ , n.s.). However, a study of chloroquine resistance in Tanga Region in 1984 showed 31.8% resistance by the *in vivo* test (Kilimali and Mkufya, 1985). The results of the present study shown in Table 1 indicates some decline in resistance in recent years.

These results may suggest that individual children had been maintaining infections of chloroquine resistant strains for a long period. From records of visits to houses a case of Makidila was noted of a household where two children live. One of the children, a forteen year old girl, had parasitaemia at all 4 examinations

whereas the other, a twelve year old boy was never found to be infected. It is suspected that the former had maintained an infection with a single resistant strain over one year period.

Where there is chloroquine resistance it is difficult to correctly evaluate Malaria control activities because even if Vector Control were to prevent any further transmission, persistent infections would maintain the malaria prevalence for a considerable period. The continuous application of effective complete treatment as well as eradication of *P.falciparum* gametocyte with primaguine should prevent chloroquine resistance spreading.

## Acknowledgements

The authors thank all the school children and teachers for their co-operation, Dr. C.F. Curtis, Dr. V.A.E.B. Kilimali for their critical reading of the muniscript, and L. Kilamile, A. Mohamed for their assistance in carrying out this work. The Ministry of Health, Tanzania, the Dar es Salaam City Council, the Tanga Municipality, the Ministry of Foreign Affairs, Japan and the Japan International Cooperation Agency supported this study.

## References

- Centre for Disease Control (1978): Chloroquineresistant malaria acquired in Kenya and Tanzania. Denmark, Geogia, New York. Mortality and Morbidity Weekly Report 27, 463–464.
- Clyde, D. F. (1967): Malaria in Tanzania, London, Oxford University Press.
- Draper, C. C., Hills, M., Kilimali, V. A. E. B. and Brubacker, G. (1988): Serial studies on the evolution of drug resistance in malaria in an area of East

Table 1	Chloroquine	resistance	in	Tanga	school	children

School	% with persistent 1989 May–June	Parasitaemia 1990 November	At day 5-7 1991 October
Kana	9 (2/20)	10 (2/16)	
	8 (3/39)	19 (3/16)	_
Mpirani	15 (6/41)	8 (1/13)	_
Mwakidila	3 (1/36)	29 (2/7)	18 (3/17)
Kiomoni	_	18 (6/34)	_
Kwanjeka	_	18 (4/24)	19 (3/16)
Mabokweni	23 (13/57)	23 (6/26)	31 (4/13)
Total	13 (23/173)	18 (22/120)	22 (10/46)

- Africa: Findings from 1979 up to 1986. J. Trop. Med. Hyg., 91, 265.
- Goosen, T. J. (1975): Studies on the sensitivity of P.falciparum to antimalarial drugs. Studies at Kicheba and Toro. Annual Report of the East African Institute of Malaria and Vector-Borne Diseases.
- 5) Kilimali, V. A. E. B. and Mkufya, A. R. (1985): In vivo and in vitro assessment of the sensitivity of P.falciparum to chloroquine in four districts of Tanga region, Tanzania. Trans. Roy. Soc. Trop. Med. Hyg., 79, 478.
- 6) Kilimali, V. A. E. B. (1989): Drug resistance of Plasmodium falciparum and the use of local herbs in the treatment of malaria in Tanzania. In: PhD thesis, London School of Hygiene and Tropical

- Medicine, University of London.
- Lelijveld, J. and Mzoo, F. (1970): The effects of small single doses of chloroquine on *P.falciparum* in north-eastern Tanzania. Bulletin of the World Health Organization, 42, 471–477.
- Nishimura, M. (1991): Proceedings of the Second Joint Technical Meeting, Dar es Salaam and Tanga Urban Malaria Control Project. 18–19 June.
- Schwats, I. K., Campbell, C. C., Payne, D. and Khatib, O. J. (1983): In vivo and in vitro assessment of chloroquine resistant Plasmodium falciparum malaria in Zanzibar. Lancet (i) 1003-1005.
- World Health Organization (1973): Chemotherapy of malaria and resistance to anti-malarials. WHO Technical Report Series. No. 529.