

Short Report

Stabilization of chloroquine resistance *in vivo* of *Plasmodium falciparum* in Edea, south Cameroon

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Chloroquine resistant falciparum malaria has rapidly spread over central and west Africa (WERNSDORFER & PAYNE, 1991). In southern Cameroon chloroquine resistance was first reported by SANSONNETTI *et al.* (1985). We measured chloroquine sensitivity *in vivo* of *Plasmodium falciparum* in May 1989 and 1991 in schoolchildren in the town of Edea, southern Cameroon, and observed considerable increase over 2 years (GAZIN *et al.*, 1990; MULDER *et al.*, 1992). Parallel studies *in vivo* in

Table 1. Characteristics of schoolchildren in Edea, Cameroon, in May of 1989, 1991 and 1993 before antimalarial treatment

	1989	1991	1993
Number	190	191	197
Age (years)	9.0	8.9	8.4
Weight (kg)	25.9	26.6	25.1
Sex (male%)	45.0	51.4	50.3
Parasite rate (%) ^a	64.5 (63.1)	67.4 (63.3)	56.9 (50.8)
GMPD ^b	447	501	489
Spleen rate	27.0	27.0	23.9
Spleen Size ^c	1.46 (±0.66)	1.70 (±0.74)	1.79 (±0.62)

^aNumbers in parentheses are the percentages of *P. falciparum* infections.

^bGeometric mean parasite density (parasitized red blood cells/mm³ of blood) on day 0.

^cAverage enlarged spleen according to Hackett (see MANSON-BAHR & BELL, 1987); standard deviations are given in parentheses).

Yaoundé, the capital of Cameroon, suggested that chloroquine resistance was stabilizing (LOUIS *et al.*, 1992a). To monitor the evolution of resistance *in vivo* of *P. falciparum* in our study population we repeated the test in the same school classes in May 1993.

All pupils present on the first day of the study (day 0) were given 25 mg/kg chloroquine base orally over 3 d under supervision. Spleen rate, weight and parasite density were assessed. Parasite densities were also assessed on days 3 to 7. Subjects with a parasitaemia on day 0 exclusively of *P. falciparum*, with parasite counts of at least 500 trophozoites/mm³ and who had taken their 3 d treatment on days 0, 1 and 2, were included in the sensitivity test.

Over the 3 studies, the groups did not differ significantly in number, age, weight, sex, spleen rate or parasite density on day 0 (Table 1). Sixty-eight children met the enrolment criteria in 1989, 52 in 1991 and 51 in 1993. Their parasitological results are given in Table 2.

Between 1989 and 1991 parasite resistance *in vivo* had increased significantly from 17.5% to 44%. In 1993 an overall resistance percentage of 31.5 was observed. Two subjects (2.9%) showed RII resistance (no reduction in parasitaemia) in 1989; in 1991 this was so for 4 (7.7%),

Table 2. Prevalence and intensity of *Plasmodium* parasitaemia in schoolchildren in Edea, Cameroon, who were included in the chloroquine resistance test *in vivo*

	1989	1991	1993
No. of children (day 0)	68	52	51
Parasite rate (%)			
Day 3	24	38	51
Day 7	17.5	44	31.5
Geometric mean parasite density (per mm ³)			
Day 0	1585	1993	2754
Day 3	40	141	85
Day 7	141	108	87

while in 1993 only 2 cases (3.9%) of RII resistance were observed.

We conclude that, after rapid emergence, chloroquine resistance has stabilized or may even be regressing in this region, as was also found for other central and west African countries (BASCO *et al.*, 1993). No explanation has been given for this phenomenon, but changing consumption towards other antimalarial drugs might play a role. In 1991 one-third of the patients presenting at a dispensary in Edea stated that they had taken quinine at home, often at insufficient doses (B. Mulder, unpublished data). Our findings indicate that chloroquine remains useful for home medication, while for first line treatment amodiaquine at a dose of 35 mg/kg over 3 d was found to be efficient (LOUIS *et al.*, 1992b). Although encouraging, stabilization of resistance *in vivo* might be temporary, emphasizing the need for constant monitoring in central African countries in order to adapt therapeutic schemes.

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References

- Basco, L. K., Ringwald, P., Simon, F., Doury, J. C. & Le Bras, J. (1993). Evolution of chloroquine resistance in central and west Africa. *Tropical Medicine and Parasitology*, **44**, 111-112.
- Gazin, P., Louis, J. P., Mulder, L., Eberle, F., Jambou, R., Moyroud, J. & Hengy, C. (1990). Evaluation par test simplifié *in vivo* de la chimiosensibilité du *Plasmodium falciparum* à la chloroquine et à l'amodiaquine dans le sud du Cameroun. *Médecine Tropicale*, **50**, 27-31.
- Louis, J. P., Louis, F. J., Trebucq, A., Migliani, R., Cot, M. & Hengy, C. (1992a). Chemoresistance of *Plasmodium falciparum* in central Africa. *Lancet*, **340**, 610-611.
- Louis, J. P., Hengy, C., Louis, F. J., Gazin, P., Jambou, R., Gardon, J., Fadat, G. & Trebucq, A. (1992b). Proposals for a new therapeutic strategy for simple *Plasmodium falciparum* malaria attacks in Cameroon. *Tropical Medicine and Parasitology*, **43**, 118-120.
- Manson-Bahr, P. E. C. & Bell, D. R. (1987). *Manson's Tropical Diseases*, 19th edition. London: Baillière Tindall, p. 43.
- Mulder, B., Gazin, P., Eggelte, T. A. & Cot, M. (1992). Increase of chloroquine resistance *in vivo* of *Plasmodium falciparum* over two years in Edea, south Cameroon. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, **86**, 376.
- Sansonetti, P. J., Le Bras, J., Verdier, F., Charmot, G. & Lapresle, C. (1985). Chloroquine resistant *Plasmodium falciparum* in Cameroon. *Lancet*, **i**, 1154-1155.
- Wernsdorfer, W. H. & Payne, D. (1991). The dynamics of drug resistance in *Plasmodium falciparum*. *Pharmacological Therapy*, **50**, 95-121.

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