In vivo seasonal assessment of *Plasmodium falciparum* sensitivity to chloroquine in two different malaria endemic communities in Southern Ghana

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SUMMARY
A two year (1992 to 1993) *in vivo* assessment of *Plasmodium falciparum* sensitivity to chloroquine was conducted in two communities at Dodowa (hyperendemic) and Prampram (mesoendemic) in Southern Ghana. A slightly modified World Health Organization standard field test (7 day test) for response of *Plasmodium falciparum* asexual parasites to chloroquine was used for the survey. In 1992, 16.2% (12/74) responses were classified as exhibiting chloroquine resistance at RI (14.8%) and RII (1.4%) in the dry season and 8.2% (10/122) responses at RI in the wet season in the hyperendemic community. Only a single response (1/144; 0.7%) at RI showed resistance in the mesoendemic community. The rest of the responses in both communities were classified as sensitive to chloroquine. In the hyperendemic community, 8.4% (13/154) of responses in the dry season showed resistance at RI and 1.3% (82/150) at RI (0.7%) and RII (0.7%) in the wet season in 1993. In the mesoendemic community 1 (1.0%) response was resistant at RI in the wet season. The rest of the responses were classified as sensitive responses to chloroquine. No RIII response was encountered in any of the communities. The pattern of RI and RII responses did not show any seasonal variations in the mesoendemic community. However, they were generally higher in the dry season than in the wet season in the hyperendemic community.

Introduction
The Ministry of Health of Ghana launched its action plans for malaria control in Ghana in November, 1992. The action plans aim principally at reducing malaria-related mortality through early diagnosis and effective treatment. The Noguchi Memorial Institute for Medical Research (NMIMR) has started collecting community-based information on malaria morbidity, mortality, transmission and extent of *P. falciparum* resistance to available antimalarial drugs as its contribution to the national effort. The information collected will serve as a basis for the evaluation of the malaria control programme in Dangme West District in Southern Ghana where the NMIMR is currently conducting its studies.

Chloroquine is the drug of choice for the treatment of malaria in Ghana. A two year *in vivo* assessment of *P. falciparum* sensitivity to chloroquine was conducted in the dry and wet seasons of the year in two different communities (hyerendemic and mesoendemic) in the Dangme West District in the Greater Accra Region of Ghana.

Materials and Methods
The study was conducted in Dodowa and in Prampram in the Dangme West District in the Greater Accra Region of Ghana in the dry (March) and wet (July) seasons in 1992 and in 1993. The two communities are rural and Dodowa is the capital of the district which was created in 1988. Dodowa is in the forest and hyperendemic area of the district and has a population of 6558 (1992 census). Prampram which has a population of 6682 (1992 census) is in the Coastal Savannah and mesoendemic area of the district. A simple random sampling method was used to select one primary school in each community in the dry and wet seasons for the sensitivity survey in 1992 and in 1993. All children aged 6 - 15 years who were present on the day of the survey in the selected primary schools were screened for the *in vivo* assay.

A slightly modified World Health Organization standard field test (7 day test) for the response of *P. falciparum* asexual parasites to chloroquine was used for the survey. Finger-prick capillary thick and thin blood films stained with Giemsa stain were used to examine school children for malaria parasitaemia. The presence of chloroquine and its metabolites in urine on the day the blood films were prepared was determined using Haskins MM II test [2]. All children with at least 500 *P. falciparum* asexual parasites per 8,000 white blood cells and with no chloroquine detected in their urine were included in the study; those with mixed infections were excluded. Children
who were seriously ill and needed admission were also excluded from the study.

Children were given (under supervision) 10mg/kg body weight of chloroquine base orally on the following day, designated as day zero, and on day one. On day two 5mg/kg body weight of chloroquine base (Pharmaceutical Division of the Ghana Industrial Holding Corporation) was given orally. Finger-prick capillary blood films were prepared on days 0, 2, 4 and 7 and stained with Giemsa's stain. 10 percent of all positive slides and all negative slides were re-examined by a second person. Urine specimens were collected on days 0, 2, 4 and 7 and tested for the presence of chloroquine or its metabolites. *P. falciparum* was considered sensitive or resistant depending on the persistence of asexual parasites during the follow-up period of 7 days after chloroquine administration [3].

**Results**

In 1992, a total of 512 children in Dodowa (hyperendemic area) and 681 in Prampram (mesoendemic area) were screened for malaria infection. The prevalence of malaria infection (patent parasitaemia) in children during the two seasons in 1992 was 53.5 - 55.6% in Dodowa and 27.7 - 44.5% in Prampram (Table 1). In 1993, 605 children in Dodowa and 689 in Prampram were screened for malaria infection. 56.9 - 57.9% and 33.1 - 42.4% of the children had patent parasitaemia in Dodowa and Prampram respectively. In 1992, the proportion of tests in the dry and wet seasons in both communities classified as sensitive responses ranged from 83.8 - 100%. 16.2% (12/74) responses were classified as exhibiting chloroquine resistance at RI (14.8%) early and RII (1.4%) in the dry season and 8.2% (10/
responses at RI early in the wet season in the hyperendemic community. Only a single response (1/114; 0.7%) at RI showed resistance in the meseoendemic community (Table 1).

In 1993, 91.6 - 100% responses in both communities in both dry and wet seasons exhibited full sensitivity to chloroquine. 8.4% (13/154) of responses showed at RI in the dry season and 1.3% (2/150) at RI (0.7) early and RI (0.7) in the wet season in the hyperendemic community while 1(1.0%) response was resistant at RI early in the wet season in the meseoendemic community while 1(1.0%) response was resistant at RI early in the wet season in the meseoendemic community (Table 2).

The pattern of RI and RII responses did not show any seasonal variations in the meseoendemic community. However, they were generally higher in the dry season than in the wet season in the hyperendemic community (Table 1 and 2).

Discussion

The level of chloroquine resistant Plasmodium falciparum in the two rural communities (Dodowa and Prampram) in this study is low and mainly RI (early). It confirms the findings that P. falciparum resistance to chloroquine in vivo is generally low and also relatively lower in the rural communities in Ghana [4]. Other studies in Nigeria [5] and in The Gambia [6] have also shown that P. falciparum resistance to chloroquine is generally lower in West Africa than in East Africa [7].

The RI (early) levels found in the hyperendemic community (Dodowa) did not increase over time. It has rather decreased from 14.8% in 1992 to 8.4% in 1993 in the dry season and from 8.2% in 1992 to 7.0% in 1993 in the wet season. The RI (early) responses were found mainly at Dodowa. Dodowa which is the capital of the newly created Dangme west district is gradually developing the characteristics of an urban community with greater accessibility to chloroquine and other antimalarial drugs. This may explain the emergence of RI (early) responses in Dodowa.

Malaria is endemic throughout the year in Ghana but the incidence is higher in the wet season than in the dry season. However, the pattern of RI and the few RII responses recorded in this study do not show any seasonal variations in the meseoendemic community, but they are generally higher in the dry season than in the wet season in the hyperendemic community. This phenomenon was observed throughout the study period of two years. It is also possible that natural selection of the parasite takes place in the dry season when transmission is generally low in endemic communities resulting in a high probability of detecting chloroquine resistant P. falciparum during the dry season.

P. falciparum sensitive responses to chloroquine, the drug of choice for the treatment of malaria, remain very high in Ghana since P. falciparum resistance in vivo to chloroquine was first reported in 1988 [8,9]. There is practically no RII and definitely no RIII P. falciparum responses to chloroquine in the two rural communities. Since the WHO 7 days test used in this study does not provide information on RI late resistance, the

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114


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