

ASSESSMENT OF THE INCIDENCE AND PREVALENCE OF CLINICAL  
MALARIA IN SEMI-IMMUNE CHILDREN EXPOSED TO INTENSE AND  
PERENNIAL TRANSMISSION.

J. F. TRAPE, A. ZOULANI, AND M. C. QUINET

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In order to determine the incidence and prevalence of clinical malaria in children exposed since birth to intense and perennial transmission, two successive longitudinal surveys, a weekly survey over four months and a daily survey over 10 days, were carried out in 1983-1984 among 182 children aged 5-13 years in Linzolo, Republic of the Congo, a village where malaria is holoendemic. By age group, prevalence of clinical malaria was found to be between 3.2% and 2.4% at ages 5-6 years, between 2.5% and 1.8% at ages 7-8 years, between 1.6% and 1.1% at ages 9-10 years, and between 0.5% and 0.3% at ages 11-13 years. For these four age groups, respectively, the annual incidence of clinical malaria was estimated during the first survey as 3.0, 2.1, 1.8, and 1.2 attacks, and during the second survey as 5.2, 2.7, 2.0, and 0.8 attacks. No difference was observed in the incidence of malarial attacks between children who use bed-nets and those who do not use them. Also investigated were the customs of the inhabitants of the village in the presence of febrile syndromes in the children, and the importance of antimalarial drug consumption in these cases. It was observed that almost all of these syndromes were rapidly treated with antimalarials, and that in half of the cases these drugs were administered by the parents themselves.

child care; child health services; longitudinal studies; malaria; morbidity; *Plasmodium falciparum*

The diagnosis of clinical malaria in semi-immune subjects presents difficult methodological problems in regions of intense malarial endemicity. The presence or absence of parasites in a febrile patient is insufficient evidence for diagnosis in these

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From the Laboratoire de Parasitologie et d'Entomologie Médicale, Centre ORSTOM, B.P. 181, Brazzaville, République Populaire du Congo.

Send reprint requests to Dr. J. F. Trape, ORSTOM, B.P. 1386, Dakar, Sénégal.

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regions, since the thick blood film is usually positive whatever the clinical context, as in healthy individuals. As a result, estimates of the incidence of clinical malaria in Africa carry a wide range of uncertainty. Few precise data are available under conditions of high endemicity, and the impact of different degrees of malaria control in terms of morbidity in each age group has never been assessed with any certainty (1, 2).

The primary health care system and the prospect of a malaria vaccine urgently require the development of operational methods for precise assessment of clinical malaria incidence and prevalence. A recent study (3) indicated that, with a small margin of error, it is possible to use the para-

site/leucocyte ratio to determine whether or not malaria is responsible for a febrile syndrome in a child living in an area of intense perennial transmission. In the present study, this method was combined with longitudinal temperature surveys in order to specify the incidence and prevalence of clinical malaria under typical conditions of holoendemicity in children aged 5–13 years. Simultaneously, certain antimalarial practices and their impact on clinical malaria were studied.

#### MATERIALS AND METHODS

##### *Study area*

The village of Linzolo is situated 25 km south-west of Brazzaville in the Republic of the Congo. There are approximately 1,000 inhabitants, whose main activity is traditional agricultural farming (fruit and food crops). Health care is available to the population through a large medical center within a Catholic mission set up in the village. Malaria transmission is perennial and remains intense for most of the year (4). From October through June, the average number of infective bites per person per night is 0.85, or 6.0 infective bites per person per week. From mid-June through September (the coolest and driest season of the year), transmission decreases, with an average of one infective bite per person per week. The main vector is *Anopheles gambiae*, which represents nearly 90 per cent of captures on human bait. The other anophelids captured on man are *A. funestus*, *A. paludis*, *A. nili*, *A. hancocki*, and *A. moucheti*, but these are epidemiologically unimportant. During the four-month clinical study, 10 night-bite captures (58 person-night) were carried out on human bait. The average number of anophelid bites per person per night was 33.8, of which 31.9 were from *A. gambiae*. The sporozoite rate was 2.18 per cent. The malaria transmission intensity was thus 4.9 infective bites per person per week.

During the 10 surveys carried out between 1980 and 1984, the average malaria prevalence was 79.0 per cent in schoolchildren

aged 5–9 years (in a total of 700 thick smears) and 82.8 per cent in schoolchildren aged 10–14 years (of 825 thick smears). No seasonal variations were observed. *Plasmodium falciparum* was found on nearly all of the positive slides (98.7 per cent), while *P. malariae* and *P. ovale* were observed on average in, respectively, 18.6 per cent and 4.5 per cent of the schoolchildren (5). In a survey carried out during the present study in January 1984, the malaria prevalence was 86.5 per cent and 82.5 per cent in two random samples, respectively, of 37 schoolchildren aged 5–9 years and 40 schoolchildren aged 10–13 years.

Infant mortality in Linzolo and the surrounding villages is 71 per thousand; child mortality (ages 1–4 years) is 49 per thousand (6). These rates, which are relatively low for Africa, are now habitual in this region of the Congo (7, 8), and malaria is responsible for only low mortality, since clinical attacks are rapidly treated (9, 10).

##### *Methods*

Two surveys were carried out in schoolchildren, the first a weekly survey over four months, and the second a daily survey over 10 days. All children over five years of age attend school in this village.

*Weekly survey.* This survey included 179 schoolchildren aged 5–13 years and lasted for 17 weeks, from November 3, 1983 through March 1, 1984. Every Thursday (except one, during the school vacation), the axillary temperature of all children present was taken. The results were recorded on individual charts. If fever was observed, a thick blood film was taken, and various other clinical and biologic examinations were carried out, and the child was systematically treated with a single dose (20 mg/kg) of amodiaquin and 500 mg of aspirin. A total of 17 weekly sessions took place.

An individual survey was carried out for all children absent from school, to determine the reason for their absence, either on the day of the visit, during the following days, or when the child returned to school.

When the child was absent for medical reasons, the exact cause was investigated, especially if clinical malaria was suspected. This was done by questioning the child or the family and by examining the results of tests carried out in the medical center or thick blood films taken at the school in the interval between two weekly sessions.

At each weekly session, the schoolchildren were questioned, to single out those who had been ill during the week. Children who said they had been ill were asked to describe their symptoms and to indicate whether or not they had visited the medical center and been given treatment. If the latter was the case, the exact nature of the disease and the treatment prescribed were investigated by questioning the child or examining the child's health card.

In between the weekly sessions, the headmistress of the school noted the axillary temperature of any child who complained of sickness while in school. If the child was feverish, a thick blood film was prepared immediately and a single-dose treatment of amodiaquin and aspirin was given.

*Daily survey.* This survey included 171 schoolchildren aged 5-13 years, and lasted for 10 days, during the period April 17-26, 1984. These were essentially the same children as in the previous survey, with the difference that 11 children had left the school and three children had arrived in the interval of time between the two surveys. On every day of the survey, except the sixth day, which was Sunday, the axillary temperature of all the children present was taken (nine sessions). If the child was feverish, a thick blood film was taken and treatment was given immediately, as in the previous study. Each absence was investigated to determine the cause, and all the children were questioned daily to find out who had been sick in the interval between visits.

*Clinical and diagnostic methods.* All children with an axillary temperature equal to or more than 38 C were considered to be feverish. This temperature was chosen after analysis of the results of an investigation

into the individual variations in axillary temperature in Linzolo schoolchildren, and of over 3,000 readings of axillary temperature combined with systematic thick blood films in schools in the Congo (J. F. Trape, unpublished data). The parasitologic and clinical methods used have been described in two previous articles (3, 11). Only cases of fever combined with a parasite/leucocyte ratio superior or equal to 2 were considered "confirmed" *falciparum* malaria cases.

## RESULTS

### *Weekly survey*

*Results for schoolchildren present during the sessions.* Theoretically, the number of temperature readings for 179 schoolchildren over a period of 17 weeks should have been 3,043. In fact, the readings numbered only 2,997 due to the departure of seven schoolchildren who transferred to another school during the survey.

The total number of schoolchildren present—and of temperatures recorded—was 2,727 during the 17 sessions (table 1). Fever was observed in 65 cases (2.4 per cent). The proportion of febrile schoolchildren was 4.1 per cent in children aged 5-6 years, 3.2 per cent in those 7-8 years, 1.5 per cent in those 9-10 years, and 1.9 per cent in those 11-13 years.

In 30 cases (1.1 per cent), the fever was combined with a parasite/leucocyte ratio on thick blood film superior or equal to 2, thus attributing the febrile syndrome to *P. falciparum*. The proportion of schoolchildren present in whom clinical malaria was found was 2.3 per cent in the children aged 5-6 years, 1.7 per cent in those 7-8 years, 0.9 per cent in those 9-10 years, and 0.3 per cent in those 11-13 years.

*Results for schoolchildren absent during the sessions (table 2).* A total of 270 absences were recorded for the 17 sessions; 210 absences were for reasons other than medical reasons (in over half of the cases the child was temporarily suspended for nonpayment of school insurance); 53 absences were for medical reasons; and seven absences were for unknown reasons. For this

TABLE 1

Attendance of schoolchildren and prevalence of fever and clinical malaria during the weekly survey, Linzolo, Republic of the Congo, November 3, 1983–March 1, 1984

Age group (years)	No. of children*	Theoretic no. of attendances†	Actual no. of attendances	Cases of fever		Cases of clinical malaria	
				No.	%	No.	%
5-6	30 (1)	501	436	18	4.13	10	2.29
7-8	40 (2)	670	601	19	3.16	10	1.66
9-10	56	952	890	13	1.46	8	0.90
11-13	53 (4)	874	800	15	1.88	2	0.25
Total	179 (7)	2,997	2,727	65	2.38	30	1.10

\* Numbers of children who left the school permanently during the study period are shown in parentheses.

† Not including the 46 absences corresponding to departures during the study period.

TABLE 2

Causes of absence of schoolchildren from the weekly survey of clinical malaria, Linzolo, Republic of the Congo, November 3, 1983–March 1, 1984

Age group (years)	Unknown cause	Non-medical cause	Medical cause		
			Other than malaria	Confirmed clinical malaria	Possible clinical malaria
5-6	1	51	7	2	4
7-8	3	48	11	2	5
9-10	3	48	4	2	5
11-13	0	63	9	1	1
Total	7	210	31	7	15

last group, the survey to investigate the reason for absence was omitted; most of these absences were probably due to reasons other than medical reasons.

Of the 53 absences for medical reasons, a diagnosis of clinical malaria was ruled out in 31 cases, either after questioning the child and the child's family, checking the child's health card, or examination of the thick blood film. In seven cases, a diagnosis of clinical *falciparum* malaria was parasitologically confirmed (parasite/leucocyte ratio  $\geq 2$ ). In 15 cases it was not possible to positively confirm the diagnosis, due to the fact that the children had generally been treated at home by their parents without the examination of a thick blood film. The majority, however, were probably cases of clinical malaria.

Results for the intervals between sessions (table 3). Apart from episodes of illness which were observed during the weekly sessions and those which were the cause of

absence, 153 other episodes were reported by the schoolchildren during the four-month study. In 55 cases, a diagnosis of clinical malaria was ruled out, either by examination of the thick blood film or the child's health card, or by questioning; in 32 cases, the diagnosis was parasitologically confirmed (parasite/leucocyte ratio  $\geq 2$ ); and in 66 cases the diagnosis could not be confirmed because although these children described symptoms compatible with the diagnosis of a malarial attack, a thick blood film had not been taken or had not been kept for the parasite count.

*Prevalence of clinical malaria.* The total number of clinical malaria episodes which occurred during the weekly sessions (including all schoolchildren present or absent) was between 37 and 52, giving a minimum clinical malaria prevalence of 1.2 per cent and a maximum of 1.7 per cent.

By age group, the prevalence was between 3.2 and 2.4 per cent at ages 5-6 years,

between 2.5 and 1.8 per cent at ages 7-8 years, between 1.6 and 1.1 per cent at ages 9-10 years, and between 0.5 and 0.3 per cent at ages 11-13 years.

*Incidence of clinical malaria.* Table 4 shows the total number of clinical malaria episodes in each age group, and the average number per child, during the four months of the survey. It was not always possible to confirm parasitologically the suspected clinical malaria, and this explains the difference between the maximum and minimum values. However, taking into account information obtained on clinical malaria in Linzolo, it can be estimated that malaria is responsible for about half of these cases, and that for each age group the total number of clinical malaria episodes during the four months of the study can be reasonably represented by the average value of the minimum and maximum values shown.

On a yearly basis, this corresponds to 3.0

attacks in children aged 5-6 years, 2.1 attacks in those 7-8 years, 1.8 attacks in those 9-10 years, and 1.2 attacks in those 11-13 years.

#### Daily survey

Nine daily sessions over a period of 10 days were carried out for 171 schoolchildren. Theoretically, the number of temperature readings should have been 1,539, but the actual number taken was 1,424. Nineteen cases of fever (1.3 per cent) were observed, of which seven (0.5 per cent) were due to *falciparum* malaria attacks. These attacks were treated immediately, and never lasted more than one day.

Of the 115 absences, 74 were for reasons other than medical, and 34 had a medical cause other than malaria. For the seven other absences, in four cases clinical malaria was parasitologically confirmed, and in three cases the diagnosis could not be

TABLE 3

*Episodes of illness in schoolchildren during the intervals between the sessions of the weekly survey, according to age group and diagnostic category, Linzolo, Republic of the Congo, November 3, 1983-March 1, 1984*

Age group (years)	No. of episodes of illness			
	Other than malaria	Possible malaria	Confirmed malaria	Total
5-6	11	11	10	32
7-8	9	9	8	26
9-10	17	23	9	49
11-13	18	23	5	46
Total	55	66	32	153

TABLE 4

*Incidence of clinical malaria in schoolchildren over the four-month period of the weekly survey, according to age group, Linzolo, Republic of the Congo, November 3, 1983-March 1, 1984*

Age group (years)	No. of children/weeks	No. of episodes of clinical malaria		Mean no. of episodes per child during four months of study	
		Minimum*	Maximum†	Minimum	Maximum
5-6	501	22	37	0.75	1.26
7-8	670	20	34	0.51	0.86
9-10	952	19	47	0.34	0.84
11-13	874	8	32	0.16	0.62
Total	2,997	69	150	0.39	0.85

\* Confirmed cases of clinical malaria during the sessions of the weekly survey (schoolchildren present and absent) and those during the intervals between the sessions.

† Confirmed and possible cases of clinical malaria.

established due to the absence of a thick blood smear. Table 5 shows the results according to age. Apart from the above-mentioned episodes of illness, five other episodes were reported during the interval between sessions, but none led to suspected clinical malaria.

Thus, over the whole 10-day period, clinical malaria attacks were observed in four out of 28 children aged 5-6 years, three out of 40 children aged 7-8, three out of 55 children aged 9-10, and one child out of 48 children aged 11-13, while, in the age group 9-10 years, a further three children had possible attacks of clinical malaria.

Annually, these results would correspond to 5.2 attacks per year in children aged 5-6 years, 2.7 attacks in those 7-8 years, 2-4 attacks in those 9-10 years, and 0.8 attacks in those 11-13 years.

#### *Antimalarial practices in Linzolo*

*Use of mosquito-nets.* Mosquito-nets are fairly widely used in Linzolo, as in the whole of this region of the Congo. It was thus possible to compare the results observed for children who used mosquito-nets with those for children who did not use them.

Of the 182 children who participated in both the weekly and daily surveys, 46 (25.3 per cent) said that they used bed-nets: nine out of 30 children aged 5-6 years (30 per cent), 10 out of 42 children aged 7-8 years (23.8 per cent), 17 out of 57 children aged 9-10 years (29.8 per cent), and 10 out of 53 children aged 11-13 years (18.9 per cent).

Of 80 parasitologically confirmed attacks of clinical malaria, 27 (33.8 per cent) were observed in children who used bed-nets, and 53 (66.2 per cent) in children who did not use bed-nets. Taking into account the departures and arrivals of children during the study, and the different rates by age group of the children who used mosquito-nets, the estimated percentage of clinical malaria attacks in children who used mosquito-nets was 27.1 per cent. It can be seen that clinical malaria attacks were slightly more frequent in children who used mos-

TABLE 5  
Results of the daily survey of clinical malaria in schoolchildren carried out over a 10-day period, Linzolo, Republic of the Congo, April 17-26, 1984

Age group (years)	No. of children	Theoretic no. of attendances	Actual no. of attendances	No. of absences	Schoolchildren present			Schoolchildren absent			Total no. of cases of clinical malaria	
					No. of cases of fever	No. of cases of clinical malaria	Non-medical causes	Medical causes other than malaria	Confirmed clinical malaria	Possible clinical malaria	Minimum	Maximum
5-6	28	252	229	23	8	3	18	4	1	0	4	4
7-8	40	360	337	23	4	1	18	3	2	0	3	3
9-10	55	495	453	42	5	3	22	17	0	3	3	6
11-13	48	432	405	27	2	0	16	10	1	0	1	1
Total	171	1,539	1,424	115	19	7	74	34	4	3	11	14

quito-nets, but the difference is not statistically significant.

*Attitude towards febrile episodes and the use of antimalarial drugs.* The inhabitants of Linzolo have easy access to health care through the medical center situated in the village, run by the mission nurses. Moreover, this medical center is well stocked with drugs, and has an excellent reputation far beyond the village and its vicinity.

This being so, we decided to study the customs of the inhabitants of Linzolo in the presence of a febrile episode in a child, and the importance of antimalarial drug consumption in these cases. This study, carried out at the same time as the weekly survey, included 53 episodes of illness (in each instance, the illness was the cause of the child's absence during the visit), and 153 episodes of illness reported during the interval between visits.

The results are shown in table 6. It can be seen that a considerable proportion of episodes of fever or "headache" in children did not lead to medical visits; only 53.4 per cent of these children were examined (and treated) at the medical center or the school.

However, most of the children who were not examined medically did receive treatment directly from their parents. Out of 75 episodes of fever or headache in children who were not examined medically, 56 (74.7 per cent) were treated with antimalarials (alone or combined with other drugs), nine (12 per cent) were treated with other drugs, and only 10 (13.3 per cent) received no treatment.

Furthermore, since at the medical center it is usual to prescribe antimalarials (either alone or combined with other drugs) to persons with episodes of fever or "headache", the total consumption of antimalarials is high: on average, at each weekly session, the proportion of schoolchildren present who had received antimalarial treatment in the preceding eight days was 12.2 per cent at ages 5-6 years, 7.5 per cent at ages 7-8, 6.5 per cent at ages 9-10, and 5.9 per cent at ages 11-13.

#### DISCUSSION

The methodological problems encountered in measuring the incidence of clinical malaria in regions of high malarial endemicity constitute the main difficulty in carrying out this type of survey. This explains why little work has been done up to this point on the subject. Precise knowledge of the semi-immune African adult comes from the studies of Miller (12) and Bruce-Chwatt (13), who each closely followed a group of adults over a long period, both clinically and parasitologically. They found the annual number of clinical malaria attacks to be 1.5 and 0.5 per person, respectively. The difference between these two values can partly be explained by the lower average age of the group studied by Miller.

To our knowledge, the only corresponding studies in children are those of Colbourne (14), Wilson (unpublished data, quoted by Colbourne), and Miller (12). Colbourne (14) observed that, annually, in Accra, Ghana, children seven years of age

TABLE 6

*Distribution of 206 episodes of illness in schoolchildren during the weekly survey (including illnesses in intervals between survey sessions), according to symptoms described, place where the child was examined, and treatment received, Linzolo, Republic of the Congo, November 3, 1983-March 1, 1984*

	Location of examination							
	Medical center		School		Child not examined		Total	
	Fever or headache	Miscellaneous	Fever or headache	Miscellaneous	Fever or headache	Miscellaneous	Fever or headache	Miscellaneous
Total no. of cases	63	21	23	0	75	24	161	45
Antimalarials given	55	1	23	0	56	4	134	5

suffered on average 5-6 days of sickness due to malaria serious enough to lead to absence from school. These results were based on data that included those from two schools in different districts of Accra where malaria transmission intensity differed considerably. The lowest incidence of clinical malaria corresponded to the highest transmission intensity. In the unpublished study by Wilson in Ghana, cited by Colbourne (14), the average number of clinical malaria attacks in adolescents aged 12-20 years was estimated to be about 0.4 per year.

The study by Miller (12) in Liberia followed 10 children, aged 3-7 years, daily for two months, and, during this period, nine clinical attacks of malaria due to *P. falciparum* and five attacks due to *P. malariae* were observed. It should be noted that, in Linzolo, *P. malariae* is rarely responsible for febrile episodes. *P. malariae* was suspected of causing a febrile episode only once during the two surveys, even though the species is relatively prevalent, and usually varies between 14 per cent and 20 per cent in schoolchildren. *P. malariae* prevalence was 20.8 per cent in January 1984.

Overall, the results of the other studies coincide well with the findings in Linzolo. The incidence of clinical malaria, which is still high at age 5-6 years, decreases rapidly until it reaches a very low level in the adolescent and adult. The role played by transmission level in the speed of decrease with age is uncertain. The absence of precise data on malaria transmission intensity in most clinical studies and the different methodologies used to evaluate the incidence of clinical malaria do not allow thorough comparisons. The incomplete protection afforded by bed-nets appears to be insufficient to modify the natural course of the infection when transmission reaches several dozen infective bites per year (15), and this also seems to be the case for the incidence of clinical attacks. However, the efficiency of bed-nets in reducing the exposure to malaria depends on various factors (e.g., the condition of the bed-nets and

the behavior of the persons who use them), which were not investigated in our study.

The total consumption of antimalarial drugs by children in Linzolo is considerable. The most interesting observation is that this widespread use is mainly a result of the practices of the parents themselves. The use of amino-4-quinolines in Linzolo can be directly compared with that of antipyretics in developed countries: a temporary treatment given by the parents in the presence of any febrile episode or simple headache. If this treatment is not rapidly effective, the child is taken to the dispensary where a quinine injection is given (and, if necessary, antibiotics are prescribed). This mode of behavior, now widespread in urban areas and the most developed rural areas of the Congo, explains the present fall in mortality due to malaria despite the fact that transmission remains at a very high level. Lastly, the high consumption of antimalarial drugs explains the apparent paradox of maximum malaria prevalence in the 10-14 years age group. The higher the incidence of febrile episodes of all kinds, the higher the number of antimalarial treatments given; this is especially true in childhood.

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