Criteria for diagnosing clinical malaria among a semi-immune population exposed to intense and perennial transmission

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Abstract

In highly malaria-endemic areas, thick smears are usually positive regardless of the clinical context. Therefore the simple positivity or negativity of the thick smear is not an adequate criterion for distinguishing malaria from other causes of fever. In order to define simple parasitological and clinical criteria for diagnosing clinical malaria with a small risk of error, a study was undertaken in a rural area in the Congo where malaria transmission is intense and perennial. Results of the systematic determination of the parasite density of 1562 samples from persons of all ages considered representative of the population of the studied area are compared to those from 327 febrile patients, 204 patients detected during medical consultations held in the villages and 123 febrile schoolchildren detected during surveys for fever. The analysis of the clinical data and the parasitological results clearly demonstrates the importance of the parasite density determination for the diagnosis of clinical malaria. Clinical *Plasmodium falciparum* malaria is unlikely to occur in children under 15 years if the parasite/leucocyte ratio is less than 1·5. On the contrary this diagnosis is very probable if the parasite/leucocyte ratio is higher than 2. Clinical criteria were too non-specific to serve as useful diagnostic criteria.

Introduction

On what criteria should the diagnosis of malaria attack be based in a semi-immune population living in a malaria-endemic area? How does one interpret a positive thick film during an attack of fever when the thick film is positive in more than three quarters of asymptomatic children and one half of asymptomatic adults? Given the non-specific clinical symptoms of malaria attacks, is it possible to make the diagnosis without significant error?

Paradoxically, very little research has directly concerned this problem which confronts doctors, nurses and health workers daily in malaria-endemic areas. Because of the uncertain reliability of clinical diagnosis, there is great uncertainty concerning those statistics on clinical malaria gathered from consultations and health unit records. Their unreliability in highly endemic regions prevents an accurate evaluation of the importance of morbidity caused by malaria. In the rural areas and many dispensaries, available equipment does not permit thick film examinations. Febrile syndromes unaccompanied by specific signs and symptoms of a definite disease are usually considered to be an attack of malaria. When a thick film is taken, the diagnosis of malaria is discarded if the results are negative, but if any parasites are present and there is no other obvious cause of the symptoms, malaria is usually diagnosed without reservation.

To define better clinical and parasitological criteria for diagnosing malaria in an area with intense and perennial transmission, a study was undertaken in several villages in the vicinity of Brazzaville (Congo).

Study Design, Material and Methods

The villages where this study was carried out (Ouaoua, M'bamou, Mvouloumamba, Yalavounga, Linzolo) lie south-west of Brazzaville, a hilly region with savannah gradually replacing the original open forest and gallery forest which have been heavily altered by exploitation for firewood and the extension of agriculture.

The entomological context of the transmission of malaria in this area has been studied by BRADY (1961), ADAM & SOUWEINE (1962) and CARNEVALE (1972, 1979)). Malaria is mainly transmitted by *Anopheles gambiae*, whose abundance throughout the year combined with sporozoïte index close to 3% contribute to a particularly high rate of inoculation, approximately one infected bite per person per night. The other known or potential vectors present in this region (*An. funestus, An. moucheti, An. nili, An. hancocki, An. bunnipes, An. paludis*) are much rarer and have little epidemiological importance. Surveys conducted during the study confirmed for the chosen villages these regional data reported earlier.

Clinical and parasitological observations which have been used in this study come from two different longitudinal surveys:

Ouaoua, M'bamou, Mvouloumamba and Yalavounga villages

Between March and November 1981, weekly or fortnightly medical consultations were held in the villages by two of the authors (P.P. and B.M.P.). A clinical record was maintained for each patient. Irrespective of associated symptoms and clinical diagnosis, a thick film was taken from every febrile patient (rectal temperature equal to or higher than 37·5°C).

Linzolo village

From November 1980, this village has been the main study area for a research project on the epidemiology of malaria and its clinical and biological impact in rural regions around Brazzaville.

For this study, we used the results of: (i) two parasitological surveys in adults and pre-schoolchildren and seven parasitological surveys in schoolchildren, performed between November 1980 and March 1982; (ii) 21 sessions of systematically taking axillary temperatures (3429 records) of 170 schoolchildren between February 1983 and February 1984 and making clinical and parasitological observations

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during those sessions, especially among the 123 febrile children; (iii) 189 leucocyte counts in schoolchildren (145 systematic counts made in January 1984 and 44 leucocyte counts in febrile schoolchildren made from December 1983 to February 1984).

All thick smears included in this study (1562 systematic samples and 327 samples from febrile patients) were examined using the same method and by the same person (J.F.T.). A qualitative and quantitative study of the parasite density was conducted including particularly: (i) systematic examination of 200 oil immersion fields in the thick smear (about 0·5 µl of blood examined); (ii) an evaluation of the parasite density for each plasmodial species based on the parasite/leucocyte ratio according to a range of five classes of parasitaemia with a geometric progression of a factor of 10 (TRAPE, 1985) (Table I); (iii) the precise determination of the parasite/leucocyte ratio for all the slides with a class 4 or 5 parasitaemia (parasites counted for 100 or 200 leucocytes).

Results

I. *Prevalence and density of parasites in the population of Linzolo*

Table II shows that about 80% of children between one and 14 years have a positive thick film and that the parasite rate only decreases gradually to 36% in subjects over 40 years old. Parasite density decreases significantly with age: 24·5% of children aged between one and four years have class 4 or 5 parasitaemia, compared with only 14·3% of those between 10 and 14 years and 5·2% of those between 15 and 19. After 20 years there is no longer a high parasite density. No significant seasonal variation of either parasite rates or parasite density was observed. Some particularities, such as the lower than expected values for parasite rates and density among infants and young children, are probably due to the frequent use of anti-malarial drugs in this population and will be discussed elsewhere.

P. falciparum was found in almost all positive slides. *P. malariae*, almost always associated with *P. falciparum*, was found in 15·7% of children under 15 years and 10·4% of adults. *P. ovale* was found in 5·2% of children aged five to nine years and 3·1% of children aged 10 to 14 years but was hardly ever seen in adults. Parasite density never reached class 4 for *P. malariae* infections and class 5 for *P. ovale* infections. In cases of association between species, parasite density of these species was generally lower than that of *P. falciparum*.

II. *Clinical and parasitological study of 204 febrile patients*

204 observations of febrile patients were collected during medical consultations held in the villages of

Table I—Classification of parasitaemia and corresponding parasite count for a mean standard leucocyte count of 8000 per µl

Class	Parasitaemia (per µl)	Parasite count
0	*no parasite observed in 200 oil immersion fields*[1]	
1	<50	Less than 1 parasite for 160 leucocytes
2	50-<500	1 to 9 parasites for 160 leucocytes
3	500-<5000	1 to 9 parasites for 16 leucocytes
4	5000-<50000	10 to 99 parasites for 16 leucocytes
5	≥50000	100 parasites and over for 16 leucocytes

[1] In thick films of normal thickness a single parasite in 200 oil immersion fields corresponds to about 2 parasites per µl.

Table II—Crude parasite density by class by age group in unselected subjects from Linzolo village

Age	Parasite density (classes)						Total
	0	1	2	3	4	5	
<1	12 (57·1%)	1 (4·8%)	4 (19%)	3 (14·3%)	1 (4·8%)		21
1-4	22 (21·6%)	18 (17·6%)	20 (19·6%)	17 (16·7%)	19 (18·6%)	6 (5·9%)	102
5-9	118 (23·6%)	88 (17·6%)	78 (15·6%)	114 (22·8%)	90 (18%)	12 (2·4%)	500
10-14	111 (18%)	109 (17·7%)	159 (25·8%)	149 (24·2%)	86 (14%)	2 (0·3%)	616
15-19	41 (29·9%)	27 (19·7%)	39 (28·5%)	23 (16·8%)	6 (4·4%)	1 (0·7%)	137
20-39	20 (44·4%)	12 (26·7%)	11 (24·4%)	2 (4·5%)			45
≥40	65 (63·7%)	21 (20·6%)	15 (14·7%)	1 (1%)			102
Total	389	276	326	309	202	21	1523

Ouaoua, M'Bamou, Mvouloumamba and Yalavounga.

Based on clinical criteria alone, the febrile patients were divided into two categories: (i) patients whose signs on clinical examination clearly indicated a disease other than malaria; (ii) patients without such signs; these subjects were therefore suspected cases of clinical malaria.

Of the 204 febrile patients, 93 were classified into the first category. 30 of the cases were bronchitis or pneumonia, 37 were ENT cases (14 otitis, and 23 rhinopharyngitis and tonsillitis cases) and 26 were a variety of diseases. The symptoms in 111 of the patients could not rule out the possibility of malarial infection and these were classified as suspected malaria.

The age groups of the patients and the distribution of rectal temperatures taken during the examination by diagnostic category are shown in Table III. For this study, it was initially decided to consider each patient with a rectal temperature over 37·5°C as febrile, but temperatures were only taken in patients who complained of fever or whose symptoms suggested the possible presence of fever. About one third of the patients respectively had a temperature between 37·5°C and 37·9°C, between 38°C and 38·4°C and 38·5°C and over. On average, suspected cases of malaria had higher temperatures than did the other patients.

Among suspected cases of malaria, fever was the only symptom in 54 cases and was accompanied by one or more symptoms in 57 cases. These were rhinitis (18 cases), cough (18 cases), diarrhoea or abdominal pains (17 cases), vomiting (13 cases), congested tympanic membrane or external otitis (10 cases).

Among the symptoms, we should distinguish those probably secondary to ENT inflammation or bronchitis (possibly associated with malaria or the true cause of fever) and those possibly secondary to malaria (vomiting and diarrhoea). The latter were found as frequently among cases of disease other than malaria and can not, therefore, be considered to be suggestive of malaria.

Various headaches and pains, which usually accompany malarial infection, have not been considered since they may not be reliably expressed by young children who constitute most of the subjects studied.

Parasitological results

Among patients not suspected of clinical malaria, *Plasmodium* was found in 74·6% of children and 34·6% of adults. 90% of the children and 66·7% of the adults suspected to be cases of malaria were positive.

P. falciparum was found in 97·9% of the positive films of suspected cases of malaria and 94·9% of the positive films of other cases. *P. ovale* and *P. malariae*, alone or more often in association with *P. falciparum*, were both found in 10·6% of the positive films of suspected cases of malaria and in 10·2% and 8·5% respectively of the positive films of the other patients. The *P. malariae* parasite density was always low (<50/µl), except in two of the cases in which disease other than malaria had been diagnosed and in one case in which there was a much higher density of *P. falciparum*. In almost half of the *P. ovale* infections, the parasite density was higher than 500/µl, but this moderate or high *P. ovale* parasitaemia was invariably associated in suspected cases of malaria with heavy *P. falciparum* infections.

The greatest difference between the two groups was in the parasite density: in those under 15 years old, 67·8% of suspected malaria patients had a parasite density belonging to class 4 or 5 compared with 19·4% in patients with other diagnoses.

To facilitate comparison between these results and those from unselected persons, we have calculated the parasite density in a control population (Linzolo) matched by age to the cases of febrile episodes.

Under 15 years of age, we can see that (Fig. 1): (i) for subjects not suspected of clinical malaria, parasite rates and density can be superimposed on those of the control population; (ii) subjects with suspected clinical malaria have a class 4 or 5 parasitaemia in significantly greater numbers than expected.

In adults the number of subjects studied were fewer and their age distribution was wider. 21 patients were classified as having diseases other than malaria and 26 patients were considered to be suspected cases of malaria. All cases of high parasite density were among the young adults (15 to 19 years) suspected of malaria. Above this age, even a parasite density above 500 per µl is rare (one case only). However the parasite rate was twice as high in the adult patients suspected of having malaria (66·7%) as in the other adults (34·6%).

III—*Observations in Linzolo schoolchildren*

Temperature surveys

From February 1983 to February 1984, 21 successive temperature surveys were conducted in schoolchildren (3429 records of axillary temperature). The mean axillary temperature was 37·3°C and 2·8%

Table III—Age distribution of febrile patients according to their rectal temperature and diagnostic category

	Suspected case of malaria				Other cases				
Age	37·5°C-37·9°C	38°C-38·4°C	≥38·5°C	Total	37·5°C-37·9°C	38°C-38·4°C	≥38·5°C	Total	Total
<1	2	2	2	6	2	3	5	10	16
1-4	7	13	19	39	17	15	10	42	81
5-9	11	10	10	31	5	2	3	10	41
10-14	2	4	8	14	1	1	3	5	19
≥15	6	9	6	21	13	9	4	26	47
Total	28	38	45	111	38	30	25	93	204

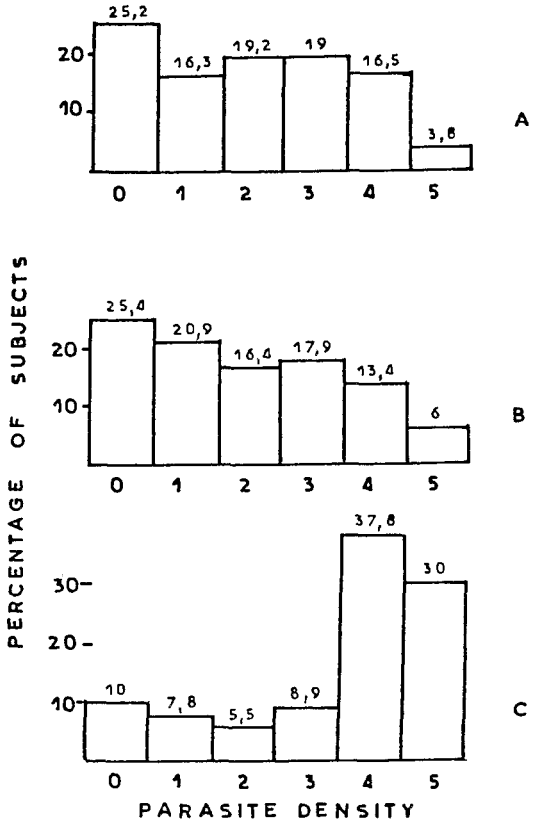

Fig. 1. Percentage distribution of children under 15 years according to their parasite density. A: control population; B: diseases other than malaria; C: suspected malaria cases.

of schoolchildren had a temperature of 38°C or higher.

In two of these surveys, thick smears were systematically taken from all schoolchildren (310 samples collected). The mean temperature of schoolchildren whose parasitaemia was of classes 0, 1, 2 or 3 was similar (37·4°C for each of these classes), but the mean temperature reached 37·7°C in those with a class 4 parasitaemia. Only one schoolchild had a class 5 parasitaemia, which was associated with a temperature of 39·5°C. In fact, the difference observed between the mean temperature of the 46 schoolchildren with a class 4 parasitaemia and the mean temperatures of the 263 schoolchildren with a class 0, 1 2 or 3 parasitaemia, was due to 12 schoolchildren with a class 4 parasitaemia (26·1%) whose axillary temperature ranged from 38·1 to 39·6°C. Only five of 263 schoolchildren (1·9%) with a class 0, 1, 2 or 3 parasitaemia had a temperature equal to or higher than 38°C.

Many authors have emphasized how difficult it is to define the normal temperature in children living in tropical regions. If we assume that the axillary temperature is about 0·5°C lower that the body temperature, most of the Linzolo schoolchildren should be considered as febrile according to standard criteria. As far as the possibility that malaria could be responsible for these high temperatures is concerned, we observed no difference between the mean temperature of two groups of Linzolo schoolchildren (numbering 75 and 78 respectively) selected at random, the first group receiving amodiaquine chemotherapy (10 mg/kg on two occasions, respectively nine and two days before recording temperature), the latter group as a control.

Furthermore, using the same methods and conditions as in Linzolo, we recorded the axillary temperature of 216 Caucasian schoolchildren from the French

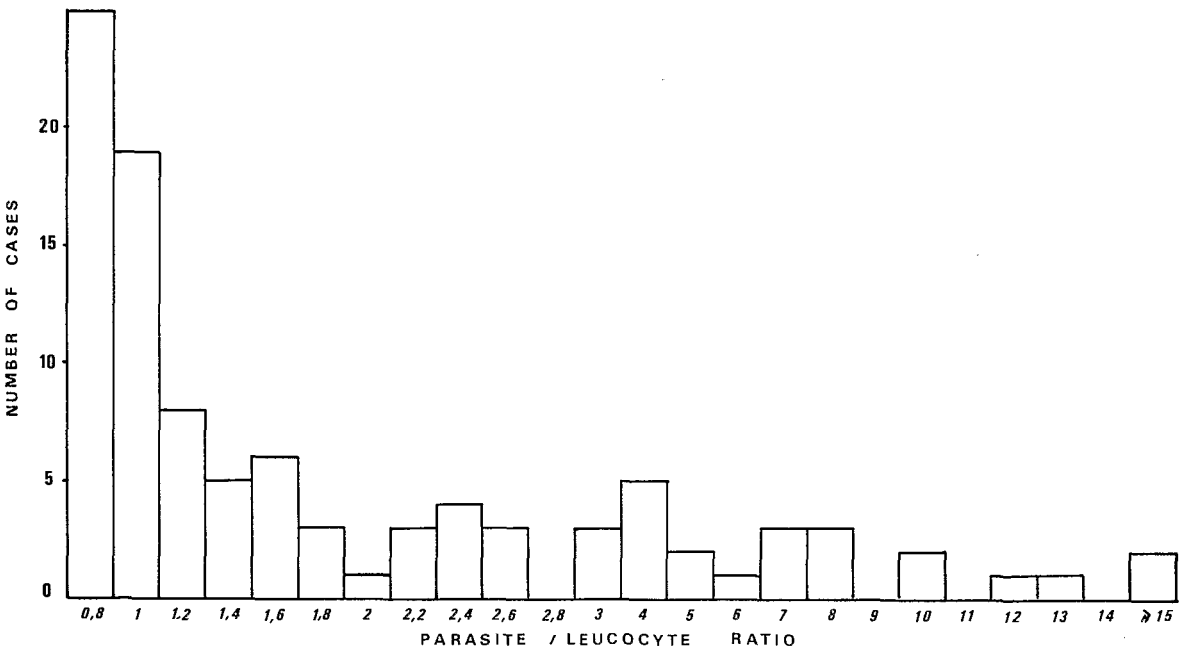

Fig. 2. Parasite/leucocyte ratio of 100 unselected schoolchildren aged 5-9 years with a class 4 or 5 parasitaemia.

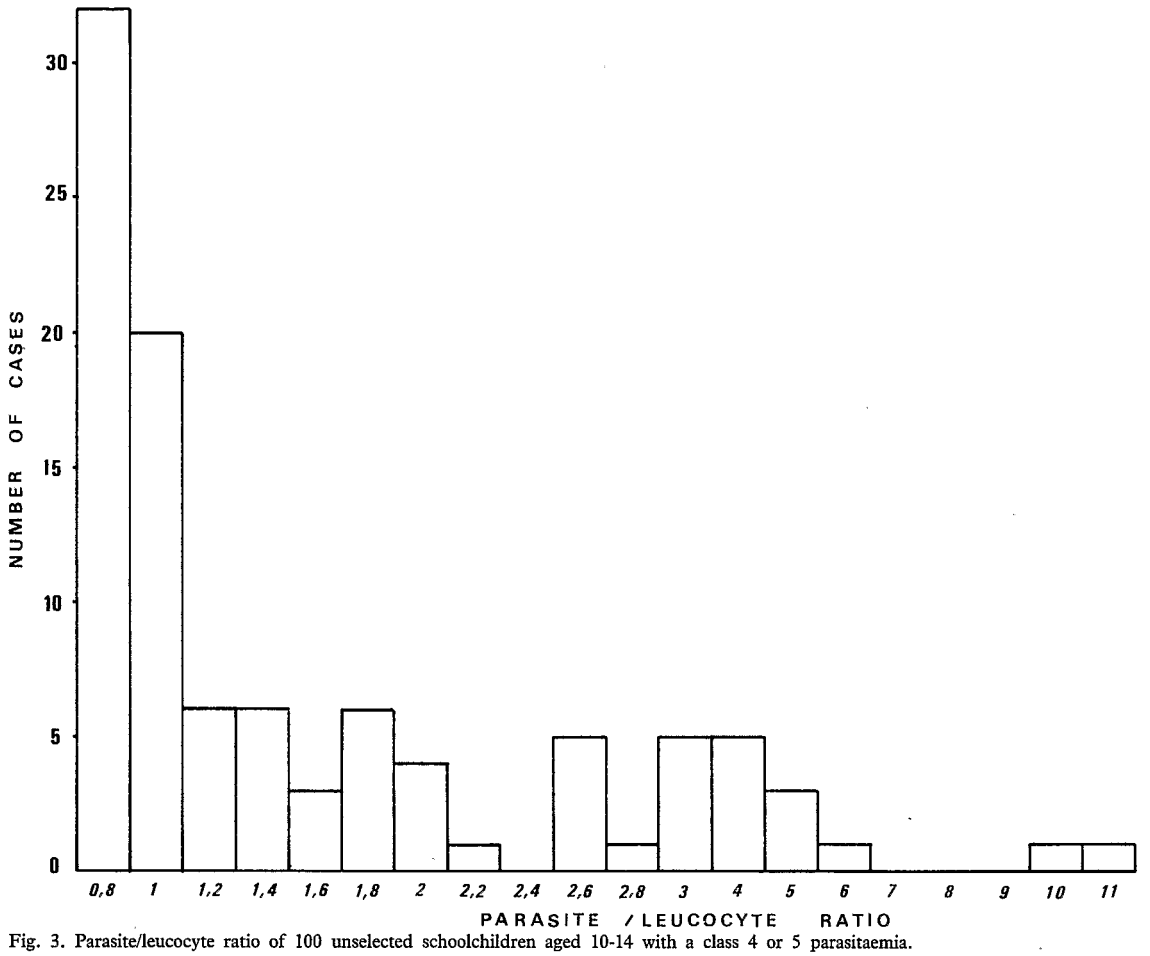

Fig. 3. Parasite/leucocyte ratio of 100 unselected schoolchildren aged 10-14 with a class 4 or 5 parasitaemia.

Table IV—Parasite density according to plasmodial species in 123 febrile schoolchildren from Linzolo village

		P. falciparum parasite density					
						4 and 5	
		0	1	2	3	P/L<2	P/L≥2
P. malariae and (*P. ovale*) parasite density	0	11	8	7	10	8	58
	1				2 (1)	4	(2)
	2	1			4 (1)	1	1
	3			2	1	1	

school in Brazzaville who were presumed to be free of malaria. The mean temperature (37.2°C) was not significantly lower and 18·5% of schoolchildren had a temperature ranging from 37·5°C to 37·9°C.

Preliminary results of a study of the weekly individual variations of axillary temperature in Linzolo schoolchildren show that a temperature of 37·8°C should be considered within the normal range of temperatures. Consequently, for all studies conducted on schoolchildren, it was decided to consider as febrile any child whose axillary temperature was 38°C or more.

Parasite/leucocyte ratio in classes 4 and 5 subjects

(i) *Unselected schoolchildren aged 5 to 14 years*: Fig. 2 and 3 show the precise parasite/leucocyte ratio

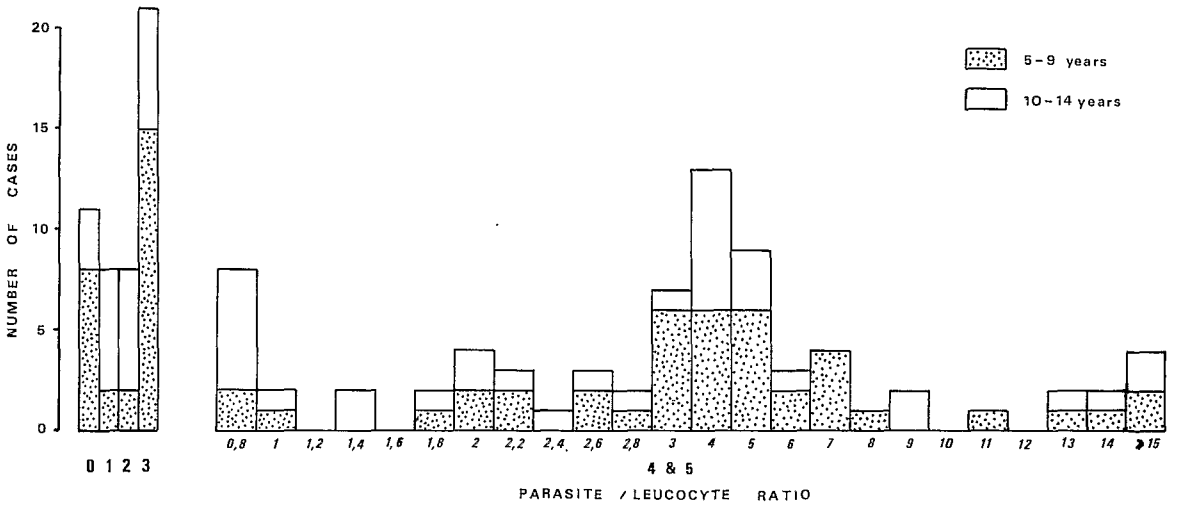

Fig. 4. Distribution of 123 febrile schoolchildren according to their parasite density. For subjects with a class 4 or 5 parasitaemia, parasite/leucocyte ratio is given.

in 200 class 4 or 5 thick smears from unselected schoolchildren aged 5 to 9 years and 10 to 14 years during seven different surveys.

A large proportion of cases observed have low values of the parasite/leucocyte ratio, and there is a rapid decrease in the number of cases when the parasite/leucocyte ratio increases. From these data it can be calculated that: (i) in schoolchildren 5 to 9 years old, 57% with classes 4 and 5 thick smears show a parasite/leucocyte ratio less than 1·5 and 66% less than 1·9; (ii) in schoolchildren 10 to 14 years old, 64% with classes 4 and 5 thick smears show a parasite/leucocyte ratio less than 1·5 and 73% less than 1·9.

(ii) *Febrile schoolchildren aged 5 to 14 years:*

Fig. 4 shows the crude parasite density in 123 febrile schoolchildren aged 5 to 14 years and Table IV shows the distribution by species. All were detected at school (95 cases during 21 temperature surveys and 28 cases between these surveys). These were 91 cases of *P. falciparum*, one of *P. malariae*, 16 cases of associated *P. falciparum-P. malariae* and four cases of associated *P. falciparum-P. ovale*. No parasite was found in 11 cases.

In 48 cases, the parasite density was lower than class 4. For the 75 cases with a class 4 or 5 parasitaemia, Fig. 4 shows that the parasite/leucocyte ratio is generally higher than 1·9 (81% of the cases).

Discussion

Parasite density

The similarity between the parasite rates and parasite density of the febrile subjects suffering from a variety of diseases other than malaria and those of the control population suggest that the fluctuations in the parasite density are independent of intercurrent diseases. When a thick film is positive it merely corresponds with parasitological malaria, whose frequency is always considerable in highly endemic areas. Furthermore, the frequency of consultation for a suspected case of malaria was not higher in those who had previously suffered from a disease other than malaria than in the rest of the population.

In febrile patients suspected of malaria, a considerable proportion have a high parasite density, even though a significant number of them must be suffering from diseases other than malaria, although they are clinically similar. In fact, many viral diseases do not have any specific signs; the symptoms are fever either alone or accompanied by non-specific signs. Many other diseases do not present any specific symptoms or signs during their early phase, and therefore do not permit a clinical diagnosis until after they have further evolved.

If we assume that parasite density in febrile patients suspected of having malaria who actually have another disease is similar to that in the first group of patients with diseases other than malaria, it appears from Fig. 1 that children under 15 years whose parasite density is below class 4 can be excluded as suspected cases of malaria.

Furthermore, comparison of the results from febrile schoolchildren and unselected schoolchildren clearly shows that the actual parasitaemia in class 4 or 5 subjects is different between these two categories of schoolchildren (Figs. 2, 3 and 4): in febrile schoolchildren the parasite/leucocyte ratio usually ranges between 3 and 12; in unselected schoolchildren the parasite/leucocyte ratio is generally close to one.

Although parasitological surveys in unselected schoolchildren have not been systematically paired with temperature surveys, it appears from the data collected during temperature surveys that most of the unselected schoolchildren with a parasite/leucocyte ratio higher than 2 or 3 were probably febrile, and this is confirmed by the results of the two surveys for which blood samples and temperatures were paired. However, in some cases we observed very high parasite densities (parasite/leucocyte ratio close to 4 or 5) in the absence of fever. In our opinion these cases must not be considered as examples of tolerance of a high parasitaemia: on three occasions during surveys in which thick smears and temperatures were syste-

matically paired, we observed schoolchildren who were initially afebrile but who developed a feverish illness one or two hours later. In these three cases parasitaemia was initially very high and remained almost unchanged during the fever attack. These observations can certainly be explained by the fact that it is not the direct effect of the parasite which induces the attack of the fever but the liberation of toxins when the erythrocytes are destroyed at the end of erythrocytic schizogony.

We interpret similarly the frequent observation in the study conducted in the villages of very high parasite density in patients consulting for fever who were not actually febrile when examined.

Concerning very high parasite densities in children with symptoms of diseases other than malaria and classified as non-suspected cases of malaria, their significance probably varies according to the cases. In four of eight children with a parasite/leucocyte ratio higher than 2, the clinical diagnoses which were reported (rhinopharyngitis in three cases and gastroenteritis in one case) suggest than the clinical criteria used were inadequate. For these four patients malaria was possibly the true cause of fever. For the four other patients (two cases of pneumopathy and two of otitis) there is no doubt that the diagnostic report explains the fever. Clinical malaria was probably associated.

In fact, the entire parasitological and clinical observations made in this study strongly suggest the lack of significant individual variability in the pyrogenic level of parasitaemia in subjects of a given age in areas of intense and perennial transmission, whether it is little affected by the variability of the individual immune response or whether the characteristics of malaria transmission in these areas tend to standardize, in most cases, the host's response after some years of exposure.

Consequently, parasite density appears to be the only available criterion for distinguishing malaria from other causes of fever, with a small and measureable risk of error. *P. falciparum* clinical malaria is unlikely to occur in children under 15 years if the parasite/leucocyte ratio is less than 1·5. On the contrary this diagnosis is very probable if the parasite/leucocyte ratio is higher than 2.

To give more precise criteria would probably be illusory and of little practical use: in more than 9 out of 10 febrile children, the parasite/leucocyte ratio is in fact sufficiently far outside the range of 1·5 to 2 to ensure that there are no difficulties in the diagnostic interpretation.

It is important to note that our results permit us to deduce similar febrile threshold values of parasitaemia as those observed for *P. falciparum* by EARLE *et al.* (1939) and MILLER (1958), who used very different methods from our own. EARLE *et al.* (1939), from observations on children in Puerto Rico, stated that clinical malaria appeared when parasite counts exceeded 12,000/µl. MILLER (1958) stated that symptoms in the children he studied in The Gambia were never produced unless the count exceeded 11,500. In his study, the mean parasite count initiating clinical attack was 18,000/µl.

In Linzolo we observed that the mean leucocyte count was 6,730/µl in febrile schoolchildren with a parasite/leucocyte ratio higher than two, 7,070/µl in febrile schoolchildren with a parasite/leucocyte ratio lower than 2, and ranged from 10,410/µl to 7,785/µl according to age in asymptomatic schoolchildren systematically tested.

The relatively low number of febrile adult patients restricted our observations. However, results indicated a rapid decrease with age of the fever threshold, thus confirming previous extensive studies by MILLER (1958) and BRUCE-CHWATT (1963). Above ages 25 to 30 a parasite density of more than 500 per µl in a febrile adult is very suggestive of a malaria attack.

Infections by P. malariae *and* P. ovale

None of the clinical attacks in the study conducted in the villages seemed to be caused by *P. malariae* or *P. ovale*, even though we admit that these species have a much lower febrile threshold than *P. falciparum*.

For these two species, the index and parasite density of the control population and of the two groups of febrile patients were similar. In suspected cases of clinical malaria, they were invariably associated with a much heavier *P. falciparum* infection. Therefore, the greatest consequence of infection with *P. malariae* or *P. ovale* in these cases would have been a contribution to raising the temperature or accentuating the symptoms.

In the study conducted in Linzolo schoolchildren, one clinical attack was probably due to *P. malariae*. Moreover there is some evidence that the febrile threshold was lowered in some cases of mixed infections by *P. falciparum* and *P. malariae*.

Clinical infections caused by *P. malariae* and *P. ovale* are rare. Hence, much larger numbers of febrile patients that we were able to observe are required to detect enough cases to establish their relative frequency and to propose criteria for diagnosis.

For *P. malariae*, MILLER (1958) in the Gambia observed that clinical attacks were initiated by parasite counts ranging from 1,650 to 5,935 µl. The mean for all attacks was 3,712/µl.

Clinical criteria

In order to specify clinical aspects of malarial infections, we must eliminate those patients initially classed as malaria suspects who had a parasite density too low to be considered true cases of clinical malaria. At the same time, we must include those cases in which clinical malaria was potentially associated with a specific disease.

By assuming that the clinical threshold in children under 15 years corresponds approximately to a parasite/leucocyte ratio of 2, malaria in our study represented: (i) 54·4% of the causes of fever in schoolchildren aged 5 to 9 years, and 43·6% for those aged 10 to 14 years; (ii) from 28·9% to 41·7% of the reasons for consultation due to febrile diseases in children under 5 years, according to the level of temperature which was used to define fever (rectal temperatures of 37·5°C or 38·5°C) and from 37·1% to 52·8% by including cases in which clinical malaria was potentially associated with a specific disease; (iii) from 41·7% to 58·3% of the reasons for consultation due to febrile diseases in children aged 5 to 14 years.

In children under 5 years, fever was the only symptom in 35·7% of cases, and was associated with

other symptoms in 64·3% of cases. There was diarrhoea or abdominal pain in 21·4% of cases, and vomiting in 10·7%. Mild intercurrent inflammation of the lungs or ENT was often present (50%), probably reflecting the high prevalence of these symptoms among young children irrespective of malaria infection.

In children aged 5 to 14 years consulting for fever, fever was the only symptom in 56% of cases. Diarrhoea or abdominal pain was present in 12% of cases, vomiting in 20% and mild intercurrent inflammation of the lungs or ENT in 24% of cases. However, in schoolchildren diagnosed at school these symptoms were much rarer.

The most useful clinical criteria for diagnosing clinical malaria in pre-schoolchildren were primarily negative: (i) absence of bronchial or pulmonary rales on ausculation, (ii) absence of tonsillitis and pharyngitis on examining the throat, (iii) absence of otitis on examining the ears.

However, these criteria do not rule out the possibility of an association with clinical malaria and were of little use in older children because of the relative rarity of diseases with specific signs. Furthermore, from 22·2% to 44·4% of the cases of fever alone or accompanied by non-specific symptoms according to age and temperature were due to a cause other than malaria.

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