Malaria Control in an Agro-industrial Settlement of Rondônia (Western Amazon Region, Brazil)

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A malaria control pilot project was developed in the Urupá agro-industrial farm that is situated in the State of Rondônia (Western Amazon Region, Brazil). Around 180 inhabitants had been surveyed for the past five years. The control measures were based on (1) training a community agent to perform on the spot microscopical diagnosis of malaria and to treat the uncomplicated cases of malaria; (2) limiting the use of insecticides to a short period before the high transmission season. This resulted in a significant reduction in the time between the onset of clinical symptoms and specific chemotherapy which fell from 3.5 to 1.3 days. In relation to the previous three reference years the total number of malaria cases was reduced to 50% in the first year and to 25% in the second year. The introduction of these measures coincided with pronounced reduction in the frequency of Plasmodium falciparum *infections but this was less marked for* P. vivax *infections. In the second year of the pilot experiment there was no* P. falciparum *transmission on the farm. During the last decade there was a general decrease in the endemicity of malaria in the State of Rondônia. The linear regression coefficient values indicate that the decline was more pronounced in Urupá than in the general municipality and that the* falciparum *malaria API in Urupá farm is significantly lower than in the general municipality of Candeias were the farm is situated.*

Key words: malaria - control - epidemiology - *Plasmodium falciparum* - *Plasmodium vivax* - Rondônia - Amazon Region

The State of Rondônia, with 234,000 km^2 and around 1.3 million inhabitants, is one of the most important endemic malaria areas of the Western Amazon Region of Brazil. There has been an intense influx of people from other parts of Brazil during the past few decades and the population increased from 116,000 inhabitants in 1970 to 1.130,000 in 1990. Concomitantly there was a marked increase in the incidence of malaria from 5,800 in 1970 (50/1,000) to 244,800 in 1989 (216.7/1,000).

In the present decade, however, the number of cases has been declining and this is thought to be associated with a reduction in the number of immigrants, a migration of the rural population to urban areas and the departure of gold miners ("garimpeiros") to other regions of Brazil. At the same time the incidence of malaria decreased from 130,000 cases in 1994 to 96,700 in 1996. The relative frequency of *Plasmodium falciparum* infections, which was high in the eighties (59% in 1988) decreased to 34% in 1992 and 25% in 1996 (Marques 1995).

Malaria is still an important endemic disease in the region, but its epidemiology has changed from 'frontier malaria' associated with the gold miners and new agricultural settlements (Sawyer 1993) to 'residual malaria' in urban/periurban areas and stable agricultural settlements.

In recent papers we described longitudinal surveys in two types of communities in Rondônia with high malaria incidence rates: the agro-industrial settlement of the Urupá farm (Camargo et al. 1994) and the urban/periurban areas of Candeias do Jamary (Camargo et al. 1996). The epidemiological profile in both localities was similar because (1) an unstable hypoendemic situation with low prevalence of malaria in the rainy season (October to April) followed by epidemic outbreaks at the end of the rains and during the dry season; (2)

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higher incidence of *P. vivax* infections, representing 70-75% of total number of cases; (3) a clear predominance of cases among adults, particularly male adults of 16 to 40 years old, indicating a relation of infection with professional activities that facilitate contact with the vector; (4) absence of asymptomatic carriers in the various longitudinal parasite surveys performed.

These characteristics of malaria in the area lead us to perform a pilot malaria control project on the Urupá farm that was based on the following measures: (1) survey of new arrivals at the farm; (2) rapid identification of parasites in patients suspected of clinical malaria followed as quickly as possible by appropriate chemotherapy; (3) limiting the use of insecticides to a period just before high transmission.

MATERIALS AND METHODS

Area and period of study - The Urupá farm, situated in the Candeias do Jamary municipality, was recently described by Camargo et al. (1994) and is 25 km from the urban site of Candeias. In March 1996 its population was composed of 145 individuals distributed in 26 families who lived in 36 houses. The control study was performed between 1 August 1995 and 31 December 1996 with a previous preparatory training period of six months.

Detection and treatment of malaria cases by the community agent - In the preparatory period performed in the farm, the community agent was trained to collect blood samples from patients, to prepare thick smears for microscopically examination and to use of a simple treatment algorithm for uncomplicated malaria. Duplicate thick smears were prepared and one was sent to the Porto Velho laboratory for quality control.

Once a week a medical doctor visited the patients who were re-examined. He collected detailed information on each case which included clinical symptoms, result of the thick smear examination and the individual's epidemiological background.

Diagnostic and treatment procedures - Case detection was passive but farm residents were encouraged to have their blood examined in case of fever or other symptoms that were compatible with malaria. To reduce the possibility of individuals with gametocytes in their blood from entering into the area any new resident on the farm was submitted to microscopical blood examination regardless of the presence or absence of symptoms. This examination was performed according to the methods described (Camargo et al. 1994, 1996).

Treatment: the schedules of the Fundação Nacional da Saúde were followed using chloroquine and primaquine for *P. vivax* infections and quinine/tetracycline for *P. falciparum* infections (Camargo et al. 1994, 1996). Sufficient drugs were provided to each patient for the complete course of treatment together with the necessary instructions. Parasite clearance was checked by microscopic examination of giemsa stained thick smears prepared 3, 7, 14, 21, 28 and 35 days after the end of treatment.

Clinical and epidemiological parameters - A malaria case was defined only when parasites were seen in a thick blood smear of an individual with fever or/and another malarial symptom. A case was defined as autocthonous if the patient had not left the farm in the 15 days preceding the onset of the symptoms. It was considered to be imported (heterocthonous) if the patient had been clearly exposed to mosquito bites in known malarial localities outside the farm, in fishing, mining, or agricultural activities. Undefined origin was assigned to patients that had been away from the farm but who had not been exposed to mosquito bites.

A "possible relapse" in *P. vivax* cases was considered when the malaria attack occurred 30 to 60 days after the first episode had been considered to be cured according to the criteria described above.

The indexes adopted to measure malaria were (1) monthly incidence – the number of new malaria cases in the month per 1,000 inhabitants and (2) annual parasite index (API) – the total number of parasitological confirmed cases in the year in relation to the average population present in the locality per 1,000 inhabitants.

To compare the evolution of malaria in the Urupá farm with that the whole region we used data from the Fundação Nacional de Saúde (unpublished) for the annual malaria prevalence over the last four years in the entire municipality of Candeias minus that of Urupá's farm (e.g. around 8,000 inhabitants, 60% rural).

Insecticide application - Between 1991 and 1995 insecticide was applied in the vicinity of the residences and the lumber cutting building of the farm where most of the male adults work. This was performed by FNS agents using the organophosphorated insecticide Desband(R) in the form of fog with a suspension at 2% concentration in Diesel oil. However, the applications were performed irregularly during all the high transmission seasons. In 1996, based on our observations on vector density throughout the previous years (Salcedo et al. unpublished observations) we decided to reduce this to a weekly application performed every Friday at 6 p.m. for the two months that corresponded to the highest vector's densities (May to July). This was done by community agents who were trained to use the fogger provided by the FNS, Rondônia.

RESULTS

Malaria prevalence on the Urupá farm before and after the introduction of additional control measures - Table I summarises the annual incidence of malaria in Urupá before and after the introduction of the control measures in August 1995 under the personal responsability of the communitary agent. The 1992 data was fragmentary and therefore discarded. Up to 1995 the diagnosis and treatment of malaria in Urupá was dependent on the ambulatory unit of the FNS in Candeias village, 25 km away from the farm. In August 1995 the community agent assumed the responsibility for the *in situ* diagnosis and treatment of malaria under the medical supervision of the principal investigator who visited the farm every week. The data in Table I and Figure, shows a clear reduction in malaria incidence from 1995 onwards with an API 50% lower than in previous years. In 1996 the reduction was in the order of 75% for the total number of malaria cases and specifically over 90% for *P. falciparum* infections. In addition, it is emphasised that the four cases of *P. falciparum* infections occurring in 1996 were imported (Table III), this means that no *P. falciparum* malaria transmission occurred at the farm after the introduction of the new control measures.

Demographic and epidemiological changes with the new control measures - The comparative age and sex distribution of *P. vivax* and *P. falciparum* malaria cases between 1991 and 1996 on the Urupá farm is shown in Table II. In spite of the important reduction in the number of cases, the general profile of malaria in the locality did not change. Males continued to be more frequently infected than females. The highest risk group was the 16 to 40 years old males (42% of cases) which is associated with their professional activities. The results of the patient inquires suggest that 48% of infections were acquired while working.

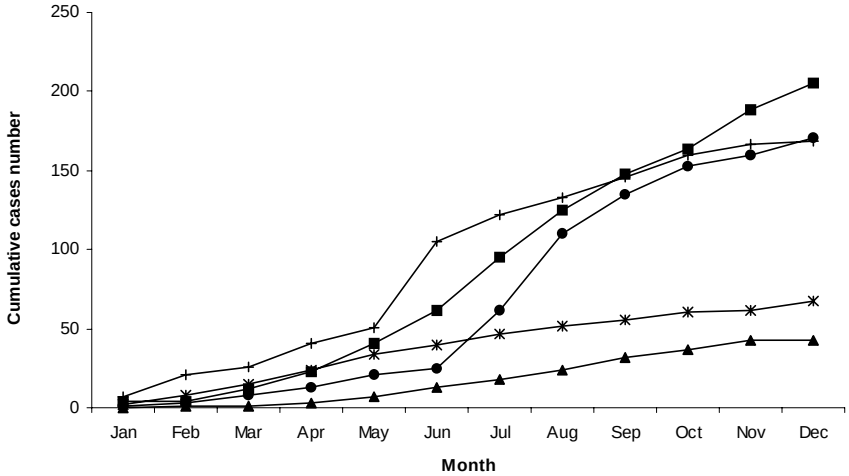
However, the seasonal distribution of malaria cases shown in Table III and Figure was modified when the new control measures were introduced. The main change was the absence in 1995 and 1996 of outbreaks at the end of the rainy season and in the dry season that typically occurred be-

TABLE I

Evolution of malaria prevalence in the Urupá farm (1991-1996)

Year	Average no. of residents	Cases of malaria			API	% *Plasmodium falciparum*
		P.v.	P.f.	Total		
1991	170	102	69	171	1,006	40.3
1993	180	137	68	205	1,139	33.2
1994	170	120	49	169	994	29.0
1995	165	54	13	67	406	19.4
1996	145	39	4	43	296	9.3

API: annual parasite index (number of parasitological confirmed malaria cases per 1,000 inhabitants); P.v.: *Plasmodium vivax*; P.f.: *Plasmodium falciparum.*



Cumulative incidence of malaria in the Urupá farm before and after the introduction of new control measures in August 1995.

tween 1991 and 1994. These changes coincide with the introduction of the new measures, in particular with the possibility of *in situ* diagnosis of malaria allowing faster application of therapeutic measures. Most significant was the reduction between the onset of symptoms and introduction of anti-malaria therapy from 3.5 to 1.3 days between 1994 and 1996.

Data in Table III also show the critical role that imported infections play in the prevalence of malaria in the farm inhabitants. Of a total 43 annual cases 12 were imported including all the four cases of *P. falciparum* malaria.

Specificity of impact of the new control measures - To confirm that the reduction in the number of malaria cases in Urupá, following the introduction of the control measures, was not related to a general decrease in malaria endemicity in the region we compared the annual prevalence in Urupá with the overall prevalence in Candeias do

TABLE II

Prevalence of malaria in the Urupá farm. Age and sex comparative distribution in years 1991 and 1996

Sex and age groups	1991					1996				
	No. of residents	No. of malaria cases				No. of residents	No. of malaria cases			
		P.v.	P.f.	Total	% total[a]		P.v.	P.f.	Total	% total
Males										
0-10	24	10	2	12	7.0	19	0	0	0	0.0
11-15	12	3	8	11	6.4	8	5	0	5	11.6
16-40	54	51	29	80	46.8	39	16	2	18	41.9
>40	13	12	5	17	9.1	11	4	1	5	11.6
Subtotal	103	76	44	120	70.3	77	25	3	28	65.1
Females										
0-10	28	3	1	4	2.3	26	7	1	8	18.6
11-15	10	7	5	12	7.0	5	1	0	1	2.3
16-40	32	12	13	25	14.6	29	5	0	5	11.6
>40	7	4	6	10	5.8	8	1	0	1	2.3
Subtotal	6726	25	51	29.8	68	14	1	15	34.9	
Total	170	102	69	171	100	145	39	4	43	100

a: % total = $\frac{\text{No. of cases in the group}}{\text{Total number of cases}}$ X 100; P.v.: *Plasmodium vivax*; P.f.: *Plasmodium falciparum.*

TABLE III

Seazonal variation and orign of malaria cases in Urupá farm

Month	*Plasmodium falciparum*				*Plasmodium vivax*			
	Auto 1996	Hetero 1996	Total 1996	Total 1991[a]	Auto 1996	Hetero 1996	Total 1996	Total 1991[a]
January	0	0	0	1	0	0	0	0
February	0	0	0	0	0	1	1	2
March	0	0	0	0	0	0	0	5
April	0	0	0	3	0	2	2	2
May	0	0	0	1	3	1	4	7
June	0	2	2	1	3	1	4	3
July	0	0	0	12	4	1	5	25
August	0	0	0	21	5	1	6	27
September	0	2	2	15	6	0	6	10
October	0	0	0	7	4	1	5	11
November	0	0	0	4	6	0	6	3
December	0	0	0	4	0	0	0	7
Total	0	4	4	69	31	8	39	102

a: (in Camargo et al. 1996); Auto: autoctonous (cases) of malaria; Hetero: heteroctonous (imported cases) of malaria.

Jamary county, where the farm is situated (Table IV). In the three FNS out patient units of Candeias, malaria control is performed by passive survey and treatment of malaria cases, backed up by periodical insecticide applications during the high transmission season. The linear regression coefficient's force values indicate that the decline in the incidence of malaria is more pronounced in Urupá than in the rest of the municipality. However only the *P. falciparum* API decline is significantly higher in the higher in Urupá (t = 2.77, 4 df). The *falciparum/vivax* API ratios showed a highly significant decrease in the last two years (Table IV).

DISCUSSION

In the present communication we have described a pilot malaria control project in an agro-industrial farm of the Brazilian Amazon region based on the participation of community agents that resulted in considerable reduction of the incidence of malaria and the interruption of *P. falciparum* malaria transmission in the locality. The introduced measures are among those recommended by the World Health Organization Malaria Ministry Conference of Amsterdam (WHO 1993). However, few controlled longitudinal experiments have been performed in the Amazon region to evaluate the impact of community based malaria control. Kroeger et al. (1995, 1997) used impregnated bednets in 84 communities in five malaria endemic areas of the Pacific coast of Ecuador, Peru and Colombia. Based on a reduction in the number of malaria attacks the protective efficacy was variable (average 40.8%). A large pilot project with an approach similar to ours was developed by Delacollette et al. (1996) in Zaire, based on the participation of community members in providing quicker treatment. However, no parasitological diagnosis was performed and the treatment was of presumptive malaria cases. An important reduction of morbidity was observed with no impact on mortality and the authors could not evaluate the effect on malaria transmission. In the beginning of our studies, in 1991, the Urupá farm, situated in Rondônia, was amongst the highest endemic malaria localities in the Western Amazon Region, with an API close to 1,000 (Camargo et al. 1994). The newly introduced measures permitted rapid *in situ* diagnosis and treatment of non complicated malaria and reduced the use of insecticides to a short period before the high transmission season.

In the period of intervention of the present study there was a sharp decline in malaria prevalence throughout the entire South-western Amazon region. In Rondônia the decline was also significant, with a 30% decline from 1994 (130,000 malaria cases) to 1996 (96,000 cases). In Candeias do

TABLE IV

Prevalence of malaria in the Urupá farm and in overall Candeias municipality from 1993 to 1996

Year	Candeias municipality						Urupá farm						
	Population	*Plasmodium vivax*		*P. falciparum*		API ratio	Population	*Plasmodium vivax*		*P. falciparum*		API ratio	χ^2 between API ratios+
		N	API	N	API			N	API	N	API		
1993	8.498	5.681	668	2.401	283	.42	180	129	761	70	378	.50	2.4972
1994	8.361	5.772	690	2.450	293	.42	170	117	706	49	288	.41	0.0001
1995	8.707	5.070	584	2.542	291	.50	165	54	327	13	79	.24	5.2430^a
1996	8.707	4.001	459	1.353	156	.34	145	39	269	4	27	.10	4.9619^a

a: significant at the 0.05 level; + with Yate's correction for continuity; API: annual parasite index (rate of parasitological confirmed malaria cases per 1,000 inhabitants).

Jamary municipality, where the Urupá farm is situated, the reduction followed the same general tendency: 34% reduction in overall malaria cases (50% reduction of *P. falciparum* malaria cases) from 1994 to 1996 (FNS, documents provided by the Coordenadoria Regional de Rondônia).

However, the linear regression analysis performed show that incidence is more pronounced in Urupá Farm than in the general municipality of Candeias. During the experimental control period the decrease in malaria incidence on the Urupá farm occurred in the first year of the project. The 90% reduction of *P. falciparum* in the second year compared to the period from 1991 to 1994 was highly significant when compared to the overall number of cases registered in Candeias municipality. Moreover, since the only four cases detected in 1996 were imported it means that *P. falciparum* transmission on the farm had been completely interrupted.

However, it should be mentioned that the total size of the population censed in 1995 was inferior to the average population censed in 1991. As we do not have data concerning oscilation of the number of inhabitants in the 1995 to 1996 period, we can not exclude size variation as causal agent of decrease in malaria incidence

It was surprising that the methods adopted produced a more pronounced reduction of *P. falciparum* than *P. vivax* infections. It is commonly claimed that drug resistance of *P. falciparum* to 4-amino-quinoleines and other synthetic anti-malarial drugs, is one of the important causes of malaria recrudescence in the world in general and in the Brazilian Amazon region in particular, where chloroquine resistance of local *P. falciparum* strains has been described as very generalized (Alecrim 1981, Reyes et al. 1985, Couto et al. 1995).

However, our experience in Rondônia over the last five years (unpublished data) coincides with that of De Souza (1992) that confirms that FNS's regimen using associations of quinine with tetracycline, or quinine with oligomycin provide very successful treatments of *P. falciparum* malaria with no recrudescence.

P. falciparum malaria is responsible for both more serious and precocious symptoms. It is thus logical that in a community that has access to immediate clinical assessment of the cases and access to prompt treatment that *P. falciparum* rather than *P. vivax* malaria transmission will be controlled. This is in fact what we saw in Urupá were the community control program resulted in a drop in the average delay between the beginning of symptoms and the onset of the treatment from 3.5 days to 1.3 days.

The problem with *P. vivax* infections is that one has to consider that recrudescences (relapses) are due to the presence of liver hypnozoites. These could represent a potential increase in the sources of infection and consequent transmission by the vector. In our sample we observed three cases of possible late recrudescences among 39 cases of *P. vivax* malaria. However, this is complicated even further by the fact that in general patients do not complete the full treatment with primaquine which has to be taken for 14 days after an initial three day chloroquine treatment. To compensate for this other complementary measures must be adopted to improve the treatment of *P. vivax* liver hypnozoites which would further reduce *P. vivax* transmission.

Finally we must also consider the possible development of some degree of premunition against *P. vivax* in the local communities. Clyde (1989) discussed the potential impact of that this has on transmission. In our previous cross-sectional surveys (Camargo et al. 1994) in Urupá we did not detect asymptomatic carriers, but in the nearby locality of Portuchuelo we have had some indirect evidence of *P. vivax* premunition in adults who have lived for many years in the endemic area (Camargo et al. 1999).

We are presently investigating the presence of premunition to *P. vivax* in local populations of Rondônia and plan to establish another pilot control project in a locality with a greater number of residents.

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