Cross-sectional Study Defines Difference in Malaria Morbidity in Two Yanomami Communities on Amazonian Boundary between Brazil and Venezuela

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It is well established that immunity to malaria is short-lived and is maintained by the continuous contact with the parasite. We now show that the stable transmission of malaria in Yanomami Amerindian communities maintains a degree of immunity in the exposed population capable to reduce prevalence and morbidity of malaria. We examined 508 Yanomami Amerindians living along Orinoco (407) and Mucajaí (101) rivers, on the Venezuelan and Brazilian Amazon region, respectively. At Orinoco villages, malaria was hyperendemic and presented stable transmission, while at Mucajaí villages it was mesoendemic and showed unstable transmission. The frequency of Plasmodium vivax *and* P. falciparum *was roughly comparable in Venezuelan and Brazilian communities. Malaria presented different profiles at Orinoco and Mucajaí villages. In the former communities, malaria showed a lower prevalence (16% x 40.6%), particularly among those over 10 years old (5.2% x 34.8%), a higher frequency of asymptomatic cases (38.5% x 4.9%), and a lower frequency of cases of severe malaria (9.2% x 36.5%). Orinoco villagers also showed a higher reactivity of the immune system, measured by the frequency of splenomegaly (72.4% x 29.7%) and by the splenic index (71.4% over level 1 x 28.6), and higher prevalence (91.1% x 72.1%) and mean titer (1243 x 62) of antiplasmodial IgG antibodies, as well as a higher prevalence (77.4% x 24.7%) and mean titer (120 x 35) of antiplasmodial IgM antibodies. Our findings show that in isolated Yanomami communities the stability of malaria transmission, and the consequent continuous activation of the immune system of the exposed population, leads to the reduction of malaria prevalence and morbidity.*

Key words: malaria - morbidity - immunity - Yanomami Amerindians - Amazon region - Brazil

Malaria is the parasitic disease of greatest prevalence and severity in the world, where 40% of the population (2.4 billion people) is exposed to the infection, especially those who live in tropical and subtropical countries. In these regions, between 300 and 500 million of cases a year are detected, what causes from 1.5 to 2.7 million deaths, mostly among children under one year old (WHO 1999).

In Americas and Caribbean, 38% of the population (308 million people) lives in areas of malaria transmission. In 1998, a total of 1.3 million cases were diagnosed, 36% of which in Brazil (OPS 1998). In 1999, 610,000 cases of malaria were registered in Brazil and 99% of them, in the Amazon region (Funasa 2000). The number of cases diminished considerably during the years of 2000 and 2001, perhaps because of control intensification. However, in 2002 and 2003 a progressive increase of malaria transmission occured, even in urban areas like Manaus (Funasa 2002, Fundação de Medicina Tropical do Amazonas 2003).

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A significant part of the Amazon Basin inhabitants is constituted of Amerindians, and the introduction of diseases, like malaria, influences their growth rate, as reported by Ribeiro (1956), Lizot (1980), and Mello (1985). The Yanomami ethnic group represents one of the biggest Amerindian communities, estimated to have 22,786 members and live in small isolated villages at the Brazilian-Venezuelan border. The way malaria was introduced in the Venezuelan Yanomami villages is not well established. According to the Venezuelan General Direction of Malariology and to reports from *Parima-Culebra* Program, malaria was introduced in that area many decades ago. On the Brazilian side, there are indications that malaria was first detected in Yanomami villages at 1987, after the arrival of gold prospectors.

The objective of this work was to characterize the profile of malaria at the Yanomami villages of Ocamo, Mavaca, and Platanal, from the Orinoco basin, Federal Territory of Amazonas (Venezuela), and to compare with that of the villages of Homoshitheri and Tireitheri, located at Mucajaí basin, state of Roraima (Brazil).

Study area localization - Yanomami lands are located at a vast region of 192,000 km^2, in the border of Brazil and Venezuela, between 1º and 4º, north latitude, and 64º to 66º, west longitude. The study areas of Orinoco basin in Venezuela, and Mucajaí basin in Brazil, present close ecological relationships and are approximately 150 km far from each other. The Orinoco region is situated at South Venezuela and is included in the Amazon Federal Territory,

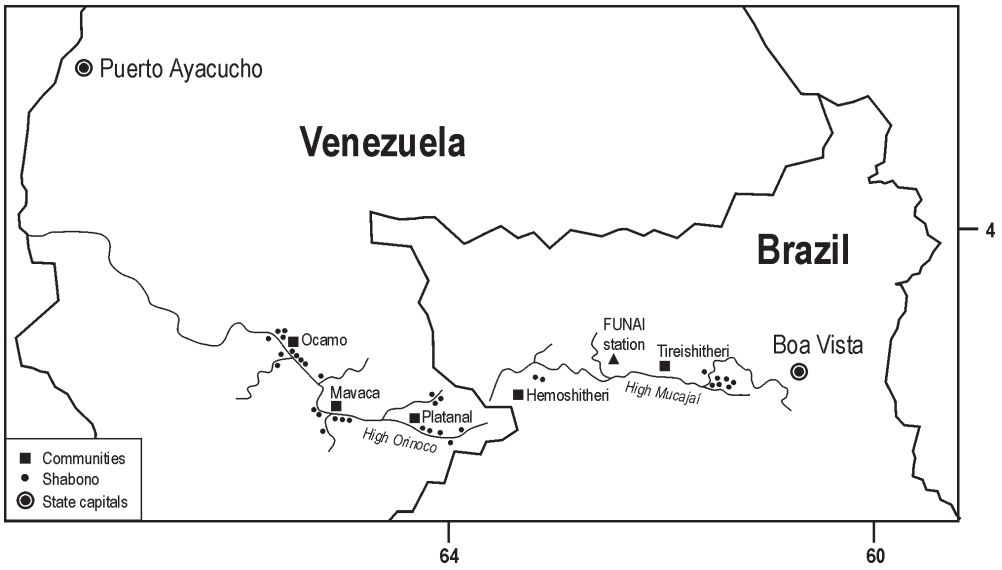

Fig. 1: location of the study areas in Brazil and Venezuela

which capital is Puerto Ayacucho. The Mucajaí region is located at North Brazil within the state of Roraima, which capital is Boa Vista (Fig. 1).

The Yanomami of the Orinoco region live in a plain, 400 m above sea level, the temperature ranges from 29 to 33ºC, during the day, and from 19 to 22ºC at night. The Yanomami of the Mucajaí basin are spread along a mountainous region, 900 m above sea level, and the temperatures ranges from 25 to 29ºC, during the day, and from 13 to 16ºC at night. In both areas, the relative humidity reaches 80% and the annual pluviometric rate is around 2000 mm, with an average higher than 100 mm per month. The villages are not provided with electricity, potable drinking water or sewage system. Health resources are incipient and reduced to a few health professionals and religious groups at the Orinoco region, and to a unit of Fundação Nacional do Índio (Indigenous National Foundation) at the Mucajaí region. No regular malaria control program is offered to the communities, and antimalarial drugs are used irregularly, mainly at the Orinoco region.

Population characteristics - The estimated Yanomami population was 22,786 people: 12,876 in Venezuela and 9910 in Brazil (Marcano 1991).

It is accepted that Yanomami people belong to a single linguistic and cultural branch, although subtle differences, either in language and in some customs have been reported. Migliazza (1967) established four linguistic subgroups: Yanomami, Yanomam, Yamam, and Sanumas. The population studied at Orinoco and Mucajaí belong, respectively, to Yanomami, and Yanomam groups. During the present study, we could observe that differences between both sub-groups, regarding language and customs, were not so evident, as stated by Lizot (1988). Thus, we will refer to the population of both areas as Yanomami.

Nowadays, the Yanomami people are agriculturist and sedentary, but they do not forget their intermittent nomadism (Chagnon 1968, Lizot 1980). Albert and Megola (1990) characterize them as hunters and horticulturists, whose energetic necessity is mainly fulfilled through agriculture and harvest (77%), while their protein necessity is satisfied by hunting and fishing (Lizot 1980). This economic model allows commercial exchange and harmonious alliances among different groups, what fulfills their social needs.

Population of both studied areas usually refers to their dwellings as “Shabono” or “Shapono”; in Mucajaí region, they also use the term “Yano”. It consists of a circular collective construction, which shelters from 20 to 120 individuals, joined according to familiar habits around a fire, near which they hung their hammocks and make their meals.

METHODOLOGY

Population and sample - On the Venezuelan side, at Orinoco basin, the population of 25 “Shabonos” of Ocamo, Mavaca, and Platanal communities consisted of 1132 individuals, while on the Brazilian side, Mucajaí basin, 289 individuals lived in the nine “Shabonos” investigated. Tables I and II show the distribution by age group and sex of the population. This population was sampled by familiar dwelling. This convenience sampling was the only possible at those circumstances and consisted of about one third of the members of each family. Therefore, this study included 508 individuals, 407 belonging to Orinoco communities (35.9% of the total), and 101 to Mucajaí communities (34.9%).

Clinical and epidemiological data collection and recording - The 508 Yanomami sampled were interviewed and submitted to clinical and parasitological exams. Results were registered into three sections: (a) *identification and epidemiological data*: name, age, sex, name and localization of the *Shabono*, migration, number of malaria episodes, use of antimalarial drugs, and mosquito-net, last insecticide application in the *Shabono*, and coincidence between malaria and pregnancy; (b) *clinical data*: including general signs and symptoms, as axillary tempera-

ture, paleness, jaundice, prostration, leanness, and dehydration; respiratory system examination (breathing frequency, dyspnea, cough, expectoration, presence of rales, and/or crepitations and history of hemoptysis); cardiovascular system examination (heart frequency, arrhythmia, heart murmurs, lower members edema, history of struggle dyspnea, and palpitations); abdominal signs and symptoms (hepatomegaly, splenomegaly, abdominal ache, diarrhea, nausea, vomits, hematemesis, ascites, abdominal venous system); (c) *parasitological and serology data*: results of blood smear and serology.

The anamnesis was always performed by the first author in Yanomami language, assisted by a bilingual interpreter (a Yanomami native, who spoke Portuguese or Spanish). In order to compare the severity of malaria in Orinoco and Mucajaí communities, some parameters were considered: frequency and level of fever, presence of cachexia, dehydration, concussion, neurological signs (convulsion, irritability, coma), respiratory signs (dyspnea, rales), and cardiovascular signs (tachycardia, low debit, third heart sound, gallop rhythm).

Blood collection and evaluation of parasitemia - Venous blood was collected with sterile disposable syringes, and used for preparing thick and thin smears. Blood smears were fixed with absolute methanol, after hypotonic lysis of thick smears, stained with 10% Giemsa solution in phosphate buffer solution pH 7.2 for 30 min, and examined by skilled microscopists from either the Venezuelan or Brazilian malaria control services. The presence and concentration of malaria parasites were evaluated in a total of 100 microscopic fields per thick smear preparation, for at least 6 min. The species of malaria parasite was established through the examination of thin smears.

Parasitemia was assessed using a semi-quantitative method, as follows:

+ = 1-10 parasites per 100 fields
++ = 11-100 parasites per 100 fields
+++ = 1-10 parasites per 1 field
++++ = more than 10 parasites per field

Positive smears were reevaluated by a highly qualified microscopist, at the Laboratory of Malaria, Núcleo de Medicina Tropical, University of Brasília. The parasite density index was calculated summing the number of positive smears of each class (in cross) divided by the total positive smears of each age group.

Assessment of IgG and IgM antiplasmodial antibodies - Blood was kept at room temperature for about 5 h for coagulation and clot retraction, and serum samples were collected, distributed in samples of 3 ml and kept at 7º to 10ºC, until they were taken to the laboratory for processing, where they were at –70ºC.

Antiplasmodial IgG and IgM antibodies were quantified by the indirect immunofluorescence technique, according to Manawadu and Voller (1978). A pool of different isolates of *Plasmodium falciparum* (PfUnB 67 Ituxi AM, PfUnB 436 Porto Velho RO, and PfUnB 434 Peixoto de Azevedo MT), kept on continuous culture, was used as antigen, prepared according to Ferreira and Sanches (1988) and Avila and Ferreira (2000). Fluorescein-conjugated rabbit anti-human IgG (1/400) or IgM (1/300) immunoglobulins (Biolab)®, were used as conjugates.

TABLE I

Yanomami population and sample from High Orinoco distributed by sex and age group

	Population (N = 1132)			Sample (n = 407)			
Age group	Males	Females	Total	Males	Females	Total	(n/N)
Years	nr	nr	nr	nr	nr	nr	%
< 2	52	42	94	9	12	21	22.3
2 - 10	165	137	302	81	58	139	46.0
10 - 16	97	92	189	31	27	58	30.7
16 - 26	96	103	199	30	38	68	34.1
> = 26	185	163	348	59	62	121	34.8
Total	595	537	1132	210	197	407	35.9

TABLE II

Yanomami population and sample High Mucajaí distributed by sex and age group

	Population (N = 289)			Sample (n = 101)			
Age group	Males	Females	Total	Males	Females	Total	(n/N)
Years	nr	nr	nr	nr	nr	nr	%
< 2	8	5	13	4	2	6	46.1
2 - 10	43	39	82	15	14	29	35.3
10 - 16	23	28	51	4	4	8	15.6
16 - 26	26	20	46	22	11	33	71.7
> = 26	49	48	97	8	17	25	25.7
Total	149	14	289	53	48	101	34.9

Antibody to *P. falciparum* SPf66 protein was detected by ELISA test. This antigen is a protein prepared by chemical synthesis of three blood merozoite peptides, joined to a NANP sequence of *P. falciparum* circumsporozoite protein (Moreno & Patarroyo 1987), provided by Dr Manuel Patarroyo from the Immunology Institute, Hospital San Juan de Dios, Bogotá, Colombia.

Evaluation of the splenic index - The spleen was considered enlarged when it was detectable by superficial abdominal palpation or during deep inspiration. Splenomegaly was classified in five levels:

0 Spleen not palpable, even on deep inspiration
1 Spleen palpable on costal margin
2 Spleen palpable half way between the costal margin and the navel
3 Spleen palpable at the navel line
4 Spleen palpable below the umbilical line, fulfilling or not the iliac cavity

The *splenic index* were determined for children between 2 and 10 years old and for those over 10 years old. The percentage of palpable spleens was computed considering the age. The *average enlarged spleen* was calculated by multiplying the number of individuals in each level of splenomegaly by the level of spleen enlargement and dividing this figure by the total number of individuals with splenomegaly.

Statistical analysis of data - The differences (0.05) in malaria prevalence and morbidity, clinical manifestations, parasitemia, and immunity between Orinoco and Mucajai areas were compared using the Chi-square (χ^2) test or Ficcher's exact test.

Ethical issues - This investigation followed the ethical rules for investigation with indigenous communities established by Venezuelan and Brazilian authorities, and was locally supervised by their representatives. All adult participants or children's parent or responsible gave their written or fingerprint consent after being informed about the investigation.

RESULTS

Malaria prevalence among the Yanomami communities of the Orinoco basin was 16% (65/407), 2.5 times less than that observed among the communities of Mucajaí, which registered 40.6% (41/101), as shown in Table III (P = 0.0000). However, no difference was found in the prevalence of malaria among children under 4 years old living at Mucajaí communities (61.5% or 8/13) and those of the Orinoco basin (50% or 27/50) (P = 0.4546). As shown in Table III, 52 of the 65 (80%) cases of malaria at Orinoco communities were diagnosed in children under 10 years old, while only 18 of the 41 cases (44%) of Mucajaí occurred in this age group (P = 0.0345). In people over 10 years old, only 5.2% (13/247) had malaria at Orinoco communities, in deep contrast with 34.8% (23/66) at Mucajaí (P = 0.0000).

Fever was the most frequent clinical sign of malaria and was present in 61.5% of the cases from Orinoco and in 95.1% of those from Mucajaí (Table IV). In Orinoco communities fever was detected in 73% (38/52) of the children under 10 years old with malaria, but only in 15.4% (2/13) of those 10 years or older (P = 0.0001). Therefore fever was not detected in 27% of children under 10 years old with malaria and in 84.6% of those older than 10 years

TABLE III

Number and percentage of malaria cases in the sample by age group in High Orinoco and High Mucajaí

	High Orinoco			High Mucajaí		
Age group	Sample	Cases	Percentage	Sample	Cases	Percentage
Years	nr	nr	%	nr	nr	%
< 4	54	27	50.0	13	8	61.5
4 - 10	106	25	23.5	22	10	45.5
10 - 16	58	5	8.6	8	3	37.5
16 - 26	68	6	8.8	33	13	39.3
> = 26	121	2	1.6	25	7	28.0
Total	407	65	15.9	101	41	40.6

TABLE IV

Number of malaria cases by age groups and percentage of febrile cases in High Orinoco and High Mucajaí

	High Orinoco			High Mucajaí		
Age group	Cases	Febrile		Cases	Febrile	
Years	nr	nr	%	nr	nr	%
< 4	27	20	74.0	8	8	100.0
4 - 10	25	18	72.0	10	10	100.0
10 - 16	5	0	0	3	2	66.6
16 - 26	6	2	33.3	13	12	92.3
> = 26	2	0	0	7	7	100.0
Total	65	40	61.5	41	39	95.1

in Orinoco communities. This pattern was different among the communities of Mucajaí: 100% of malaria cases under 10 years old presented fever, while for those 10 years old, only 91.3% did so (P = 0.1996). Moreover, children under 10 years old living in Orinoco had less fever than those of Mucajaí (P = 0.0138).

No relevant difference was found in the frequency of *Plasmodium* species between Orinoco and Mucajaí communities. At the former, 67.7% of malaria cases were caused by *P. vivax*, 13.8% by *P. falciparum*, 13.8% by *P. malariae* and 4.6% by mixed infections (*P. vivax* and *P. falciparum*), while at Mucajaí, 78% of cases were caused by *P. vivax* and 22% by *P. falciparum* (Fig. 2). However, the individuals from the Orinoco communities presented a lower parasite density index (1.8) than that of Mucajaí individuals (2.5) (P = 0.0000), mainly in those over 10 years old.

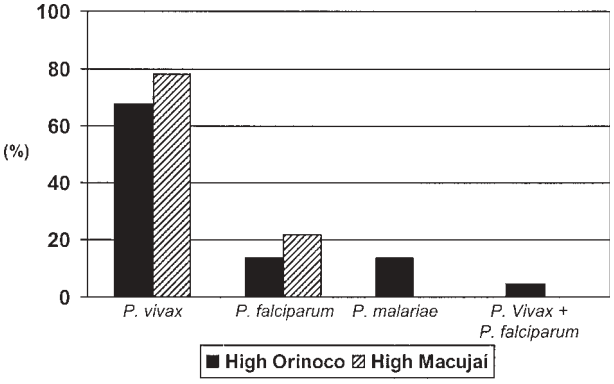

Fig. 2: percentage of *Plamodium* species in the High Orinoco and High Mucajaí areas

The cases of severe malaria were characterized by one or more of the following presentations: high parasitemia (+++ or ++++), prostration, dehydration, cerebral edema, convulsion, stupor or coma, respiratory distress syndrome, or any other situation that demanded parenteral treatment. As shown in Table VI, the frequency of severe cases of malaria was significantly lower among those living at Orinoco communities (9.2% or 6/65), than at Mucajaí (36.5% or 15/41) (P = 0.0005). Interestingly, severe cases of malaria occurred exclusively in patients under 10 years old at Orinoco region, while at Mucajaí 60% of severe cases were detected in patients 10 years old or more.

Splenomegaly was 2.4 times more frequent in patients from the Orinoco area, where it occurred in 72.4% (295/407) of the cases of malaria, than in Mucajaí (29.7% or 30/101) (P = 0.0000). Table VII shows the frequency of splenomegaly according to age group in both areas. The degree of splenomegaly was also higher among those living in the Orinoco area, where the average splenomegaly level was 2.0, and 1.2 in Mucajaí. This occurred because the frequency of big spleens was higher at the Orinoco basin (28.5%, 48.8% , 10.8% e 11.8% for levels 1, 2, 3, and 4, respectively) than at Mucajaí (73.3%, 26.6%, 2% and, 0%, respectively).

As shown in Table VIII, the individuals from Orinoco area presented a higher prevalence of IgG antiplasmodial antibody (91.1% or 360/395) than those from Mucajaí (72.1% or 70/97) (P = 0.0000), and the mean titer was 20 fold higher in Orinoco than in Mucajaí (1243 and 62, respectively) (P = 0.0000). This difference was detected exclusively among 10 years old or older patients. In this group the mean titers were 1535 and 65, respectively in Orinoco and Mucajaí areas (P = 0.0000). A similar pattern was found in relation to IgM antiplasmodial antibody. As shown in Table IX, the frequency of this antibody was 77.4% at Orinoco communities and 24.7% at Mucajaí (P = 0.0000), with mean titers of 120 and 35, respectively (P = 0.0000). Mean titers of individuals under 10 years old were 53 at Orinoco and 27 at Mucajaí, while this difference was four fold higher in the group of 10 years old or older: 164.3 and 40.3, respectively. IgG anti-SPf66 antibodies was detected in 93.3% (322/345) of the individuals from Orinoco

TABLE VI

Number and percentage of severe cases of malaria, by age group in High Orinoco and High Mucajaí

Age	High Orinoco			High Mucajaí		
group	Cases	Severe cases		Cases	Severe cases	
Years	nr	nr	%	nr	nr	%
< 4	27	5	18.5	8	4	50.0
4 - 10	25	1	4.0	10	2	20.0
10 - 16	5	0	0	3	1	33.3
16 - 26	6	0	0	13	6	46.1
> = 26	2	0	0	7	2	28.5
Total	65	6	9.2	41	15	36.5

TABLE V

Index and parasitic density by age group of the malaria cases, in High Orinoco and High Mucajaí

Age	High Orinoco						High Mucajaí					
group	Smear	Parasitic density				Index	Smear	Parasitic Density				Index
Years	Positive	+	++	+++	++++		Positive	+	++	+++	++++	
	nr	nr	nr	nr	nr		nr	nr	nr	nr	nr	
< 4	27	8	10	3	6	2.2	8	2	2	3	1	2.3
4 - 10	25	6	17	1	1	1.8	10	2	4	2	2	2.4
>= 10	13	12	1	0	0	1.0	23	3	8	5	7	2.6
Total	65	26	28	4	7	1.8	41	7	14	10	9	2.5

communities, and in only 54.7% (52/97) of those from Mucajaí. A positive correlation was found between the mean titers of IgG and IgM antiplasmodial antibodies and IgG anti-SPf66 antibody, and the levels of splenomegaly in both studied areas.

DISCUSSION

An important aspect of malaria epidemiology is the characterization of the degree of endemicity, which depends on the dynamics of malaria transmission and control. The splenic index of children from 2 to10 years old has been used as a marker of malaria transmission since its adoption by the WHO in 1951. Areas of malaria transmission are classified as hypoendemic, mesoendemic, holoendemic, and hyperendemic according to the occurrence of splenic index lower than 10%, 10 to 50%, 50 to 75% or higher than 75%, respectively. This classification is no more useful for areas where diagnosis and treatment of malaria are systematically applied. However, the scarcity of medical intervention among Yanomami communities may warrant the application of this classification of endemicity. Accordingly, the Orinoco area was considered as hyperendemic and Mucajaí as mesoendemic.

Mac Donald (1957) showed that the intensity and regularity of malaria transmission influence the degree of acquired immunity. In areas of *stable* malaria, where transmission is intense and constant throughout the year, exposed people develop a higher level of immunity, while in areas of *unstable* malaria, where transmission intensity and frequency are not so high, with irregular bursts, varying from month to month and from year to year, exposed people develop low immunity. According to this classification, malaria was considered stable at Orinoco communities, and unstable at Mucajaí communities. The stabil-

TABLE VII

Number and percentage of cases with splenomegaly by age group in High Orinoco and High Mucajaí

	High Orinoco			High Mucajaí		
Age group	Examined	Splenomegaly		Examined	Splenomegaly	
Years	nr	nr	%	nr	nr	%
< 4	54	46	85.1	13	3	23.0
4 - 10	106	83	78.3	22	8	36.3
10 - 16	58	39	67.2	8	3	37.5
16 - 26	68	47	69.1	33	7	21.2
> = 26	121	80	66.1	25	9	36.0
Total	407	295	72.4	101	30	29.7

TABLE VIII

Prevalence of IgG anti-plasmodium and mean geometric titers (MGT), by age group in High Orinoco and High Mucajaí

	High Orinoco				High Mucajaí			
Age group	Examined	Positives		MGT	Examined	Positives		MGT
Years	nr	nr	%		nr	nr	%	
< 4	51	40	78.4	204	12	9	75.0	37
4 - 10	101	96	95.0	905	21	15	71.4	70
10 - 16	57	50	87.7	1194	8	7	87.5	54
16 - 26	66	63	95.4	1493	31	24	77.4	69
> = 26	120	111	92.5	1920	25	15	60.0	80
Total	395	360	91.1	1243	97	70	72.1	62

TABLE IX

Prevalence of IgM anti-plasmodium mean of geometric titers (MGT) by age group in High Orinoco and High Mucajaí

	High Orinoco				High Mucajaí			
Age group	Examined	Positives		MGT	Examined	Positives		MGT
Years	nr	nr	%		nr	nr	%	
< 4	51	27	52.9	44	12	2	16.6	28
4 - 10	101	77	76.2	62	21	5	23.8	26
10 - 16	57	44	77.1	117	8	2	25.0	57
16 - 26	66	57	86.3	154	31	8	25.8	37
> = 26	120	101	84.1	222	25	7	28.0	27
Total	395	306	77.4	120	97	24	24.7	35

ity of malaria transmission depends on several factors including climate conditions, species of the vector, its anthropophylia, and vectorial capacity, on one hand, and to the effectiveness of the malaria control measures and the degree of host immune response on the other (Petersen et al. 1992, Snow & Marsh 2002, Gu et al. 2003). Orinoco and Mucajaí Yanomami communities live about 150 km far from each other, in comparable epidemiological conditions of malaria transmission, and were not submitted to any effective program of malaria control. The major difference between them was the degree of immunity of both populations. While over 90% of those from Orinoco communities presented IgG antibodies to plasmodium and to SPf66 protein of *P. falciparum*, at high titers, only 72.1% and 54.7%, respectively, of those from the Mucajaí communities presented these antibodies, and at lower titers. Moreover, splenomegaly, a marker of immune reactivity, was present in 72.4% of those from Orinoco and in only 36.5% of the cases from Mucajaí. The higher degree of immunity in the Orinoco population involved both anti-parasite and clinical immunity; parasitemia was lower at this area, particularly among those older than 10, and the frequency of asymptomatic infection was very high, reaching 38.5% of infected people, in contrast to 4.9% in Mucajaí. On the other hand only 9.2% of cases of severe malaria was diagnosed in Orinoco, while this frequency reached 36.5% in Mucajaí.

Our data point out an intriguing situation: malaria is hyperendemic and its transmission is stable among Orinoco communities, nevertheless, in this area, its prevalence and morbidity are lower than those found in Mucajaí communities, where the infection is mesoendemic and transmission unstable. A possible explanation for this finding is the fact that Orinoco villagers have experienced malaria for a long time, while this infection was recently introduced to Mucajaí communities, due to the outburst of gold prospectors that has broken population isolation. The prolonged and continuous contact with malaria parasite, as happened in Orinoco villages, has been considered as necessary to build up an effective immunity to malaria (Nielsen et al. 2002). Antimalarial immunity can suppress gametocytemia (Baird et al. 1991), and therefore reduce malaria transmission, and control parasitemia (Bull & Marsh 2002), leading to a reduction in malaria morbidity. It can be assumed that the relative isolation of Yanomami villagers (Laserson et al. 1999) restricted the variety of circulating isolates of malaria parasites (Maitland et al. 2000) and contributed to the efficacy of immunity.

Our findings show that in isolated Yanomami communities the stability of malaria transmission and the consequent continuous activation of the immune system of the exposed population leads to the reduction of malaria prevalence and morbidity.

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