Am. J. Trop. Med. Hyg., 76(4), 2007, pp. 619–625

MALARIA RISK FACTORS IN AMERINDIAN CHILDREN IN FRENCH GUIANA

SARAH HUSTACHE,* MATHIEU NACHER, FÉLIX DJOSSOU, AND BERNARD CARME

Equipe EA 3593, Laboratoire Hospitalo Universitaire de Parasitologie Mycologie, Université Antilles Guyane, Campus Saint Denis; Department of Health Centers, Cayenne General Hospital, Cayenne, French Guiana

Abstract. Malaria is a major public health problem in French Guiana. This study was conducted in children <1–5 years of age in Camopi, an Amerindian village in eastern French Guiana. Medical, environmental, and behavioral predictive factors of malaria were studied using the Kaplan-Meier method and Cox modeling. Variables included were clearing vegetation around the home (hazard ratio [HR] = 0.62, 95% confidence interval [CI] = 0.43–0.88 for 50–75% cleared and HR = 0.5, 95% CI = 0.31–0.81 for > 75% cleared) relative to homes surrounded by vegetation; distance of a home from a river (HR = 0.56, 95% CI = 0.37–0.85 for distances between 20 and 40 meters, HR = 0.72, 95% CI = 0.47–1.09 for distances between 40 and 80 meters, HR = 0.52, 95% CI = 0.28–0.94 for distances between 80 and 120 meters, and HR = 0.5, 95% CI = 0.30–0.86 for distances > 120 meters) relative to distances < 20 meters; the number of occupants in the home (HR = 1.54, 95% CI = 0.98–2.44 for 7 occupants, HR = 1.9, 95% CI = 1.29–2.81 for 8–11 occupants, and HR = 2.03, 95% CI = 1.27–3.23 for > 11 occupants); clothing (HR = 0.64, 95% CI = 0.46–0.90 for children wearing western-style clothes relative to those wearing the traditional kalimbe), and ethnicity (Wayampi children had a lower hazard of malaria relative to Emerillon children: HR = 0.55, 95% CI = 0.40–0.80). The environment near the home was strongly associated with malaria. This suggests that simple pragmatic protection measures would be useful in Camopi.

INTRODUCTION

Malaria is a major public health problem in French Guiana, an overseas French region located in the Amazon Basin in South America. Malaria control measures in French Guiana are based mainly on systematic treatment of attacks and house spraying. Since the 1970s, disease incidence has constantly increased, partly because of Brazilian and Surinamese immigration.[1] To date, malaria incidence rates in French Guiana are among the highest in South America.[2] This may also be caused by increased human activities that favor malaria transmission. The epidemiology of malaria in French Guiana is very heterogeneous, probably because of highly diverse environmental conditions and a wide range of population densities and mixed ethnic groups.

More than 90% of the malaria cases occur in foci of stable transmission disseminated along the Maroni River (Western border with Surinam) and the Oyapock River (Eastern border with Brazil). The coastal area along the Atlantic Ocean has almost no malaria transmission. The malaria parasites responsible for most cases reported each year include mainly *Plasmodium falciparum* and *P. vivax*. The former is most predominant in the Maroni area and the latter is more frequent in the Oyapock area. Knowledge about the epidemiology of malaria is sketchy in this region, notably about places and circumstances of infection. The principal vector mosquito is *Anopheles darlingi*, which is the most anthropophilic mosquito in South America, and is known to be endophagic and exophagic, to breed mainly along the rivers, and to have a nocturnal activity.[3] However, *An. darlingi* seems to be able to modify and adapt its behavior according to the characteristics of the region.[4]

Malaria transmission can vary from village to village but also from household to household in the same village. These patterns probably reflect a composite of heterogeneities in the environment, vector distribution, human vector contact, and household and human host factors. Successful control of malaria depends upon detailed knowledge of its epidemiology, including social and economic factors. This study attempted to identify risk factors of such variations in a forest setting in Camopi village in French Guiana among Amerindian children less than five years of age, a population that is most vulnerable to malaria.

METHODS

Study site. Camopi is an Amerindian village located in the Amazon forest along the Oyapock River. It is made up of 22 hamlets covering an area of 15 km^2. The inhabitants are mainly of the Wayampi and Emerillon ethnic groups. They live in traditional huts or *carbets*, which have a wooden floor and a roof of steel sheet, canvas sheet, or palm leaves. These structures traditionally have no walls, but some are now enclosed by wood or canvas sheets. The Wayampis hamlets are located near the Oyapock River and the Emerillons hamlets are located near the Camopi River. A study conducted in 2002 in Camopi showed particularly high malaria incidence rates among children (661 cases per 1,000 person-years among those less than 15 years of age) caused by *P. vivax* in 60% of the cases.[5]

Study design and population. A retrospective study using an open cohort design was carried out with all Wayampi and Emerillon children less than 1 to 5 years of age between January 1 and December 31, 2001. Informed consent was provided by the legal guardian of every child before admission into the study. The study was reviewed and approved by the Ethical Committee of Antilles-Guyane.

Follow-up and all medical data were managed by the Camopi Health Center by two physicians, two nurses, and one Amerindian assistant. The children came to the health center approximately once a month, generally at the time of illness. Data for children for whom follow-up by the Health Center had been interrupted were right censored at the interruption date.

Clinical and parasitologic diagnosis. Malaria was defined as fever (temperature ≥ 38°C at consultation or fever within the

* Address correspondence to Sarah Hustache, Laboratoire Hospitalo-Universitaire de Parasitologie-Mycologie, Centre Hospitalier de Cayenne, BP 6006, 97300 Cayenne, French Guiana. E-mail: sarah.hustache@yahoo.fr

past 48 hours) associated with *Plasmodium* asexual forms on a thin blood smear. All thin blood smears were first analyzed in Camopi by a trained nurse and then checked at the parasitologic laboratory at Cayenne Hospital. The list of all clinical malaria episodes, their date of occurrence, and *Plasmodium* species identified was based on records of treated malaria patients obtained from the Cayenne Hospital. This list was then used in Camopi with the "carnet de santé" (a personal booklet of medical information kept at the Camopi Health Center) for each child.

Retrospective collection of risk factors. Environmental exposure was evaluated by direct observation of the patients' houses. All distances (to the river, the nearest home, the forest, and the health center) were evaluated by s geographic positioning system or direct measurement for distances < 50 meters. A standardized questionnaire about behavioral habits, use of prophylactic measures, knowledge of malaria, and social and economic status was administered individually to every child's mother during the visits.

Statistical analysis. Possible risk or protective factors were adjusted for potential confounders using the Cox proportional-hazards model. Entry date into the study was January 1, 2001 or the birth date for children born after this date. Exit date was December 31, 2001 or the fifth birthday of a child if he or she was born before January 1, 2001. Time under risk was the time from entry in the study until exit. We did not substract any period for any children receiving treatment for a current episode because some children may have had a *P. falciparum* malaria attack shortly after a *P. vivax* malaria attack (all malaria attacks were treated when diagnosed).

The influence of each variable on malaria incidence was assessed using the Kaplan-Meier method and Cox modeling. The proportional hazards assumption was tested graphically and with tests based on Schoenfeld residuals.

Changes in the risk of a first malaria attack were investigated using a single-failure Cox model. This concerned the first episode after inclusion in the study, assuming that some children may have had a malaria attack before inclusion. Factors influencing all the malaria attacks were then investigated using a multiple-failure Cox model (taking into account all the malaria attacks and making no difference between a relapse case and a new malaria case). In both instances, univariate and a multivariate analysis was carried out.

All models were stratified by year of birth, accounting for age (which violated the proportional hazards assumption) and the period of birth (malaria incidence variations according the year). The most parsimonious model was obtained using the log-likelihood ratio test to remove variables from the saturated model. Convergence of this model with both forward and backward automatic stepwise elimination was checked. STATA version 8 software was used for all statistical analyses (STATA Corporation, College Station, TX).

RESULTS

Three hundred sixty-nine children were admitted into the cohort, which was composed of children living permanently in Camopi. There were 177 (47.9%) girls and 192 (52.1%) boys. During the follow-up, 676 malaria cases were observed: 178 caused by *P. falciparum*, 472 by *P. vivax*, 20 by mixed infections, and 6 by unidentified species.

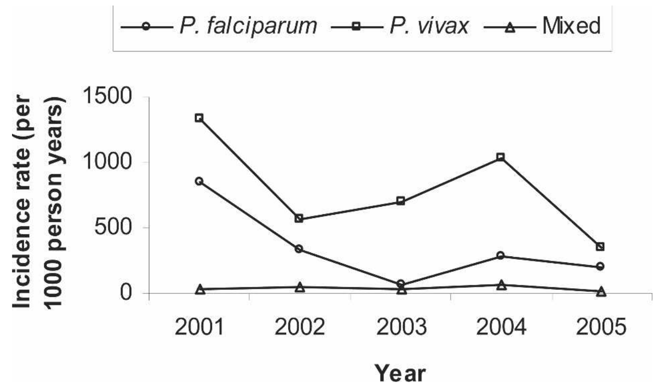

FIGURE 1. Malaria incidence rate by year, Camopi, French Guiana. *P.* = *Plasmodium*.

Description of the population. Forty four percent of the children were Emerillon, 53.5% were Wayampi, and 2.5% were mixed Wayampi-Emerillon. Eighteen percent of the children lived in Camopi village and the others lived on the Oyapock River (59.9%) and the Camopi River (40.1%). The median survival time without a malaria attack was two years, seven months. One percent of the children had their first attack before the age of four months. There were only nine hospitalizations (1.33%) and there were no deaths during follow-up.

Only 25.3% of the mothers could name at least one antimalarial treatment, and only 39.5% mentioned mosquitoes as malaria vectors. However, malaria was considered a severe and urgent disease by most people (75.3%). In Camopi, 69.8% of the children spent all their nights under bed nets. Many families used insecticides and cutaneous repellent (65.7% and 67.7%, respectively).

Malaria incidence. Overall annual incidence during the study period was 935 per 1,000 person-years with 246 per 1,000 person-years attributed to *P. falciparum* and 643 per 1,000 person-years attributed to *P. vivax*. This varied greatly from year to year (Figure 1). However, *P. vivax* remained the most incriminated species (69.8% of all malaria cases). Malaria incidence also varied by age with a peak of clinical malaria episodes in children between 2 and 3 years of age (Figure 2). We did not observe any significant variation of malaria incidence between the dry season (from July to December) and the rainy season (from January to June) ($P = 0.143$, by chi-square test).

Risk factors of first attack using a single failure Cox model. Time to first malaria attack (*P. falciparum* and *P. vivax*) was

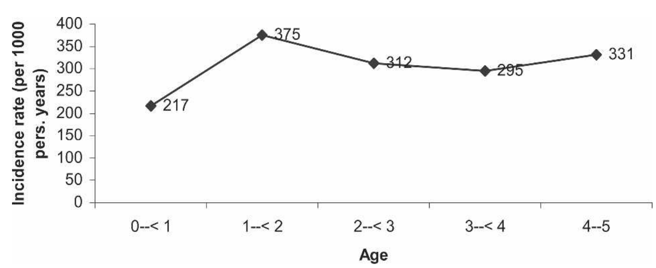

FIGURE 2. First malaria attack incidence rate by age, Camopi, French Guiana. Pers. = person.

considered. Univariate analysis showed that 12 variables were associated with malaria incidence (Figure 3 and Table 1). Hematinic treatment was the only medical variable significantly associated with malaria. With regard to environmental exposures, clearing vegetation around the home and living in a home far from the river were associated with a lower risk of malaria. Conversely, children living in homes surrounded by water (river or swamp) were at higher risk. Living in an isolated village (more than 3 km from Camopi village) or in a home with more than 6 occupants was associated with an increased risk of malaria. With regard to interview data, parents' income was associated with malaria: children from couples receiving at least one salary had a lower risk of malaria than those receiving less (the same applied for family having a television set or other socioeconomic proxies). It was noteworthy that Wayampi children had a much lower hazard ratio than Emerillon children.

Multivariate analysis using Cox modeling identified five

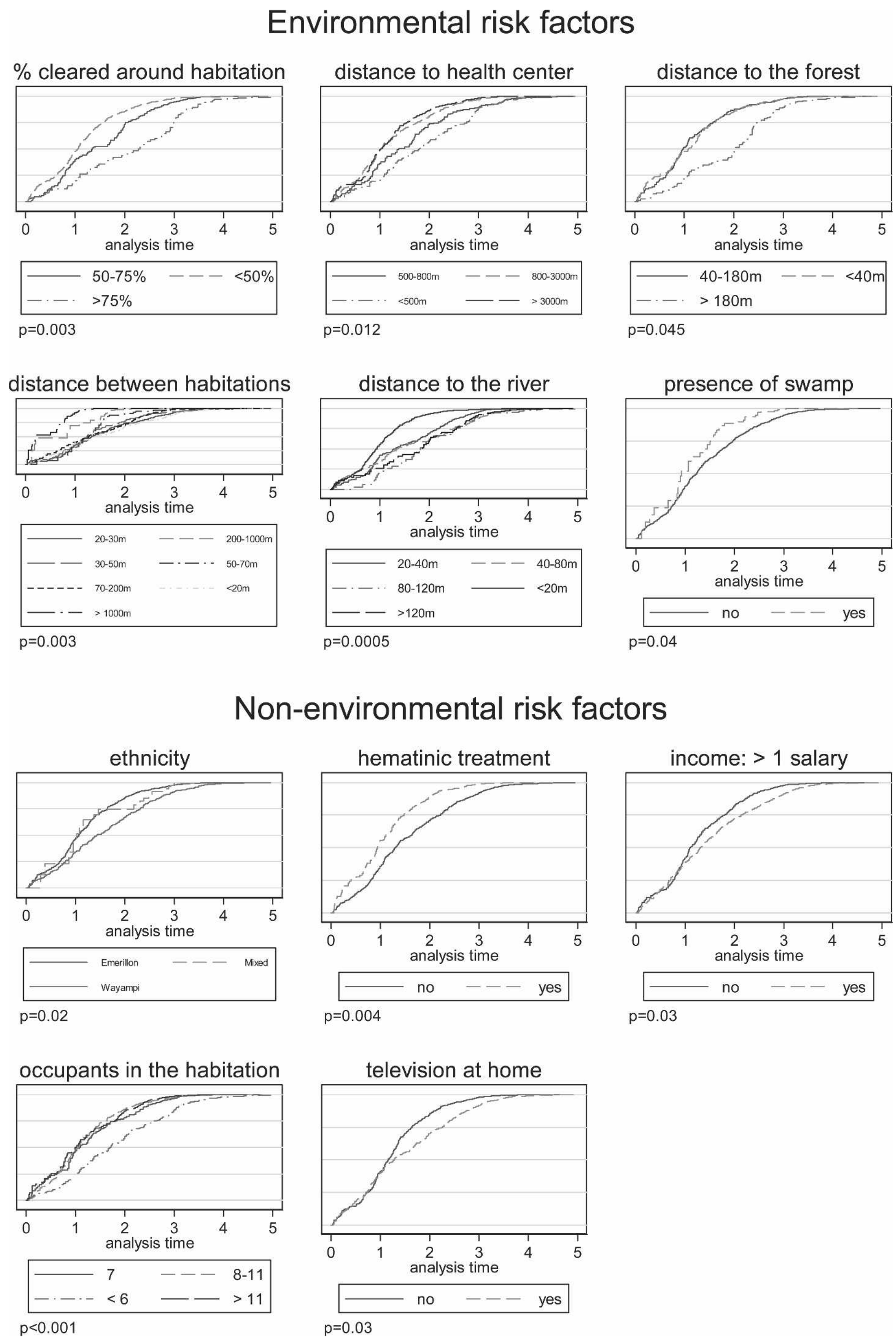

FIGURE 3. Risk factors of first malaria attack, by univariate analysis, Camopi, French Guiana. Estimation of the function 1 − survival was determined by the Kaplan-Meier method. The *P* value for analysis time in years was obtained by the log rank test.

TABLE 1
Risk factors of first malaria attack by univariate analysis, French Guiana*

		No. of children	Hazard ratio	95% CI	P
Hematinic treatment	No	272	1		
	Yes	67	1.59	1.15–2.19	0.004
% cleared around home	< 50	175	1		
	50–75	101	0.76	0.55–1.04	0.095
	> 75	75	0.51	0.34–0.77	0.001
% with river around home			1.01	1.003–1.02	0.003
Distance to nearest home, meters	< 1,000	267	1		
	1,000–1,500	73	2.77	1.20–6.42	0.017
	> 1,500	11	2.34	1.07–5.15	0.033
Distance to Camopi, meters	< 500	89	1		
	500–800	67	1.06	0.67–1.69	0.777
	3,000–5,000	118	1.74	1.19–2.54	0.004
	> 5,000	77	1.45	0.96–2.22	0.078
Distance to the river, meters	< 20	104	1		
	20–40	77	0.63	0.43–0.92	0.019
	41–80	86	0.57	0.39–0.83	0.004
	81–120	38	0.37	0.21–0.65	0.001
	> 120	46	0.50	0.32–0.80	0.004
Distance to the forest, meters	< 40	92	1		
	40–100	90	0.98	0.67–1.42	0.915
	101–180	83	0.58	0.38–0.88	0.012
	> 180	86	0.79	0.54–1.15	0.226
Presence of swamp	No	335	1		0.04
	Yes	16	1.77	1.005–3.11	
No. of occupants	< 6	128	1		
	7	66	1.87	1.25–2.81	0.02
	8–11	100	2.33	1.62–3.33	< 0.001
	> 11	57	1.65	1.07–2.56	0.024
Ethnicity	Emerillon	162	1		
	Wayampi	198	0.67	0.50–0.89	0.006
Parents income	< 1 salary	175	1		
	≥ 1 salary	166	0.73	0.55–0.97	0.032
Television	No	135	1		
	Yes	206	0.73	0.55–0.97	0.032

* Univariate analysis of risk of first malaria attacks estimated from a single failure Cox model. Analysis time = 563.68 person-years. CI = confidence interval.

variables associated with occurrence of a first malaria attack (Table 2). Clearing vegetation around the home was strongly associated with a decreased risk of malaria after adjusting for potential confounders. The was also true for the occupants of homes more than 20 meters from the river relative to those living less than 20 meters from the river. Human aggregation in the household was associated with malaria (higher risk for children living in a home occupied by more than six persons). Ethnicity remained strongly associated with malaria risk, even after adjusting for other environmental and behavioral factors, with Emerillon children being at higher risk. Modern clothing was a protective factor relative to kalimbe (traditional Amerindian loincloth).

Risk factors of malaria attack using a multiple failure Cox model. All malaria attacks were analyzed regardless of the *Plasmodium* species involved (observations were not censored after the first attack). Univariate analysis identified all variables associated with malaria in single-failure analysis. In addition, hard roofs (steel sheet or wood), indoor residual spraying (IRS), use of bed nets, and use cutaneous repellents were associated with protection. A past history of treatment for intestinal protozoa, going regularly into the forest for less than a day, and going daily to the river were associated with malaria (Table 3).

In addition to variables previously identified in single failure analysis, multivariate analysis identified remoteness from the forest and use of cutaneous repellents as protective factors. Hematinic treatment and treatment for intestinal protozoa remained associated with an increased risk of malaria after adjusting for confounders. Conversely, distance from the river and ethnicity were no longer significantly associated with the risk of malaria (Table 4).

TABLE 2
Risk factors of first malaria attack, by multivariate analysis, French Guiana*

		Hazard ratio	95% CI	P
% cleared	< 50	1		
	50–75	0.62	0.43–0.88	0.008
	> 75	0.5	0.31–0.81	0.005
Distance to the river, meters	< 20	1		
	20–40	0.56	0.37–0.85	0.006
	41–80	0.72	0.47–1.09	0.128
	81–120	0.52	0.28–0.94	0.033
	> 120	0.5	0.30–0.86	0.012
No. of occupants	≤ 6	1		
	7	1.54	0.98–2.44	0.061
	8–11	1.9	1.29–2.81	0.001
	> 11	2.03	1.27–3.23	0.003
Ethnicity	Emerillon	1		
	Wayampi	0.552	0.401–0.796	< 0.001
Clothing	Kalimbe	1		
	Modern	0.64	0.46–0.90	0.011

* Multiivariate analysis of risk of first malaria attacks estimated from a single failure Cox model, statified for year of birth (saturated model with 23 variables, which were significant at $P > 0.25$ in univariate analysis. The most parsimonious model was selected manually using the loglikelyhood ratio test. Automated forward and backward stepwise elimination were convergent with the manual procedure hereabove. Analysis time = 563.68 person-years. Proportional hazards assumption checked (Schoenfeld: $P = 0.862$). CI = confidence interval.

TABLE 3
Risk factors of malaria attacks, by multiple failure univariate analysis, French Guiana*

		No. of children	Hazard ratio	95% CI	*P*
Hematinic treatment	No	272	1		< 0.0001
	Yes	67	1.69	1.43–1.99	
Passed intestinal parasitic treatment	None	98	1		0.07
	For helminths	78	1.13	0.84–1.51	
	For protozoa	9	1.83	1.12–3.01	
	Both	154	1.24	0.97–1.61	
Presence of hard roof	No	93	1		< 0.0001
	Yes	258	0.55	0.41–0.73	
Distance to health center, meters	< 500	89	1		< 0.0001
	50–800	67	1.12	0.86–1.45	
	801–3,000	118	1.68	1.35–2.09	
	> 3,000	77	1.86	1.49–2.33	
Distance to the river, meters	< 40	181	1		< 0.0001
	40–120	124	0.56	0.47–0.67	
	> 120	46	0.61	0.47–0.78	
Distance to the forest, meters	< 100	182	1		< 0.0001
	> 100	169	0.60	0.51–0.71	
Presence of swamp	No	335	1		0.011
	Yes	16	1.50	1.09–2.05	
> 1 family in home	No	206	1		0.0006
	Yes	145	1.30	1.12–1.52	
No. of occupants	≤ 6	128	1		< 0.0001
	7	66	1.74	1.38–2.18	
	8–11	100	1.91	1.56–2.33	
	> 11	57	1.98	1.59–2.46	
House spraying	No	122	1		< 0.0001
	Yes	229	0.71	0.61–0.83	
Ethnicity	Emerillon	162	1		< 0.0001
	Wayampi	198	0.67	0.57–0.78	
Use of bed net	Never	49	1		0.02
	Sometimes	40	0.77	0.57–1.03	
	Often	15	1.03	0.71–1.48	
	Always	239	0.75	0.61–0.92	
Use of cutaneous repellents	Never	110	1		< 0.0001
	Regularly	232	0.60	0.49–0.73	
Parents income	< 1 salary	175	1		< 0.0001
	≥ 1 salary	166	0.72	0.62–0.84	
Television at home	No	135	1		< 0.0001
	Yes	206	0.70	0.60–0.81	
Having a boat motor	No	175	1		0.006
	Yes	165	0.80	0.69–0.94	
Going to the river	< 3times/week	20	1		< 0.0001
	3–7 times/week	22	2.37	1.26–4.44	
	Several times/day	301	3.17	1.93–5.21	
Going to the forest	Rarely	115	1		0.02
	Regularly	228	1.22	1.07–1.39	

* Univariate analysis of risk of malaria attacks estimated using a multiple failures Cox model. Analysis time = 722.59 person-years. CI = confidence interval.

DISCUSSION

The environment near the home was strongly associated with malaria incidence in children 0–5 years old in this study. Proximity to the river and to the forest were associated with a higher risk of malaria, as observed elsewhere.[6] The minimum distances needed for protection differ in various studies.[7–9] In Camopi, a distance of 40 meters from the river and 100 meters from the forest were associated with a lower risk of malaria. Clearing the vegetation around the home was associated with a two-fold reduction of malaria incidence in children. This could be a practical, simple, and efficient intervention that had never been explicitly formulated. Conversely, activities near the river or in the forest, as well as trip by children with their parents (a few days spent in the forest for hunting or cultivation) were not associated with malaria in this study. This suggests that transmission predominantly occurs in the villages, contrary to a popular belief that transmission is linked to forest activity in French Guiana.

Apart from the high risk associated with proximity to the river, the presence of water around the home (swamps, puddles, wells, containers) was associated with malaria only for swamps and only by univariate analysis. This suggests that river banks may be the essential vector breeding sites in Camopi. This is consistent with another study conducted in Belize, in which the malaria vector is the same as in Camopi.[10]

Children living in isolated villages, as well as those living in isolated homes, had an increased risk of malaria. However, a higher number of people in the same home (more than six occupants) was associated with a higher risk of malaria. Human aggregation is likely to increase the probability for vectors near homes to be infected. Similar observations have also been made in northeastern Venezuela.[11]

Hematinic treatment was associated with subsequent malaria attacks by univariate single failure analysis, and after adjustments, by multiple-failures analysis. This association has been previously described.[12,13] Hematinic treatment could increase the number of reticulocytes and transform a latent infection into a symptomatic attack.[14] This suggests that increased surveillance of children receiving hematinic treatment may be useful. The role of treatment for intestinal protozoa is difficult to explain; the presence of parasites was not documented and it was not a time-dependent variable. Therefore, it is unclear if being infected with intestinal worms was a protective factor. Conversely, if treated children were infected, this would imply that intestinal protozoa infections would be associated with a higher risk of malaria.

Family income was associated with the risk of malaria in Camopi, as in other parts of the world. However, construction with poor materials and closure of the house did not play a major role in the occurrence of attacks. These findings differed from those in other studies.[15,16]

Use of cutaneous repellents and bed nets was associated with a lower risk of malaria by univariate analysis in the multiple failure Cox model. However, this association with bed nets was not observed by multivariate analysis. This could be explained by the fact that nets commonly have holes and are not insecticide-treated. Moreover, several people often share the same bed net, which is often too small. This would result in children being against the edge of the bed net, thus exposing them to anopheline bites. It would be important to evaluate the impact of an insecticide-treated net distribution campaign, which surprisingly has never been conducted in this French administrative region where bed nets are already largely used and well-accepted. House spraying did not play a major role in protection against malaria in Camopi. This could be linked to its irregular use in this remote part of French Guiana. Moreover, the efficiency of this method for Amerindian homes, which are incompletely closed by walls, may not be optimal.[17]

The strong association of ethnicity with malaria incidence was noteworthy. Wayampi children were protected more from first malaria attack relative to Emerillon children, even after adjusting for behavioral and environmental factors. Some behavioral factors were not examined in this study and should be further explored.[18] However, a difference in genetic susceptibility could be involved in Amerindian tribes of different origins. This would explain some of the apparent clustering of the cases in Camopi, where, as shown by Smith and others, few children had most of the attacks.[19] Wayanas and Emerillons came to French Guiana in the 18th century from different parts of South America, and could have had a different history of malaria, with different selection pressures on their immunogenetic background. Differences in vector density between Camopi (where Emerillons live) and near the Oyapock River (where Wayampis live) also cannot be ruled out.

Different analyses (single and multiple Cox models) suggest different risk factors for malaria. The multiple failure analysis was more powerful and concerned all malaria attacks, but it did not find any difference between real new attacks and relapses because there was no molecular evidence of a different strain available. The single-failure Cox modeling analysis concerned only the first attack, and therefore could be more valid because it excluded relapses.

This study suggests additional research questions and some testable interventions such as clearing vegetation around homes. Malaria continues to be a major public health problem in Camopi, especially in children. Better comprehension of the epidemiology of malaria in this region could lead to pragmatic, efficient, and locally adapted measures in an integrated control program. These factors may be also relevant in other villages in similar ecotopes.

Received June 22, 2006. Accepted for publication October 31, 2006.

Acknowledgments: We the staff of the Health Center of Camopi, particularly Alain Maniglier, Anne Viaud, and Christelle Monnerville, for their assistance.

Authors' addresses: Sarah Hustache and Bernard Carme, Laboratoire Hospitalo-Universitaire de Parasitologie-Mycologie, Centre Hospitalier de Cayenne, BP 6006, 97300 Cayenne, French Guiana, E-mail: sarah.hustache@yahoo.fr. Mathieu Nacher, Centre d'Information et de Soins de l'Immunodéficience Humaine, Centre Hospitalier de Cayenne, BP 6006, 97300 Cayenne, French Guiana. Félix Djossou, Départements des Centres de Santé, Centre Hospitalier de Cayenne, BP 6006, 97300 Cayenne, French Guiana.

REFERENCES

1. Carme B, Venturin C, 1999. Malaria in the Americas. *Med Trop (Mars) 59:* 298–302.
2. Carme B, 2005. Substancial increase of malaria in inland areas of eastern French Guiana. *Trop Med Int Health 10:* 154–159.
3. Harris AF, Matias-Arnèz A, Hill N, 2006. Biting time of *Anopheles darlingi* in the Bolivian Amazon and implications for control of malaria. *Trans R Soc Trop Med Hyg 100:* 45–47.
4. Tadei WP, Thatcher BD, Santos JM, Scarpassa VM, Brandao Rodrigues I, Silva Rafael M, 1998. Ecologic observations on anopheline vectors of malaria in the Brazilian Amazon. *Am J Trop Med Hyg 59:* 325–335.
5. Carme B, Lecat J, Lefebvre P, 2005. Malaria in an outbreak zone in Oyapock (French Guiana): incidence of malaria attacks in the Amerindian population of Camopi. *Med Trop (Mars) 65:* 149–154.
6. Brooker S, Clarke S, Njagi JK, Polack S, Mugo B, Estambale B, Muchiri E, Magnussen P, Cox J, 2004. Spatial clustering of malaria and associated risk factors during an epidemic in a highland area of western Kenya. *Trop Med Int Health 9:* 757–766.
7. Van Der Hoek W, Konradsen F, Amerasinghe PH, Perera D, Piyaratne MK, Amerasinghe FP, 2003. Toward a risk map of malaria for Sri Lanka: the importance of house location relative to vector bredding sites. *Int J Epidemiol 32:* 280–285.
8. Staedke SG, Nottingham EW, Cox J, Kamya MR, Rosenthal PJ, Dorsey G, 2003. Short report: proximity to mosquito breeding sites as a risk factor for clinical malaria episodes in an urban cohort of Ugandan children. *Am J Trop Med Hyg 69:* 244–246.
9. Kleinschmidt I, Sharp BL, Clarke GP, Curtis B, Fraser C, 2001. Use of generalized linear models in the spatial analysis of small-area malaria incidence rate in Kwazulu Natal, South Africa. *Am J Epidemiol 153:* 1213–1221.
10. Hakre S, Masuoka P, Vanzie E, Roberts DR, 2004. Spatial correlations of mapped malaria rates with environmental factors in Belize, Central America. *Int J Health Geogr 22:* 3–6.
11. Barrera R, Grillet ME, Rangel Y, Berti J, Aché A, 1999. Temporal and spatial patterns of malaria reinfection in northeastern Venezuela. *Am J Trop Med Hyg 61:* 784–790.
12. Nacher M, McGready R, Stepniewska K, Cho T, Looareesuwan S, White NJ, Nosten F, 2003. Haematinic treatment of anaemia increases the risk of *Plasmodium vivax* malaria in pregnancy. *Trans R Soc Trop Med Hyg 97:* 273–276.
13. Sazawal S, Black RE, Ramsan M, Chwaya HM, Stoltzfuz R, Dutta A, Dhingra U, Kabole I, Deb S, Othman M, Kabole FM, 2006. Effects of routine prophylactic supplementation with iron and folic acid on admission to hospital and mortality in preschool children in high malaria transmission setting: Community-based, randomised, placebo-controlled trial. *Lancet 367:* 133–143.

14. Nacher M, 2005. Charming the mosquito: do malaria symptoms increase the attractiveness of the host vector? *Med Hypotheses 64:* 788–791.
15. Klinkenberg E, van Der Hoek W, Amerasinghe FP, 2004. A malaria risk analysis in an irrigated area in Sri Lanka. *Acta Trop 89:* 215–225.
16. Van der Hoek W, Konradsen F, Amerasinghe PH, Perera D, Piyaratne MK, Amerasinghe FP, 2003. Toward a risk map of malaria for Sri Lanka: the importance of house location relative to vector breeding sites. *Int J Epidemiol 32:* 280–285.
17. Raccurt CP, 1997. Malaria, *Anopheles*, the anti-malaria campaign in French Guiana: between dogmatism and judgment. *Med Trop (Mars) 57:* 401–406.
18. Garcia A, Dieng AB, Rouget F, Migot-Nabias F, Le Hesran JY, Gaye O, 2004. Role of environment and behaviour resemblances of *Plasmodium falciparum* infection in a population of Senegalese children. *Microbes Infect 6:* 68–75.
19. Smith DL, Duschoff J, Snow RW, Hay SI, 2005. The entomological inoculation rate and *Plasmodium falciparum* infection in African children. *Nature 438:* 492–495.