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ABSTRACT

Objectives: To investigate the epidemiology of falciparum malaria in workers from a highland tea plantation in western Kenya with very seasonally limited malaria transmission to determine what factors are associated with increased risk of malaria transmission in the Kenyan highlands.

Design: A cross-sectional study with rolling, random subject enrollment from April 1998 through October 1999.

Setting: Highland tea plantation located at 0°22' south and 35° 17' east in the Rift Valley highlands of western Kenya, an area with seasonally limited malaria transmission.

Subjects: The data for the study were obtained from enrollment of outpatients from the healthcare system of a major tea company, which has 18 estates with 22,000 workers and approximately 50,000 persons eligible for health care. Of the 2796 patients evaluated during the study period, 798 cases of malaria were confirmed by positive peripheral blood smear; 1998 smear-negative patients were pressured to be non-infected and served as controls (Ratio: 2.52: 1).

Interventions: Tea estate workers do not receive malaria chemoprophylaxis, but were given easily available free treatment for any symptomatic infections.

Main outcome measures: Smear-positive cases were compared with smear-negative patients for multiple demographic and disease variables, including sex, age, travel history, ethnic origin, home district transmission risk index and length of residence. Disease characteristics, including parasite types, counts and clinical symptoms, and treatments administered were described.

Results: Malaria was predominantly *P. falciparum* (>99%); asexual parasite counts ranged from 1-10,440 per mm³, with a mean of 803.6 (95% confidence interval: 695.2, 912.0). Gametocytemia was present in 7.5% of smear-positive malaria cases, but was rare in the absence of blood asexual forms (0.5%). Prior use of a variety of antimalarial drugs was extremely common and negatively predictive of parasitemia in patients presenting for clinical treatment (Pearson Chi-square 50.81, $p < 0.001$), as was a subjective history of previous malaria infection in the past year ($F = 26.65$, 14 df, $p < 0.001$; univariate ANOVA). Amodiaquine was the most commonly used drug to treat cases of either smear-proven or clinically suspected malaria, accounting for 56% of therapy; pyrimethamine/sulfadoxine was used to treat 27%, artemisinin 8% and chloroquine was administered to only 3%, while combination therapy was used in 5% of cases, and only a single treatment (0.1%) was recorded using quinine. Subjects with a prior history of treatment for malaria were statistically less likely to be infected again (Pearson Chi-square 50.81, $p < 0.001$). Presenting with symptoms suggestive of malaria was statistically associated with parasitemia, particularly fever, headache and dizziness, ($p < 0.001$ for all, univariate ANOVA), but in general, clinical symptoms were not an effective discriminator of malarial disease. Ethnic group predicted malaria infection with groups traditionally from the Lake Victoria lowland regions having a greater prevalence of parasitemia ($F = 2.04$, 4 df, $p = 0.002$, univariate ANOVA). Parasitemia was significantly associated with age less than ten years (Pearson Chi-Square 145.99, $p < 0.001$), with a history of travel more than twenty kilometers from site within six weeks (Pearson Chi-square 58.28, $p < 0.001$) and with time since arrival on the plantation of one year or less (Pearson Chi-square 185.12, $p < 0.001$).

Conclusion: Lower infection rates in persons with a history of prior infection implies a protective effect; the predilection of malaria for young and immunologically naive victims was confirmed. The proclivity in some ethnic groups for travel to holoendemic areas also accounts for the strong associations between recent travel, lowland ethnic group and infection. These findings taken together suggest that importation of malaria to the highlands, as well as travel away from the highlands, are important sources of new infections among persons living and working there.

INTRODUCTION

The epidemiology of falciparum malaria in workers from a highland tea plantation in western Kenya with very seasonally limited malaria transmission was investigated. Since the early 1950's, highland regions of western Kenya were considered to be free of indigenous malaria, with only imported cases occurring, but local epidemics have been shown to be increasing since about 1990(1). A severe disease outbreak affecting 314 plantation workers and 97 dependent family members at the Brooke Bond Kenya Ltd. tea company in Kericho from January through March 1998 prompted renewed interest in disease control in the workers of this key export industry. The lowland regions around Lake Victoria are notorious for holoendemic, chloroquine-resistant, falciparum, malaria transmission, with a high degree of naturally occurring host immunity in those indigenous to the region. The population of the highland tea plantation consists largely of workers and their families attracted to the region by steady wages. While many of the workers on the tea plantation bring their families and work for years, some migrate from lowland areas near Lake Victoria and return to the lowlands to visit relatives frequently. The worker population studied consisted of approximately 22,000 employees and about the same number of dependants residing on the tea plantation. The study was conducted from April 1998 through October 1999.

Background: The factors necessary for malaria transmission are the *Plasmodium* parasite, the *Anopheles* mosquito vector, and the human host. Both parasite and vector are affected by temperature and rainfall. Although temperature extremes kill *Anopheles* mosquitoes, temperatures between 15°C-3°C increase their rate of development. The gonotrophic cycle (interval between blood meals) shortens with increasing temperature, and the effect of a small temperature increase is greatest at the cooler ambient temperatures. Thus, a small rise in temperature from 19°C to 21°C shortens the gonotrophic cycle from 4 to 3 days, greatly increasing the vectorial capacity of the mosquito(2). Altitude is thought to be a proxy for temperature, so the actual limiting factor for malaria at high altitude is the effect of the lower temperature on the parasite(3). Despite the effect of altitude on ambient temperature, microclimatic factors (e.g. heated houses) can play an important role in facilitating malaria transmission and epidemics at higher elevations.

Unlike the parasite, the mosquito vector can commonly be found at altitudes from >1,600m to 3,000m(4,5), demonstrating that the limiting factor for malaria transmission at high altitude is the survival of the *Plasmodium* parasite. The *Anopheles* population is very sensitive to rainfall, which increases the availability of mosquito breeding sites. *A. gambiae*, the primary malaria vector of western Kenya, lays its eggs in small pools and puddles; in this region, rainfall of 150 mm per month leads to rapid expansion of the *A. gambiae* population(5,6) and hence increased risk for malaria transmission. Finally, epidemic malaria requires sufficient numbers of human gametocyte carriers to infect *Anopheles* mosquitoes and susceptible human hosts to acquire clinical infection(7).

Malaria apparently did not exist in the western Kenyan highlands until the second decade of the 20th century(8). In 1901, completion of a railway from the Kenya coast to Lake Victoria along with increased road transport facilitated the gradual spread of infective mosquitoes into the highlands from the low-lying holoendemic-disease areas(6). The development of tea estates in the highlands, with the concomitant clearing of the forests, provided suitable mosquito breeding grounds. Arrival of asymptomatic, gametocytemic individuals from other parts of Kenya completed the conditions necessary for malaria transmission. The first reported epidemic was in 1918 to 1919 when Kenyan soldiers returned from Tanzania after World War I(8). Two epidemics were recorded in the 1920's and four in the 1930's. Garnham(3) reported epidemics of malaria in the Londiani area of western Kenya from 1941 to 1944, close to the site of the present study, at an altitude of approximately 2,200 m. After the military camp in the area was disbanded in 1944, the local outbreaks ceased, but highland malaria continued to be a serious public health problem into the 1950's, when an extensive control programme essentially eliminated the disease(9). The highlands were considered free of malaria through the 1980's, but since 1990 malaria has been increasing(10).

More than 90% of malaria in Kenya is caused by *P. falciparum* (4,6) and is transmitted most often by *A. gambiae*, with *A. funestus* as a secondary vector. It had generally been assumed that malaria in the highlands of western Kenya was not due to local transmission, but was imported from the nearby holoendemic areas around Lake Victoria by the frequent travel of the tea plantation workers and their families, until Malakooti *et al.* (1) showed otherwise.

Geography: This study was conducted in the Kericho tea-growing area at 0° 22'south and 35° 17' east in the Rift Valley highlands of western Kenya, 80 from the holoendemic malaria area of the Lake Victoria basin. The altitude of the tea estates is 1,780 m to 2,225 m; the mean monthly temperature is 18.7°C. February is the warmest month of the year, with a mean maximum daily temperature of 28.3°C and mean minimum daily temperature of 10.8°C; July is the coolest month, with a mean maximum daily temperature of 25.4°C and mean minimum daily temperature of 10.2°C. Annual rainfall is 1.79 m with a March-to-June rainy season, and relative humidity is generally slightly below 60% except for May to July. April is the wettest month, with mean rainfall of 252 mm; December is the driest with a mean rainfall of 78 mm.

Population: The data for the study were obtained from enrollment of outpatients from the health-care system of a major tea company, which has 18 estates with 22,000 workers and approximately 50,000 persons eligible for health care; 32% of company employees belong to ethnic groups whose traditional home areas have holohyperendemic malaria. Given that marriage between ethnic groups is not common, it follows that about 15,000 workers and dependents are from malarious areas; most of these travel back to their home regions at least once per year. Approximately 31% of employees originate from the highland areas and the remaining 37% front intermediate disease areas around the country. This labour composition has remained stable for at least 20 years. The employees and families generally live in cement-walled, corrugated metal-roofed duplex style houses, situated close together in large housing areas. The houses usually have two rooms, with a wood or charcoal-burning fireplace, one door, and two unscreened windows. The Brooke Bond central hospital has 67 beds, two physicians, and two clinical officers, and averages 50 to 80 hospitalized patients per day and 20,000 outpatients per year three outlying medical centers, each with a clinical officer, see 15,000 to 20,000 inpatients per year; and 26 dispensaries, each with a nurse provider, see approximately 180,000 to 240,000 outpatients per year. During the study, patients presenting with fever (defined as temperature >38.2 Celsius) or other clinical sign suggestive of malaria were referred to our on-site field laboratory for a peripheral blood smear examination. Patients with positive smears were returned back to the referring physician for anti-malarial treatment, or to the central hospital in the event of severe illness requiring inpatient therapy. Patients with negative smears were presumed to be free of malaria, and referred back to the outpatient clinic for appropriate treatment of their other clinical illnesses. These patients provided a population of non-infected persons, with which to compare the demographic characteristics of patients with malaria. Tea estate workers do not receive malaria chemoprophylaxis, but

are given easily available free treatment for any symptomatic infection.

MATERIALS AND METHODS

This study was done under a protocol approved by the Kenya National Ethical Review Committee and the Human Subjects Research Review Board of the US Army Surgeon General. A questionnaire based upon prior experience from workers in the region (L Malakooti 1998) was administered to outpatients presenting with clinical symptoms suggestive of malaria infection at the tea plantation hospital and outlying clinics. The questionnaire asked for demographic information and medical history and was administered by a local field worker/translator. A total of 2796 completed questionnaires were entered into the study database. Every patient completing a questionnaire also had a peripheral blood smear that was read by a trained microscopist on-site. Patients with positive smears were defined as malaria cases, while those with negative smears were defined as non-infected. Subjects with either sexual or asexual blood parasite forms on their peripheral smear were classified as infected cases and received treatment for malaria. Parasite counts were estimated by counting the number of parasites per 100 white blood cells and extrapolating from the patient's white blood cell count. Lab officers and study investigators performed periodic weekly review of positive and negative sample slides from the study population for the purpose of quality assurance.

Data from the questionnaires was extracted by transcriptionists using a Microsoft Access (11: 1997) data manager shell and dual-entered by independent workers. The data was then exported to Epilinfo® Version 6.04c (12: CDC 1998) for dual-entry verification, errors were identified and verified line-by-line by comparison with the original questionnaires, and the verified data set was exported to SPSS® Base 9.0 (13: SPSS 1999) for statistical analysis. Incomplete data entries from individual records were treated as missing points rather than as null values.

Demographic characteristics of patients presenting with illness and negative peripheral blood smears for malaria were compared to those of patients with positive smears. Because plantation workers were mainly from four ethnic groups, with only a small minority drawn from others, these groups were characterized based upon the elevation of their region of origin, with highland defined as 1500m or more above sea level, and whether the ethnic groups were of Bantu or Nilotic extraction. Accordingly, these are Bantu highland one, Bantu Highland two, Bantu lowland, Nilotic lowland and others. The distinction between Bantu highland groups one and two is based upon geographic region of ethnic origin.

Subjects were also grouped according to an ordinal index of infection risk in their home district as proposed by Omumbo *et al*(14). This scale rates risk of infection by each district in Kenya, from almost none(0) to holoendemic(4). Descriptive statistics and simple frequencies were obtained, and Pearson Chi-square and general linear model univariate analysis of variance (ANOVA) statistical tests were used to test for associations.

RESULTS

Subject Characteristics: Of 2796 patients evaluated at the tea plantation during the study period, 798 cases of malaria were confirmed by positive peripheral blood

smear, with 1998 patients with negative smears presumed to be non-infected (Ratio: 2.52:1). Each of these visits represents a unique patient; repeat visits by the same patient were excluded from the analysis. Plantation workers were 48.7% female, 51.3% male, with no statistical association between sex and malaria infection (Pearson Chi-Square 1.19, $p = 0.553$). The age range for those infected with malaria was 0.3-85 years, with a mean of 14.7 (95% confidence interval 13.7, 15.7) and a median age of eight years in infected subjects and a mean age of 19.6, (95% confidence interval 18.9, 20.3) median age of 20 in non-infected patients, for which a strong statistical association between age under ten years and infection was present (Pearson Chi-square 145.99, $p < 0.001$). A graphical depiction of the age distribution among malaria cases and non-infected controls shows the trend for infection affecting children under age ten (Figure 1).

There was a statistically significant association between ethnic group and malarial infection ($F = 2.04$, 4 df, $p = 0.002$; ANOVA), with a slight bias toward infection in the Nilotic Lowland group (31.0%); the Bantu Highland Two group had a lower prevalence of malaria infection (24.3%) in comparison to the other

ethnic groups, although the intergroup differences are too slight to be clinically relevant (Table 1). There was a statistically significant association between high infection risk index of home region and malaria infection, with disproportionately more infections in persons from regions rated as three or four ($F = 4.25$, 4 df, $p = 0.002$; ANOVA). A history of recent travel, defined as more than twenty kilometers from site within six weeks, was strongly associated with malaria infection (Pearson Chi-Square 58.28, $p < 0.001$).

A statistically significant association was also present between ethnic group and positive travel history for malaria cases ($F = 2.06$, 4 df, $p = 0.020$; ANOVA), with lower infection prevalence in those groups with low travel frequency (Table 1). When stratified for ethnic group, a strong significant association between traveling and malaria infection was confirmed for both lowland ethnic groups and the Highland Bantu 1 group, but was non-significant for the Highland Bantu 2 and other groups (Table 1). The proportion of travellers infected was roughly correlated with the proportion of travellers when stratified by ethnic group; the more travellers, the higher the proportions of infections and of infected travellers in each ethnic group (Table 1).

Figure 1

Age of patients with malaria (black) contrasted with uninfected patients (gray)

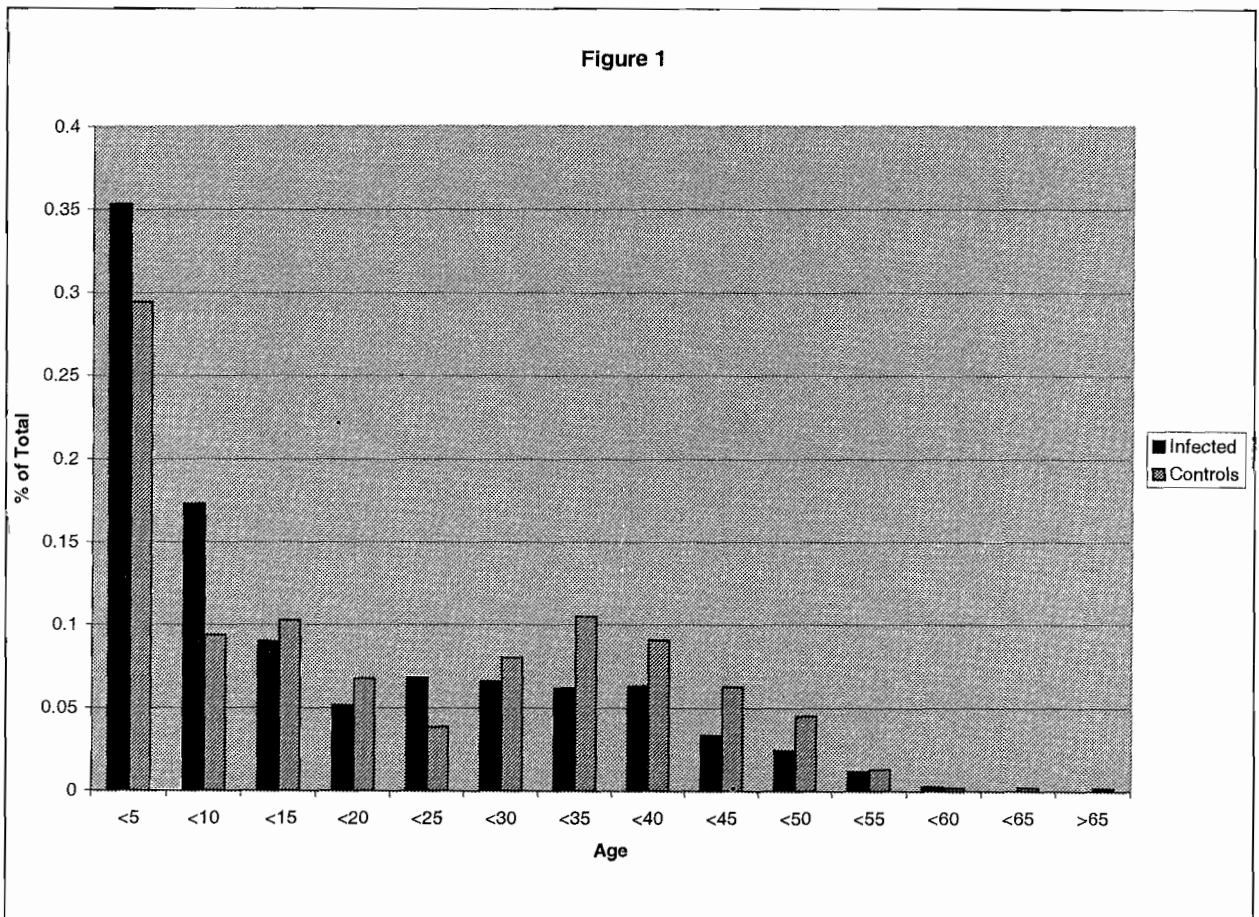


Table 1

Ethnic group affiliation, prevalence of malarial infection and associated with travelling

Ethnic Group	Ethnic Group Pop'n	Malaria Infected Cases	Infection Prevalence	Uninfected Controls	Number Travellers	Infected Travellers	Proportion Travelling	Proportion Infected Travellers	Infected Travellers vs. all cases	Odds Ratio, Travel vs Infection (95% CI)	Chi-square*	p-value
Nilotic	758	250	250/758	508	336	145	336/758	145/336	145/250	2.29	28.22	<.001
Lowland Bantu	(27.1)	(31.3)	(33.0%)	(25.4)	(37.9)	(42.9)	(44.3%)	(43.2%)	(58.0%)	(1.66-3.16)		
Bantu	360	97	97/360	263	122	54	122/360	54/122	54/97	3.60	28.04	<.001
Lowland Highland	(12.9)	(12.1)	(26.9%)	(13.2)	(13.7)	(16.0)	(33.9%)	(44.3%)	(55.7%)	(2.15-6.04)		
Bantu 1	872	252	252/872	620	181	72	181/872	72/181	72/252	1.78	13.14	<.001
Highland	(31.2)	(31.6)	(28.9%)	(31.0)	(20.4)	(2.13)	(20.8%)	(39.8%)	(28.6%)	(1.31-2.68)		
Bantu 2	711	173	173/711	538	227	60	227/711	60/227	60/173	1.18	0.80	.372
Highland	(25.4)	(21.7)	(24.3%)	(26.9)	(25.6)	(17.8)	(31.9%)	(26.4%)	(34.7%)	(0.81-1.72)		
Bantu 2	95	26	26/95	69	21	7	21/95	7/21	7/26	1.45	0.48	.490
Other	(3.3)	(3.3)	(27.4%)	(3.5)	(2.4)	(2.0)	(22.1%)	(33.3%)	(26.9%)	(0.45-4.61)		
Column Total	2796	798	798/2796	1998	887	338	887/2796	338/887	338/798	-	-	-
Total	(100)	(100)	(28.5%)	(100)	(100)	(100)	(31.7%)	(38.1%)	(42.4%)			

Figures shown in parentheses express each cell value as a percentage of column total. "Other" includes those ethnic groups with less than 2.0% representation. "CI" = Confidence Interval. *Mantel-Haenszel; for travelled vs. infected.

Subjects were asked about how long they had resided at the respective sites in years; the range reported was from 0-55 years, with 90% reporting less than 12 years. A strong statistical association exists between living for one year or less on site and malaria infection. Fully 77.7 percent of infected subjects were residents for one year or less, compared with only 53.0% of non-infected subjects (Pearson Chi-square 185.12, $p < 0.001$), with recent arrivals at the tea estates being more likely to have malaria.

Malaria Characteristics: Malaria parasites identified on peripheral blood smears were almost exclusively *P. falciparum*, with less than 1% identified as *P. ovale* or *P. malariae*. Asexual parasite counts in patients with positive smears ranged from 1-10,440 per mm^3 , with a mean of 803.6 (95% confidence interval: 695.2, 912.0). Gametocyte counts in peripheral blood of patients infected with asexual parasites ranged from 1 to 80 per mm^3 , with a mean of 9.4 ($N = 60$; 95% confidence interval 5.6, 13.2). The highest values were found in cases with concurrent asexual parasitemia; the gametocyte in Persons without asexual parasitemia (instances of carriage as an incidental finding) ranged from 1- 12 per mm^3 ($N = 10$; 95% confidence interval 2.6, 8.4). Gametocytemia was present in 7.5% of subjects with asexual parasitemia, and in only 0.5% of subjects lacking asexual Parasitemia forms.

Subjects were questioned as to whether they had been infected with presumptive malaria in the year before this illness. This was a highly subjective estimate of prior disease history. Sixty percent of infected

subjects reported having had a prior illness attributed to malaria within the past year, but fully 88% of non-infected subjects reported having had malarial illness in the past twelve months. This, was statistically significant ($F = 26.65$, 14 df, $p < 0.001$; ANOVA). The range of positive responses varied from 1-20 annual malaria "attacks", with a median of two bouts in the past year in both infected and non-infected patients.

Subjects reported a range of 0-60 days with a median of three days ill (zero days' illness implies presentation on day of onset, which was encouraged by the tea company's provision of readily available health services). Infected plantation workers reported 0-20 lost workdays from illness, with a mode of zero; non-infected subjects reported 0-30, with a mode of zero days lost. When asked to report prior treatment for malaria within the past two months, 304/798 (38.1%) of infected and 492/1998 (24.6%) of non-infected subjects reported recent prior treatment, either for presumed or diagnosed malaria.

From those reporting treatment for malaria in the past two months, a total of only 82/304 (26.7%) malaria cases and 209/492 (42.5%) non-infected patients reported having had prior peripheral blood smears, of which 52/82 (63.4%) and 107/209 (51.2%) were reportedly positive, respectively. There was no significant association between a history of having had a prior smear and malaria infection (Pearson Chi-square 0.021, $p = 0.885$). Infected and non-infected patients reported symptoms and complaints associated with their illness, (Table 2), along with their associated tests for statistical significance.

Table 2

Symptoms reported by malaria-infected and non-infected subjects with values for tests of statistical significance

Symptom	Malaria Cases (N=798)	Uninfected Controls (N=1998)	Pearson Chi-square	Pearson p-value	F-Statistic (ANOVA)	ANOVA p-value
Fever	328(41.1)	504(25.2)	68.78	.000	31.16	.000
Headache	353(44.2)	639(32.0)	37.40	.000	53.80	.000
Dizziness	97(12.2)	372(18.6)	17.06	.000	15.26	.000
Coughing	203(25.4)	625(31.3)	9.34	.002	11.38	.001
Backache	126(15.8)	365(18.3)	2.42	.120	8.82	.003
Nausea	42(5.3)	169(8.5)	8.35	.004	0.048	.489
Vomiting	267(33.5)	461(23.1)	31.94	.000	3.26	.071
Diarrhea	81(10.2)	241(12.1)	2.05	.153	0.18	.671
Stomachache	221(27.7)	499(25.0)	2.21	.138	0.76	.783
Skin Rash	16(2.0)	58(2.9)	1.78	.182	0.78	.377
Joint pain	229(28.7)	596(29.8)	0.35	.553	2.64	.104
Seizures	4(0.5)	5(0.3)	1.12	.290	0.85	.357

Figures in parentheses express each cell value as percentage of column total

Treatment Administered: Both treatment for historical illness and current anti-malarial treatment administered at time of presentation to our study group were documented. The most common historical treatment reported was with chloroquine, accounting for 60% of prior therapy; amodiaquine and pyrimethamine/sulfadoxine were next most common, accounting for 24% and 11%, respectively. Three percent of all subjects had been previously treated with quinine, only one percent reported therapy with artemisinin, and 1% had been treated with some combination of the above drugs. In contrast, amodiaquine was the most commonly used drug to treat cases of either smear proven or clinically suspected malaria in plantation subjects, accounting for 56% of malaria therapy pyrimethamine/sulfadoxine was used to treat 27%, and artemisinin 8% of subjects. Chloroquine was administered to only three percent, while combination therapy was used in five percent of cases, and only a single treatment (0.1 %) was recorded using quinine. Subjects with a prior history of treatment for malaria were statistically less likely to be infected again (Pearson Chi-square 50.81, $p < 0.001$).

DISCUSSION

This study was a preliminary step in evaluating the epidemiologic pattern of epidemic highland malaria in western Kenya prior to any intervention programs. The major strength of this study was the large number of subjects, which increased the power of the statistical analysis. Weaknesses included the lack of a true control group and the likely presence of confounding by unevaluated variables, such the nature of other illnesses leading to clinic visits.

The strong statistical association between age less than ten and malaria infection in plantation children confirms the predilection of the disease for these young and immunologically naive victims. The lack of association between sex and parasitemia was not unexpected. The increased prevalence of infection in lowland origin plantation workers is likely related to a proclivity in these groups for travel to the holoendemic lowland areas, which also accounts for the strong associations between recent travel, lowland ethnic group and infection. Many lowland workers at the tea plantation have relatives in neighbouring districts, and travel between these areas increases both their own risk, as well as serving as a source of gametocytes, which contributes to the risk of epidemic highland malaria. The significant risk of infection for travellers in the Highland Bantu 1 ethnic group (OR 1.78, $p < 0.001$; Table 1), given this group had the lowest overall travel frequency (21%) suggests a higher susceptibility to infection among those members, of this group who do travel. The apparent protective effect observed in the Highland Bantu 2 and Other ethnic groups is likely because of a tendency to remain in and travel to areas of lower malaria risk. The association between parasitemia and a high infection risk class (three or four on the scale of zero to four) of home districts among plantation workers likely reflects relative risk of areas to where the workers travel when away from the plantation, as does the association between years living on the plantation and malaria infection. These findings taken together suggest that importation of malaria to the highlands, as well as travel away from the highlands, are important sources of new infections among persons living and working there. The strong association between reported malarial illness within the past year and having

a negative peripheral smear suggests a protective effect of prior infections. The rather low number of lost workdays and the mode of zero lost days suggest that malaria is well tolerated by most workers.

The common treatment of malaria with chloroquine is attributable to its ready availability and low cost, despite known widespread parasite resistance to this drug. Because many patients receive presumptive therapy for malaria without establishing the presence of parasitemia, the usual diagnosis of malaria is on clinical grounds. The association between a history of prior treatment for malaria and the absence of parasitemia is consistent with a protective effect from recent prior infection. Treatment of laboratory-proven malaria consisted most commonly of amodiaquine or pyrimethamine/sulfadoxine, or less often, these drugs given either together, or in combination with another medication.

Regarding disease symptomatology, although fever, dizziness and headache are significantly more frequent in patients with malaria than in those with other illnesses (Table 3), the differences are too slight to be clinically helpful in case management. Nausea was more common in non-infected cases, but vomiting was more frequent in infected subjects, an intuitively illogical relationship that was disproved by testing with the general linear model (ANOVA test, Table 2). Coughing was more likely to be associated with other illness, but this finding is of no real clinical use.

The presence or absence of symptoms suggestive of malaria is of little value by itself in distinguishing parasitic infections from non-specific afflictions, and the statistical power to find small but significant differences proved to be of no practical utility. Control of epidemic malaria is one of the goals of the World Health Organization's "Roll Back Malaria programme". Our data suggest that even in classic malaria epidemic situations, such as seasonal highland outbreaks, there is a wide spectrum of findings related to the geographic and immunologic complexity of malaria infection.

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