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Changing patterns of clinical malaria since 1965 among a tea estate population located in the Kenyan highlands*

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Abstract

The changing epidemiology of clinical malaria since 1965 among hospitalized patients was studied at a group of tea estates in the western highlands of Kenya. These data indicate recent dramatic increases in the numbers of malaria admissions (6·5 to 32·5% of all admissions), case fatality (1·3 to 6%) and patients originating from low-risk, highland areas (34 to 59%). Climate change, environmental management, population migration, and breakdown in health service provision seem unlikely explanations for this changing disease pattern. The coincident arrival of chloroquine resistance during the late 1980s in the sub-region suggests that drug resistance is a key factor in the current pattern and burden of malaria among this highland population.

Keywords: malaria, *Plasmodium falciparum*, epidemiology, highlands, drug resistance, climate change, Kenya

Introduction

Changing patterns of infectious diseases, such as AIDS, bovine spongiform encephalopathy and Ebola, provoke much public interest. These 'epidemics' focus political attention and resources. Across much of sub-Saharan Africa *Plasmodium falciparum* malaria has always posed a major public health challenge but has never achieved the dubious political significance of infections with either HIV or haemorrhagic viruses. Nevertheless, there is a growing commentary on the changing patterns of malaria on the continent, highlighting the increasing risks of severe complicated disease and mortality among communities exposed to both stable and unstable transmission since the late 1980s (GREENBERG *et al.*, 1989; MOUCHET, 1998; TRAPE *et al.*, 1998). This increase has variously been attributed to changes in environmental management (LINDSAY & MARTENS, 1998; MOUCHET *et al.*, 1998), population migration (LINDSAY & MARTENS, 1998), breakdown in health service provision (LINDSAY & MARTENS, 1998; MOUCHET, 1998; MOUCHET *et al.*, 1998), drug resistance (GREENBERG *et al.*, 1989; TRAPE *et al.*, 1998) and global warming (LOEVINSOHN, 1994; MOUCHET, 1998).

Long-term trends in diseases affecting the developed world can be defined through sophisticated systems of national morbidity and mortality reporting. Conversely, national disease reporting in much of the developing world is either erratic or non-existent. To provide adequate descriptions of changing clinical patterns demands contiguous data spanning several decades among relatively stable populations. This paper reports on a unique series of malaria data for 1965–97 from the Brooke Bond Kenya Ltd tea estates, located at 1780–2225 m altitude in western Kenya, to define the extent and timing of changes in clinical risks from *P. falciparum*.

Methods

Brooke Bond Kenya Ltd began farming at Kericho in 1925 and developed rapidly into a large collection of tea estates. The company currently has 18 estates employing about 18 000 workers. Two-thirds of the company employees have historically originated from highland areas, including Kericho district, whilst one-third of the employee population belong to ethnic groups whose traditional home areas are endemic for malaria. As early as 1931 Brooke Bond Kenya Ltd was the sole provider of clinical care for its employees and their dependants. These services began with mobile clinics which, during the 1930s, were formed into a series of static health posts. Presently, there are 26 dispensaries and 3 medical centres. The company central hospital was opened in November 1955 to provide inpatient clinical care and has averaged 60 beds staffed by at least 2 physicians and 2 clinical officers.

Admissions to the central hospital have been systematically recorded in ward registers since 1965. These registers were located at the hospital records department, archives and stores. All admissions to the hospital with suspected malaria were confirmed through microscopy which, in conjunction with other clinical and laboratory procedures, was used to define a primary diagnosis. Data were transcribed by 2 supervised field staff according to monthly counts of admissions by cause, age and ethnic group. Ten percent of the data were entered twice and used for cross-checking purposes, with less than 2% transcription errors noted.

Results

Between 1965 and 1997 a total of 10 169 admissions were recorded with a primary diagnosis of malaria. Between 1965 and 1989 malaria accounted for between 5·3 and 11·4% of all admissions, between 1990 and 1994 approximately 20% of hospitalized patients were diagnosed as having malaria, and this proportion rose to 32·5% between 1995 and 1997 (Table). The incidence of malaria admissions was relatively low between 1965 and 1989 and rose significantly during the 1990s (Fig. 1). Trend analysis on the annual admission data showed this rise to be significant ($B = 1{\cdot}318$ (mean annual monthly cases/year), $r^2 = 0{\cdot}407$, $P = 0{\cdot}00003$). The company claims that employee and dependant numbers eligible for health care have remained relatively constant over the period of observation. We were able to obtain employee numbers from the company records only for the period 1986 through to 1997 and these numbers have been used to express 'rates' of malaria hospitalization among all age-groups per 1000 employees (Fig. 2). These data show a changing disease pattern consistent with total numbers shown in Figure 1. Records of inpatient survival were obtained from independent records at the hospital and matched to admission records. Data were available only for the periods 1965–72 and 1990–97. During the late 1960s malaria case fatality was 1·3% (22/1717) compared with 6·0% (326/5427) during the 1990s. Finally malaria admissions have increasingly included

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Table. Summary of data on malaria admissions to Brooke Bond Ltd central hospital, Kericho, Kenya 1965–97

Years	Numbers of malaria admissions	Percentage of all admissions due to malaria	Percentage of malaria admissions among highlanders[a]
1965–69	1099	6·5	33·6
1970–74	1125	8·9	34·7
1975–79	568	5·3	32·2
1980–84	1115	6·0	50·1
1985–89	1061	11·4	47·2
1990–94	2650	19·8	50·6
1995–97	2551	32·5	59·0

[a]Highlanders were defined as persons whose ethnic group traditionally came from areas in Kenya >1500 m elevation.

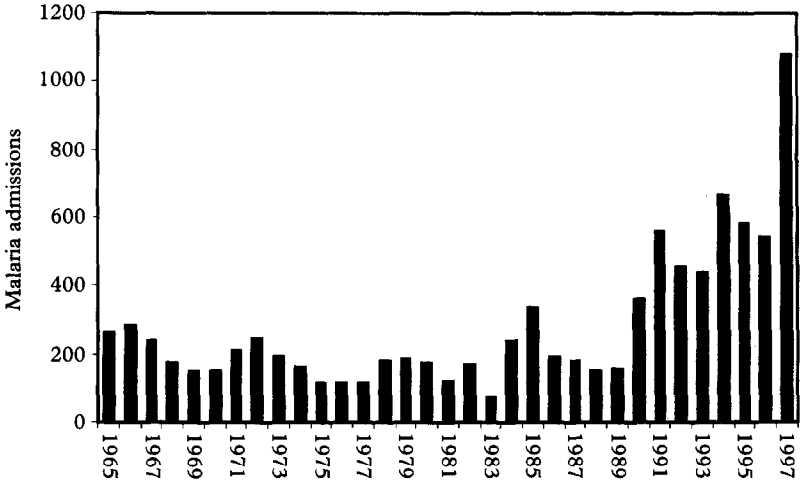

Fig. 1. The numbers of malaria admissions to the Brooke Bond Kenya Ltd tea estate hospital between 1965 and 1997.

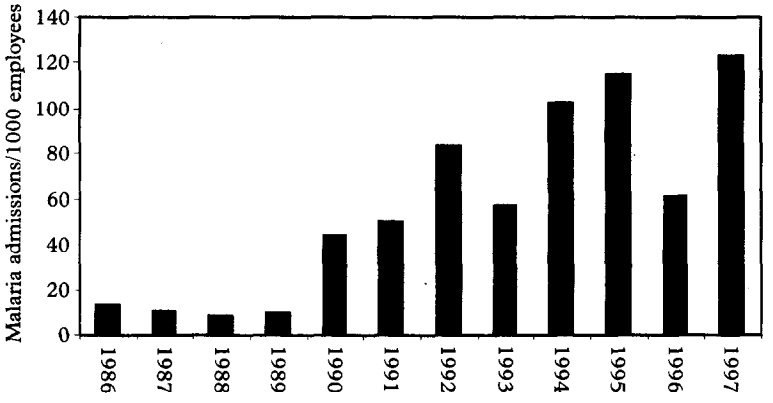

Fig. 2. The annual number of malaria admissions to the Brooke Bond Kenya Ltd tea estate hospital, expressed per 1000 employees.

people who originate from areas of low or unstable malaria risk (B = 4·393 (percentage admission change/5-year interval), r^2 = 0·789, P = 0·004) (Table).

Climate data were available between 1965 and 1997 as mean monthly ambient temperature (°C) and monthly rainfall totals (mm) recorded at the centre of the estates by the Tea Research Foundation (NG'ETICH, 1997). There has been no significant change in the mean annual monthly mean temperature (B = 0·009 (°C/year), r^2 = 0·04, P = 0·14, not significant) or mean annual monthly total rainfall (B = −0·232 (mm/year), r^2 = −0·03, P = 0·642, not significant) during the period 1965–97. While these analyses do not exclude complex, combined temperature and rainfall changes it seems plausible to assume that factors other than climate change would have led to the precipitous rise in malaria warranting inpatient care during the 1990s at the Kericho tea estates.

Discussion

Mass proguanil administration to tea estate residents was adopted periodically during the late 1940s and early 1950s (STRANGEWAYS-DIXON, 1950). No preventative strategies (chemoprophylaxis, house spraying with residual insecticide or bednet distribution), however, have been used since the late 1950s (MALAKOOTI *et al.*, 1998). Rather, the company has relied upon the use of rapid access to therapy with chloroquine for uncomplicated clinical malaria. Since the late 1980s this cheap and effective drug has rapidly become ineffective in the management of uncomplicated malaria across Kenya

(RAPUODA *et al.*, 1996). There are no chloroquine sensitivity data for the tea estate population; however, at the neighbouring district of Nandi in 1981 studies *in vitro* on 15 parasite isolates showed all to be sensitive to chloroquine (MASABA *et al.*, 1985). In 1996 within the same area, 50% of patients treated with chloroquine were unable to clear infections by day 7 (RAPUODA *et al.*, 1996).

We did not set out to study prospectively the relative contributions of climate change, drug resistance and health service delivery upon the changing incidence of clinical malaria at Kericho. Rather, we have constructed retrospectively a long-term series of clinical data covering 33 years from a fixed estate population located above 1700 m in the western highlands of Kenya. This employee population and their dependants have had good access to curative services since the 1940s. The hospital is well equipped and provides 24-h cover for about 100 000 people. An examination of the frequency of hospitalization with clinical malaria over the past 3 decades supports the public health communities' claim of a changing clinical epidemiology within areas of East and the Horn of Africa located between 1500 and 2000 m (LOEVINSOHN, 1994; LINDSAY & MARTENS, 1998; MOUCHET *et al.*, 1998). Since the early 1990s there has been a dramatic rise in malaria admissions to the company hospital. Whilst it is well established that malaria transmission in these highland areas is affected by the effects of low ambient temperature upon the development of the sporozoite stages of the parasite in the vector (LINDSAY & MARTENS, 1998) our preliminary analysis of climate variables does not indicate any major transition in either ambient temperature or rainfall since 1965. Similarly the stability in demographic structures and health service provision make these unlikely explanations for the dramatic rise in malaria admissions seen during the early 1990s. Rather, we suspect that a major contributor to the changing clinical epidemiology of malaria in this population is that of changing drug sensitivity. This proposition is supported by the changing malaria inpatient case fatalities which themselves are unlikely to be much affected by changes in climate. We speculate that chloroquine resistance increased the number of treated but not-cured malaria cases in the tea estates thus increasing the pool of gametocytaemic individuals available to infect mosquitoes during the brief mid-year period when transmission was possible.

Indeed it could be argued that the prevailing situation in many African countries is best described as an 'epidemic' of drug-resistant malaria. This changing epidemiology may manifest itself most acutely in communities, like Kericho, located at the borders of stable transmission. Such areas of Africa demand special attention for 2 principal reasons: (1) they are densely populated and of economic and political significance due to their agricultural potential, and (2) the historical epidemiological data shown in this report demonstrate that prompt access to efficacious drugs can maintain the severe consequences of infection at acceptable levels. New therapeutic strategies involving combinations with artesunate (PRICE *et al.*, 1996; WHITE *et al.*, 1999) may have a significant impact on local disease risks among low transmission areas of stable and unstable malaria in Africa.

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References

Greenberg, A. E., Ntumbanzondo, M., Ntula, N., Mawa, L., Howell, J. & Davachi, F. (1989). Hospital-based surveillance of malaria-related paediatric morbidity and mortality in Kinshasa, Zaire. *Bulletin of the World Health Organization*, **67**, 189–196.

Lindsay, S. W. & Martens, W. J. M. (1998). Malaria in the African highlands: past, present and future. *Bulletin of the World Health Organization*, **76**, 33–45.

Loevinsohn, M. E. (1994). Climatic warming and increased malaria incidence in Rwanda. *Lancet*, **343**, 713–718.

Malakooti, M. A., Biomndo, K. & Shanks, G. D. (1998). Re-emergence of epidemic highland malaria in western Kenya. *Journal of Emerging Infectious Diseases*, **4**, 671–676.

Masaba, S. C., Anyona, D. B. & Chepkwoni, D. K. (1985). *In vitro* response of *Plasmodium falciparum* to chloroquine in the Nandi District, Kenya. *Bulletin of the World Health Organization*, **63**, 593–595.

Mouchet, J. (1998) L'origine des épidémies de paludisme sur les plateaux de Madagascar et les montagnes d'Afrique de l'est et du sud. *Bulletin de la Société Pathologie Exotique*, **91**, 64–66.

Mouchet, J., Manguin, S., Sircoulon, J., Laventure, S., Faye, O., Onapa, A. W., Carnevale, P., Julvez, J. & Fontenille, D. (1998). Evolution of malaria in Africa for the past 40 years: impact of climatic and human factors. *Journal of the American Mosquito Control Association*, **14**, 121–130.

Ng'etich, W. K. (1997). *An assessment of the effects of drought in tea areas*. Tea Research Foundation of Kenya. Internal Document.

Price, R. N., Nosten, F. Luxemburger, C., ter Kuile, F. O., Paiphun, L., Chongsuphajaisiddhi, T. & White, N. J. (1996). Effects of artemisin derivatives on malaria transmissibility. *Lancet*, **347**, 1654–1658.

Rapuoda, B. A., Ouma, J. H. Njagi, K., Khan, B. & Omar, S. (1996). Status of antimalarial drug sensitivity in Kenya. *Malaria and Infectious Diseases in Africa*, **8**, 25–43.

Strangeways-Dixon, D. (1950). Paludrine (proguanil) as a malarial prophylactic amongst African labour in Kenya. *East African Medical Journal*, **28**, 1–4.

Trape, J. F., Pison, G., Preziosi, M. P., Enel, C., Desgrees du Lou, A., Delaunay, V., Samb, B., Lagarde, E., Molex, J. F. & Simondon, F. (1998). Impact of chloroquine resistance on malaria mortality. *Comptes Rendus de L'Academie des Sciences, Paris, Série III*, **321**, 689–697.

White, N. J., Nosten, F., Looareesuwan, S., Watkins, W. M., Marsh, K., Snow, R. W., Kokwaro, G., Ouma, J., Hien, T. T., Molyneux, M. E., Taylor, T. E., Newbold, C. I., Ruebush, T. K. 2nd, Danis, M., Greenwood, B. M., Anderson, R. M. & Olliaro, P. (1999). Averting a malaria disaster. *Lancet*, **353**, 1965–1967.

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