ISBN 1188–4169

Canada Communicable Disease Report

FAX

Vol . 22-20

Date of publication: 15 October 1996

Contained in this FAX issue: *(No. of pages: 7)*

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FATAL *FALCIPARUM* MALARIA IN CANADIAN TRAVELLERS

Introduction

Malaria continues to be a major cause of mortality worldwide and is responsible for an estimated 1.5 to 3.5 million deaths annually[1,2]. With current international travel and immigration patterns, imported malaria has become an increasingly common problem in many developed countries, including Canada[3-6]. Each year, approximately 3 million Canadians cross international borders with a large number travelling to or through malaria-endemic areas[7]. The majority of these travellers rely on their family physicians to provide accurate information on malaria prevention, personal protection measures to prevent mosquito bites, and appropriate chemoprophylaxis[6].

Approximately 90% of travellers who acquire malaria will not become symptomatic until they return home[3]. Delays in diagnosis and treatment increase malaria-associated morbidity and mortality: malaria can progress from an asymptomatic state to death in as little as 36 to 48 hours[2,3]. Furthermore, the mortality of severe malaria is $\geq$ 30%, even for previously healthy adults managed in moderate intensive care units. Therefore, preventing imported malaria deaths requires prompt recognition of cases, accurate identification of species, and appropriate initial management. However, recent studies indicate that several problems exist in the recognition and management of malaria in non-endemic areas, including Canada[4,6]. The following illustrates two fatal outcomes as a result.

Case 1

A previously healthy 66-year-old Caucasian male travelled through South Africa, including Krueger National Park and Victoria Falls in Zimbabwe. He did not seek pre-travel advice while in Canada; however, he began proguanil and chloroquine chemosuppressive therapy while on route from Johannesburg to Zimbabwe. He was well in Africa but discontinued malaria chemosuppression shortly after returning to Canada on 5 April 1996 because of gastrointestinal upset. Approximately 1 week later, he developed nausea, anorexia, and headaches. No fever was noted. On the morning of 19 April 1996, he was found unresponsive and incontinent. He was taken to a local hospital. He was afebrile, disoriented, tachypneic, and in atrial fibrillation. Initial blood work revealed hypoglycemia and acidosis. A complete blood court (cbc) was not performed at that time. He was transferred to a larger regional hospital where a cbc revealed a platelet count of 21 billion/L and a smear indicated approximately 50% parasitemia with *Plasmodium falciparum* malaria. No parenteral quinidine was available: he was treated with mefloquine 1,500 mg orally, and three tablets of Fansidar®. Ten hours later, he was transferred to a regional tertiary care hospital to receive parenteral therapy for *falciparum* malaria. He arrived in a coma and with acute renal failure. Parenteral quinidine was no longer stocked by the pharmacy of the tertiary care hospital but intravenous (IV) quinine was received on an urgent basis from Ottawa. The patient was managed with exchange transfusion, parenteral quinine, and doxycycline. Despite this, he developed irreversible shock and died the following day. Postmortum examination confirmed typical findings of severe and cerebral malaria.

Case 2

A previously healthy 45-year-old Caucasian female travelled with her three children and her husband for 1 month to Nigeria from December 1995 to January 1996. Prior to her departure, she sought pre-travel advice from her family physician and was prescribed chloroquine for chemosuppression. She and her family were compliant with this medication. No other personal protection measures, such as insect repellents or bed nets, were used.

She developed general malaise, and watery, non-bloody diarrhea, and back pain 3 weeks after arriving in Nigeria. After developing fevers, chills, rigors, and delirium, she was assessed by a local physician. Initially, therapy consisted of an analgesic and diazepam, despite a presumptive diagnosis of malaria. A thick blood film report, received the following day, revealed *P. falciparum* malaria. She became obtunded and developed jaundice. Therapy was switched to IV hydration and parenteral chloroquine. After a transient response, she lapsed into a coma and died of cerebral malaria 2 days later. Postmortum examination, following the return of her body to Canada 3 weeks later, confirmed the diagnosis of *P. falciparum* malaria.

Upon returning to Toronto, all three of her children subsequently developed *P. falciparum* malaria. They were admitted to hospital with parasitemias ranging from 0.5 % to 3%. Each was treated with quinine (600 mg PO t.i.d. for 3 days) and doxycycline (100 mg PO b.i.d. for 7 days). All three were slow to respond to therapy and their thick blood films cleared by day 5. Follow-up films at day 28 were negative in all three.

Comments

These cases illustrate important problems in the prevention, diagnosis, and management of *falciparum* malaria in Canadian travellers.

Accurate pre-travel advice: Accurate pre-travel advice about the use of personal protection measures to prevent insect bites and malaria chemosuppression is essential to prevent malaria in Canadian travellers. In a recent study of malaria acquired by Canadians, the majority of travellers had sought pre-travel advice from their family physicians[6]. In many cases, inappropriate chemoprophylactics were prescribed and few travellers were advised about personnel protection measures. Given the constantly changing situation with drug-resistant malaria, many physicians may not be able to keep abreast of rapidly changing chemosuppressive recommendations. Therefore, unless physicians are willing to keep current in this field, travellers should be referred to a travel or tropical medicine specialist for up-to-date malaria prevention recommendations.

Chloroquine is no longer effective in preventing *falciparum* malaria for most of the malaria-endemic world, with the exception of Central America, the Caribbean, and a decreasing area of the Middle East. Chloroquine and proguanil as combination chemosuppression are only 60 % to 70% efficacious in sub-Saharan Africa. Weekly mefloquine or daily doxycycline continue to provide substantial protection against drug-resistant *falciparum* malaria in most malaria-endemic areas, except on the borders of Thailand with Myanmar (Burma) and Cambodia.

Unreliable management in developing countries: Medical treatment received in developing countries may not be reliable, particularly as non-immune travellers represent an unfamiliar patient population for local health-care workers. In addition, adequate laboratory diagnosis and appropriate medications are not available in many remote areas. For Case 2, therapy for suspected malaria was delayed and the initial management for a non-immune patient infected with *P. falciparum* was not appropriate.

Early diagnosis and appropriate treatment: Early recognition and appropriate management can prevent imported cases of malaria with subsequent death[3,6-9]. Delays in diagnosis and treatment increase the risk of complications and mortality[9,10]. Fever in the returned traveller or recent immigrant must be considered to be malaria and, in particular, *P. falciparum* until proven otherwise. The failure of physicians to take a travel history is the major reason for delays in the diagnosis of malaria. Bad outcomes are most often the results of physician misjudgments regarding the severity and potential complications of this life-threatening infection. *Falciparum* malaria in a non-immune patient constitutes a medical emergency and generally requires admission to hospital for initial management and follow-up[11].

Availability of appropriate medication: The World Health Organization and the Institute of Medicine have identified drug-resistant malaria as a re-emerging infectious disease and a threat to global health[12,13]. Recognition of malaria as an emerging pathogen necessitates the availability of emergency medications for the treatment of severe malaria in non-endemic areas. Parenteral quinidine gluconate remains the treatment of choice for severe or complicated malaria throughout North America[11]. As newer antiarrhythmic agents have replaced quinidine for its cardiac indications, some hospitals and health facilities have discontinued quinidine gluconate from their formularies. The Centers for Disease Control and Prevention in Atlanta have reported that delays in obtaining quinidine gluconate for parenteral therapy were thought to have played a role in two recent fatal cases of *falciparum* malaria[14]. None of the three hospitals to which Case 1 was admitted had parenteral quinidine gluconate in their hospital formularies. Although the alternative drug for the treatment of severe malaria, quinine dihydrocholoride, is available in Canada through Emergency Drug Release, unacceptable delays may occur in acquiring this drug when it is urgently needed. Directors of hospital formularies need to co-ordinate their efforts with the drug industry to ensure that parenteral therapy for severe malaria remains readily available.

Conclusion

With the resurgence of malaria worldwide, increasing drug resistance, and current travel and immigration patterns, the number of cases of drug-resistant malaria imported into Canada will continue to rise. To prevent malaria deaths, travellers need to be adequately informed about prevention of malaria using personal protection measures and appropriate chemosuppression. As these measures will never be completely protective, physicians in Canada must be able to recognize malaria, to request malaria smears on an urgent basis, and to institute prompt and effective therapy in order to prevent imported malaria deaths.

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Source: *S Sharma, MD, A Humar, MD, KC Kain, MD, Tropical Disease Unit, Division of Infectious Diseases, University of Toronto and The Toronto Hospital, Toronto, Ontario; D Zoutman, MD, Medical Microbiology and Infectious Disease, Kingston General Hospital, Kingston, Ontario.*

MALARIA—BOUNDARY HEALTH UNIT, BRITISH COLUMBIA, 1995

Introduction

In 1995, 104 cases of malaria were reported to the Boundary Health Unit (BHU) of the municipalities of Delta, Langley, Surrey, and White Rock in the Lower Mainland of British Columbia (BC). This is a substantial increase compared to previous yearly case counts and rates (Table 1). A similar increase was not noted in any other BC health unit. The 104 cases were reviewed to determine if any were caused by local transmission, and if a lack of pre-travel counselling and an inadequate use of malaria chemoprophylaxis and personal protective measures were significant factors.

Table 1
Number of malaria cases and rate, 1990-95

Year	Number of cases	Case rate (per 100,000)
1990	37	10.60
1991	79	21.85
1992	51	13.57
1993	76	19.64
1994	36	9.10
1995	104	25.43

Methods

Cases were defined as individuals who had a positive malaria blood smear reported to the BHU in 1995. Malaria is reportable by BC laboratories. Case name, age, gender, treating physician, and the identified malarial subspecies were obtained from the laboratory report. Individuals who had multiple positive blood smear reports were counted as one case.

For each case, standardised questionnaires were given by phone or during an office visit to the treating physician. The first questionnaire asked about prior history of malaria, country of birth, year of immigration, overseas travel within the last 5 years, pre-travel prescription of malaria chemoprophylaxis, and details of the clinical course and treatment of the current episode of malaria. A second questionnaire asked treating physicians about their clinical practice pertaining to the recommendation and prescription of malaria chemoprophylaxis. Due to limited time and resources, no further information was obtained from cases whose only identified risk factor for malaria was immigration to Canada within the last 5 years.

A third questionnaire was given by phone to those cases who had travelled overseas within the last 5 years or who had no documented risk factors. A Punjabi-speaking physician asked further details about recent overseas travel, use of malaria chemoprophylaxis and other preventive measures, number of physician visits, and days of disability resulting from the current episode of malaria.

Descriptive statistics were calculated using EpiInfo 6.02 (Centers for Disease Control and Prevention, Atlanta, GA. 1994).

Results

First physician questionnaire: Laboratory reports and information from the treating physicians were obtained for 103 of 104 cases (99%) (Table 2). The 103 cases were distributed among 27 different treating physicians, with the number of cases per physician ranging from one (12 physicians) to 10 (1 physician). The median number of cases per physician was 2.0.

Of the 103 cases, 46 (45%) were female and 57 (55%) were male. Ages ranged from 0 (a congenital case) to 86 years with a mean age of 37 years. Only 16 cases (16%) had prior histories of malaria documented in their medical files. No histories were documented in a further 34 cases (33%). In the remaining 53 cases (51%), files contained no information about prior malaria histories. Twelve cases (12%) were born in Canada, 89 (86%) in India and 2 (2%) in Pakistan. In all cases born outside of Canada, the country of emigration was the same as the country of birth. There were 84 laboratory reports (82%) of *Plasmodium vivax*, one (1%) with suspected *P. vivax* (but *P. falciparum* could not be excluded) and one (1%) of possible *P. malariae*. Seventeen (17%) could not be speciated.

Table 2
Risk factors for malaria among 1995 BHU malaria cases (n=104)

Risk factor	Number of cases (%)	
Immigration within past 5 years	58	(56%)
Overseas travel in past 5 years	37	(36%)
Immigration and overseas travel in past 5 years	5	(5%)
No risk factor documented in medical file	3	(3%)
No case information available	1	(1%)

A known risk factor for malaria was documented for 100 of the 103 cases. The 100 cases included one congenital case where the mother was a recent immigrant from India. Fifty-eight cases had recently immigrated (within 5 years), and 87% of these had immigrated in 1994 and 1995. Thirty-seven cases had recently travelled overseas, and 93% of these had travelled in 1994 and 1995. Five cases had both recent immigration and recent travel overseas as risk factors.The remaining three cases were believed to have had recent travel and/or immigration to South Asia, but this could not be confirmed.

Of the 42 cases with recent overseas travel as a risk factor, only 11 (26%) had prescriptions for malaria chemoprophylaxis documented in their medical files. No malaria chemoprophylaxis had been prescribed in a further 17 cases (41%). No information was documented for the remaining 14 cases (33%).

Of the entire 103 cases, a prescription for primaquine was documented in only 58 cases (56%). Primaquine was not prescribed in 37 cases (36%). In the remaining 8 cases (8%), medical files contained no information.

Second physician questionnaire: Of the 27 treating physicians, 25 (93%) stated that they always or usually recommend malaria chemoprophylaxis for patients travelling to malaria areas. Twentyone (81%) also stated that they always or usually prescribe chemoprophylaxis. Of the physicians who indicated that they did not always prescribe chemoprophylaxis, 16 (59%) indicated that if they did not give a prescription they would send patients to a travel clinic.

Patient questionnaire: As mentioned above, 42 cases had recent overseas travel as a documented risk factor for malaria and three had no documented risk factors. Of these 45 cases, 25 completed the patient questionnaire.

Twenty-three of these 25 cases (92%) had travelled to India, one (4%) to Brazil, and one (4%) to numerous countries in Central and South America. Of the cases that had travelled to India, all but one had travelled to Punjab. The remaining case had travelled to Delhi. Twenty-one cases (84%) reported travelling only to a rural area while the other four (16%) reported travelling to both urban and rural areas. The range for duration of stay was 4 to 70 weeks, with a mean of 19.8 weeks and a median of 8.0 weeks. All 25 cases were at their destinations during summer; eight also during spring, eight also during fall, and seven also during winter.

The use of malaria prevention measures by the 25 cases is presented in Table 3. The nine cases who obtained travel advice were among the 10 cases who were aware of the need to take chemoprophylaxis, and were the same nine who obtained a prescription for chemoprophylaxis. Reasons given for not taking the full prescription were forgetting to take the pills (four cases), losing the pills, difficulty swallowing the pills, and a belief that the risks of the medication were greater than the risk of malaria (one case each). Cases who received pre-travel advice were not more likely to have taken at least one preventive measure, but due to small numbers the study's power was very low.

Table 3
Preventive measures taken by malaria cases with recent overseas travel as a risk factor (n=25)

Preventive Measure	Number of Cases (%)	
Aware of need for chemoprophylaxis	10	(40%)
Obtained travel advice	9	(36%)
Obtained Px for malaria chemoprophylaxis	9	(36%)
Took full course of malaria chemoprophylaxis	2	(8%)
Used insect repellent	4	(16%)
Used long-sleeved and long-legged clothing	6	(24%)
Stayed in house/hotel with window screens	16	(64%)
Used mosquito net over bed	12	(48%)
Stayed indoors between dusk and dawn	10	(40%)
No precautions taken	6	(24%)

Discussion

Assessment of methods: Although an increased number of malaria cases were reported to the BHU in 1995, it is not clear if this represents all cases that occurred in 1995. Also, if a case of malaria was diagnosed clinically and without a confirmatory blood smear, that case would not have been included in the survey. It is expected that the number of cases where no blood smear was performed would have been very small. Overall, the 104 cases probably underrepresent the actual number of malaria cases. The study did not attempt to determine reasons for the observed increase, rather, its purpose was to look at risk factors and preventive measures.

To assess recent risk factors for malaria, information from the medical files was relied upon in the majority of cases. The lack of verification does raise some concern about the accuracy of the information but in all 25 cases, where a patient questionnaire was also completed, the information obtained from the medical file was consistent with that provided by the patient.

Risk factors: The fact that almost all (101/103) of the malaria cases occurred in individuals from the South Asian community is important when discussing risk factors and possible preventive interventions. Ninety-seven percent of the cases had documented risk factors for malaria and in all of these cases the risk factors were the expected ones of recent travel and/or immigration. There were no cases where local transmission was suspected, and,

furthermore, none of the species of mosquito that inhabit British Columbia's Lower Mainland are capable of malaria transmission (Dr. P. Belton, Simon Fraser University, British Columbia: personal communication, 1996).

It is expected that a portion of immigrants from a country such as India would suffer an episode of malaria after arrival in Canada. Whether such immigrants should be screened for malaria on arrival or simply be treated if they develop symptoms is beyond the scope of this report. Of greater importance is the lack of preventive measures taken by overseas travellers in this study, especially since the majority travelled in situations with high risk of malarial transmission (i.e. tropical country, rural location, summer travel, long length of stay). Of those interviewed, only 40% were even aware of the need to take malaria chemoprophylaxis, only one-third sought pre-travel medical advice, and less than 10% took a full course of malaria chemoprophylaxis. Non-medical preventive measures were used somewhat more frequently but still at relatively low levels.

There is a private travel clinic in Surrey but patients must pay a fee to attend. The Vancouver Health Department runs a travel clinic but it is extremely busy, requires a fee, and is not very convenient for BHU residents to attend. Although barriers to seeking pre-travel advice were not specifically addressed, these factors may well limit the use of travel clinics.

Barriers to the use of malaria prevention measures were also not specifically addressed, but in discussion with the treating physicians, many of whom are South Asian, it became apparent that, in the South Asian community, malaria is frequently viewed "as a disease that you almost inevitably get and when you get symptoms you take quinine." Prevention of malaria is either not considered or not viewed as being worth the time, effort, and money. This view is presumably based on the experience of living with malaria in South Asia, but it persists in local South Asian communities.

Physician practice: The large majority of physicians (> 80%) either always or usually personally prescribe malaria chemoprophylaxis for patients travelling to countries with a risk of malaria transmission. However, > 60% of the physicians also refer patients to a travel clinic.

Travel medicine and, in particular, malaria prevention is an area in which it is especially difficult for physicians to keep up to date. The fact that fewer than one half of the cases in this study who should have received primaquine as part of their treatment actually received it may reflect this difficulty.

Conclusions

1) Information about the need for pre-travel advice and malaria prevention measures needs to be specifically developed for and targeted toward the South Asian community in the BHU area.
2) Ways should be explored to give BHU-area physicians access to up-to-date travel information.
3) Given physician practice in the BHU area, at least in those serving the South Asian community, an easily accessible local travel clinic could be of benefit to the community.
4) BHU-area physicians could benefit from continuing education about malaria diagnosis and treatment.

Although these recommendations are specific to the BHU area, increasing world travel and immigration make them widely applicable. Undoubtedly, culturally specific educational materials and improved access for both physicians and the public to up-to-date travel medicine information are necessary nationwide.

Source: *R Strang, MD, Department of Health Care and Epidemiology, University of British Columbia, A King, MD, BC Centre for Disease Control, Vancouver; M Hutcheon, MD, Y Tarif, MD, Boundary Health Unit, Surrey, British Columbia.*

Editorial Comment

Malaria presents most commonly as a non-specific febrile illness that can rapidly progress to death if not recognized and treated immediately. In general, Canada reports approximately 400 malaria cases annually with up to one death per year. Statistics do not include speciation. However, in 1991, a total of 674 cases and five deaths were reported. All reported Canadian malaria cases have been imported from endemic countries.

Although malaria deaths are an occasional occurrence, recent episodes serve to reinforce the need for increased awareness of the ever-changing international malaria situation. Malaria, especially the potentially lethal *falciparum* malaria, has developed drug resistance throughout most of the world where the disease occurs. Awareness of these changing patterns is imperative when choosing preventive chemosuppression and treatment for malaria. Physicians must recognize that malaria is a life-threatening illness that can affect any Canadian who has travelled to an endemic area.

None of the measures to prevent the acquisition of malaria are 100% effective. As well, health-care workers may not even consider malaria in the differential diagnosis of a febrile illness, especially if they have not inquired about a recent travel history. Many physicians do not routinely counsel the travelling public, and due to the ever-changing recommendations for the prevention and treatment of malaria, it may be prudent to refer these patients to a travel clinic. A list of 10,221 travel clinics can be found in the brochure ***Health Information for Canadian Travellers*** available from the Canadian Society for International Health, (613) 230-2654.

Recommendations for the prevention and treatment of malaria are reviewed constantly. A copy of the 1995 Committee to Advise on Travel and Tropical Medicine guidelines can be obtained through the LCDC Faxlink Service by calling 613-941-3900 from a fax telephone. These guidelines are also available on the internet through the LCDC BBS or by telephone request at 613-954-5146.

Notice

REQUEST FOR RESEARCH PROPOSALS

Division of STD Prevention and Control, Bureau of HIV/AIDS and STD, Laboratory Centre for Disease Control

The Division of STD Prevention and Control, Laboratory Centre for Disease Control is seeking proposals from researchers on emerging issues in national STD prevention and control, or on the following topics as recommended by the STD Targeted Research working group:

- Cost-effectiveness and appropriateness of new testing strategies (particularly those which are non-invasive, such as polymerase chain reacation) for *Chlamydia* and gonorrhea (both as a screening and diagnostic tool);
- Cost-effective methods for partner contact tracing and notification, and their efficacy as behavioural interventions;
- Effectiveness of pre-teen/teen reproductive health education interventions (influencing knowledge, attitudes, and behaviour);
- Variations in health-seeking behaviour among certain subgroups (e.g. homeless, ethnic groups, immigrants, etc.) and their relationships with burden of illness;
- Proportion of ectopic pregnancies in Canada attributable to chlamydial and gonococcal infection;
- Cost-benefit analysis of inpatient versus outpatient treatment of pelvic inflammatory disease;
- Impact of presence or absence of STD clinics on STD control in communities;
- Evaluating and improving degree of compliance to STD treatment (e.g. effects of free treatments on compliance);
- Transmission dynamics of STDs both within and between communities;
- Burden of viral STDs (prevalence, transmission, basic epidemiology) in the Canadian population; and
- Assessments of knowledge, attitudes, and behaviours of health-care providers involved in STD treatment/counselling.

The Division is looking to fund six to eight projects with funding ceilings up to $50,000 each. University researchers, governmental and non-governmental organizations, and private researchers throughout Canada are eligible. Funding decisions will be determined on the basis of scientific merit (through a competitive, peer-review process), cost-effectiveness, and relevance to the research needs identified by a consensus meeting and/or emerging issues in national STD prevention and control. Researchers should write to the **Division of STD Prevention & Control, Bureau of HIV/AIDS & STD, Tunney's Pasture, Ottawa, Ontario K1A 1B5, Address Locator 0202A, or Fax: 613-957-0381**. Submissions will be accepted until **1 December 1996**.

International Notes

WORLD MALARIA SITUATION IN 1993

Population at risk

In 1993, some 90 countries or territories were considered malarious; almost half of them are situated in Africa south of the Sahara (Figure 1). For comparison, in the mid-1950s there were some 140 countries or territories where malaria was endemic.

The total world population of about 5,540 million people may be classified according to the status of malaria and their area of residence (all figures are rounded).

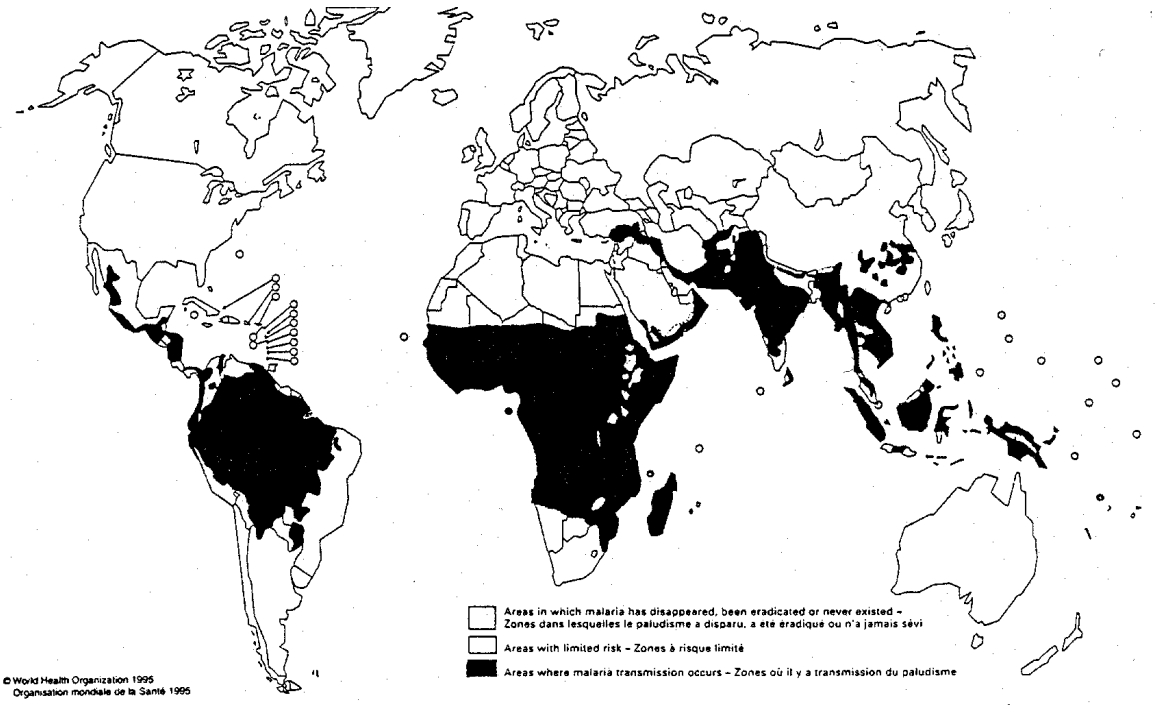
1) Malaria-free areas [3,500 million people (63%)]:
   - areas with 1,540 million people (28%), where malaria has never existed or has disappeared without specific antimalaria measures; and
   - areas inhabited by 1,960 million people [35%], where the disease has disappeared or has been eliminated by antimalaria campaigns, and the malaria-free status has been maintained (small areas with very low risk are also included in this category).
2) Areas considered malarious [2,020 million people (36%)]:
   - areas where endemic malaria was considerably reduced or even eliminated but transmission was reinstated and the situation is unstable or deteriorating [1,620 million people (29%)] (these areas include zones with the most severe malaria problems which developed following major ecologic or social changes, such as agricultural or other economic exploitation of jungle areas, sociopolitical unrest, and population migration); and
   - areas, situated mainly in tropical Africa, where endemic malaria remains basically unchanged and most control programs are in a planning or an early implementation stage with very limited human and material resources [400 million people (7%)].

Mortality

Severe malaria and malaria mortality are caused by *Plasmodium falciparum*, which is the predominant species in tropical Africa, eastern Asia, Oceania and the Amazon area. In the rest of the world it is far less common.

Estimates of malaria mortality vary from 1.5 to 2.7 million malaria deaths worldwide per year, the great majority of them in Africa. Outside of tropical Africa, deaths from malaria occur principally among non-immune people becoming infected with

Figure 1
Epidemiological assessment of the status of malaria, 1993



The designations employed and the presentation of material on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries.

Les désignations utilisées sur cette carte et la présentation des données qui y figurent n'impliquent, de la part de l'Organisation mondiale de la Santé, aucune prise de position quant au statut juridique de tel ou tel pays, territoire, ville ou zone, ou de ses autorités, ni quant au tracé de ses frontières.

falciparum malaria in areas where appropriate diagnosis and treatment are not available.

Resistance to drugs

Among the countries where *falciparum* malaria is endemic, only those of Central America have not recorded resistance of *P. falciparum* to chloroquine. Chloroquine resistance of various levels is now common in practically all endemic countries in Afria, and in many of them, especially in eastern Africa, high levels of resistance pose increasing problems for the provision of adequate treatment. In western and middle South Asia, as well as in Malaysia, Indonesia, the Philippines, and Oceania, levels of chloroquine resistance are variable.

Resistance to sulfadoxine/pyrimethamine is widespread in South-East Asia and South America but is focal and uncommon in other parts of the world. In Thailand, more than 50% of *falciparum* infections in certain areas bordering Cambodia and Myanmar no longer respond to mefloquine therapy.

Reduced susceptibility of *P. falciparum* to mefloquine has been detected by in vitro studies in Africa, but only rarely has this been reflected in in vivo studies. It has not been reported from the Americas.

There is commonly cross-resistance between halofantrine and mefloquine, although halofantrine has retained some efficacy in the areas with mefloquine resistance in Thailand.

In several countries of South-East Asia as well as in Brazil, where quinine plus tetracycline is now the standard treatment for uncomplicated malaria, the sensitivity to quinine is diminishing. Consequently, artemisinin and its derivatives are being deployed for first-line treatment in certain areas.

The resistance of *vivax* malaria strains to chloroquine, first documented in 1989 in infections from Papua New Guinea, has been confirmed in Indonesia, Myanmar, and Vanuatu. In some localized foci in Indonesia and Papua New Guinea, 20% to 30% of patients infected with *vivax* malaria now have recurrences of parasitemia 1 to 3 weeks after a course of 25 mg chloroquine base/kg.

Source: *WHO Weekly Epidemiological Record, Vol 71, No 3, 1996.*