Updated July 2010

Malaria

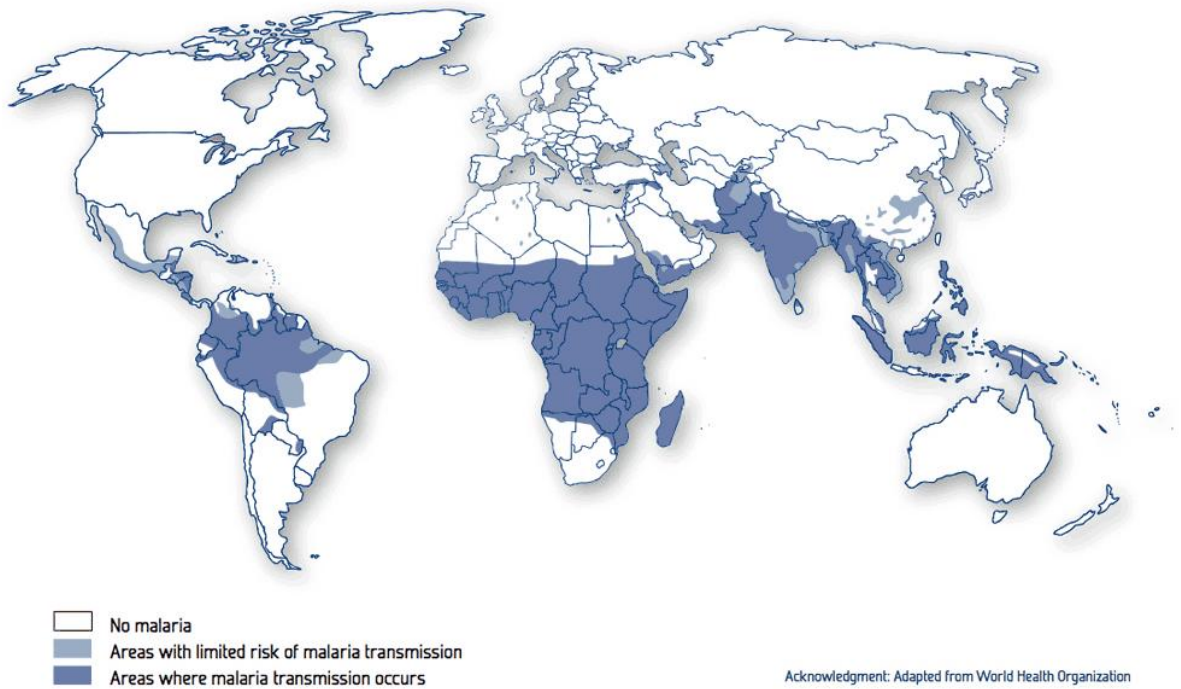
Introduction

Malaria is caused by protozoan parasites of *Plasmodium* and is transmitted to humans by *Anopheles* spp. mosquitoes. There are five species of *Plasmodium* that cause disease in man; *P. falciparum, P. vivax, P. malariae*, *P. ovale* and *P. knowlesi. P. knowlesi* is usually restricted to monkeys in South East Asia but has recently been identified as a cause of malaria in humans [1].

Malaria is endemic in more than 100 countries worldwide where approximately 3.3 billion people are exposed to the disease [2].

Epidemiology

Figure 1. Malaria risk areas, 2009



View larger image (opens in new window)

Map from: Health Information for Overseas Travel, 2010.

Malaria is widely distributed throughout tropical regions of the world in Africa, Hispaniola, Central and South America, Asia, the Middle East and Oceania. In 2008 there were 247 million cases of malaria and nearly one million deaths worldwide, mostly amongst children living in Africa [3].

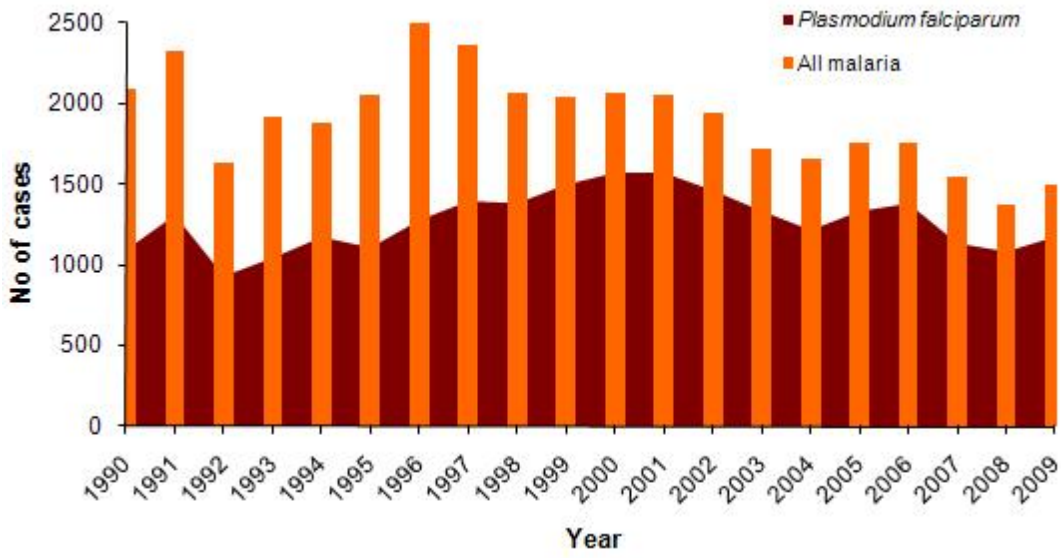
The global prevalence of malaria species differs. While there is overlap, *P. falciparum* is most common in Africa, Hispaniola and Papua New Guinea and *P. vivax* is more common in the Indian subcontinent and Central America. South America and South East Asia have both species. *P. ovale* and *P. malariae* are relatively uncommon. *P. knowlesi* occurs in South East Asia with cases widely distributed in Sabah and Sarawak in Malaysian Borneo, and peninsular Malaysia [1]. Single cases

have been reported from other parts of South East Asia [1], and sporadic cases have occurred in travellers [4].

Malaria-endemic areas can be classified into areas of stable and unstable malaria transmission. In stable areas, for example many countries of sub-Saharan Africa, malaria transmission is year-round with high rates of infection. The population, particularly adults, may therefore develop a degree of immunity and the majority of clinical cases occur in infants and children. In areas of unstable malaria, for example India, transmission tends to be seasonal with short epidemics of varying intensity. Malaria transmission in these unstable areas is less intense, therefore communities have poor immunity and all age groups may be affected.

Malaria in travellers from the United Kingdom

Figure 2. Imported malaria cases, (with P. falciparum cases) United Kingdom: 1990 – 2009 [5]



Courtesy of the Health Protection Agency Malaria Reference Laboratory

Between 2005 and 2009, an average of 1,600 cases of malaria were reported annually in travellers returning to or arriving in the UK from malaria endemic countries [6]. Of these cases, there were between five and 15 deaths reported each year. In 2009, there were 1,495 malaria cases reported, with six deaths [5, 7]. Seventy nine percent of cases were caused by P. falciparum, the severe form of malaria. The first imported case of P. knowlesi was reported in 2006 [8].

Where a destination was stated, 67% (813/1207) of cases in 2009 were acquired in West Africa. Among travellers who are normally resident in the UK, and where a reason for travel is stated, 81% (584/722) of the reported cases in 2009 were amongst travellers returning to their country of origin for the purpose of visiting friends and relatives (VFRs) [5]. The risk of dying from malaria depends on several factors: not realising there is a risk, not taking malaria prevention tablets, not seeking prompt medical care, and not making the correct diagnosis and initiating treatment.

Risk for travellers

All travellers visiting malaria endemic regions are at risk of acquiring malaria, including migrants to the UK who were born in malaria risk areas and return to visit friends and relatives in their country of birth. Any immunity VFR travellers may have acquired in their country of origin wanes rapidly on migration. Their UK-born children will have no protection from the disease.

The risk of malaria varies according to season, geographic location, activities, type of accommodation and the use of malaria prevention tablets and bite avoidance measures. The UK malaria guidelines provide country specific information on malaria risk. This information is also available on the NaTHNaC Country Information Pages.

Transmission

Malaria is transmitted to humans via the bite of an infected female Anopheles mosquito. The female mosquito requires protein from blood in order for her eggs to mature. A diagram illustrating the life cycle of the malaria parasite can be found in the UK malaria guidelines.

Anopheles mosquitoes generally bite between sunset and sunrise and are attracted to humans by several factors including heat, odour and carbon dioxide expired during breathing. The sporozoite stage of the malaria parasite migrates from the mosquito gut to the salivary glands, and is injected into humans when the mosquito takes a blood meal. Although the salivary glands can contain as many as 60,000 sporozoites, only a few are inoculated during feeding.

Once sporozoites enter the human they are rapidly carried to the liver where they infect liver cells and undergo further development. After a period of time that varies according to malaria species, parasites within liver cells mature and are released as merozoites. At this point they infect red blood cells and the symptoms of malaria occur. Two species of malaria, P. vivax and P. ovale, can persist in the liver for several months in a hypnozoite form.

Merozoites further develop within erythrocytes forming a schizont. When the schizont is fully developed, the red cell bursts and releases daughter merozoites that will infect other red cells. In order for malaria to infect a new person, sexual forms of the parasite termed gametocytes, must develop in infected red blood cells and be taken up by an Anopheles mosquito when it feeds. These develop into sporozoites in the mosquito, and the lifecycle is completed.

Signs and symptoms

The incubation period of malaria (the time from injection of sporozoites to the onset of clinical symptoms) in *P. falciparum* is 7- 14 days, but can be longer where there is partial immunity or where the parasite has been suppressed by chemoprophylaxis. In *P. vivax* or *P. ovale* infection, the incubation period is usually between 12 to 18 days, but can be several months or rarely, years, due to the emergence into the bloodstream from the liver of latent liver hypnozoites.

Malaria begins with a non-specific prodrome characterised by fever, headache and myalgia. Cough and diarrhoea can also be seen. Symptoms can progress to high fever and severe muscle aches and pains.

Although symptoms of malaria from all species can be disabling, illness with *P. falciparu*m can progress rapidly and develop serious life-threatening complications if prompt treatment is not given. The most serious complication of falciparum malaria is cerebral malaria, which can lead to coma and death. Other potential complications include renal failure, anaemia, hypoglycaemia, metabolic acidosis, disseminated intravascular coagulation, shock, and pulmonary oedema. Infection with *P. knowlesi* can also be severe [9].

The fever pattern in patients with *P. vivax* or *P. ovale* malaria may become cyclical, recurring every 48 hours. There are cold and hot phases; the cold stage with shivering lasts 15 to 60 minutes, and the hot stage lasts two to six hours, followed by profuse diaphoresis. Although *P. vivax* can cause severe symptoms, fatalities are uncommon [10].

All travellers should be aware of the signs and symptoms of malaria and should be advised to seek immediate medical attention if these occur either whilst abroad or up to a year after their return.

Treatment

All patients who present with fever and a history of travel within malaria risk areas should be evaluated urgently for malaria. Clinical diagnosis is usually by thick and thin blood smears, which are examined by microscopy. Results should be confirmed on the same day and if positive the patient should be referred to a specialist centre. If blood tests for malaria are negative, tests should be repeated daily for a further two days.

P. falciparum malaria is a medical emergency especially if complications have developed, and patients often require intensive therapy. Infection with any species of malaria should be treated promptly. ACMP malaria treatment guidelines have been published [11] and an algorithm for initial management of malaria has been published by the British Infection Society [12].

The choice of drug treatment depends on the causative parasite species and whether or not there is resistance of *P. falciparum* to chloroquine or other drugs. Travellers with *P. falciparum* malaria should be admitted to hospital where they can receive careful evaluation and monitoring. If the patient does not have complications and can swallow pills without difficulty, usual treatments are quinine plus doxycycline, atovaquone/proguanil (Malarone™), or artemether/lumefantrine (Riamet™). If a patient has complications, then intravenous treatment with quinine (followed by doxycycline) is usually given. Consideration should be given to accessing artesunate, a highly effective artemisinin derivative, in severe cases [11, 12]. Formal treatment guidelines from the ACMP should be consulted [11, 12], as well as advice from an infection or tropical medicine unit. Chloroquine can be used for treatment when chloroquine-resistant parasites are not causing illness.

Travellers who develop malaria overseas in remote areas where appropriate supervised treatment may not be available, can consider self-treatment with emergency standby medication. Although rapid test kits have been given to travellers for help in the diagnosis of febrile episodes during travel, they are often not used correctly [13], and the ACMP do not recommend their use by travellers [14].

Emergency standby treatment is intended for travellers who believe they have malaria whilst overseas; it is not a replacement for malaria prevention tablets. Such travellers should still seek medical assistance as soon as possible if they develop a fever, in order for definitive diagnosis and treatment to be made. Guidelines for the use of emergency standby treatment can be found in the UK malaria guidelines.

Prevention

The prevention of malaria involves several steps that have been termed the A, B, C, D of malaria prevention:

A awareness of the risk
B employing bite avoidance measures
C compliance with the appropriate malaria chemoprophylaxis (prevention tablets)
D prompt diagnosis should the symptoms of malaria develop

The choice of chemoprophylaxis to prevent malaria depends on the parasite species and whether or not there is resistance of P. falciparum to chloroquine or other drugs. Chemoprophylactic agents are either causal (directed at the liver phase of the malaria parasite life cycle) or suppressive (directed at

the red blood cell phase of the malaria parasite life cycle). Information on the places in the life cycle targeted by the available chemoprophylatic agents is available in the UK malaria guidelines

Country specific advice regarding malaria is available on the NaTHNaC Country Information Pages

References

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Links

ACMP Guidelines for the prevention of malaria in travellers from the United Kingdom
NaTHNaC Health Information Sheets. Malaria chemoprophylaxis
NaTHNaC Health Information Sheets. Insect bite avoidance
ACMP malaria treatment guidelines
British Infection Society malaria treatment algorithm
Health Protection Agency: Malaria