

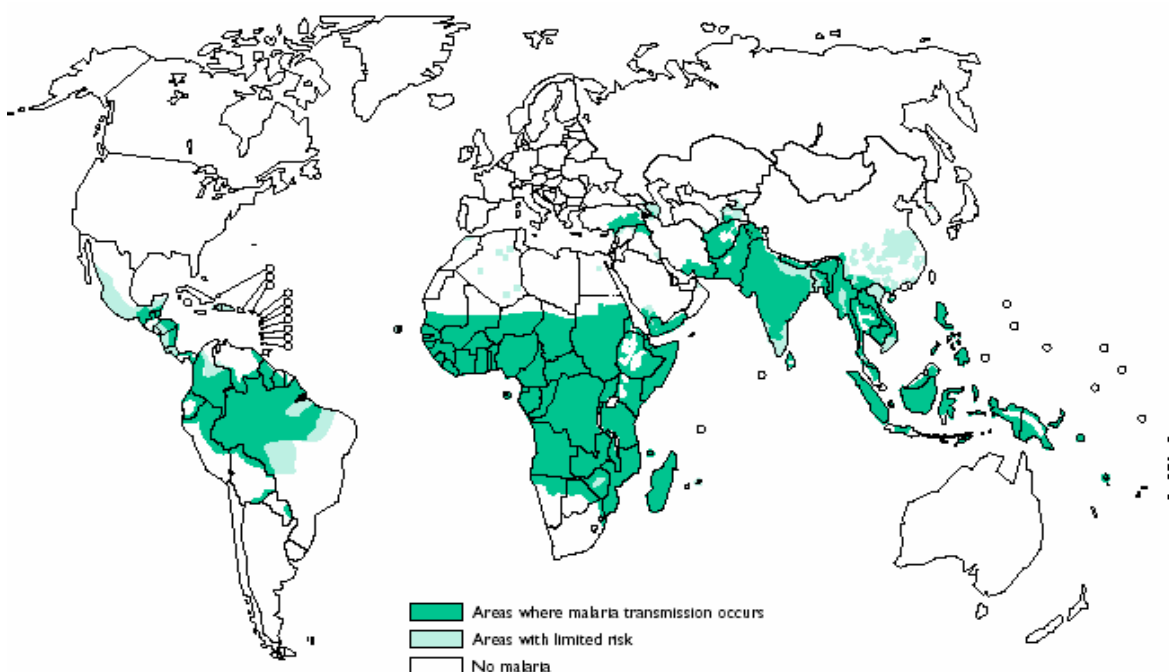
## Malaria

### Introduction

Malaria is caused by protozoan parasites of *Plasmodium* spp and is transmitted to humans by *Anopheles* mosquitoes. There are four species of *Plasmodium* that cause disease in man; *P. falciparum*, *P. vivax*, *P. malariae*, and *P. ovale*. In 2006, the first imported case of *P. knowlesi* in the United Kingdom was reported [1]; this is a species that is usually restricted to monkeys. Malaria is widely distributed throughout tropical regions of the world in Africa, Hispaniola, Central and South America, Asia, the Middle East and Oceania. Recent estimates indicate that as many as 500 million cases of *P. falciparum* occur each year [2].

### Epidemiology

Figure 1. Global Malaria Distribution, 2005 (courtesy of the World Health Organization [3])



Malaria is endemic in over 100 countries world-wide where approximately 3.2 billion people are exposed to the disease (Figure 1) [4].

There is a difference in the global prevalence of malaria species. While most species overlap, *P. falciparum* is more common in Africa, Hispaniola and Papua New Guinea and *P. vivax* is more common in the Indian subcontinent and Central America. South



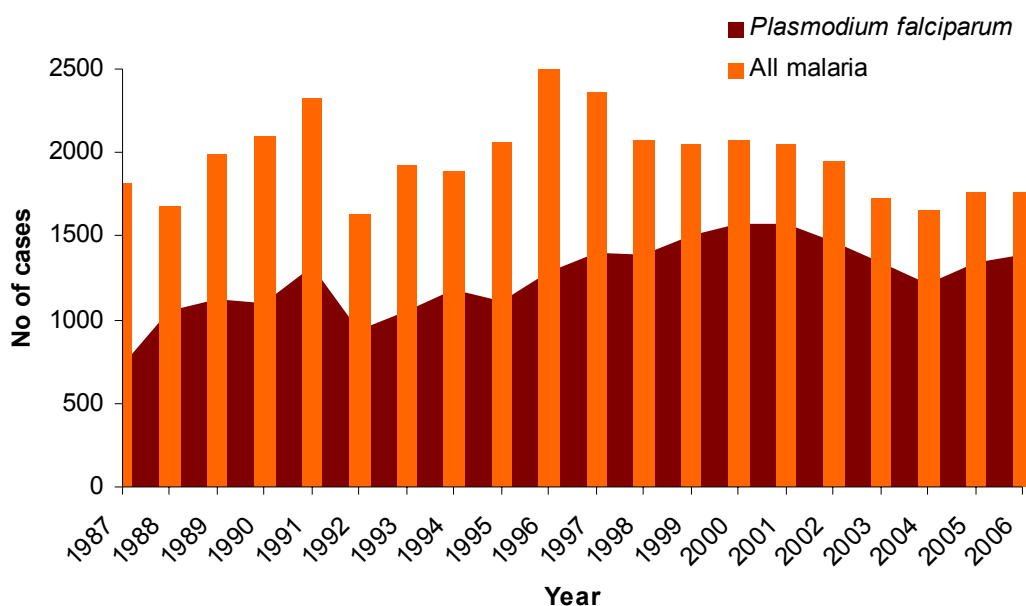
America and South East Asia have both species. *P. ovale* and *P. malariae* are relatively uncommon.

Malaria-endemic areas can be classified into areas of stable malaria transmission and unstable areas. 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 endemicity, 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 are affected.

Malaria is a huge global burden with an estimated 300 million cases, and at least one million deaths occurring each year [5]. Ninety percent of malaria deaths occur in countries in sub-Saharan Africa, and most of these are young children.

### Malaria in travellers from the United Kingdom

Figure 2. Imported malaria cases, (with *P. falciparum* cases) United Kingdom: 1987 – 2006. (Courtesy of the Health Protection Agency Malaria Reference Laboratory [6])



Approximately 1,750 cases of malaria are imported into the United Kingdom (UK) each year, with the majority due to infection with *P. falciparum*. Of these, there are between five and 15 deaths reported each year. In 2006, there were 1,758 malaria cases reported, with eight deaths [7]. All eight deaths occurred as a result of *P. falciparum* infection acquired in Africa. 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. Among travellers who are normally resident in the UK, and where a reason for travel is stated, 77% (589/764) of the reported cases in 2006 were amongst travellers to their country of origin who were visiting friends and relatives (VFRs) [8].

Failure to take malaria prevention tablets is a key factor in both acquiring malaria. A history of the use of malaria prevention tablets was recorded for 917 cases in 2006, of these 81% (740) were not taking malaria prevention tablets. A high proportion of the remainder were taking tablets not currently recommended by the HPA Advisory Committee on Malaria Prevention (ACMP) [8].

### **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 this group 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 risk on malaria and can be found at the link provided.

### **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 on the HPA website.

*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 malaria parasites is carried in the mosquito's salivary glands and injected into humans when the mosquito takes a blood meal. Although the salivary glands may 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.

Merozoites further develop within erythrocytes forming a schizont. When the schizont is fully developed (usually one to several weeks), 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) can be as short as eight days in *P. falciparum* infection, or as long as several months (usually with *P. vivax* or *P. ovale*).

Infections due to *P. falciparum* can progress rapidly and be life-threatening if prompt treatment is not given.

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

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 symptoms of malaria from all species can be disabling, illness with *P. falciparum* can progress rapidly and develop serious complications. 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.

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 year after their return.

## Treatment

All patients who present with fever and a history of travel within malaria risk areas should be evaluated for malaria.

Clinical diagnosis of malaria is usually by thick and thin blood smears, which are examined by microscopy. Rapid diagnostic tests for malaria antigen may be available in some laboratories. Although rapid test kits have been given to travellers in the past for help in the diagnosis of febrile episodes during travel, there is evidence that they are often not used correctly [9]. The ACMP do not recommend their use by travellers [10].

*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 recognised and treated promptly. ACMP malaria treatment guidelines have recently 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 is not showing signs of 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. It may be possible to access artesunate, an 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 may 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. Emergency standby treatment is intended for travellers who believe they have malaria; 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 [ACMP 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), and D – prompt diagnosis should the symptoms of malaria develop. The [ACMP malaria guidelines](#) should be consulted for country specific recommendations for the prevention of malaria in travellers.

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  12. British Infection Society. Malaria – algorithm for initial assessment and management in adults. February 2007. [Accessed 17 August 2007] Available at  
<http://www.britishinfectionsociety.org/documents/Malariaalgorithm07.pdf>

## Links

ACMP Guidelines for the prevention of malaria in travellers from the United Kingdom  
[http://www.hpa.org.uk/infections/topics\\_az/malaria/guidelines.htm](http://www.hpa.org.uk/infections/topics_az/malaria/guidelines.htm)

NaTHNaC Health Information Sheets. Malaria chemoprophylaxis  
<http://www.nathnac.org/pro/factsheets/malariaproph.htm>

NaTHNaC Health Information Sheets. Insect bite avoidance.  
<http://www.nathnac.org/pro/factsheets/iba.htm>

ACMP malaria treatment guidelines  
[http://www.hpa.org.uk/infections/topics\\_az/malaria/pdf/mal\\_treat\\_Jol07.pdf](http://www.hpa.org.uk/infections/topics_az/malaria/pdf/mal_treat_Jol07.pdf)

British Infection Society malaria treatment algorithm  
<http://www.britishinfectionsociety.org/K210%20malaria%20algorithmFINAL.pdf>

Health Protection Agency  
[http://www.hpa.org.uk/infections/topics\\_az/malaria/default.htm](http://www.hpa.org.uk/infections/topics_az/malaria/default.htm)