Malaria is a mosquito-transmitted parasitic infection that can cause the destruction of red blood cells, leading to severe illness and death. Taking antimalarials can reduce the risk of infection.

Malaria clinical features and prevention

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Malaria is a potentially life-threatening infection caused by the protozoan parasite Plasmodium, transmitted via female anopheles mosquitoes. It is one of the most common causes of fever among people returning from abroad.1

Epidemiology

In 2012, there were an estimated 207 million cases of malaria worldwide and an estimated 627,000 deaths.2 Malaria is most prevalent in tropical regions of Africa, Asia, South and Central America, the Middle East, Hispaniola and Oceania. Most deaths caused by malaria occur in Africa.3

There has been a 45% global reduction in malaria mortality since 2000. This is likely to be attributable in part to a series of World Health Organization initiatives, such as the provision of long-lasting insecticidal nets, indoor residual spraying and the introduction of measures to ensure the quality of artemesia-based combination therapies.

In the UK, around half of all cases reported are in London. Cases generally peak over the summer months (July to September), with a smaller peak observed in January. Most cases occur in adults aged 20–49 years, with men having a slightly higher infection rate than women.4 Some 60% of malaria cases occur in people of African or South Asian origin, over half of whom develop symptoms after a visit to family and friends in an endemic area. Most of these patients will not have taken adequate malaria prophylaxis.5 Mortality rates in the UK have been shown to increase with age.6

Very rarely, malaria is reported in the UK in people with no relevant travel history. These cases are thought to be caused by the carriage of an infected mosquito into the UK in luggage or on an airplane from an endemic area.7

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Microbiology

There are five species of Plasmodium that can cause malaria in humans. They are:

- Plasmodium falciparum
- Plasmodium vivax
- Plasmodium ovale
- Plasmodium malariae
- Plasmodium knowlesi

Infections with P. falciparum is the most common cause of malaria in the UK — accounting for 73% of all reported cases in 2012.8

Anopheles mosquitoes can carry the malaria-causing Plasmodium parasite.
The clinical picture of malaria varies depending on the causative species. *P. falciparum* infection generally causes the most severe disease and is responsible for most deaths. Infection with *P. vivax*, *P. ovale* or *P. malariae* does not tend to cause as severe an illness as *P. falciparum*, but can occasionally be life-threatening, particularly during pregnancy.

In the past, *P. knowlesi* has only been known to infect monkeys but reported human cases are on the increase — particularly in travellers returning from the Asia-Pacific region. Patients with *P. knowlesi* malaria can deteriorate quickly and, because of the species' morphological resemblance to *P. malariae*, misdiagnosis is possible, which can have a detrimental effect on prognosis.3

*P. falciparum*, *P. malariae* and *P. ovale* are most frequently contracted in sub-Saharan Africa, and *P. vivax* is most commonly detected in patients who have a history of travel in South Asia (mainly the Indian subcontinent).1

The process by which plasmodium parasites produce disease is complex and not fully understood. Haemolytic anaemia is known to be caused by the rupture of infected red blood cells (see Box 1), the removal of affected red blood cells by the spleen and bone marrow dyserythropoesis.

During *P. falciparum* infection, infected red blood cells adhere to endothelial cells in the microvasculature. This prevents the removal of infected cells by the spleen. It is thought that the higher the concentration of *P. falciparum*-infected red blood cells there are, the greater the severity of the disease.4

### Clinical features

The minimum incubation period for malaria to develop is six days. *P. falciparum* malaria usually develops within three months after returning from an endemic area, but the incubation period may be longer for patients who have taken prophylaxis. Occasionally, the incubation period for non-falciparum malaria will be greater than six months. Therefore, malaria should be suspected in any patient with a febrile illness presenting between six days and 12 months of return from an endemic area.

Because the clinical features of malaria are non-specific, there are no signs or symptoms that can predict a diagnosis of malaria accurately. Possible symptoms include:1

- Fever
- Sweats
- Chills
- Malaise
- Myalgia
- Headache
- Diarrhoea
- Thrombocytopenia
- Cough

Occasionally, symptoms can be misleading, especially in children, with patients experiencing symptoms such as gastrointestinal disturbances, lower respiratory tract infections and sore throat.1

Signs and symptoms of severe or complicated malaria include confusion, impaired consciousness, seizures, renal

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**Box 1: Life cycle of the plasmodium parasite**

When an infected mosquito bites a human, plasmodium sporozoites are injected into a human host where they invade liver cells (see below Figure; stage 1). During the liver stages (stage 2), the parasites mature to form schizonts and multiply, this takes around 5–20 days.4

Once mature the liver schizonts will rupture, releasing merozoites. The invasion of red blood cells by merozoites marks the beginning of the erythrocytic cycle (stage 3) wherein the parasites continue to grow and divide. It is when the parasites are in this stage of their life cycle that they begin to destroy their host's red blood cells and the symptoms of malaria emerge.

A proportion of infected red blood cells will develop into male and female gametocytes (stage 4). When a mosquito ingests both male and female gametocytes, they mature, mate and multiply to form sporozoites, which are stored in its salivary glands.

For people who are infected with *P. vivax* or *P. ovale*, parasites can remain dormant in the liver for months before being reactivated — causing a relapse of the infection.4
be or she should stop immediately because this can prevent detection of the parasite.\(^1\)

Thick and thin blood films should be collected promptly and examined for the presence of plasmodium parasites. If parasites are detected, the species, parasitic stage and stage of life cycle (see Box 1, p58) should be reported. Although the initial parasite count is highly dependent on the stage of the infection, it can be a useful predictor of severity of disease. There is an increased risk of developing severe disease if more than 2% of red blood cells are parasitized.\(^3\)

If the initial blood film is negative, repeat films should be examined 12–24 hours later and again after a further 24 hours. Generally, malaria is unlikely if parasites cannot be detected on three blood film slides.

RAPID DIAGNOSTIC TESTS

RAPID DIAGNOSTIC TESTS should always be used in addition to blood films in the diagnosis of malaria. These are used to test for the presence of parasite antigens or enzymes. Rapid diagnostic testing is almost as accurate as examining blood films in the diagnosis of P. falciparum malaria, but is not as reliable in the diagnosis of other types.

A full blood count should be taken to assess the level of anaemia and thrombocytopenia. Blood glucose, urea, electrolytes and liver function should be checked. For more severely ill patients, blood gases, haemoglobin and clotting function tests should also be performed.\(^6\)

A chest X-ray, urine and stool cultures (the latter if the patient has diarrhoea) should be taken to rule out other origins of infection. If a febrile patient presents with impaired consciousness or is having repeated seizures, a lumbar puncture should be considered to exclude meningitis or encephalitis. HIV and viral hepatitis should be tested in certain circumstances. Other travel-related infections should also be considered, eg typhoid, dengue fever, severe acute respiratory infection and Chagas disease.

Malaria is a notifiable disease and confirmed cases must be reported to the local health protection unit.\(^7\) Other members of the group who travelled with the patient are likely to have been exposed to the same risk and should be advised to seek urgent medical advice if they develop symptoms suggestive of malaria. Pregnant women with malaria (especially if infected with P. falciparum) are susceptible to severe and complicated disease, especially during the third trimester of pregnancy. The placenta can contain higher levels of the parasite than the circulating red blood cells, which can lead to difficulties in diagnosis. Stillbirth or early delivery can occur and there is a risk of maternal death.\(^8,9\)

Prevention

Some individuals possess genetic or immunological factors that confer protection against malaria or that result in less severe disease. For example, the absence of the Duffy antigen in red blood cells prevents P vivax malaria, and the sickle cell gene is known to reduce the severity of disease and mortality from all causes of malaria.\(^10\)

It is essential that travellers are informed about the need to adhere to chemoprophylaxis and the importance of completing the course. Photo-sensitivity reactions with doxycycline are possible and individuals should be advised accordingly. Methotrexate should be started two to three weeks before departure, this is to assess tolerability to the medicine.

MODERATION

MALARIA EXPUSURE IS INFLUENCED BY THE NUMBER OF MOSQUITO BITES WHICH AN INDIVIDUAL RECEIVES, WHICH CAN BE AFFECTED BY TEMPERATURE, ALTITUDE, TIME OF YEAR AND LENGTH OF STAY.

Bite prevention: People travelling to malaria-endemic areas should be advised to minimise the amount of exposed skin to prevent being bitten by mosquitoes. Loose-fitting clothing is recommended and arms, legs and feet should be covered with trousers after sunset. There is limited evidence to support the use of herbal remedies, vitamin B supplements and garlic to prevent mosquito bites and these options are not recommended.\(^11\)

Explorers travelling to areas with high risk of malaria should ideally have a pyriproxyfen to prevent mosquito bites and these options are not recommended.\(^11\)

The cost of the medication and treatment course may also be an issue for some people.

There are two approaches to prophylaxis: chemoprophylaxis or suppressive prophylaxis. Chemoprophylaxis aims to prevent the plasmodium parasite from leaving the liver and infecting red blood cells. It takes approximately seven days for a parasite to reach this stage, therefore, chemoprophylaxis is recommended for at least seven days after leaving the endemic area. The combination of proguanil and atovaquone is used in this approach. Suppressive prophylaxis acts on the parasite after it has infected the red blood cells of a host and must be taken for several weeks after leaving an endemic area.\(^6\)

Some recommendations should only be used on exposed areas of skin and care should be taken to avoid inhaling or contact with eyes or mouth. DEET can reduce the efficacy of sunscreen and should always be used after sunscreen has been applied.\(^12\)

There have been concerns raised about the safety of DEET and its potential to cause toxic encephalopathy in children. However, there have been just 17 case reports of this, some of which cannot amputate the encephalopathy to DEET alone.\(^13\) Systemic toxicity following topical application is very rare, with only two cases being reported so far of one which resulted in psychosis, the other in cardiovascular complications.\(^13\) Use of DEET is considered safe and is recommended by Public Health England. However, travelers should be advised to take care not to ingest or inhale these products.\(^13\)

People should be advised to take precautions to protect themselves while sleeping, too. Air-conditioning reduces the risk of bites and mosquito screens on doors and windows can prevent mosquitoes entering the room overnight. Rooms should be sprayed with insecticide (pyrethroid is recommended) before dusk to kill any mosquitoes that may have entered during the day.

Insect repellents are useful if effective, mosquitoes containing insecticide can be used.
Vaccines  Research into the use of vaccines to prevent malaria began in the 1960s, but a licensed product has yet to be developed. Studies into malaria vaccines are ongoing and one product, which targets *P. falciparum*, is currently in phase III trials.6

Reserve courses  Reserve courses of antimalarials are recommended for travellers who are taking chemoprophylaxis and intending to visit remote areas where they are unlikely to be able to seek medical attention, if needed, within 24 hours. Travellers should be advised to start reserve courses of antimalarials at the onset of fever and to seek medical attention as soon as possible. Reserve courses should not be considered as a substitute for prophylactic measures. To minimise drug toxicity and prevent resistance it is recommended that the medicine used for the reserve course should not be the same as the one taken for chemoprophylaxis.7

References

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