International travel and health

Module 3: Malaria

World Health Organization

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Cover photo: Credit: WHO
Congo. Vector control is a vital component of malaria control and elimination strategies as it is highly effective in preventing infection and reducing disease transmission. The 2 core interventions are insecticide-treated nets (ITNs) and indoor residual spraying (IRS).

Contents

Foreword

Depending on the health profile of the traveller, the type of travel to be undertaken, and the place of transit and destination, travellers may face various health risks during travel. The *International travel and health* collection is an update of International travel and health (2012) and serves as an entry point for other World Health Organization (WHO) publications that provide further information. Its primary target audience is travel health practitioners and travel health professionals, who provide health advice to travellers on appropriate precautions to be taken to minimize any travel-related health risks in unfamiliar environments, before, during and after travel. The guidance may also be of interest to health authorities who intend to support travel health professionals in their jurisdiction or develop health advice for their population. It may also be of interest to travellers who wish to obtain such information for themselves as well as those working in the travel industry, such as agents and organizers, airlines and shipping companies.

Module 3 outlines the clinical features, geographical distribution and chemoprophylaxis against malaria, as well as personal protection measures against mosquitoes that travellers should take during their journey and at destinations, and treatment for those who are infected.

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Declaration of interest

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Credit: WHO / Simon Lim
A member of the Yunnan Institute of Parasitic Diseases prepares to collect water from a bamboo grove as he looks for mosquito larvae. Simao, Yunnan Province, China. 19 May 2010.

Module 3: Malaria

1. Background

Malaria is a common and life-threatening disease in many tropical and subtropical areas. There is currently a risk of malaria transmission in 91 countries and territories, which are visited by more than 125 million international travellers every year.

Each year many of these international travellers fall ill with malaria while visiting countries and territories where malaria is endemic, and well over 10 000 are reported to become ill with malaria after returning home. However, underreporting means that the real figure may be considerably higher. International travellers to countries/territories with local malaria transmission who arrive from countries with no transmission are at high risk of malaria infection and its consequences because they lack immunity. Migrants from countries/territories with malaria transmission living in malaria-free countries and returning to their home countries to visit friends and relatives are similarly at risk because of waning or absent immunity.

Travellers who fall ill while travelling may find it difficult to access reliable medical care. Those who develop malaria upon returning to a country that is malaria-free face particular problems. For example, medical personnel may be unfamiliar with malaria, the diagnosis may be delayed, and effective antimalarial medicines may not be registered and/or available. This can result in progression to severe malaria with complications and, consequently, high case fatality rates.

Fever occurring in a traveller within 3 months of leaving a country in which there is a risk of malaria is a potential medical emergency and should be investigated urgently to exclude malaria. In the rare situations in which there is no rapid access to reliable diagnostic facilities, standby emergency treatment (SBET) is indicated (see section **3.2**).

1.1 Cause

Malaria is caused by the protozoan parasite Plasmodium. Human malaria is caused by five different species of Plasmodium: *P. falciparum*, *P. malariae*, *P. ovale*, *P. vivax* and *P. knowlesi*. Of these, *P. falciparum* and *P. vivax* are the most prevalent, and *P. falciparum* is the most dangerous, with the highest rates of complications and mortality. This deadly form of malaria is a serious public health concern in most countries in sub-Saharan Africa. *P. knowlesi*, a species that normally infects animals, can occasionally infect humans. As yet there are no reports of human-mosquito-human transmission of such “zoonotic” forms of malaria.

1.2 Transmission

The malaria parasite is transmitted by female *Anopheles* mosquitoes, which bite mainly between dusk and dawn.

1.3 Nature of the disease

Malaria is an acute febrile illness with an incubation period of 7 days or longer. Thus, malaria should always be considered when a febrile illness develops 1 week or more after the first possible exposure.

The most severe form of malaria is caused by *P. falciparum* and has variable clinical features that include fever, chills, headache, muscle aches and weakness, vomiting, cough, diarrhoea and abdominal pain. Other symptoms related to organ failure may supervene, such as acute renal failure, pulmonary oedema, generalized convulsions and circulatory collapse, followed by coma and death. The initial symptoms are nonspecific and cannot be distinguished from those of other febrile illnesses that might be common in the locality, such as acute respiratory infections, dengue fever and septicaemia.

It is important to consider the possibility of falciparum malaria in all patients with unexplained fever starting at any time between 7 days after the first possible exposure to malaria and 3 months (or, rarely, later) after the last possible exposure. Any person who experiences a fever during this period should immediately seek diagnosis and effective treatment and should inform medical personnel of their possible exposure to malaria infection. Falciparum malaria may be fatal if treatment is delayed beyond 24 hours after the onset of clinical symptoms.

Young children, pregnant women, travellers who are immunosuppressed and older travellers are particularly at risk of severe disease. Malaria, particularly *P. falciparum*, in non-immune pregnant travellers increases the risk of maternal death, miscarriage, stillbirth and neonatal death.

Human malaria caused by other Plasmodium species results in significant morbidity and can occasionally cause life-threatening disease. Cases of severe *P. vivax* malaria have been reported among populations living in (sub)tropical countries with malaria risk. *P. vivax* and *P. ovale* can remain dormant in the liver; relapses caused by the persistent liver forms ("hypnozoites") may occur months and, rarely, several years after exposure, except when specific anti-relapse medications are administered. Latent blood infection with *P. malariae* may be present for many years, but it is very rarely life-threatening.

P. knowlesi malaria is primarily a public health problem among populations living or working in forested areas in south-east Asia. In recent years, sporadic cases of travellers' malaria due to *P. knowlesi* have been reported. Humans can be infected with this "monkey malaria" parasite while staying in – or on the fringes of – rainforests, within the range of the natural monkey hosts and mosquito vector of this infection. These areas include parts of Brunei Darussalam, Cambodia, China, Indonesia, Lao People's Democratic Republic, Malaysia, Myanmar, Philippines, Singapore, Thailand and Viet Nam. Symptoms may be atypical of malaria. Severe *P. knowlesi* malaria with organ failure may occur, and sporadic fatal outcomes have been described. *P. knowlesi* has no persistent liver forms and relapses do not occur. Travellers to forested areas of south-east Asia where human *P. knowlesi* infections have been reported should protect themselves against mosquito bites between dusk and dawn to prevent infection and take chemoprophylaxis where indicated.

1.4 Geographical distribution

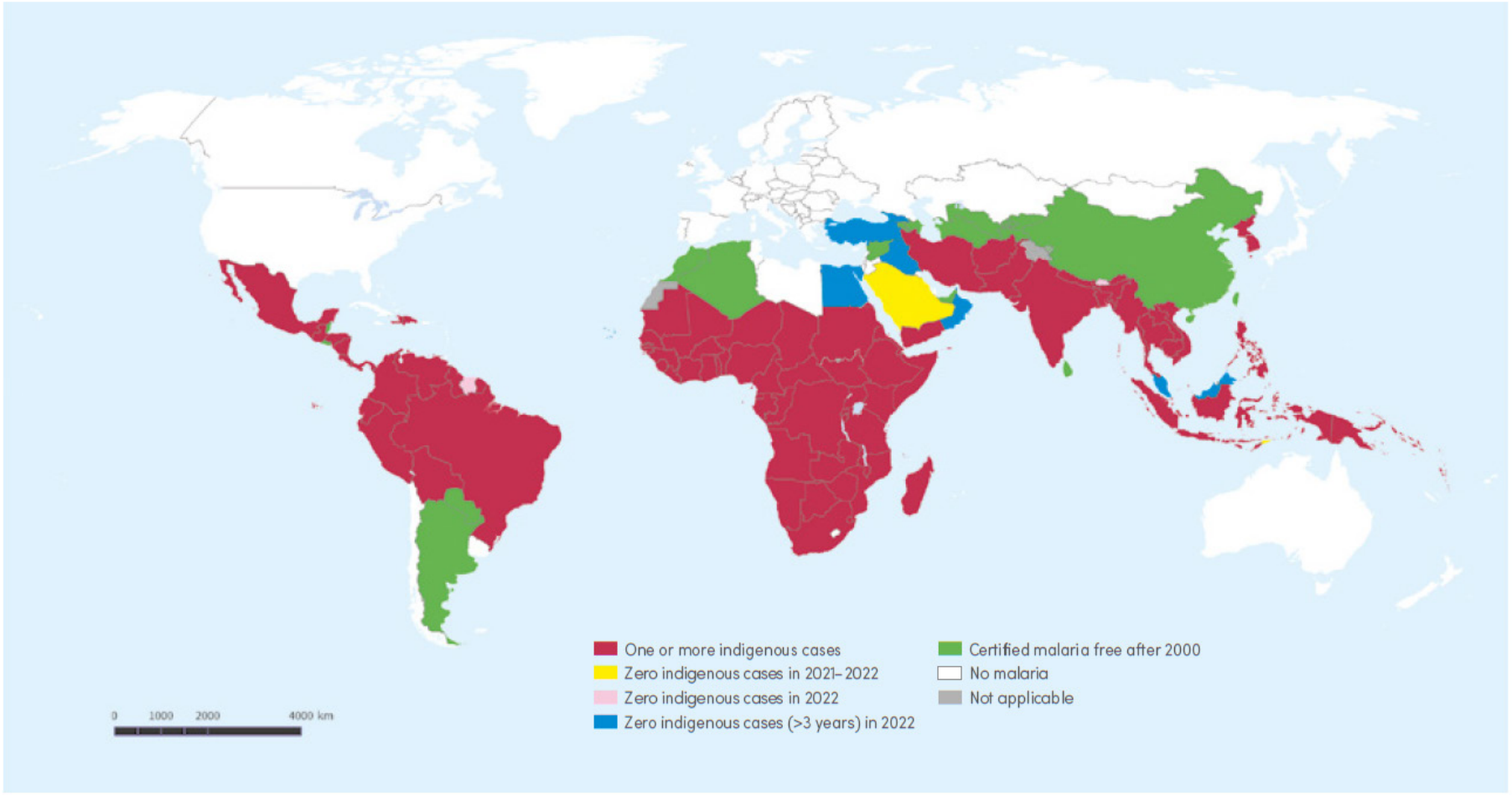
The current distribution of malaria in the world is available from WHO's *World malaria report* (WHO, 2023). The risk for travellers of contracting malaria varies greatly from country to country and even between areas within a country, and this must be considered in any discussion of appropriate preventive measures.

In most countries/territories with malaria risk, the centres of large urban areas – although not necessarily the periurban areas – are free of malaria transmission. However, malaria can be transmitted throughout urban areas of Africa and, to a lesser extent, India. There is usually less risk at altitudes above 1500 metres, although in favourable climatic conditions the disease can be contracted at altitudes up to almost 3000 metres. The risk of infection may also vary according to the season, being highest at the end of, or soon after, the rainy season.

There is no risk of malaria in many tourist destinations in south-east Asia, the Caribbean and Latin America, and information on malaria risk in each country/territory is given in the Country List: Country vaccination requirements and WHO recommendations for vaccination against yellow fever, poliomyelitis, and malaria prophylaxis in international travellers (hereafter Country list).

Since 2000, there has been a significant increase in the number of countries that have moved towards malaria elimination. Between 2000 and 2023, 25 countries that were malaria endemic achieved 3 consecutive years of zero indigenous malaria cases, and 15 of these countries were certified malaria-free by WHO. However, malaria remains endemic in 85 countries and areas.

Credit: WHO / Shatha Al-Eryani
Combat against mosquito-borne diseases, Yemen, June 2024. Community health volunteers knock on doors to ensure that health information reaches the households that need it most.



Countries with indigenous cases in 2000 and their status by 2022[a,b] *Source: WHO database.*

WHO: World Health Organization.

[a] Malaysia has a significant number of indigenous malaria cases caused by *Plasmodium knowlesi* infection.

[b] Countries with zero indigenous cases for at least 3 consecutive years are considered to have eliminated malaria. In 2022, Malaysia reported zero indigenous cases caused by human *Plasmodium species*[a] for the fifth consecutive year and Cabo Verde reported zero indigenous cases for the fourth year. Belize was certified malaria free in 2023, following 4 years of zero malaria cases.

1.5 Risk for travellers

During the transmission season in countries/territories with malaria risk, all non-immune travellers who are exposed to mosquito bites, especially between dusk and dawn, are at risk of malaria. This includes previously semi-immune travellers who have lost or partially lost their immunity during stays of 6 months or more in countries or areas of no risk. Children who have migrated to countries and areas of no risk are at particular risk when they travel to malarious areas to visit friends and relatives.

Most cases of falciparum malaria in travellers occur because of poor adherence to, or use of inappropriate, prophylactic malaria drug regimens, combined with failure to take adequate precautions against mosquito bites. Studies of travellers' behaviour have shown that adherence to chemoprophylaxis can be improved if travellers are informed of the risk of infection and believe in the benefit of prevention strategies. Late-onset vivax and ovale malaria may occur despite effective prophylaxis because these parasites cause relapses that cannot be prevented with medicines that are currently recommended for chemoprophylaxis.

Malaria risk is not evenly distributed where the disease is prevalent. Travellers to any country/territory in which malaria transmission varies by area should seek advice on the risk of infection in the particular zones that they will be visiting. If specific information is not available before travelling, it is recommended that precautions appropriate for the highest reported risk in the country/territory be taken. This applies particularly to individuals backpacking to remote places and visiting areas where health facilities are not readily accessible. Travellers staying in rural areas at night may be at highest risk.

Credit: WHO / Valerie Fernandez
Malaria prevention in Vanuatu. A member of the community receives bed nets for his household.

2. Precautions

Travellers and their advisers should note the five principles – the ABCDE – of malaria protection:

- Be **A**ware of the risk, the incubation period, the possibility of delayed onset and the main symptoms.
- Avoid being **B**itten by mosquitoes, especially between dusk and dawn.
- Take antimalarial drugs (**C**hemoprophylaxis) when appropriate, at regular intervals to prevent acute malaria attacks.
- Immediately seek **Di**agnosis and treatment if a fever develops 1 week or more after entering an area where there is a malaria risk and up to 3 months (or, rarely, later) after departure from a risk area.
- Avoid outdoor activities in **E**nvironments that are mosquito breeding places, such as swamps or marshy areas, especially in the late evenings and at night.

2.1 Protection against mosquito bites

All travellers should be advised that personal protection from mosquito bites between dusk and dawn is their first line of defence against malaria.

Travellers may protect themselves from mosquitoes by the means outlined below.

Insect repellents are substances applied to exposed skin or to clothing to prevent human/vector contact. The active ingredient in a repellent repels insects but does not kill them. Choose a repellent containing DEET (N,N-diethyl-3-methylbenzamide), IR3535 (3-[N-acetyl-N-butyl]-aminopropionic acid ethyl ester) or icaridin/picaridiin (1-piperidinecarboxylic acid, 2-(2-hydroxyethyl)-1-methylpropylester). Insect repellents should be applied to provide protection at times when insects are biting. Care must be taken to avoid contact with mucous membranes; insect repellents should not be sprayed on the face, applied to the eyelids or lips, or to sensitive, sunburned or damaged skin or deep skin folds. Always wash the hands after applying the repellent. Repeated applications may be required every 3–4 hours, especially in hot and humid climates when sweating may be profuse. When the product is applied to clothes, the repellent effect lasts longer. However, label instructions should be followed to avoid damage to certain fabrics. Repellents should be used in strict accordance with the manufacturers' instructions and the dosage must not be exceeded, especially for young children and pregnant women.

Mosquito nets are excellent means of personal protection while sleeping. Nets can be used either with or without insecticide treatment. However, treated nets are much more effective. Pretreated nets may be commercially available. Nets should be strong and have a mesh size no larger than 1.5 mm. The net should be tucked in under the mattress after ensuring that it is not torn and that there are no mosquitoes inside. Nets for hammocks are available, as are nets for cots and small beds.

Mosquito coils are the best-known example of insecticide vaporizer, usually with a synthetic pyrethroid as the active ingredient. A more sophisticated product, which requires electricity, is an insecticide mat that is placed on an electrically heated grid, causing the insecticide to vaporize. Battery-operated vaporizers are also available. Such devices can also be used during daytime if necessary.

Aerosol sprays intended to kill flying insects are effective for quick knockdown and killing. Indoor sleeping areas should be sprayed before bedtime. Treating a room with an insecticide spray will help to free it from insects, but the effect may be short-lived. Spraying before bedtime, combined with the use of a vaporizer or a mosquito net, is recommended.

Protective clothing can help at times of the day when vectors are active. The thickness of the material is critical. When applied to clothing, insect repellent is effective for longer than it may be on the skin. Extra protection is provided by treating clothing with permethrin or etofenprox, to prevent mosquitoes from biting through the material.

Travellers camping in tents should use a combination of mosquito repellents and screens. The mesh size of tent screens often exceeds 1.5 mm, in which case special mosquito screens are necessary.

Screening of windows, doors and eaves reduces exposure to flying insects. Accommodation with these features should be sought where available.

Air-conditioning is a highly effective means of keeping mosquitoes and other insects out of a room as long as there are no gaps around windows or doors. In air-conditioned hotels, other precautions are not necessary indoors.

2.2 Chemoprophylaxis

The most appropriate chemoprophylactic antimalarial drug for the destination should be prescribed in the correct dosage (see Country list and Table 1).

Travellers and their doctors should be aware that **no antimalarial prophylactic regimen gives complete protection**, but good chemoprophylaxis (adherence to the recommended drug regimen) significantly reduces the risk of fatal disease. The following should also be taken into account:

- Dosing schedules for children should be based on body weight.
- Weekly mefloquine should preferably be started 2–3 weeks before departure to achieve protective levels in the blood and to allow possible side-effects to be detected before travel so that alternatives can be considered. Before mefloquine is prescribed, all users should be made aware of the adverse events associated with its use.
- Daily prophylaxis with doxycycline or atovaquone–proguanil should be started 1–2 days before arrival in the malaria risk area (or earlier if drug tolerability needs to be checked before departure).
- Weekly chloroquine should be started 1 week before arrival at the destination.
- All prophylactic drugs should be taken with unfailing regularity for the duration of the stay in the malaria risk area. They should continue to be taken for 4 weeks after the last possible exposure to infection since parasites may still emerge from the liver during this period. The single exception is atovaquone–proguanil, which can be stopped 1 week after return because it is effective against early liver-stage parasites (liver schizonts). However, if daily doses have been skipped while the traveller was

exposed to malaria risk, atovaquone–proguanil prophylaxis should also be taken for 4 weeks after return.

- Depending on the type of malaria at the destination, travellers should be advised about possible late-onset malaria caused by the persistent hepatic forms of *P. vivax* and *P. ovale*.

Depending on the type of malaria risk in the specific area of the country/territory visited (see Country list), the recommended prevention method may be mosquito bite prevention only, or mosquito bite prevention in combination with chemoprophylaxis and/or standby emergency treatment (SBET), as shown in Table 2 (see also Table 1 for details of individual drugs).

Credit: WHO / Panos Pictures / Saiyna Bashir
Pakistan: Malaria response following 2022 floods. On 14 March 2023, WHO medical entomologist Syed Baseer Ahmed visits a village during a door-to-door campaign for malaria outbreak response and prevention in Sohbatpur.

Table 1 Use of antimalarial drugs for prophylaxis in travellers

Generic name	Dosage regimen	Duration of prophylaxis	Use in special groups			Main contraindications[a]	Comments[a]
			Pregnancy	Breastfeeding	Children		
Atovaquone–proguanil combination tablet	One dose daily. 11–20 kg: 62.5 mg atovaquone plus 25 mg proguanil (1 paediatric tablet) daily 21–30 kg: 2 paediatric tablets daily 31–40 kg: 3 paediatric tablets daily > 40 kg: 1 adult tablet (250 mg atovaquone plus 100 mg proguanil) daily	Start 1 day before departure and continue for 7 days after leaving malaria endemic area	No data, not recommended	No data, not recommended	Not recommended < 11 kg (< 5 kg in Belgium, Canada, France and the United States of America) because of limited safety data	Hypersensitivity to atovaquone and/or proguanil; severe renal insufficiency (creatinine clearance < 30 ml/min)	Take with food or milky drink to increase absorption. Registered in European countries for chemoprophylactic use with a restriction on duration of use (varying from 5 weeks to 1 year). Plasma concentrations of atovaquone are reduced when it is co-administered with rifampicin, rifabutin, metoclopramide or tetracycline. May interfere with live typhoid vaccine. The non-recommended status in pregnancy has been replaced with a warning label in France.
Chloroquine	5 mg base/kg weekly in one dose, or 10 mg base/kg weekly divided into six daily doses. Adult dose: 300 mg chloroquine base weekly in one dose, or 600 mg chloroquine base weekly divided over 6 daily doses of 100 mg base (with one drug-free day per week)	Start 1 week before departure and continue for 4 weeks after return. If daily doses, start 1 day before departure	Safe	Safe	Safe	Hypersensitivity to chloroquine; history of epilepsy; psoriasis	Concurrent use of chloroquine may reduce the antibody response to intradermally administered human diploid-cell rabies vaccine.

Table 1 Contd.

Generic name	Dosage regimen	Duration of prophylaxis	Use in special groups			Main contraindications[a]	Comments[a]
			Pregnancy	Breastfeeding	Children		
Doxycycline	1.5 mg salt/kg daily Adult dose: 1 tablet of 100 mg daily	Start 1 day before departure and continue for 4 weeks after return	Contraindicated	Contraindicated	Contraindicated under 8 years of age	Hypersensitivity to tetracyclines; liver dysfunction	Doxycycline makes the skin more susceptible to sunburn. People with sensitive skin should use a highly protective (UVA) sunscreen and avoid prolonged exposure to direct sunlight, or switch to another drug. Doxycycline should be taken with plenty of water to prevent oesophageal irritation. Doxycycline may increase the risk of vaginal *Candida* infections. Studies indicate that the monohydrate form of the drug is better tolerated than the hyclate.
Mefloquine	5 mg/kg weekly Adult dose: 1 tablet of 250 mg weekly	Start at least 1 week (preferably 2–3 weeks) before departure and continue for 4 weeks after return	Safe	Safe	Not recommended under 5 kg because of the lack of safety data	Hypersensitivity to mefloquine; psychiatric (including depression) or convulsive disorders; history of severe neuropsychiatric disease; concomitant halofantrine treatment; treatment with mefloquine in previous 4 weeks	May prolong QT interval or cause sinus bradycardia; consider other options in those with conduction disorders or taking medications such as beta blockers or calcium channel blockers. Co-administration of mefloquine with anti-arrhythmic agents, beta-adrenergic blocking agents, calcium channel blockers, antihistamines including H1-blocking agents and phenothiazines may contribute to prolongation of QTc interval. Do not give mefloquine within 12 hours of quinine treatment. Ampicillin, tetracycline and metoclopramide may increase mefloquine blood levels. Do not give concomitantly with oral typhoid vaccine. In the United States of America, mefloquine is recommended as a chemoprophylaxis option for all trimesters of pregnancy.

[a] See package insert for full information on contraindications and precautions.

Table 2 Malaria risk and type of prevention

	Malaria risk	Type of prevention
Type A	Very limited risk of malaria	Mosquito bite prevention only
Type B	Risk of non-falciparum malaria	Mosquito bite prevention plus chloroquine, or doxycycline or atovaquone–proguanil or mefloquine chemoprophylaxis (select according to parasite sensitivity, reported side-effects and contraindications)[a]
Type C	Risk of *P. falciparum* malaria	Mosquito bite prevention plus atovaquone–proguanil or doxycycline or mefloquine chemoprophylaxis (select according to reported drug-resistance pattern, side-effects and contraindications)[a,b]

[a] Alternatively, for travel to rural areas with low risk of malaria infection, mosquito bite prevention can be combined with standby emergency treatment.

[b] In certain areas with multidrug-resistant malaria, mefloquine chemoprophylaxis is no longer recommended. At present these areas include Cambodia, south-eastern Myanmar and Thailand.

All antimalarial drugs have specific contraindications and possible side-effects. Adverse reactions attributed to malaria chemoprophylaxis are common, but most are minor and do not affect the activities of the traveller. Serious adverse events – defined as events constituting an apparent threat to life, requiring or prolonging hospitalization or resulting in persistent or significant disability or incapacity – are rare and normally identified in post-marketing surveillance after a drug has been in use for some time. Severe neuropsychiatric disturbances (seizures, psychosis, encephalopathy) occur in approximately 1 in 10 000 travellers receiving mefloquine prophylaxis and have also been reported for chloroquine at a similar rate. The risk of drug-associated adverse events should be weighed against the risk of malaria, especially *P. falciparum* malaria, and local drug-resistance patterns.

Each of the antimalarial drugs is contraindicated in certain groups and individuals, and the contraindications should be carefully observed (see Table 1) to reduce the risk of serious adverse reactions. Pregnant women, people travelling with young children and people with chronic illnesses should seek individual medical advice. Travellers who develop severe adverse effects while using an antimalarial should stop taking the drug and seek immediate medical attention so that they can switch to a different antimalarial drug. This applies particularly to neurological or psychological disturbances experienced with mefloquine prophylaxis. Mild nausea, occasional vomiting or loose stools should not prompt discontinuation of prophylaxis, but medical advice should be sought if symptoms persist.

2.3 Long-term chemoprophylaxis

Adherence and tolerability are important aspects of chemoprophylaxis for people with long-term exposure to risk of malaria infection. Few studies have been done on chemoprophylaxis use for more than 6 months.

- The risk of serious side-effects associated with long-term prophylactic use of chloroquine is low, but retinal toxicity is a concern when a cumulative dose of 100 g of chloroquine is reached. Anyone who has taken 300 mg of chloroquine weekly for more than 5 years and requires further prophylaxis should be screened twice yearly for early retinal changes. If daily doses of 100 mg chloroquine have been taken, screening should start after 3 years.

- Data indicate no increased risk of serious side-effects with long-term use of mefloquine if the drug is tolerated in the short term. Pharmacokinetic data indicate that mefloquine does not accumulate during long-term intake.
- Available data on long-term chemoprophylaxis with doxycycline (more than 12 months) are limited but reassuring. There are few data on long-term use of doxycycline in women, but use of this drug is associated with an increased frequency of vaginitis due to infection with Candida spp..
- Atovaquone–proguanil is registered in European countries, with a restriction on duration of use (varying from 5 weeks to 1 year); such restrictions do not apply in the United Kingdom of Great Britain and Northern Ireland (the United Kingdom) or the United States of America (USA).

Credit: WHO / National Malaria Control Program
Insecticide treatment of bednets to prevent malaria in Bangladesh

3. Treatment

Patients who are non-immune are at high risk of malaria and its consequences. Early diagnosis and appropriate treatment can be life-saving.

For travellers who are treated for malaria in countries or areas of no risk, the following principles apply:

- All patients with suspected clinical malaria should be tested for malaria at a reliable diagnostic centre with microscopy or a rapid diagnostic test. If no parasites are found in the first blood film, a series of blood samples should be taken at intervals of 6–12 hours and examined very carefully. If laboratory diagnostic results are delayed, treatment should be started on the basis of clinical indicators and travel history.
- If the patient has taken malaria chemoprophylaxis, the same medicine should not be used for treatment.
- The possibility of mixed *P. falciparum–P. vivax* infections must always be considered.
- Travellers who acquire malaria while still in the malaria-endemic country should be treated in accordance with the national policy of the country.

P. falciparum

Chemoprophylaxis and treatment of falciparum malaria are becoming more complex because *P. falciparum* is increasingly resistant to various antimalarial medicines. Chloroquine can no longer be used for prevention and treatment of falciparum malaria.

The following combination therapies are suitable for treatment of uncomplicated falciparum malaria in travellers upon their return to countries or areas of no risk:

- artemether–lumefantrine
- dihydroartemisinin–piperaquine
- artesunate–amodiaquine
- artesunate–mefloquine
- artesunate–pyronaridine

Note: Antimalarials other than those listed above that are registered for use in the non-endemic country may be used for treatment of travellers on their return. Nevertheless, the artemisinin combination therapies are preferred because treatment failures are consistently lower than 5% in settings without resistance to the partner drug. The choice of medicine should also be guided by the parasite sensitivity in the country of infection.

P. vivax and P. ovale

The treatment for vivax or ovale malaria in travellers is as follows:

- An artemisinin-based combination therapy (ACT) (except artesunate + sulfadoxine–pyrimethamine) or chloroquine, combined with primaquine, is the treatment of

choice to achieve radical cure (that is, to cure both the blood-stage and liver-stage infections, and thereby prevent both recrudescence and relapse).

- An ACT (except artesunate + sulfadoxine–pyrimethamine) should be given for chloroquine-resistant vivax malaria. Where ACT is not available, quinine can be used instead. All these treatments should be combined with primaquine.
- Travellers must be tested for glucose-6-phosphate dehydrogenase (G6PD) deficiency before receiving primaquine anti-relapse treatment. Primaquine is contraindicated in pregnant women.
- In mixed (falciparum, vivax or ovale) infections, the treatment for *P. falciparum* will usually also cure *P. vivax*. After G6PD testing, primaquine should be given to achieve radical cure and prevent relapses.

Resistance of *P. vivax* to chloroquine is still rare but is increasing. Focal chloroquine resistance or failure of prophylaxis and/or treatment of *P. vivax* has now been observed in 23 countries: Afghanistan, Bolivia, Brazil, Cambodia, China, Colombia, Ethiopia, Guyana, India, Indonesia, Madagascar, Malaysia (Borneo), Myanmar, Pakistan, Papua New Guinea, Peru, Republic of Korea, Solomon Islands, Sri Lanka, Thailand, Turkey, Vanuatu and Viet Nam.

P. malariae

Malaria caused by *P. malariae* can be treated with the standard regimen of an ACT or chloroquine, but it does not require radical cure with primaquine because no hypnozoites are generated by this species. Chloroquine-resistant *P. malariae* has been reported from Indonesia.

P. knowlesi

On microscopical examination, the mature forms of *P. knowlesi* may be mistaken for *P. malariae*, while its ring forms may resemble *P. falciparum*. Knowlesi malaria can be treated with a standard regimen of chloroquine or with the antimalarials recommended for uncomplicated falciparum malaria. The clinical condition of patients infected with *P. knowlesi* may deteriorate quickly. Severe *P. knowlesi* malaria with organ failure may occur and its treatment should be as for severe falciparum malaria.

P. knowlesi infection should always be considered in patients with a microscopy diagnosis of *P. malariae* and a history of travel to forested areas of south-east Asia, including areas where malaria is not normally present.

The dosage regimens for the treatment of uncomplicated malaria are given in Table 3. Details of the clinical management of severe malaria are addressed in other WHO publications (see “Further reading” at the end of this module).

Credit: WHO / TDR / Steven Lindsay
Mosquito coils are burnt indoors to help repel mosquitos, reduce biting rates and so lower the incidence of disease.

Table 3 Use of antimalarial drugs for treatment of uncomplicated malaria in travellers

Generic name	Dosage regimen	Use in special groups			Main contraindications[a]	Comments[a]
		Pregnancy	Breastfeeding	Children		
Artemether–lumefantrine combination tablet	3-day course of six doses in total, taken at 0, 8, 24, 36, 48 and 60 hours 5–14 kg: 1 tablet (20 mg artemether plus 120 mg lumefantrine) per dose 15–24 kg: 2 tablets per dose 25–34 kg: 3 tablets per dose > 35 kg: 4 tablets per dose	Safe	Safe	Apparently safe in children < 5 kg, but limited data	Hypersensitivity to artemether and/or lumefantrine	Must be taken with fatty foods to improve absorption. A flavoured dispersible paediatric formulation is available, facilitating its use in young children.
Atovaquone–proguanil combination tablet	One dose daily for 3 consecutive days 5–8 kg: 2 paediatric tablets daily (62.5 mg atovaquone plus 25 mg proguanil per tablet) 9–10 kg: 3 paediatric tablets daily 11–20 kg: 1 adult tablet (250 mg atovaquone plus 100 mg proguanil) daily 21–30 kg: 2 adult tablets daily 31–40 kg: 3 adult tablets daily > 40 kg: 4 adult tablets (1 g atovaquone plus 400 mg proguanil) daily	No data, not recommended	No data, not recommended	Apparently safe in children > 5 kg, but limited data	Hypersensitivity to atovaquone and/or proguanil; severe renal insufficiency (creatinine clearance < 30 ml/min)	Take with food or milk drink to increase absorption. Plasma concentrations of atovaquone are reduced when the drug is co-administered with rifampicin, rifabutin, metoclopramide or tetracycline. May interfere with live typhoid vaccine.
Chloroquine	25 mg base/kg divided into daily doses of 10, 10 and 5 mg base/kg for 3 days	Safe	Safe	Safe	Hypersensitivity to chloroquine; history of epilepsy; psoriasis	Use only for malaria caused by *P. vivax, P. ovale, P. malariae* or *P. knowlesi*. Concurrent use of chloroquine may reduce the antibody response to intradermally administered human diploid-cell rabies vaccine.

Table 3 Contd.

Generic name	Dosage regimen	Use in special groups			Main contraindications[a]	Comments[a]
		Pregnancy	Breastfeeding	Children		
Clindamycin	Under 60 kg: 5 mg base/kg four times daily for 5 days > 60 kg: 300 mg base four times daily for 5 days	Safe	Safe	Safe	Hypersensitivity to clindamycin or lincomycin; history of gastro-intestinal disease, particularly colitis; severe liver or kidney impairment	Use only in combination with quinine in areas where an effective ACT is not available
Dihydroartemisinin–piperaquine	One dose daily for 3 consecutive days Target dose = 4 mg/kg per day dihydroartemisinin and 18 mg/kg per day piperaquine Adults > 50 kg: 3 tablets daily for 3 days	Recommended, if artemether–lumefantrine is not available. Limited data on its use in first trimester	Safe	Safe in children ≥ 5 kg	Hypersensitivity to dihydroartemisinin and/or piperaquine	
Doxycycline	Adults > 50 kg: 800 mg salt over 7 days, taken as two tablets (100 mg salt each) 12 hours apart on day 1, followed by one tablet daily for 6 days Children 8 years and older: 25–35 kg: 0.5 tablet per dose 36–50 kg: 0.75 tablet per dose > 50 kg: 1 tablet per dose	Contraindicated	Contraindicated	Contraindicated under 8 years of age	Hypersensitivity to tetracyclines; liver dysfunction	Used only in combination with quinine in areas where an effective ACT is not available

Table 3 Contd.

Generic name	Dosage regimen	Use in special groups			Main contraindications[a]	Comments[a]
		Pregnancy	Breastfeeding	Children		
Mefloquine	25 mg base/kg as split dose (15 mg/kg plus 10 mg/kg 6–24 hours apart)	Not recommended by manufacturer in first trimester because of lack of safety data (see Comments)	Safe	Apparently safe in children < 5 kg, but data are limited	Hypersensitivity to mefloquine; psychiatric (including depression) or convulsive disorders; history of severe neuropsychiatric disease; concomitant halofantrine treatment; treatment with mefloquine in previous 4 weeks	Mefloquine is used with artesunate as ACT. Do not give mefloquine within 12 hours of the last dose of quinine treatment. Mefloquine and other related compounds (such as quinine and quinidine chloroquine) may be given concomitantly only under close medical supervision because of possible additive cardiac toxicity and increased risk of convulsions; co-administration of mefloquine with anti-arrhythmic agents, beta-adrenergic blocking agents, calcium channel blockers, antihistamines including H1-blocking agents and phenothiazines may contribute to prolongation of QTc interval. Ampicillin, tetracycline and metoclopramide may increase mefloquine blood levels.
Primaquine	0.25–0.5 mg base/kg with food once daily for 7 or 14 days In Oceania and south-east Asia the dose should be 0.5 mg base/kg	Contraindicated	Contraindicated for mothers breastfeeding infants < 6 months of age	Contraindicated < 6 months of age	G6PD deficiency; active rheumatoid arthritis; lupus erythematosus; conditions that predispose to granulocytopenia; concomitant use of drugs that may induce haematological disorders	Used as anti-relapse treatment for *P. vivax* and *P. ovale* infections
Quinine	8 mg base/kg three times daily for 7 days	Safe	Safe	Safe	Hypersensitivity to quinine or quinidine; tinnitus; optic neuritis; haemolysis; myasthenia gravis. Use with caution in persons with atrial fibrillation, cardiac conduction defects or heart block. Quinine may enhance effect of cardiosuppressant drugs. Use with caution in people taking beta blockers, digoxin, calcium channel blockers, etc.	In areas of emerging resistance to quinine, give in combination with doxycycline, tetracycline or clindamycin. Quinine may induce hypoglycaemia, particularly in (malnourished) children, pregnant women and patients with severe disease.

ACT, artemisinin-based combination therapies.

[a] See package insert for full information on contraindications and precautions.

Severe malaria

Returning travellers with severe malaria should be managed in an intensive care unit. Initiate antimalaria treatment with parenteral artesunate (artemether or quinine can be used only if artesunate is not available), and complete with a full course of an ACT for at least 24hr and until the patient is able to tolerate oral medication.

3.1 Treatment during travel

A person who experiences a fever 1 week or more after entering an area with malaria risk should consult a physician or qualified malaria laboratory immediately to obtain a correct diagnosis and safe and effective treatment. In principle, travellers can be treated with an ACT in accordance with the national policy in the country they are visiting.

National antimalarial drug policies for all countries/territories with risk are available from the WHO website and the World malaria report (WHO, 2023).

In light of the spread of counterfeit drugs in some malaria-endemic settings, travellers are advised to buy sufficient antimalarial medicines from reliable sources before departure.

3.2 Standby emergency treatment (SBET)

Many travellers will be able to obtain proper medical attention within 24 hours of the onset of fever. For travellers staying in remote locations where prompt access to medical care may be difficult, it is advisable to carry antimalarial drugs for self-administration (SBET).

SBET may also be indicated for travellers in some occupational groups who make frequent short stops in countries or areas with malaria risk over a prolonged period. Such travellers may choose to reserve chemoprophylaxis for high-risk areas and seasons only. However, they should continue to take measures to protect themselves against mosquito bites and should be prepared for an attack of malaria. For this reason, they should always carry a course of antimalarial drugs for SBET, seek immediate medical care in case of fever, and take SBET if prompt medical help is not available.

Furthermore, SBET – combined with protection against mosquito bites – may be indicated for short-term travellers spending 1 week or more in certain remote rural areas where there is a very low risk of infection (see Country list).

Studies on the use of rapid diagnostic tests have shown that untrained travellers experience major problems in the performance and interpretation of these tests, with an unacceptably high number of false-negative results. When performed by well-trained staff, good-quality rapid diagnostic tests are reliable, and several tests have demonstrated good diagnostic performance.

Successful SBET depends crucially on travellers' behaviour, and health advisers need to spend time explaining the strategy. Travellers provided with SBET should be given clear and precise written instructions on the recognition of symptoms, when and how to take the treatment, and the possible side-effects. They should also be made aware of the possibility of inadequate response to treatment. If several people travel together, the individual dosages for SBET should be specified. Weight-based dosages for children must be clearly indicated. **Travellers should realize that self-treatment is a first-aid measure and that they should still seek medical advice as soon as possible.**

In general, travellers carrying SBET should observe the following guidelines:

- Consult a physician immediately if fever occurs 1 week or more after entering an area with malaria risk.
- If it is impossible to consult a physician and/or establish a diagnosis within 24 hours of the onset of fever, start the SBET and seek medical care as soon as possible for complete evaluation and to exclude other serious causes of fever.
- Do not treat suspected malaria with the same drugs as were used for prophylaxis.
- Vomiting of antimalarial drugs is less likely if fever is first lowered with antipyretics. A second full dose should be taken if vomiting occurs within 30 minutes of taking the antimalarial medicine. If vomiting occurs 30–60 minutes after a dose, an additional half-dose should be taken. Vomiting with diarrhoea may lead to treatment failure because of poor drug absorption.
- Complete the SBET course and resume antimalarial prophylaxis 1 week after the *first* treatment dose.
- The drug options for SBET are in principle the same as the options for treatment of uncomplicated malaria (section 3). The choice will depend on the type of malaria in the area visited and the chemoprophylaxis regimen taken. Artemether–lumefantrine has been registered (in Switzerland and the United Kingdom) for use as SBET for travellers. Quinine is less feasible for SBET because it is less effective than the ACTs, it requires a long and complex treatment regimen, and it has several dose-dependent side-effects. If quinine is taken for SBET, at least 12 hours should elapse between the *last* treatment dose of quinine and resumption of mefloquine prophylaxis to reduce the risk of drug interactions. Table 3 provides details on individual drugs.

3.3 Multidrug-resistant malaria

Multidrug-resistant malaria is defined as malaria that is resistant to drugs of more than two different chemical families. The term is most often used when, in addition to chloroquine and sulfadoxine–pyrimethamine resistance, resistance of *P. falciparum* to mefloquine and/or artemisinins has been reported.

Mefloquine resistance

Mefloquine resistance affects travellers' choices of prophylaxis and SBET, and is currently reported in Cambodia, south-eastern Myanmar and Thailand. In these areas, the choice of chemoprophylaxis is limited to doxycycline and atovaquone–proguanil.

Artemisinin resistance

WHO's Global Malaria Programme issues regular updates about artemisinin resistance in affected countries on its website. Artemisinin resistance has no implication for the choice of prophylaxis, but it has an impact on treatment; it is reported in Cambodia, Myanmar, Thailand and Viet Nam and most recently in the Lao People's Democratic Republic. In these countries, SBET options are limited to atovaquone–proguanil only. Local treatment should be with the ACTs recommended at national level. To reduce the danger of spreading artemisinin-resistant parasites to other malaria-endemic parts of the world, all malaria patients who have travelled to these areas should be promptly diagnosed and treated effectively. The addition of a single oral dose of primaquine (0.25 mg base/kg body weight) to treatment will accelerate the removal of *P. falciparum* gametocytes and thereby reduce the risk of onward transmission in other endemic areas. Medical staff should follow national reporting requirements, especially for imported falciparum malaria cases that originated from travel to the above areas of multidrug-resistance.

4. Special groups

Some groups of travellers, especially young children, pregnant women and immunosuppressed people, are at particular risk of serious consequences if they become infected with malaria. Recommendations for these groups are difficult to formulate because drug safety data are limited.

Immigrants increasingly travel to their place of origin to visit friends and relatives (VFR). VFRs from endemic countries/territories who live in malaria-free countries and return to their home countries are at increased risk of travel-related malaria. Because of familiarity with their place of origin, they may perceive less risk, which may result in lower rates of malaria prophylaxis, higher risk of exposure and insufficient protective measures. Improving the access of VFRs to pre-travel health counselling is of increasing public health importance.

4.1 Pregnant women

Malaria in a pregnant woman increases the risk of maternal death, miscarriage, stillbirth and low birth weight with the associated risk of neonatal death. Pregnant women should be advised to avoid travelling to areas where malaria transmission occurs. When travel cannot be avoided, it is essential to follow the recommendations given below.

Mosquito bite prevention during pregnancy

Pregnant women are particularly susceptible to mosquito bites and should therefore be vigilant in using protective measures, including insect repellents and insecticide-treated mosquito nets. They should take care not to exceed the recommended usage of insect repellents.

Chemoprophylaxis during pregnancy

In areas with exclusively *P. vivax* transmission, chloroquine prophylaxis may be used. In areas with *P. falciparum* transmission, mefloquine prophylaxis may be given. In light of the danger of malaria to mother and fetus, experts increasingly agree that **travel to a *P. falciparum* transmission area during the first trimester of pregnancy should be avoided or delayed; if this is truly impossible, good preventive measures should be taken, including prophylaxis with mefloquine where this is indicated**. Doxycycline is contraindicated during pregnancy. Data on the safety of exposure to atovaquone–proguanil during pregnancy are limited and this combination is therefore not recommended for use in pregnant women or is recommended only with relevant warnings and information on risk.

Treatment during pregnancy

Artemether–lumefantrine is the drug of choice for treatment of malaria in the first trimester, however, if artemether–lumefantrine is not available, any of the other ACTs can be used except artesunate–sulphadoxine/pyrimethamine and artesunate–pyronaridine . Any of the ACTs can be used to treat uncomplicated malaria in the second and third trimesters. Chloroquine can be safely used for treatment of vivax malaria during pregnancy, but primaquine anti-relapse treatment should be postponed until after delivery. Pregnant women

treated for vivax malaria should continue weekly chloroquine prophylaxis post-treatment until delivery to avoid relapse during the pregnancy.

Pregnant women with falciparum malaria, particularly in the second and third trimesters of pregnancy, are more likely than other adults to develop severe malaria, often complicated by hypoglycaemia and pulmonary oedema. The risk of maternal mortality is significantly increased by severe malaria. Fetal death and premature labour are common. **Pregnant women with severe malaria** must be treated without delay with full doses of parenteral antimalarial treatment: artesunate is the treatment of choice, and artemether or quinine should be used if artesunate is not available. Treatment must be started without delay. Information on the safety of antimalarial drugs during breastfeeding is provided in Tables 1 and 3.

4.2 Women who may become pregnant during or after travel

Malaria prophylaxis may be taken by women who may become pregnant during or after travel, but pregnancy should preferably be avoided during the period of drug intake and for 1 week after doxycycline, 3 weeks after atovaquone–proguanil and 3 months after the last dose of mefloquine prophylaxis. If pregnancy occurs in a woman taking antimalarial prophylaxis, this is not considered to be an indication for pregnancy termination.

4.3 Young children

Falciparum malaria in a young child is a medical emergency. It may be rapidly fatal. Early symptoms are atypical and difficult to recognize, and life-threatening complications can occur within hours of the initial symptoms. Medical help should be sought immediately if a child develops a febrile illness within 3 months (or, rarely, later) of travelling to a malaria-endemic country or territory. Laboratory confirmation of diagnosis should be requested immediately, and treatment with an effective antimalarial drug should be initiated as soon as possible. In infants, malaria should be suspected even in the case of a non-febrile illness. **Parents should be advised not to take infants or young children to areas where there is risk of falciparum malaria.** If travel cannot be avoided, children must be very carefully protected against mosquito bites and given appropriate chemoprophylactic drugs. Long-term travellers and expatriates should adjust the chemoprophylaxis dosage according to the increasing weight of the growing child.

Mosquito bite prevention for young children

Infants should be kept under insecticide-treated mosquito nets as much as possible between dusk and dawn. The manufacturer's instructions on the use of insect repellents should be followed diligently, and the recommended doses must not be exceeded.

Chemoprophylaxis in youngchildren

Chloroquine and mefloquine are considered compatible with breastfeeding. Breastfed, as well as bottle-fed, infants should be given chemoprophylaxis since they are not protected by the mother's prophylaxis. Dosage schedules for children should be based on body weight, and tablets should be crushed and ground as necessary. The bitter taste of the tablets can be disguised with jam or other foods. Chloroquine is safe for infants and young children, but its use is now very limited because of chloroquine resistance. Mefloquine may be given to infants of more than 5 kg body weight. Atovaquone–proguanil is generally not recommended for prophylaxis in children who weigh less than 11 kg, because of limited safety data; in Belgium,

Canada, France and the USA, atovaquone–proguanil is given for prophylaxis to infants of more than 5 kg body weight. Doxycycline is contraindicated in children under 8 years of age. All antimalarial drugs should be kept out of the reach of children and should be stored in childproof containers; chloroquine is particularly toxic in case of overdose.

Treatment of young children

Acutely ill children with falciparum malaria require careful clinical monitoring as their condition may deteriorate rapidly. Every effort should be made to give oral treatment and to ensure that it is retained. ACT may be used, in accordance with national policy, as first-line treatment while abroad. Oral treatment options for SBET and returning travellers are: artemether–lumefantrine, dihydroartemisinin–piperaquine, artesunate–mefloquine and artesunate–pyronaridine. Parenteral treatment and admission to hospital are indicated for young children who cannot swallow antimalarials reliably.

Chloroquine or dihydroartemisinin–piperaquine or artemether–lumefantrine can be safely given to treat *P. malariae*, *P. ovale* or *P. vivax* infections in young children. Anti-relapse treatment should be guided by the G6PD activity of the patient. Information on the safety of drugs for prophylaxis and treatment of young children is provided in Tables 1 and 3.

4.4 Immunosuppressed travellers

Immunosuppressed travellers are at increased risk of malaria disease, and prevention of malaria through avoidance of mosquito bites and the use of chemoprophylaxis is particularly important. Individual pre-travel advice should be diligently sought. There may be an increased risk of antimalarial treatment failure in people living with HIV/AIDS. At present, however, there is insufficient information to permit modifications to currently recommended treatment regimens for this specific population group.

Credit: WHO / Diane Abad-Vergara
WHO Certification of Cabo Verde's Elimination of Malaria (January 2024) A general view in Praia.

5. Countries and territories with malarious areas

The following list shows all countries/territories for which some information on malaria is included in the country list. In some of these countries/territories, malaria is present only in certain areas or up to a particular altitude. In many countries, malaria has a seasonal pattern. Some countries have not reported any cases in recent years. These details as well as information on the predominant malaria species, status of resistance to antimalarial drugs and recommended type of prevention are provided in the Country list.

Afghanistan
Angola

Bangladesh
Benin
Bolivia, Plurinational State of
Botswana
Brazil
Burkina Faso
Burundi

Cambodia
Cameroon
Central African Republic
Chad
Colombia
Comoros
Congo
Congo, Democratic Republic of the
Costa Rica
Côte d'Ivoire

Djibouti
Dominican Republic

Ecuador
Equatorial Guinea
Eritrea
Eswatini
Ethiopia

French Guiana

Gabon
Gambia
Ghana
Guatemala
Guinea
Guinea-Bissau
Guyana

Haiti
Honduras

India
Indonesia
Iran, Islamic Republic of

Kenya
Korea, Democratic People's Republic of[1]
Korea, Republic of[1]

Lao People's Democratic Republic
Liberia

Madagascar
Malawi
Mali
Mauritania
Mexico
Mozambique
Myanmar

Namibia
Nepal
Nicaragua
Niger
Nigeria

Pakistan

Panama
Papua New Guinea
Peru
Philippines

Rwanda

Sao Tome and Principe
Senegal
Sierra Leone
Solomon Islands
Somalia
South Africa
Sudan
South Sudan

Thailand
Togo

Uganda
United Republic of Tanzania

Vanuatu
Venezuela, Bolivarian Republic of
Viet Nam

Yemen

Zambia
Zimbabwe

[1] *P. vivax* risk only.

Further information

The documents listed below are available on the WHO Global Malaria Programme website;

Global Malaria Programme (who.int)

- Drug efficacy and resistance [web page]. Geneva: World Health Organization (https://www.who.int/teams/global-malaria-programme/case-management/drug-efficacy-and-resistance, accessed 24 September 2024).
- Malaria vector control and personal protection: report of a WHO Study Group. Geneva: World Health Organization; 2006 (WHO Technical Report Series, No. 936; https://iris.who.int/handle/10665/43425, accessed 1 September 2024).
- Management of severe malaria: a practical handbook, third edition Geneva: World Health Organization; 2012 (https://iris.who.int/handle/10665/79317, accessed 1 September 2024).
- WHO Guidelines for malaria, Geneva: World Health Organization; 2023 (https://iris.who.int/handle/10665/366432, accessed 1 September 2024).
- World malaria report 2023. Geneva: World Health Organization; 2023 https://iris.who.int/handle/10665/374472, accessed 1 September 2024).

Credit: WHO / Budi Chandra
Malaria in Indonesia. Malaria and other mosquitoes breeding place in remote areas of Java. Argowilis Village, Kulon Progo, DI Yogyakarta.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