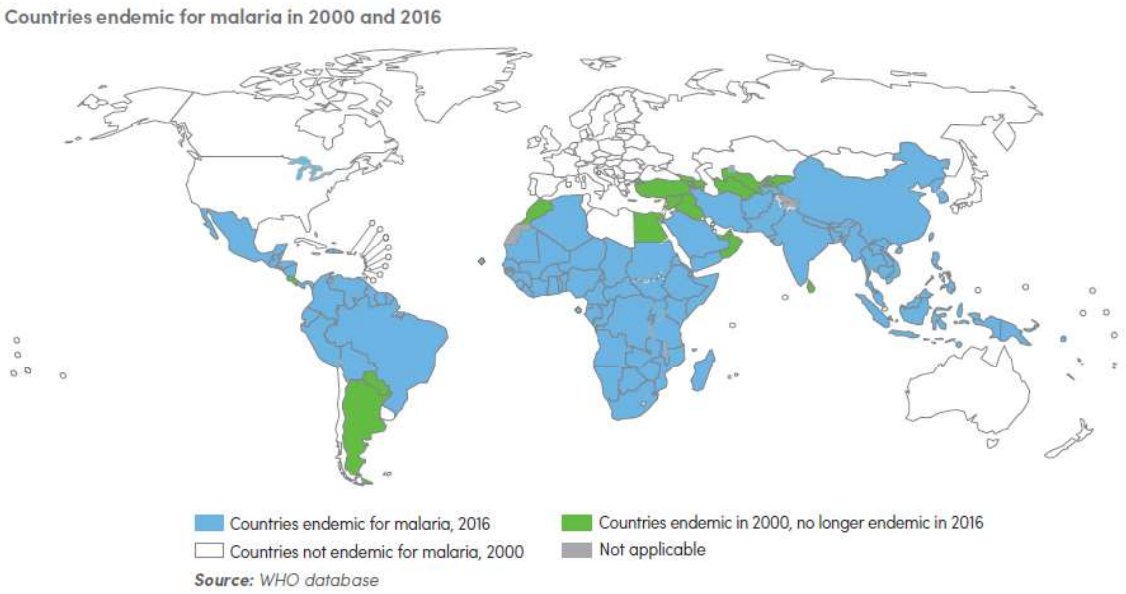
Malaria information sheet

Malaria is a mosquito-borne infectious disease of humans and other animals caused by eukaryotic protists of the genus *Plasmodium*. The disease results from the multiplication of *Plasmodium* parasites within red blood cells, causing symptoms that typically include fever and headache, in severe cases progressing to coma or death. It is widespread in tropical and subtropical regions, including much of Sub-Saharan Africa, Asia, and the Americas.



According to the WHO World Malaria Report 2020, there were 229 million cases of malaria and >400,000 deaths in 2019. Most deaths occur among children living in Africa where a child dies every 68 seconds of malaria and the disease is a major cause of childhood mortality. According to the report, fewer than half of the 91 malaria-affected countries and territories are on track to achieve the 2020 milestone of a 40% reduction in case incidence and mortality.

Malaria is caused by Plasmodium parasites. The parasites are spread to people through the bites of infected Anopheles mosquitoes, called "malaria vectors", which bite mainly between dusk and dawn. There are five types of human malaria:

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

Plasmodium falciparum and Plasmodium vivax are the most common. Plasmodium falciparum is the most deadly.

Key interventions to control malaria include: prompt and effective treatment with artemisinin-based combination therapies (ACTs); use of insecticidal nets by people at risk; and indoor residual spraying with insecticide to control the vector mosquitoes.

Transmission

Malaria is transmitted exclusively through the bites of Anopheles mosquitoes. The intensity of transmission depends on factors related to the parasite, the vector, the human host, and the environment. About 20 different Anopheles species are locally important around the world. All of the important vector species bite at night. Anopheles mosquitoes breed in water and each species has its own breeding preference; for example some prefer shallow collections of fresh water, such as puddles, rice fields, and hoof prints. Transmission is more intense in places where the mosquito lifespan is longer (so that the parasite has time to complete its development inside the mosquito) and where it prefers to bite humans rather than other animals. For example, the long lifespan and strong human-biting habit of the African vector species is the main reason why more than 89% of the world's malaria deaths are in Africa.

Transmission also depends on climatic conditions that may affect the number and survival of mosquitoes, such as rainfall patterns, temperature and humidity. In many places, transmission is seasonal, with the peak during and just after the rainy season. Malaria epidemics can occur when climate and other conditions suddenly favour transmission in areas where people have little or no immunity to malaria. They can also occur when people with low immunity move into areas with intense malaria transmission, for instance to find work, or as refugees.

Human immunity is another important factor, especially among adults in areas of moderate or intense transmission conditions. Immunity is developed over years of exposure, and while it never gives complete protection, it does reduce the risk that malaria infection will cause severe disease. For this reason, most malaria deaths in Africa occur in young children, whereas in areas with less transmission and low immunity, all age groups are at risk.

Signs and symptoms

Symptoms of malaria include fever, shivering, arthralgia (joint pain), vomiting, anemia (caused by hemolysis), hemoglobinuria, retinal damage and convulsions. The classic symptom of malaria is cyclical occurrence of sudden coldness followed by rigor and then fever and sweating lasting four to six hours, occurring every two days in *P. vivax* and *P. ovale* infections, and every three days for *P. malariae*. *P. falciparum* can have recurrent fever every 36–48 hours or a less pronounced and almost continuous fever. For reasons that are poorly understood, but that may be related to high intracranial pressure, children with malaria frequently exhibit abnormal posturing, a sign indicating severe brain damage. Malaria has been found to cause cognitive impairments, especially in children. It causes widespread anemia during a period of rapid brain development and also direct brain damage. This neurologic damage results from cerebral malaria to which children are more vulnerable. Cerebral malaria is associated with retinal whitening, which may be a useful clinical sign in distinguishing malaria from other causes of fever.

Severe malaria is almost exclusively caused by *Plasmodium falciparum* infection, and usually arises 6–14 days after infection. Consequences of severe malaria include coma and death if untreated—young children and pregnant women are especially vulnerable. Splenomegaly (enlarged spleen),

severe headache, cerebral ischemia, hepatomegaly (enlarged liver), hypoglycemia, and hemoglobinuria with renal failure may occur. Renal failure is a feature of blackwater fever, where hemoglobin from lysed red blood cells leaks into the urine. Severe malaria can progress extremely rapidly and cause death within hours or days. In the most severe cases of the disease, fatality rates can exceed 20%, even with intensive care and treatment. In endemic areas, treatment is often less satisfactory and the overall fatality rate for all cases of malaria can be as high as one in ten. Over the longer term, developmental impairments have been documented in children who have suffered episodes of severe malaria.

For both *P. vivax* and *P. ovale*, clinical relapses may occur weeks to months after the first infection, even if the patient has left the malarious area. These new episodes arise from "dormant" liver forms (absent in *P. falciparum* and *P.malariae*), and special treatment – targeted at these liver stages – is mandatory for a complete cure.

Diagnosis

The mainstay of malaria diagnosis has been the microscopic examination of blood, utilizing blood films. Although blood is the sample most frequently used to make a diagnosis, both saliva and urine have been investigated as alternative, less invasive specimens. More recently, modern techniques utilizing antigen tests or polymerase chain reaction have been discovered, though these are not widely implemented in malaria endemic regions. Areas that cannot afford laboratory diagnostic tests often use only a history of subjective fever as the indication to treat for malaria.

WHO recommends that all cases of suspected malaria be confirmed using parasite-based diagnostic testing (either microscopy or rapid diagnostic test) before giving treatment. Results of parasitological confirmation can be available in a few minutes. Treatment solely on the basis of symptoms should only be considered when a parasitological diagnosis is not possible.

Treatment

Combination therapy with two antimalarial agents is now widely regarded as essential to prevent the development and spread of resistance. In its 2006 guidelines for the treatment of malaria (updated in 2013), WHO recommends that malaria be treated with the potent antimalarial drug artemisinin as part of combination therapy. Almost all African countries have now adopted ACTs (artemisinin-based combination therapy) as first-line treatment for uncomplicated malaria.

The risk of death from severe malaria is greatest in the first 24 h, yet, in most malaria endemic countries, the transit time between referral and arrival at health facilities able to administer intravenous treatment is usually prolonged; this delays the commencement of appropriate antimalarial treatment. As during this time the patient may deteriorate or die, it is recommended that patients be treated with the first dose of one of the recommended treatments before referral (unless the referral time is less than 6 h). Recommended pre-referral treatment options include intramuscular artesunate, artemether, or quinine, or rectal artesunate. Evidence from recent studies demonstrates that in situations where parenteral medication is not possible and intramuscular injection impractical, using a single dose of rectal artesunate as pre-referral treatment reduces the risk of death or permanent disability in young children.

Drug resistance

Growing resistance to antimalarial medicines has spread very rapidly, undermining malaria control efforts. When treated with an artemisinin-based monotherapy, patients may discontinue treatment prematurely following the rapid disappearance of malaria symptoms. This results in incomplete treatment, and such patients still have persistent parasites in their blood. Without a second drug given as part of a combination (as is done with an ACT), these resistant parasites survive and can be passed on to a mosquito and then another person. Such monotherapies are therefore one of the primary forces behind the spread of artemisinin resistance which has led to an intensification of efforts to prohibit the marketing of oral artemisinin-based monotherapies.

First evidence of resistance to artemisinins has been detected in the Greater Mekong subregion (Cambodia, Myanmar, Thailand and Viet Nam). The consequences of a further spread of the resistance to ACTs could be dire, as no alternative antimalarial medicines will be available for at least three years.

Vaccines

In October 2013, a third set of results on the efficacy of the RTS,S/ AS01 vaccine were reported for 6–14 week and 5–17 month age groups. In the 5–17 month age group, efficacy estimates, pooled across all trial sites, remained statistically significant against clinical malaria (46%) and severe malaria (35.5%). By contrast, in the 6–14 week age group, the efficacy estimate for severe malaria was not statistically significant (although efficacy against clinical malaria remained statistically significant at 27%). The reasons for this difference between the age groups are unclear, but co-administration with DTP-containing vaccines and the presence of maternally acquired antibodies to malaria may contribute to a lower immune response in infants aged 6–14 weeks. In October 2015, two independent WHO advisory groups recommended the pilot implementation of RTS,S/ASO1 in parts of three to five sub-Saharan African countries. RTS,S/AS01 is being assessed as a complementary malaria control tool that could potentially be added to – and not replace – the core package of proven malaria preventive, diagnostic and treatment measures. It should be noted, however, that the current malaria vaccines are only effective on P.falciparum and while they reduce the severity of the illness, they do not prevent transmission.

The economic cost of malaria

In addition to the human cost of malaria, the economic burden of the disease is enormous based on the Roll Back Malaria (RBM) partnership report for 2001-2010. It is estimated that malaria causes an average loss of 1.3% of annual economic growth in countries with intense transmission. Over the long term, these aggregated annual losses have resulted in substantial differences in GDP between countries with and without malaria, particularly in Africa. Malaria affects productivity – adults with malaria cannot go to work and children with malaria cannot go to school. Malaria disproportionately affects poor people who cannot afford treatment or have limited access to health care. The health costs of malaria include both personal and public expenditures on prevention and treatment. In some heavy-burden countries, the disease accounts for:

- up to 40% of public health expenditures
- 30% to 50% of inpatient hospital admissions
- up to 60% of outpatient health clinic visits