PRIMEVIEW

MALARIA

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Malaria is caused by infection with a protozoan parasite of the *Plasmodium* spp. (mainly *Plasmodium falciparum* and *Plasmodium vivax*), which is transmitted by the bite of an infected mosquito of the *Anopheles* genus. Malaria can be asymptomatic, uncomplicated or severe.

EPIDEMIOLOGY

The global burden of malaria is estimated at >200 million cases; around half a million people died of malaria in 2015, mostly children <5 years of age. Africa accounts for the majority of cases, followed by Southeast Asia. Malaria is endemic, particularly in resource-limited tropical areas owing to the most deadly pathogen, *P. falciparum*, which requires a hot climate to mature inside its mosquito vector.

PREVENTION

Indoor residual spraying, the use of insecticide-treated bed nets and access to effective drug therapies account for the recent reduction in malaria-associated morbidity and mortality.

With seasonal malaria chemoprevention, antimalarial drugs are regularly distributed to large populations.

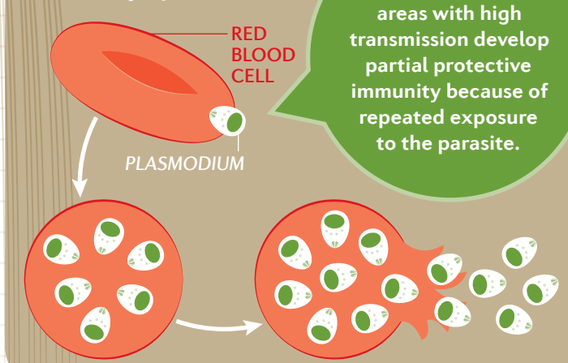
MANAGEMENT

The mainstay treatments of uncomplicated malaria are oral artemisinin-based combination therapies (ACTs), which combine an artemisinin derivative with a quinine derivative. In severe malaria, an artemisinin derivative (artesunate) is administered parenterally to rapidly clear the parasites from the blood. Chloroquine is the first-choice drug in cases of malaria not caused by *P. falciparum*.

Artemisinin is extracted from the leaves of the plant *Artemisia annua*; since its introduction in 1970s, millions of lives have been saved.

MECHANISMS

In the human host, *Plasmodium* spp. replicate inside red blood cells, causing haemolysis and the release of parasites and by-products of haemoglobin digestion, which stimulates the host's immune response and leads to malaria symptoms.



Individuals living in areas with high transmission develop partial protective immunity because of repeated exposure to the parasite.

Symptoms of uncomplicated malaria include fever, shaking chills, sweating, gastrointestinal disturbances and anaemia. Severe malaria also presents with end-organ damage, in particular, cerebral, pulmonary and renal complications.

DIAGNOSIS

The WHO diagnostic criteria are fever and the presence of the parasite in the bloodstream (parasitaemia). *Plasmodium* spp. can be detected by light microscopy examination or rapid diagnostic tests, which are based on the immunological detection of parasite antigens and provide rapid, point-of-care diagnosis.

QUALITY OF LIFE

Malaria has a high socioeconomic burden; loss of school time for sick children means limited education opportunities, whereas loss of work time for adults results in loss of productivity and income. Neurological complications in children can lead to cognitive defects, further aggravating the strain on families.

Intermittent preventive treatment is recommended for pregnant women, as parasites in the placenta increase the risk of complications for both the mother and the baby.

OUTLOOK

The emergence of drug-resistant *Plasmodium* strains is a serious threat to the progress that has been made so far towards global malaria elimination. The new drugs pipeline is plentiful, with four compounds in phase II clinical development; however, even the most advanced candidates are still years away from approval, and, currently, no vaccine has been deployed against malaria. Insecticide-resistant mosquitoes are also a concern. Future vector control approaches include gene drive systems (to modify mosquitoes so their progeny is sterile or refractory to *Plasmodium* spp. infection) and biocontrol (via the release of mosquitoes that are infected with bacteria of the *Wolbachia* spp. and, therefore, cannot transmit the infection to human hosts).

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