

***Plasmodium falciparum* malaria**

Every year 300 to 500 million people suffer from malaria, causing an estimated 1 to 2.7 million deaths. Ninety percent of these deaths occur in sub-Saharan Africa, mostly among children younger than five.

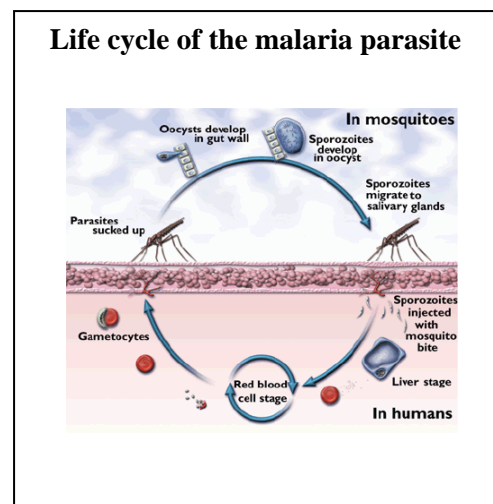


Malaria is endemic to over 100 nations and territories in Africa, Asia, Latin America, the Middle East, and the South Pacific. It is caused by a parasite that is transferred by the bite of an infected *Anopheles* mosquito. *Plasmodium (P.) falciparum* is by far the deadliest of the four human malarial species; (*Plasmodium falciparum*, *malariae*, *ovale*, and *vivax*). *P. vivax* is the most widespread.

P. malariae and *P. ovale*, although also significant, cause fewer cases and less severe forms of the disease.

Symptoms of malaria include cyclical fever and shivering, pain in the joints, headache, weakness, and repeated vomiting. In severe cases, convulsions and kidney failure can result. Complications of *P. falciparum* include acute anemia and cerebral malaria. In some patients who seemingly recover, another bout of malaria may occur if the treatment does not completely clear the parasite from the blood and liver.

Life Cycle: All types of malaria have a similar life cycle. Sporozoites, the infectious form of the malaria parasite, are injected into a human host through the saliva of an *Anopheles* mosquito. These sporozoites enter the liver cells within minutes, take on a new form, and multiply. When the liver cells rupture, blood stage parasites—known as merozoites—are released. Each merozoite invades a red blood cell, and for two days multiplies into more merozoites. The red blood cell full of merozoites ruptures to release more merozoites. It is this stage of the life cycle that causes disease and, too often, death. Some merozoites change into the form called gametocytes, which do not cause disease but remain in the blood until they are cleared by drugs or the immune system, or taken up by the bite of a mosquito. In the mosquito's stomach a "male" gametocyte fertilizes a "female" to form an egg, or oocyst, which matures into thousands of sporozoites that swim to the mosquito's salivary glands to be injected into another human at the next bite.



Why is *P. falciparum* worse than other types of malaria?

In addition to being the deadliest form of malaria, *P. falciparum* destroys red blood cells, which can cause acute anemia. Adherence to cells in certain tissues may cause problems within those organs, such as the lungs, kidneys and brain. A major complication of *P. falciparum*, cerebral

malaria, can lead to coma, transient or permanent neurological effects, and death. Compared to *P. vivax*, *P. falciparum* is less widespread, but more likely to result in severe complications and be fatal.

Treatment: Traditional first-line treatments such as chloroquine and Sulphadoxine/Pyrimethamine have lost much of their effectiveness in many countries. This has led to the need for new and more expensive antimalarial drugs, including combination therapies (such as artemisinin combination therapy—ACT) now being introduced by some governments. More information on treatment is available at:
<http://www.cdc.gov/travel/diseases/malaria/index.htm>.

Burden of Disease: Companies, governments, and public-private partnerships continue working to develop new drugs, since *P. falciparum* is the most common cause of morbidity and mortality in Africa, killing more African children than any other single disease. It accounts for 9 to 10 percent of Africa's entire disease burden—with severe economic consequences. Countries with a high incidence of malaria can suffer a 1.3 percent annual loss of economic growth. A Harvard/World Health Organization study suggests that if malaria had been eliminated 35 years ago, Sub-Saharan Africa's gross domestic product could be \$100 billion greater.

Vaccine Development: The development and implementation of a vaccine against malaria are critical to the long-term solution to this age-old killer. Malaria vaccines could save millions of lives and are likely to be hugely cost-effective. Much progress has been made in understanding the immune mechanisms and in identifying potential vaccine targets. Key challenges right now are to produce clinical-grade vaccines for evaluation in people and to implement clinical trials that answer key questions that will further accelerate progress toward a vaccine. Several different malaria vaccine approaches, using the latest advances in technology, are now in human clinical trials in Africa, Asia, Europe, and the United States. Although vaccine development is reaching maturity, it could be ten years before an effective vaccine is licensed and introduced.

MVI's *P. falciparum* Strategy: The PATH Malaria Vaccine Initiative (MVI) seeks to accelerate the development of promising malaria vaccines and ensure their availability and accessibility in the developing world. In partnership with companies, government agencies, and academic institutions, MVI is moving forward several *P. falciparum* vaccine candidates, targeting all stages of the parasite's life cycle. As the leading killer of African children, *P. falciparum* is the primary focus of MVI's work.



Photos courtesy of Richard Franco

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The PATH Malaria Vaccine Initiative (MVI) is a global program established at PATH through an initial grant of \$50 million from the Bill & Melinda Gates Foundation. MVI's mission is to accelerate the development of malaria vaccines and ensure their availability and accessibility in the developing world. For more information, please visit www.malariavaccine.org. **PATH** is an international, nonprofit organization that creates sustainable, culturally relevant solutions that enable communities worldwide to break longstanding cycles of poor health. By collaborating with diverse public- and private-sector partners, PATH helps provide appropriate health technologies and vital strategies that change the way people think and act. PATH's work improves global health and well-being. For more information, please visit www.path.org.