

# Malaria Fact Sheet

Malaria is a life-threatening disease transmitted by mosquitoes infected with parasites of the genus *Plasmodium*. The most serious forms of the disease are caused by *Plasmodium falciparum* and *Plasmodium vivax*, but other related species can also infect humans. Malaria is a preventable and treatable disease. Nonetheless it infects between 300-500 million people annually and kills between 1-3 million people each year, making malaria a cause of poverty, a hindrance to economic development, and a major public health concern, especially in children.

No vaccine is currently available for malaria; however medicines are available for prevention and for the treatment of malaria infections. Unfortunately, preventative medicines must be taken continuously and are too expensive for most people living in the endemic countries and the most affordable treatments for malaria have become ineffective due to drug resistance across Asia and Africa. In 2001, the World Health Organization recommended using Artemisinin-based Combination Therapy (ACT) as first-line treatment for uncomplicated malaria in areas experiencing resistance. Drug compounds derived from artemisinin which is extracted from the wormwood plant *Artemisia annua*, has over a 90% efficacy rate. While many countries have adopted the WHO recommendations into their malaria treatment policies, the artemisinin supply available is not meeting the demand for number of treatments and cost of the ACTs create a barrier to use in these countries.

## OneWorld Health's Role

In 2004, the Institute for OneWorld Health received a grant from the Bill & Melinda Gates Foundation to develop an affordable, stable, non seasonal, second source of artemisinin using synthetic biotechnology. Under this grant, OneWorld Health sponsors research at the University of California at Berkeley and at Amyris Biotechnologies. These three organizations have formed a partnership to drive the drug development process through the necessary research, product development and regulatory steps to manufacture semisynthetic artemisinin for use in ACTs at a lower cost than the currently used material.

University of California, Berkeley scientists discovered the metabolic pathway and identified the genes required to make artemisinic acid. They inserted this genetic pathway into microorganisms to enable them to manufacture copious amounts of artemisinic acid, the precursor to artemisinin. Amyris Biotechnologies is working with Berkeley's "microbial factories" to optimize the microbial host system and develop robust fermentation and purification processes to deliver high-quality, low cost and high quantities of artemisinic acid. Simultaneously, Amyris Biotechnologies is developing a novel, scalable chemical process to convert artemisinic acid to artemisinin.

To help ensure affordability in developing countries, UC Berkeley has issued a royalty-free license to OneWorld Health and Amyris Biotechnologies to develop the technology for malaria treatment in the developing world. iOWH has responsibility for directing this collaborative effort and also works with the Bill & Melinda Gates Foundation and scientific and business advisors to determine the best overall strategy to achieve the goals of the project. This includes determining the manufacturing and commercial strategy, key decision points, and the future partnerships necessary to transition the research and laboratory-scale development work to manufacture at commercial scale and integrate the semisynthetic artemisinin into the supply chain and ultimately into life saving ACTs.

Our goal is to make a significant difference in the development of affordable antimalarials for patients with malaria.

## **Disease Transmission**

The life cycle of the malaria parasite *Plasmodium* begins when an infected female anopheles mosquito bites a human. The *Plasmodium* sporozoites enter the bloodstream and travel to the liver where they divide repeatedly. New morphological stages of the parasite called merozoites emerge and infect red blood cells. Some merozoites in the blood develop into special cells called gametocytes. When a female anopheles mosquito bites the infected person, it ingests these gametocytes. Then, in the mosquito's digestive system, the gametes combine to form a zygote. The zygote goes through several developmental stages to form more sporozoites. The sporozoites migrate to the salivary glands of the mosquito; when the insect bites another person, the life cycle begins anew. In most cases of *Plasmodium* infection, the incubation period is from seven to 30 days, but varies if the individual has taken a preventive medicine. The most malignant (*P. falciparum*) cases develop within three months upon infection, while the forms transmitted by *P. vivax* and *P. ovale* may not appear until three years later.

## **Disease Characteristics**

Malaria is characterized by extreme exhaustion associated with high fever, sweating, shaking and chills. By destroying red blood cells, malaria can also lead to anemia. The disease may present as uncomplicated malaria, characterized by flu-like symptoms, or severe malaria, in which infected red blood cells block vessels to the brain or damage other vital organs, often resulting in death. Non-immune patients with uncomplicated malaria are prone to the development of severe *P. falciparum* malaria. Severe malaria usually occurs in persons who have no immunity to malaria or whose immunity has decreased. In some instances, people in highly endemic areas who are infected frequently may develop immunity to the disease and become asymptomatic carriers of malaria, contributing to epidemics.

## **Prevalence**

Malaria causes nearly 600 million new infections, more than 300 million acute illnesses and 1 million deaths annually. The burden of this disease falls heaviest among children under the age of 5. Also, malaria poses a risk to pregnant women, developing fetuses, and newborn babies. Malaria infection in pregnant women is largely asymptomatic in the areas of greatest transmission rates.

## **Geographic Distribution**

Malaria is a disease of poverty, with 58 percent of malaria occurring in the poorest 20 percent of the world's population. It is endemic in over 100 countries worldwide, notably in sub-Saharan Africa, where 90 percent of deaths occur, mostly among young children. Malaria kills an African child every 30 seconds. In other areas of the world, malaria is a less prominent cause of death, but can cause substantial disease and incapacitation, especially in rural areas of some countries in South America and Southeast Asia.

## **Current Therapies**

There are a number of drugs capable of preventing *Plasmodium* infection. However, chronic use of these drugs is not recommended because of serious side effects. These options are usually only available to occasional travelers, expatriate workers or military personnel in endemic areas.

For people in malaria-endemic countries, traditional first-line treatments, such as chloroquine and sulphadoxine/pyrimethamine are no longer effective due to increasing drug resistance. Today there are reported cases of *Plasmodium*-resistant strains for each of the currently available first-line therapies, leading to the spread of malaria to new areas and the re-emergence of the disease in areas where it had previously been eradicated. In response, scientists have developed new treatments using combinations of artemisinin-based drugs with other antimalarials (artemisinin combination therapy or ACTs). At present, there has not been a documented clinical case of artemisinin drug resistance. Unfortunately, because of their supply shortage and cost, even at \$2.20 per treatment, these therapies are not widely affordable to the people who most need them.

Vaccines are ideal in preventing disease, and several different malaria vaccine candidates are now in human clinical trials in Africa, Asia, Europe, and the United States. However, it could be a decade before an effective vaccine is licensed and deployed. Effective preventive measures, such as insecticides and

insecticide-treated bed nets (ITNs), also play an important role in reducing disease incidence in malaria endemic areas.

### **Sources**

Centers for Disease Control (CDC), <http://www.cdc.gov/malaria/index.htm>

World Health Organization, <http://www.who.int/topics/malaria/en/>

World Malaria Report 2005, <http://rbm.who.int/wmr2005/html/1-1.htm>

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