

CHALLENGES IN ELIMINATING MALARIA

MALARIA CAN EXIST ALMOST EVERYWHERE

Approximately 40% of the world's population lives in malaria-infested countries; countries with hot, humid climates, including India and countries in South America and Africa. Those of us living in the United States may assume that we are safe because malaria ceased to be a problem years ago. But in fact, malaria exists on every continent except Antarctica, and as recently as 2005, 1,528 cases of malaria were reported in the United States, including 7 deaths. All but 2 of these cases came from areas where malaria is endemic, particularly from humans who had visited West Africa.(1)

Malaria may not be endemic in the US, but it has not been completely eliminated for some of the same reasons it exists in other countries:

1. The complex lifecycle of malaria parasites
2. Difficulty of obtaining an accurate diagnosis
3. Lack of access to current medical cures
4. The persistent challenge of maintaining effective medication and treatments.

MOSQUITOE SURVIVAL ENSURES MALARIA SURVIVAL

A malarial parasite requires 2 host animals to complete its lifecycle and spread disease: the female Anopheles mosquito and either a human or animal.

Of the 430 species in the genus Anopheles, 30 to 50 are carriers of malaria. To produce eggs, female mosquitoes require a blood meal, which is obtained by biting a host:(2)

1. In the host, sporozoites go through several stages of development, first infecting liver cells, and then red blood cells. Some eventually mature into the sexual form of the parasite, the gametocyte.
2. When a mosquito bites a malaria-infected human, it ingests both the female and male gametocyte forms of the malaria parasite.
3. In the mosquito's stomach, the male penetrates the female gametocyte, creating zygotes.
4. The zygotes develop into oocysts, which grow and rupture, releasing sporozoites.
5. The sporozoites make their way to the salivary glands and are injected into a host when the mosquito bites, completing the lifecycle of the parasite.

PLASMODIUM: THE PARASITE CAUSING MALARIA

Of the 100 species of the genus *Plasmodium*, 4 can infect humans. Which species of the parasite infects a human, the severity of illness, and the drugs and insecticides used to prevent or cure malaria depend on where the human was exposed to the disease.(3)

Plasmodium falciparum is found world-wide and, the most severe and potentially fatal form of malaria. Because this species multiplies rapidly in the blood, it

quickly destroys red blood cells, which can lead to severe anemia or abnormal blood clotting, seizures, coma, and other neurologic abnormalities.(3)

Plasmodium vivax is found mostly in Asia, Latin America, and in some parts of Africa. This species rarely causes death and can remain dormant in the liver for long periods. When the parasite is active, a human experiences fever that spikes every 48 hours. If left untreated, symptoms will re-occur.(3)

Plasmodium ovale is found mostly in Africa (especially West Africa) and in the islands of the western Pacific. It is similar to *P vivax*, in that it can remain dormant in the liver for long periods, with symptoms reoccurring over time. However, it differs from *P vivax* in that it can infect humans who do not have the Duffy antigen group. These humans, including most humans of African descent, cannot produce an immune response to the organism.(3)

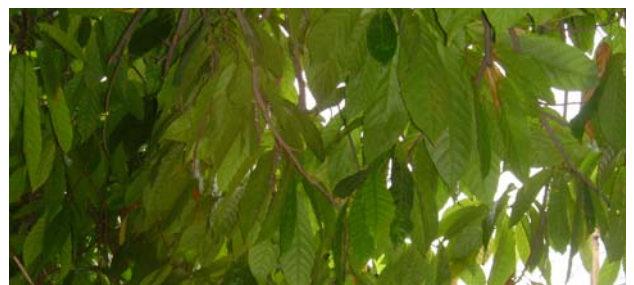
Plasmodium malariae is found world-wide and is perhaps the least lethal and produces the mildest and most chronic symptoms of the 4 species. Left untreated, symptoms will reoccur every 36 hours. This species can remain dormant for long periods during which the human experiences no symptoms. Left untreated, the parasite can severely damage the kidneys.(3)

LIVING CONDITIONS AND BEHAVIORS THAT PUT HUMANS AT RISK

Unknowingly, humans may put themselves at risk of infection when they travel to malaria-infested countries. Humans can become infected even when they employ all the precautions if the species of either the mosquito or the parasite have developed resistance to the available medications. In certain areas of the world, treatment may not be available, or an inaccurate diagnosis may prevent a human from receiving treatment at all.(4)

Cultural mores, local living conditions (no access to medicines, nearness to swamps or stagnant water, houses with no screens or insecticide-treated mosquito netting), poverty, and mobility of the local population can increase the risk of exposure to malaria.

Because the parasite lives in the blood of an infected human, it can be transmitted to another human who receives a transfusion of infected blood. A



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mother can transfer malaria to her unborn child.(5)

THE CHALLENGE OF ACCURATE DIAGNOSIS

Malaria, in its early stage, is difficult to diagnose because its symptoms-fever, chills, sweats, headaches, muscle pain, nausea, and vomiting-are similar to other less life-threatening diseases, such as the flu or the common cold.

The reference standard for confirming the diagnosis of malaria is to examine blood cells (obtained from a blood smear) under a microscope to see if the human is infected and by which species of parasite. Each species has distinct microscopic characteristics that allow for diagnosis. Factors such as the quality of the reagents used to stain the blood sample, the quality of the microscope and laboratory equipment, and the experience of laboratory personnel can affect the accuracy of a diagnosis.

Rapid diagnostic tests (RDTs) are used in some countries to diagnose malaria within 15 minutes. However, the results of RDTs may be limited by false negatives if the human has been recently infected. Rapid diagnostic tests cannot identify the extent of infection. Whether RDTs can accurately diagnose the 2 less-common parasites *Plasmodium ovale* and *Plasmodium malariae* is not known. With these limitations, it may be difficult to prescribe an effective medical treatment without examining a blood smear under a microscope.(6,7)

In countries where medical expertise, drugs, and equipment are in short supply, a local physician may diagnosis malaria on the basis of symptoms, without a blood test for confirmation. Antimalarial medications may then be prescribed without knowing whether the human is in fact infected or which species of parasite is causing the disease. Because each species must be treated with different medication or combinations of medications, prescribing medicines that are ineffective against a particular species is not only costly in terms of human suffering, but if the malaria parasite is frequently exposed to drugs or insecticides, it can quickly develop resistance leaving local communities at higher risk of acquiring a form of malaria for which a cure is no longer effective.(6)

An opposite clinical practice may be the norm in countries where malaria has essentially been eradicated, such as in the United States. A human may be experiencing the symptoms of malaria and actually have the disease, but the physician will not likely consider malaria until tests that eliminate the possibility of more common infections have been run with negative results. If a human is infected by a species (that remains dormant) and experiences no symptoms he or she may carry malaria for months or years before the disease is diagnosed.(6)

EFFECTIVE MEDICINES AND INSECTICIDES

Because both the female Anopheles mosquito and the malarial parasites rapidly reproduce, they quickly become resistant to current preventative treatments and cures. Maintaining effective cures and preventative measures requires that medical personnel accurately diagnose the species of the parasite that caused the infection, and prescribe the most effective medicines for treatment or prevention. The Centers for Disease Control and Prevention has developed a complex treatment table and a clinical guidance document that describe treatment options based on severity, the species of parasite, the location where the infection occurred, and whether the patient is a child or an adult.(5,8)

WHAT CAN BE DONE?

Biologically, 3 factors must be present to continue the survival of malaria:

1. A female Anopheles mosquito.
2. A malaria parasite.
3. A host such as a human.

However, with 30 to 50 species of mosquitoes and 4 species of parasites involved in the survival of malaria in almost every part of the world, maintaining effective preventive measures and medicinal cures on a global scale is a daunting challenge. It requires significant resources dedicated to research and development of future cures to keep one step ahead, as the parasite and mosquito become resistant to current measures.

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