Malaria is a disease caused by infection with *Plasmodium* parasites. These parasites are spread from person to person by infected female *Anopheles* mosquitoes. After transmission, the parasites first pass through the liver before invading red blood cells, where exponential expansion of the parasite population leads to the manifestation of malaria. Regardless of prior infection, individuals can be infected with *Plasmodium* parasites and contract malaria with any exposure to infected mosquitoes. Five species of *Plasmodium* are capable of causing malaria in humans, but infections by *Plasmodium falciparum* (*P. falciparum*) and *Plasmodium vivax* are the most prevalent. *P. falciparum* accounts for the highest number of deaths worldwide. Largely controlled in North America and Europe, malaria remains a major burden in Africa, Asia, and Central and South America. Adding to this burden in malaria endemic regions, co-infections with other pathogens are common: including HIV, tuberculosis, and parasitic worms.

Symptoms of malaria usually manifest 7-28 days post-infection, and typically include fever, headache, muscle pains, chills, vomiting, and fatigue. However, clinical outcomes vary depending on the age, sex, nutritional status, and previous infection, among other factors, of each patient. Examples of severe cases of malaria include cerebral malaria (infection affecting the brain) and severe malarial anemia.

The Global Burden of Malaria

Over half of the world’s population is considered at risk for malaria; in 2020 alone it was responsible for approximately 241 million cases and 627,000 deaths. The vast majority of these cases (95%) and fatalities (96%) occur in Africa. Children under 5 years of age are the most vulnerable, accounting for 80% of deaths in Africa and the largest percentage globally.

$12 Billion:
Estimated annual economic impact in Africa, factoring in healthcare costs, decreased productivity, days lost in education, and loss of international investment and tourism (in USD).

Progress and Continuing Challenges

Despite remarkable progress in mosquito control and other interventions, malaria remains a significant global threat due to insecticide resistance in mosquitoes, increasing resistance of *Plasmodium* parasites to first-line antimalarial medications, and the lack of an effective vaccine.

Global Malaria Deaths Over the Last 20 Years

Source: World Malaria Report 2021, Table 3.1

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i. Though very rare, malaria can be transmitted through blood transfusion, organ transplant, or the use of blood-contaminated needles or syringes. An infected mother can also transmit the disease to her unborn infant before or during delivery (known as congenital malaria).

ii. About 2,000 cases are diagnosed in the United States each year, with the vast majority from recent travelers or immigrants, however small and isolated outbreaks have occurred.
Malaria Treatments

Since its introduction in the 1970s, the drug **Artemisinin** has had a major impact on the treatment of malaria. Frontline treatments worldwide for *P. falciparum* malaria are **artemisinin-based combination therapies**, where derivatives of artemisinin and quinine are combined. Recent evidence suggests the emergence of parasite resistance to existing antimalarials, underscoring the importance of mosquito control measures and novel drug development.  

A Vaccine for Malaria?

In October 2021, the **RTS,S/AS01** vaccine became the first malaria vaccine recommended by the World Health Organization for use in children in high-risk areas of the world. Development of the vaccine began in the 1980s, becoming a collaborative effort between GlaxoSmithKline and the Walter Reed Army Institute of Research (WRAIR), with support from the PATH Malaria Vaccine Initiative and the Bill and Melinda Gates Foundation. This first-of-its-kind vaccine offers hope for future development and approval of a vaccine for broader use.

Federally-funded Research at Work

Once endemic in temperate regions of the United States, malaria was successfully eliminated in the early 1950s largely through the establishment of what would become the Centers for Disease Control and Prevention (CDC) in 1942. The U.S. federal government still plays a pivotal role in malaria surveillance, research, and development because continuing to fight this disease is both a humanitarian and economic imperative.

The U.S. Department of Defense has played a crucial role throughout history in the global fight against malaria, with research taking place at **WRAIR** and the **Naval Medical Research Center (NMRC)**, including at overseas laboratories. WRAIR co-led the development of the RTS,S/AS01 vaccine, and both WRAIR and NMRC have played a role in the development of every prevention drug approved by the U.S. Food and Drug Administration.

The **National Institute of Allergy and Infectious Diseases** at the **National Institutes of Health** conducts extensive research into the biology of *Plasmodium* parasites and mosquito control measures.

The **U.S. Agency for International Development (USAID)** works with international governments to strengthen the capacity of malaria endemic countries to prevent and treat malaria. USAID leads the **U.S. President’s Malaria Initiative**, in coordination with the CDC.

Sources: