Malaria

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Malaria; Etiologic agents: *Plasmodium vivax; Plasmodium falciparum; Plasmodium ovale; Plasmodium malariae* and the zoonosis *Plasmodium knowlesi* (1).

Transmission:

Malaria is transmitted mainly by the bite of an infected female *Anopheles* mosquito (9). In rare cases, it can be transmitted through blood transfusion, organ transplants, and contaminated medical devices such as syringes and needles (1). Congenital malaria may also rarely occur (6). Zoonotic transmission from *P. knowlesi* to humans is possible, too (1).

Reservoirs:

Humans and some animals (monkeys) are reservoirs of transmission (1).

General characteristics of *Plasmodium*:

All the five species responsible for malaria in humans are obligate intracellular parasites. They are classified as protozoan under the phylum apicomplexa. They are unicellular and lack a cell wall. They do not have locomotor organelles. They have a complex of special organelles at the apexes of their cells, which help them to penetrate a host’s tissues. *Plasmodium spp.* grows sexually (sporozoite) in the anopheles mosquito gut (definitive host) and asexually (merozoite) in humans (intermediate hosts) (9).

Key tests for identification:

Many tests can be used to identify the *Plasmodium spp.* It is usually recommended to start with a thick and a thin blood smear with special stains (2). Thick smears help to see the parasite more easily while thin smears help to differentiate the species. The rapid diagnostic test (antigen testing) is used to detect the malaria antigen (protein). A positive result is indicated by a color change on the test strip. The Polymerase Chain Reaction (PCR) can also be used to amplify and then identify the nucleic acid’s parasite in the infected blood (3). Serology tests can also be used to detect the antibodies produced by the body to fight the specific malaria agent (3).

Signs and symptoms of the disease:

The signs and symptoms of the malaria disease include chills and fever, and sometimes headache, fatigue and sweating. Depending on the severity of the disease (which is related to the species), the infected patient can also suffer from anorexia, anemia, seizures, confusion, coma, cerebral malaria, and even death (9). The period of incubation varies from 3 to 12 days (for *P. falciparum* which is the most dangerous) to 3 to 40 days (for *P. malariae*). Some species such as *P. vivax* and *P. ovale* are hypnozoites with relapses that can occur after weeks, months or even years.

Historical Information:
The word “malaria” comes from Italian “mala aria” which literally means “bad air” (7). In 2700 BC, Chinese described the symptoms of the disease and attributed it to the bite of some insects. Quinine plants were found effective to treat fever in the 17th century by Indian tribes. It is in 1880 that the French army surgeon Laveran discovered the malaria parasite in an infected human blood. Italian investigators named the different species of malaria parasites in 1890 *P. vivax* and *P. malariae*. The American Welch named *P. falciparum* in 1897. Watson Stephen named the forth species *P. ovale*. *P. Knowlesi* was named in 1931, and its first human infection was documented in 1965. Ronald Ross was the first to discover that malaria parasite could be transmitted from an infected patient to mosquitoes in 1897. Two years later, Italian researchers conducted an experiment. They collected infected mosquitoes and sent them to London to be fed on healthy volunteers. Both volunteers developed the malaria disease (7).

**Virulence Factors:**

The *Plasmodium spp.* has many strains which cause low to moderate forms of malaria in humans (5). The most dangerous species is *P. falciparum* which can cause cerebral malaria and death in humans. Its virulence factors are primarily the adherence of infected cells to endothelial surfaces (5), and secondly the antigenic variation of this strain due to *Plasmodium falciparum* erythrocyte membrane protein 1 (pfemp1) which is responsible of “sequestration within the vital organs” (1). The special apical organelles that help the entire apicomplexa phylum to enter host tissue, also constitute another virulence factor (9).

**Control/Treatment:**

The treatment of the malaria disease depends on the type of malaria (malignant or benign) the patient is suffering from, depends on whether suppressive, radical, or preventive treatment is required, and also on the drug resistance. Anti-malaria drugs of choice include oral drugs (chloroquine, or malarone in chloroquine-resistant area), suppository and intravenous drugs. The method of administration depends on the degree of infection (9).

Control measures of the *Plasmodium spp.* are mostly based on vector control programmes such as DDT programmes, and on the use of insecticides spray, insecticides-treated bed nets, screens, and insect repellants, to avoid the mosquito bites.

**Prevention:**

There is no effective vaccine against the *Plasmodium spp.* (8). The barriers to developing an effective vaccine include the complexity of the malaria parasites’ life cycle, and the fact that acquired immunity does not provide a long lasting immunity. The only approved vaccine which is still on its third trial is the RTS,S. It is a recombinant vaccine which consists of the *P. falciparum* protein from pre-erythrocytic stage (8). It requires four injections and is of low efficacy. That is why is not recommended to be used in children younger than three months of age. However, research for new vaccines is still ongoing (8). The prevention of infection is mainly made through vector control. To prevent the malaria disease in vulnerable groups such as pregnant women and children, anti-malaria drugs can be used to eliminate parasites in the blood (suppression). The disease can also be prevented by a complete treatment of any prior malaria in order to avoid spread and resurgence. Travelers to tropical or endemic areas should use bed nets, insect repellants, and prophylactic drugs.

**Local Cases/Outbreaks:**
In the United States, mosquito control and the reduction of human carriers dropped the reported cases below 100 in 1960 (9). However, a resurgence of malaria due to immigration and travelers to endemic regions has been noted. The southeast part of the United States is the most affected region with more than 1500 cases every year. The highest number of cases was in 2013 with 1727 cases reported, out of which 61% were caused by \textit{P. falciparum}. Ten people died that year of malaria.

**Global Cases/Outbreaks:**

Malaria affects 10% of the world population with at least 300 million of new cases every year (9). There has been an estimated 37\% global decrease in malaria incidence between 2000 and 2015, and a 60\% decrease in global malaria deaths between 2000 and 2015. Ninety percent of malaria deaths occurred in the African region and in children aged less than 5 years.

**References**