2. BIOLOGY OF MALARIAL PARASITES

Malaria is a disease caused by protozoan (unicellular) blood parasite belonging to the sporozoans, genus *Plasmodium*. 150 species are known which are specific to various reptiles, birds and mammals (Kreier and Baker, 1987; Bogitsh and Cheng, 1999 and Wikipedia, 2010). Human malaria is caused by four species, *Plasmodium falciparum, P. vivax, P. malariae* and *P. ovale* (figures 1-4). Of these, the most dangerous is *P. falciparum*. This species is particularly harmful because it causes a high rate of medical complications, many of which can result in death.

2.1. Taxonomy of malarial parasite *Plasmodium*

<table>
<thead>
<tr>
<th>Phylum</th>
<th>Protozoa</th>
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<tbody>
<tr>
<td>Subphylum</td>
<td>Sporozoa</td>
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<tr>
<td>Class</td>
<td>Telospora</td>
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<tr>
<td>Order</td>
<td>Eucoccidia</td>
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<td>Suborder</td>
<td>Haemosporidia</td>
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<tr>
<td>Family</td>
<td>Plasmodiidae</td>
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<tr>
<td>Genus</td>
<td><em>Plasmodium</em></td>
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<tr>
<td>Species</td>
<td><em>falciparum</em> (<em>vivax, ovale and malariae</em>)</td>
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</table>
Figure 1. Red blood cells infected with *Plasmodium falciparum*.

Figure 2. Red blood cells infected with *Plasmodium vivax*.
Figure 3. Red blood cells infected with *Plasmodium ovale*.

Figure 4. Red blood cells infected with *Plasmodium malariae*. 
2.2. Morphology

The matured malarial parasite, \textit{Plasmodium} in adult condition is called trophozoite. It is amoeboid, uninucleated, having vacuolated and granular cytoplasm. It has double membrane, the plasmalemma closely applied to the cytoplasm. The nucleus, mitochondrion, apicoplast and the microtubules of \textit{Plasmodium} sporozoites are linked to the parasite pellicle via long tethering proteins. The tethers originate from the inner membrane complex and are arranged in a periodic fashion following a 32 nm repeat. The tethers pass through a subpellicular structure that encompasses the entire parasite, probably as a network of membrane-associated filaments.

2.3. Life cycle

\textit{Plasmodium} parasites have an indirect life cycle (figure 5), i.e. they require two hosts (Arie, 2010). The intermediate host (humans) harbours sexually immature stages, the final host (in human malaria many mosquito species of the genus \textit{Anopheles}) harbours sexually mature stages. Malaria is caused by infection with four species of \textit{Plasmodium}. The life cycles of all the malarial parasites are very similar (Matteelli and Castelli, 1997 and Fujiokaa, and Aikawab, 2002).
Figure 5. Schematic drawing of the life cycle of malaria parasites.
Mosquitoes inject malaria sporozoites into the blood stream of humans when sucking blood. These stages penetrate into cells of the liver parenchyma, where they grow up to large cells, so-called megaschizonts (although some sporozoites of \textit{P. vivax} and \textit{P. ovale} may survive as “sleeping stages” (= hypnozoites) for long periods in the blood plasma before infecting host cells).

After a number of days these stages multiply by asexual fission (= preerythrocytic or exoerythrocytic schizogony) giving rise to small merozoites, which are released into the bloodstream to infect erythrocytes. They are now referred to as trophozoites (= feeding stages). They grow up to schizonts smaller than those in the liver, which again multiply by asexual fission (= erythrocytic schizogony), producing several to many (depending on the species) daughter cells, the merozoites. Host cells are destroyed during schizogony, their toxic substances released into the blood. Importantly, schizogony in the infected blood cells is synchronized, i.e. toxic substances from many destroyed cells are released at more or less the same time, leading to the malaria symptoms (chills, fever attacks, severe headache, etc.). Merozoites infect other erythrocytes and the process of asexual reproduction is repeated many times. At a later stage, some of the
merozoites are not transformed into feeding stages and schizonts, but into sexual cells (= male and female gametocytes). These circulate in the blood, where they cannot develop further until ingested by an Anopheles-mosquito. In the digestive tract of the mosquito, male gametocytes give rise to several male gametes by a process called exflagellation (many flagella-like gametes arranged around a central residual body), whereas the female gametocyte is transformed into a single female gamete. One male gamete penetrates into a female one and fertilizes it forming a zygote which is mobile and therefore called an ookinete. It penetrates into the wall of the mosquito’s digestive tract and surrounds itself with a cyst wall, thus becoming an oocyst, containing a large number of sporozoites. After some time, the cyst wall of the oocyst ruptures, releasing numerous sporozoites into the body cavity, from where they migrate mainly into the salivary glands of the mosquito. They enter the bloodstream of humans when they are injected by the mosquito.

The four major human species of malaria differ in morphology and symptoms produced, but in all species the first disease symptoms occur only once schizogonies in the blood have produced large numbers of merozoites infecting erythrocytes with subsequent breakup of large numbers of blood cells leading to the release of large quantities of toxic
substances. In other words, no symptoms can be expected as long as infection is restricted to the liver, and during the early stages of the erythrocytic cycle. Depending on the malaria species and the health condition of the infected person, this prepatent period (= period without symptoms) can last a number of days or even several months.

They undergo asexual multiplication (exoerythrocytic Schizogony) resulting in the production of many uninucleate merozoites. These merozoites flood out into the blood and invade red blood cells (Scott 1939). They initiate a second phase of asexual multiplication (erythrocytic Schizogony) resulting in the reproduction of about 8-16 merozoites which invade new red blood cells. This process in repeated almost indefinitely and is responsible for the disease, malaria. As the infection progress, some young merozoites develop in to male and female gametocytes that circulate in the peripheral blood until they taken up by a female Anopheline mosquito when it feeds (Rusell, 1965). The gametocytes mature into male and female gametes (Foster, 1965), fertilization occurs and a motile zygote (ookinite) is formed within the lumber of the mosquito gut. The ookinite penetrates the gut wall and becomes a conspicuous oocyst with in another phase of multiplication occurs resulting in the formation of sporozoites that migrates to the
salivary glands of a mosquito and are injected when the mosquito feeds on a new host.

2.4. Signs and symptoms

Symptoms of malaria include fever, shivering, arthralgia (joint pain), vomiting, anemia (caused by hemolysis), hemoglobinuria, retinal damage, and convulsions. The classic symptom of malaria is cyclical occurrence of sudden coldness followed by rigor and then fever and sweating lasting four to six hours, occurring every two days in \( P. \) \textit{vivax} and \( P. \) \textit{ovale} infections, while every three days for \( P. \) \textit{malariae} and \( P. \) \textit{falciparum} can have recurrent fever every 36-48 hours or a less pronounced and almost continuous fever. For reasons that are poorly understood, but that may be related to high intracranial pressure, children with malaria frequently exhibit abnormal posturing, a sign indicating severe brain damage. Malaria has been found to cause cognitive impairments, especially in children. It causes widespread anemia during a period of rapid brain development and also direct brain damage. This neurologic damage results from cerebral malaria to which children are more vulnerable. Cerebral malaria is associated with retinal whitening, which may be a useful clinical sign in distinguishing malaria from other causes of fever.

2.5. Transmission
Malarial disease is usually transmitted through the bite of an infected female *Anopheles* mosquito (Sharma *et al.*, 2004). Less commonly, it may occur through contact with infected blood. This type of mosquito becomes infected with one of the four *Plasmodium* parasites that cause malaria in humans, through a previous blood meal from an infected person. When an *Anopheles* mosquito bites an infected person, a small amount of blood infected with microscopic malaria parasites is taken. The parasite grows and matures in the mosquito's gut for a week or more, then travels to the mosquito's salivary glands. When the mosquito next takes a blood meal, these parasites mix with the saliva, are injected with the bite, and the transmission of malaria is complete.

Once in the blood, the parasites travel to the liver and enter liver cells, to grow and multiply. After as few as seven days or as long as several years, the parasites leave the liver cells and enter red blood cells, which normally carry oxygen in the blood to tissues that need it.

Once in the red blood cells, the malaria parasites continue to grow and multiply. After they mature, the infected red blood cells
rupture, freeing the parasites to attack and enter other red blood cells. Toxins released when the red cells burst are what cause the typical symptoms of malaria, such as fever, chills and flu-like symptoms.

**Other methods of malaria transmission:** Because the malaria parasite is found in red blood cells, transmission may also occur through contact with infected blood. This can occur through:

1. **Blood transfusion (Transfusion malaria):** This is fairly common in endemic areas.

   Following an attack of malaria, the donor may remain infective for years (1-3 years in *P. falciparum*, 3-4 years in *P. vivax*, and 15-50 years in *P. malariae*.)

   Most infections occur in cases of transfusion of blood stored for less than 5 days and it is rare in transfusions of blood stored for more than 2 weeks. Frozen plasma is not known to transmit malaria. The clinical features of transfusion malaria occur earlier and any patient who has received a transfusion three months prior to the febrile illness should be suspected to have malaria.
2. **Mother to the growing fetus (Congenital malaria):** Intrauterine transmission of infection from mother to child is well documented. Placenta becomes heavily infested with the parasites. Congenital malaria is more common in first pregnancy, among non-immune populations.

3. **Needle stick injury:** Accidental transmission can occur among drug addicts who share syringes and needles. (Therapeutic inoculation of malarial parasites, so as to induce fever, was a mode of treatment for neurosyphilis).

   If a mosquito bites this infected person and ingests certain types of malaria parasites, the malaria transmission cycle continues.

2.7. **Preventive measures**

   Of course, preventing malaria in the first place is better than needing a cure. Prevention of malaria in individuals will generally involve the reduction of human-mosquito contact. If we live in, or will be visiting, an area where the risk for malaria is high, malaria prevention strategies are recommended. Some of these include:

   - Keeping mosquitoes from biting, especially at night.
Wearing insect repellent and long-sleeved clothing.

Sleeping under bed nets, which are especially effective if they have been treated with insecticide.

Taking anti-malaria medications for malaria prophylaxis (prevention of spread).

Eliminating places around your home where mosquitoes breed.

Spraying insecticides on your home's walls to kill adult mosquitoes that come inside.

Chemoprophylaxis is another strategy used primarily for persons visiting an endemic area for a relatively short period of time. However, chemoprophylaxis only suppresses parasitemia and does not prevent infection. Furthermore, chemoprophylaxis should not be used on a mass scale to control malaria since it promotes the development of drug resistance.

2.8. Treatment

Anti-Malaria is divided into four categories according to the stage in the life cycle they attack. The commonly used antimalarial drugs are,
Chloroquine, Primaquine, Mepacrine, Proguanil and Sulphone drugs (Anvikar, 2009).

The anti-malarial drugs are effective against all stages of the malarial parasites found in the vertebrate host. The choice of anti-malarial drug for use in man will depend on whether it is for prophylactic purpose. It also depends on which species of malaria parasites to be controlled (WHO, 2010).

2.9. Control

The fight against malaria has been fought on several fronts:

- Prevention of infection by using mosquito nets and insect repellents.

- Mosquito eradication using insecticides (Hexa Chlorocyclo Hexane and dieldrin), combined with detailed ecological studies to permit the correct application of insecticides.

- Prophylactic drugs, and drugs used for treatment like quinine, chloroquine, artemisinin, atebrin, etc. However, malarial parasites developed the resistance and are developing fairly fast, so that new medications have to be developed continually.
Development of vaccines. To date, projects to develop vaccines against malaria have been successful only to a marginal degree. No vaccine exists that protects the majority of people against several strains of even one species of malaria.

The new approaches to mosquito control are only at the developmental stage. These include genetic control, by using sterile male technique in which the fecundity of the population is reduced by releasing sterile male into it (Phillips, 2001).