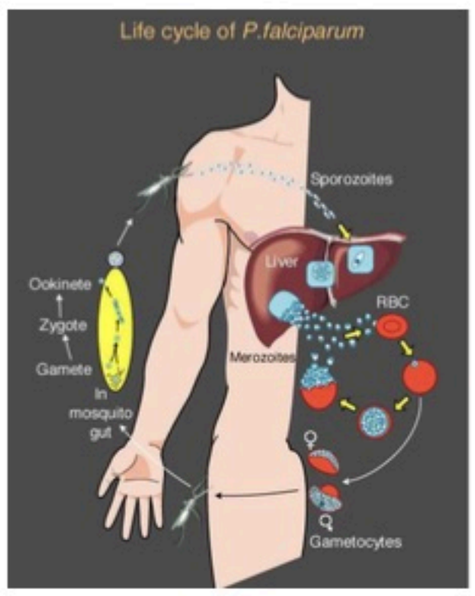
Life Cycle of Plasmodium in Anopheles Mosquito

Three stages:

1. Mosquito stage: sexual reproduction
2. Liver stage: asexual reproduction
3. Blood-stage: asexual reproduction, major amplification stage

The life cycle of the Plasmodium parasite can be divided into three major stages, primarily occurring in the mosquito and the human host. The mosquito serves as the definitive host where sexual reproduction of the parasite occurs (1-2 weeks). This involves fertilization and meiosis, resulting in a haploid form of the parasite known as sporozoites, which are injected into humans during a mosquito bite (30 mins).

- **Definitive Host:** The mosquito, where sexual reproduction occurs.
- **Haploid Form:** Sporozoites with one set of chromosomes (14 chromosomes).
- **Diploid Forms:** Zygotes and ookinetes in the mosquito, which have two sets of chromosomes.



Three stages:

1. Mosquito stage - sexual reproduction

2. Liver stage - asexual reproduction)

3. Blood-stage - asexual reproduction, major amplification stage

Upon entering the human bloodstream, sporozoites travel to the liver, where they recognize and enter hepatocytes (1-2 weeks). Initially, the infection is asymptomatic, and the liver functions normally. After approximately 10 days, the parasites emerge from the hepatocytes as merozoites, which then infect red blood cells, initiating the symptomatic phase of malaria.

- **Initial Infection:** Sporozoites enter the liver and grow in hepatocytes.
- **Asymptomatic Phase:** No clinical illness occurs during the initial liver infection.
- **Merozoite Release:** After 10 days, merozoites burst from hepatocytes and infect red blood cells.

Once inside red blood cells, each merozoite can replicate asexually, producing 16 to 32 new merozoites every 48 hours. This cycle leads to a significant increase in the number of infected red blood cells, potentially affecting 1% to 5% of the total red blood cell count. The clinical symptoms of malaria arise during this phase, primarily due to the high biomass of parasites in the bloodstream.

- **Replication Cycle:** Merozoites replicate every 48 hours.
- **Clinical Symptoms:** Fever and chills occur due to the synchronous rupture of infected red blood cells.
- **Infection Scale:** A small fraction of red blood cells can become infected, leading to significant disease.

Disease occurs a week to a month after infection.

Gamete Formation and Mosquito Reinfection

During the red blood cell cycle, some haploid organisms transform into gametocytes, which are male and female forms of the parasite. When an uninfected mosquito feeds on infected blood, it ingests these gametocytes, which then undergo fertilization in the mosquito's midgut. This process completes the life cycle of the Plasmodium parasite, allowing it to return to the mosquito's salivary glands and be transmitted to another human host.

- **Gametocyte Formation:** Some merozoites become gametocytes in the human host.
- **Fertilization:** Gametocytes are fertilized in the mosquito's midgut.
- **Life Cycle Continuation:** The parasite returns to the mosquito's salivary glands for transmission.

Introduction to PfEMP1

In this section, we will explore the parasite protein PfEMP1, which is encoded by the Plasmodium falciparum genome. This parasite has 14 chromosomes that encode approximately 5200 proteins. PfEMP1 is one of these proteins and plays a significant role in the pathology of malaria.

Clinical Presentation of Malaria

Malaria caused by P. falciparum can present with various symptoms, including:

- Fever and chills
- Severe anemia
- Cerebral malaria, which may lead to fitting or coma
- Placental malaria in pregnant women, which may not show other clinical effects

It is important to note that Plasmodium vivax, while significant for morbidity, is not the primary cause of severe malaria (low mortality). It has a dormant phase in the liver (hypnozoite), leading to recurring malaria episodes, unlike Plasmodium falciparum, which does not have this dormant phase.

Mechanism of Infection

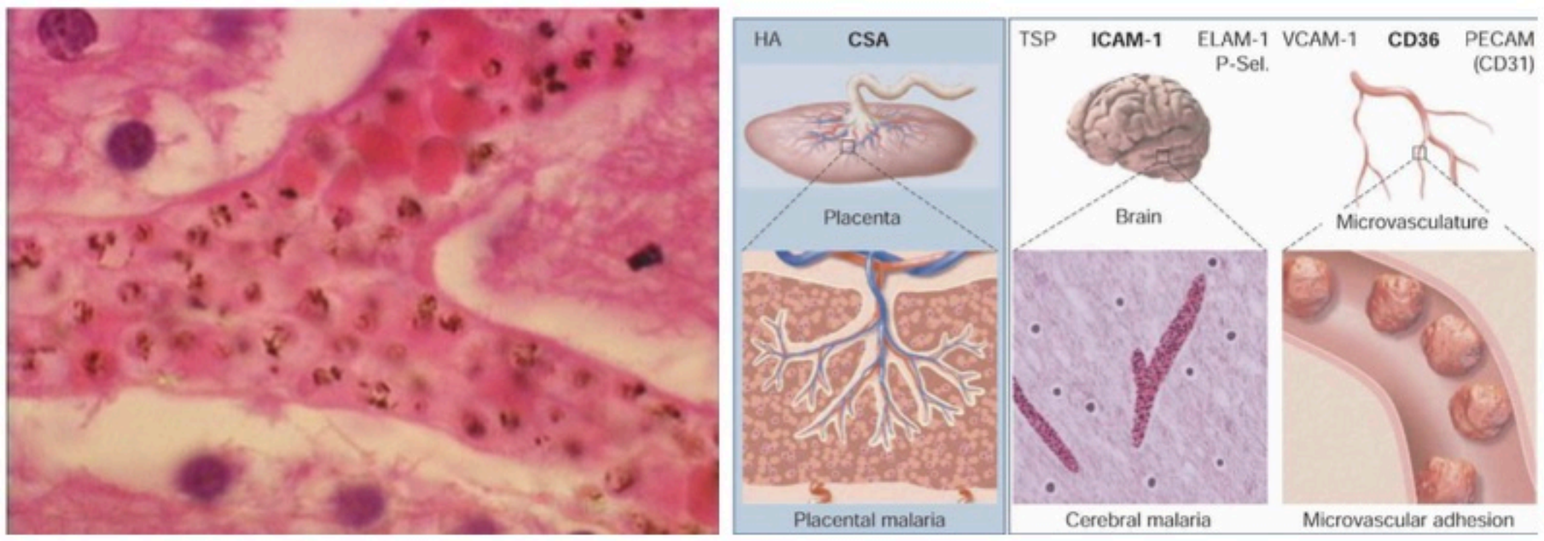
Infected red blood cells (RBCs) do not remain in circulation; instead, they adhere to blood vessel walls through a process called cytoadherence. This allows the parasites to sequester in various tissues, such as:

- Skeletal muscle
- Fat tissue
- Kidneys
- Brain

This sequestering helps the parasites avoid detection and destruction by the spleen, which filters out abnormal RBCs.

Histopathology of Severe Malaria

In cases of severe malaria, histopathological examination reveals blood vessels packed with parasites, particularly in the brain. The presence of crystallized heme, which is a detoxified form of heme, indicates the presence of mature parasites. This crystallization is crucial for the parasite's survival as heme is toxic to them.



PFEMP1 Structure and Function

The PFEMP1 protein is expressed on the surface of infected RBCs and is crucial for binding to specific receptors on blood vessel walls. The parasite has multiple genes (approximately 60) encoding different variants of PFEMP1 (clonal antigenic variation), allowing it to switch its expression and adapt to different tissues. This switching can lead to:

- Binding to CD36 in some tissues
- Binding to E-selectin in others
- Binding to chondroitin sulfate A in placental tissue

This ability to change binding partners contributes to the unpredictability of malaria severity, as different PFEMP1 variants can lead to different disease manifestations.