

- During that division, the nucleus of trophozoite divides into a large number of
- nuclei, followed by division of cytoplasm to form thousands of merozoites inside the liver cell.
- The time needed for the pre-erythrocytic schizont (incubation period) to form and the number of merozoites in, it differ according to species of *Plasmodium*.
- The incubation period for *P. vivax* is eight days, *P. malaria* 12 days, *P. ovale* nine days and finally five days for *P. falciparum*.

## **2. Secondary tissue phase**

- At the same time, some of the pre-erythrocytic merozoites invade the red blood cells thus initiating the erythrocytic schizogony.
- In *P. falciparum*, once pre-erythrocytic merozoites are liberated from the liver
- cells, they invade only the red blood cells and never reinvade the liver, so the relapses are absent in *P. falciparum*.
- The reinvasion of the liver cells in the three benign malaria species is responsible for relapses after apparent cure.

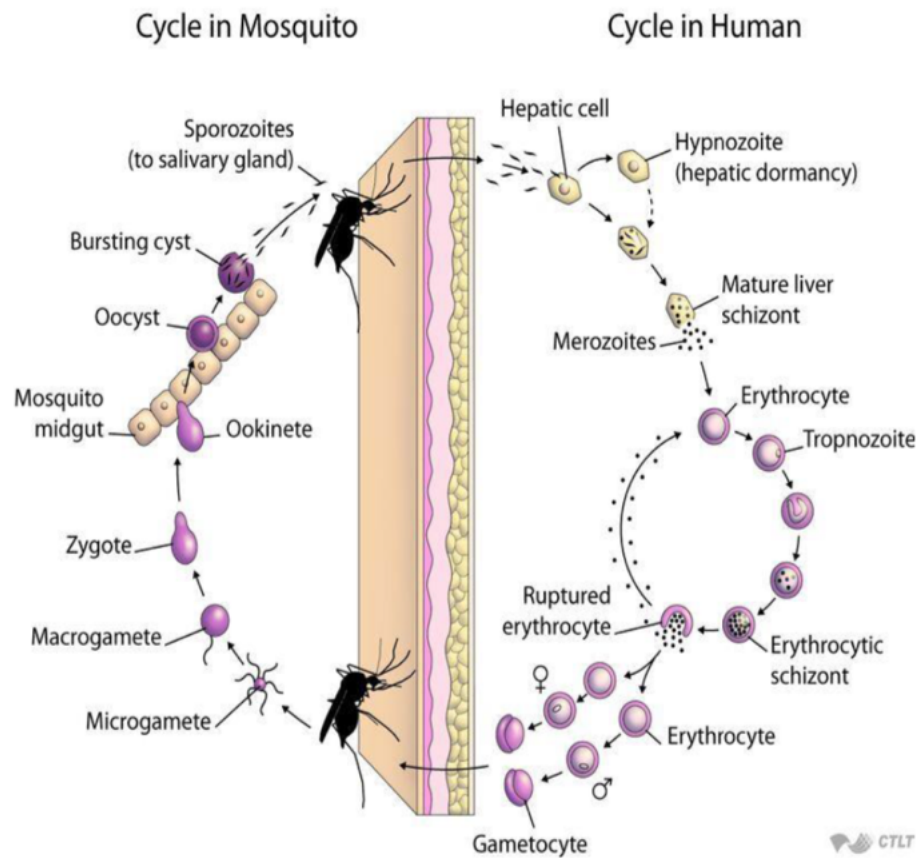
## **3. Erythrocytic Schizogony**

- Merozoites discharged from pre-erythrocytic schizont enter the red cells by invagination of its cell membrane.

- The merozoite is transformed into:
  - 1) Ring stage or young trophozoite
  - 2) Amoeboid stage or old trophozoite, which digests hemoglobin to form the
  - 3) malarial pigments namely **Schuffner's dots in *P. vivax*** and ***P. ovale*, Ziemann's**
  - 4) **dots in *P. malaria*** and **Maurer's dots in *P. falciparum*.**
- The old trophozoite undergoes schizogony to form schizont stage containing merozoites. The liberated merozoites invade new red blood cells, repeating the cycle. Rupture of erythrocytic schizonts release haematin pigments and parasite toxins, which responsible for fever and sweating.
- When the schizonts rupture, fever and other symptoms take place, and this reoccurs every third day, and thus the fever is **called tertian fever**, and the disease is **called benign tertian malaria**.
- In *P. falciparum*, the **fever is irregular**, it may be tertian, quatrain or even continuous.
- After completing few schizogony cycles, some merozoites develop into male microgametocytes and female macrogametocytes.
- All erythrocytic stages of *Plasmodium* are found in peripheral blood, except trophozoites and **schizonts of *P. falciparum*, which are trapped in blood vessels of internal organ.**

#### 4. The Sexual cycle (Sporogony)

- This occurs inside the insect which is an anopheline mosquito. When it sucks a blood meal of a patient containing all stages and the gametocytes, all stages of malaria are digested in the insect mid-gut except the gametocytes.
- The male microgametocyte nucleus divides into 4-8 fragments, to form finally the microgametes.
- The female macrogametocyte throws two polar bodies to reduce its chromatin before the fertilization occurs.
- After fertilization by fusion of the macro and micro gametes, the zygote is formed.
- The zygote throws out pseudopodia to form a motile stage called Ookinete.
- Ookinete penetrates the mucous membrane of gut, to settle beneath it, which is called oocyst.
- Its nucleus divides many times to produce fine spindle shaped called sporozoites.
- The oocyst ruptures and sporozoites are free to migrate to the salivary glands, they pass with saliva into human body while the mosquito is taking a blood meal.



### Pathogenesis]

Three organs show gross pathological lesions namely the liver, the spleen and bone marrow. Liver shows necrosis and enlargement, spleen may enlarge and tender, bone marrow becomes vascular, chocolate brown due to deposition of pigment.

- In *P. falciparum*, the disease is characterized by its common malignant features, due to:
  1. Agglomeration of parasitized and non-parasitized red blood cells inside capillaries of the internal organs, this causes plugging of the human capillaries, and causes thrombosis and sometimes hemorrhages

2. In chronic malignant malaria, rapid intravascular haemolysis occurs, leads to passage of dark urine due to presence of haemosiderin, which called "**black water fever**".

### [Diagnosis]

- Clinical symptoms and signs such as fever, sweating, enlarged and tender spleen and liver, and Jaundice may occur.
- Direct methods such as thin and thick blood film.
- Serological test.

### [Prevention and control]

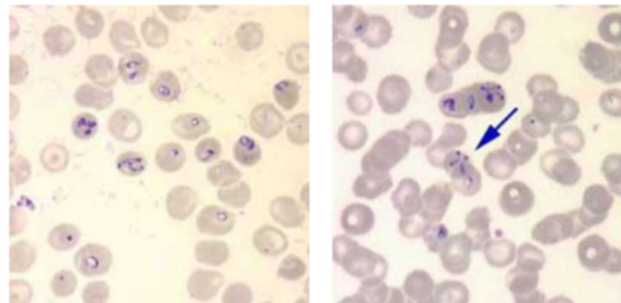
- Treatment of patients.
  - control the *Anopheles* mosquitoes, adults and larvae
1. **Transmission:** - naturally acquired infections are via the bite of infected female *Anopheles* mosquitoes. Malaria is also transmitted via blood transfusion, sharing of contaminated needles among IV drug abusers, and congenital transmission also has been documented.
  2. **Immunity:** - incomplete immunity follows infection. Some persons get reinfected over and over.
    - a. **Sickle cell trait:** - the malaria parasite is not successful at utilizing the "S" haemoglobin. This trait does not confer immunity to infection, but does offer resistance to infection.
    - b. **Duffy factor** :- represents the "portal of entry" antigen for

*P. vivax*. Persons without the factor are immune to this species (but not the others).

**Pathology/Pathogenesis:**

1. **Prodromal stage** :- a time period which can include premonitory symptoms such as headache, myalgia, anorexia & nausea prior to the paroxysm.
2. **Paroxysm**: - period of chills & fever followed by profuse sweating.

**A. Babesia:-**



*Babesia sp. rings in red blood cells*

*Babesia sp. "maltese cross" (arrow)*

Babesia are intraerythrocytic sporozoan parasites that morphologically resemble *plasmodium* and cause tickborne malaria like illness in domestic and wild animals. It causes opportunistic infection in humans.

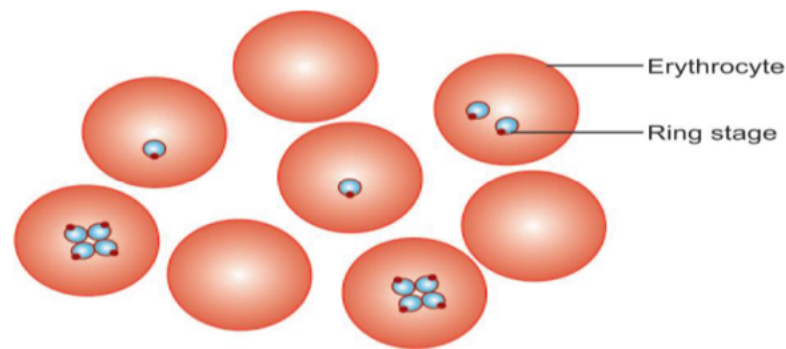
**Habitat**

The parasite is present in erythrocytes and resembles the ring stage of *P. falciparum*.

**Morphology:****Morphology**

Trophozoites are pleomorphic 2–5  $\mu\text{m}$  in diameter found inside the red cells. The shape may be pyriform, amoeboid, or spindle-like, usually in pairs and are often mistaken as ring form of *Plasmodium*. Merozoites may be spherical or oval or pyriform bodies, found in pairs.

**Disease name:** - babesiosis, piroplasmosis. “Piro” from “pyro”- Latin for “fire”. Because the disease is fever (fire) inducing. The “piroplasms” are a group of fever-inducing organisms or infections. Malaria is a piroplasm also.

**Life Cycle**

**Definitive host:** *Ixodid* ticks.

**Intermediate host:** Man or other mammals.

**Infective form:** Sporozoites are the infective form for humans.

**Mode of Transmission:** Infection in vertebrate occurs through bite of the nymphal stage of *Ixodid* ticks.

Incubation period is 1–6 weeks Babasiosis can also be transmitted via blood transfusion. Transovarian transmission in ticks also occurs.

In their life cycle, merogony takes place in vertebrate hosts and sporogony in the invertebrates.

Man acquires infection by bite of the infected ticks  
**(definitive host).**

Sporozoites present in the salivary glands of tick are introduced in man or other mammals **(intermediate host).**

Sporozoites change to trophozoites in the circulation, which then invade the RBCs and multiply asexually by binary fission or schizogony to form 4 or more trophozoites. Newly formed trophozoites are released by rupturing erythrocytes and invade new erythrocytes.

Some of the sporozoites grow slowly inside red cells and become folded like an accordion. These are thought be gametocytes.

Female ticks become infected by feeding the host blood.

In the digestive tract of tick, the gametocytes multiply sexually and later migrate to the salivary glands where they divide by multiple fission into smaller forms known as ‘**vermecules**’.

Vermecules undergo secondary schizogony to produce sporozoites, which are the infective forms for human.

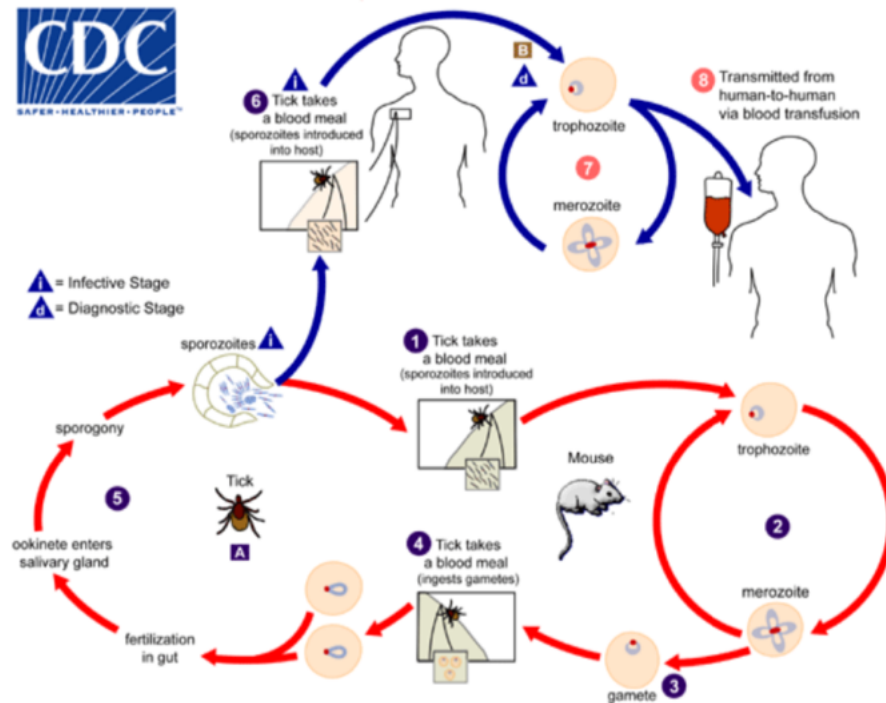
### **Pathogenecity and Clinical Features**



Hemolysis of the infected erythrocytes is primarily responsible for many clinical manifestations.

There is accumulation of parasites in the capillaries of liver, spleen, and kidneys which leads to cellular degeneration and necrosis.

In acute disease, there is malaise, fatigue, fever, myalgia, arthralgia, dry cough and anorexia. Fever exceeds 38°C and can reach 40.6°C accompanied by chill and sweat.



### Diagnosis:

Molecular techniques, including qPCR on EDTA blood  
Serological testing, microscopic examination for blood film

### Prevention:

Avoidance of known tick areas, particularly during “tick seasons”, use of an effective anti-tick product and daily checking for/effective removal of ticks may help reduce the risk of disease transmission.

## Differences between the human species of plasmodium

	Plasmodium vivax	Plasmodium malariae	Plasmodium falciparum	Plasmodium ovule
1. Geographical distribution	Tropical and temperate region. Very common.	Tropical and temperate region. Not very common.	Tropical region. Very common.	West Africa and South America.
2. Age of erythrocytes preferred	Young	Old	All ages	Unknown
3. No. of parasites per cubic mm. of blood.	20-40,000	5-10,000	50-1,00,000	-
4. Trophozoite	Ring like form is large and grows into a highly amoeboid form with prominent vacuoles.	Ring like form is large and grows into a slightly amoeboid band like form with inconspicuous vacuoles.	Ring like form is rather small and grows into a compact amoeboid form. There may be 2 or more parasites in one erythrocyte.	Ring like form is large and grows into amoeboid form.
5. Schizont	Large than a normal erythrocyte.	Slightly smaller than a normal erythrocyte.	Much smaller than a normal erythrocyte.	Smaller than a normal erythrocyte.
6. Infected erythrocyte	Becomes enlarged and frequently distorted.	Does not enlarge.	Does not enlarge may get slightly distorted.	Becomes enlarged and oval.
7. Haematin	Light brown in fine granules evenly	Dark brown in coarse granules	Dark in one or two solid masses.	Light brown scattered.