Parasitology
Blood & tissue sporozoa

Lec -5-

2nd stage

Toxoplasma

- ***Toxoplasma gondii***, causes of toxoplasmosis, which is an obligate intracellular sporozoan.
- It differs from ***Plasmodium*** in that both sexual and asexual reproductive cycles occur within the gastrointestinal tract of felines (the definitive host) and the disease is transmitted to other host species by the ingestion of **oocysts** passed in the feces of infected felines.
- **General properties:**
- The parasite is a crescent or banana shape ,the nucleus is sub-terminal.
- The major morphologic forms of the parasite are the **tachyzoite**, **tissue cyst** & **oocyst.**
- **All parasite stages are infectious**.
- The definitive host is the **domestic cat** and other felines; humans and other mammals are **intermediate hosts**.

- **Epidemiology:**
- Human infections are found in every region of the globe.
- In general, the incidence is higher in the tropics and lower in cold regions.
- **Transmission:**
- Transmission of Toxoplasma is by three ways :

1- Congenital : from mothers to their fetus during pregnancy(tachyzoite).

2- Ingestion of contaminated food and water with sporulated oocysts from cat feces

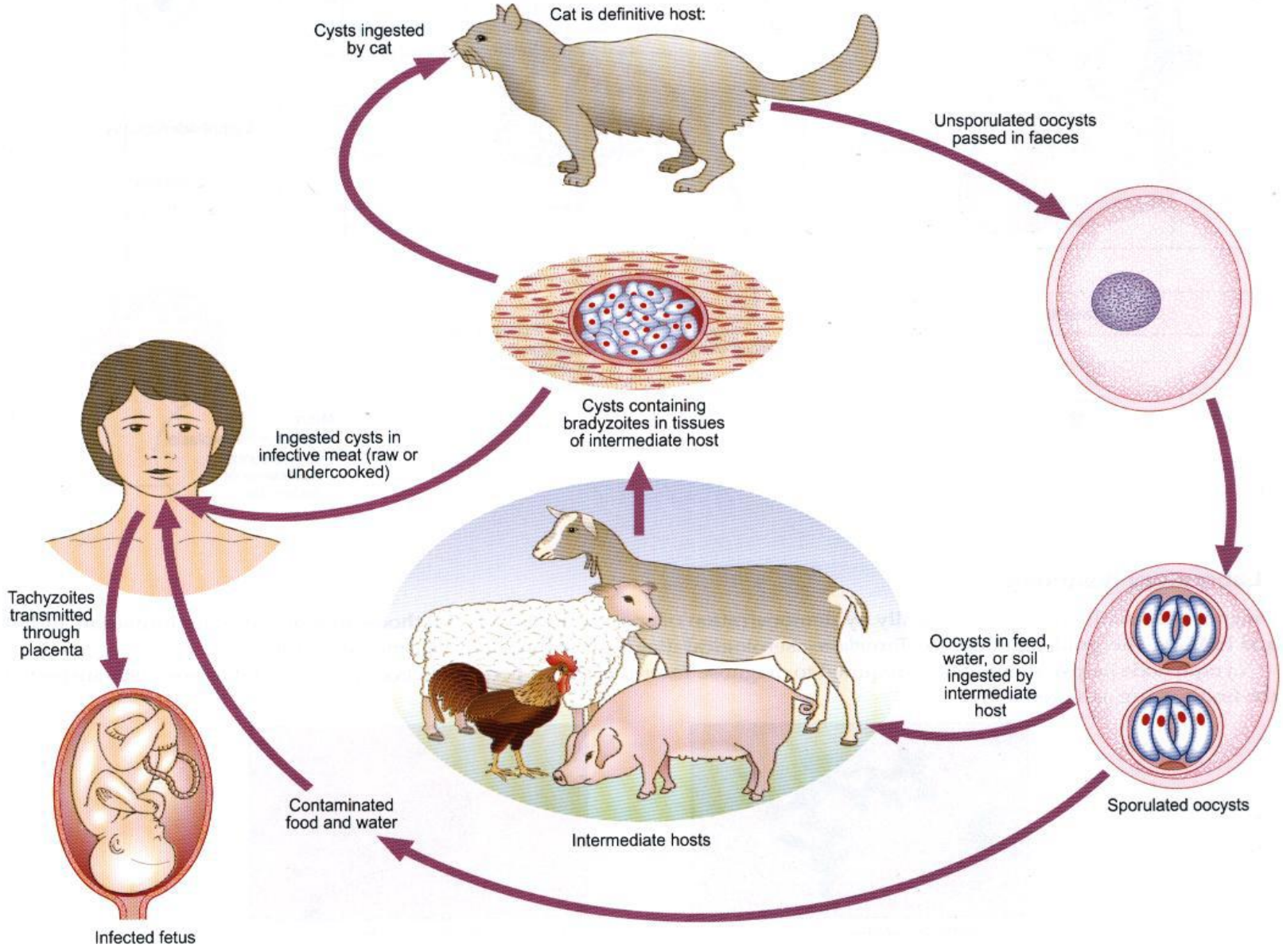
3. Ingestion of bradyzoites (tissue cysts) in infective meat(row or undercooked meat) are common mode of transmission.

Toxoplasma

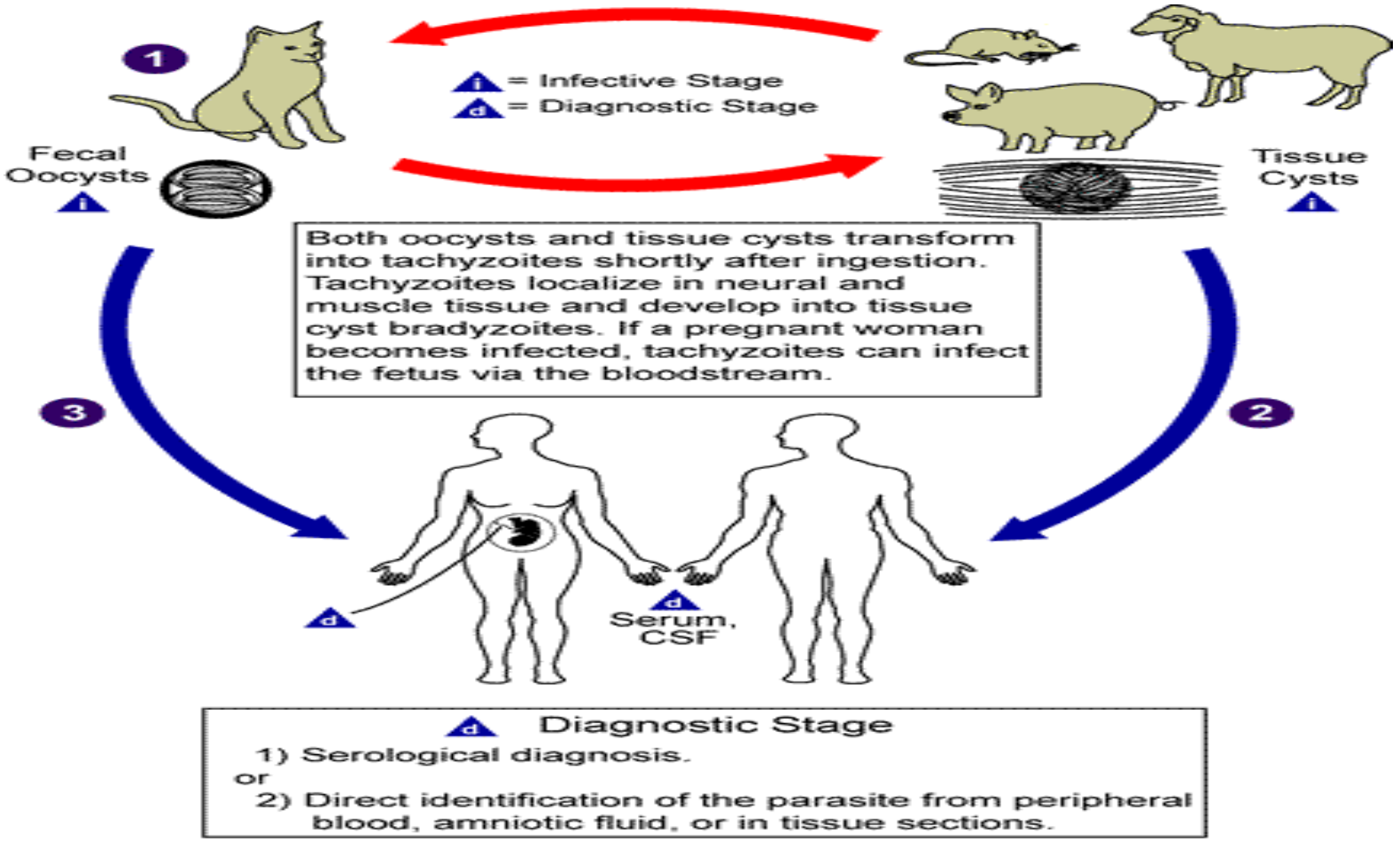
- **Life cycle in definitive host**
- Sexual reproduction of *T. gondii* occurs only in the intestinal tract of felines, most commonly in the domestic cat.
- Ingested parasites enter the epithelial cells of the ileum.
- Intracellularly, the **trophozoites** reside within a membrane-bound vacuole and undergo schizogony.
- With cell rupture, **merozoites** are released.
- The **merozoites** infect adjacent epithelial cells; they then repeat another asexual cycle or eventually differentiate into **gametocytes**, initiating sexual reproduction.
- Fusion of the mature male and female gametes leads to the formation of an oval, thick-walled **oocyst** that is then shed in the feces.

Toxoplasma

- **Life cycle in intermediate hosts:**
- After ingestion by a susceptible animal or human, sporozoites are released from the disrupted oocyst.
- In the small intestine, the cysts rupture and release forms that invade the gut wall, where they are ingested by macrophages and differentiate into rapidly multiplying (**tachyzoites**), which kill the cells and infect other cells.
- Tachyzoites enter host cells in the brain, muscle, and other tissues, where they develop into cysts in which the parasites multiply slowly. These forms are called **bradyzoites** .


Cysts ingested by cat
Cat is definitive host:
Unsporulated oocysts passed in faeces
Cysts containing bradyzoites in tissues of intermediate host
Ingested cysts in infective meat (raw or undercooked)
Tachyzoites transmitted through placenta
Infected fetus
Oocysts in feed, water, or soil ingested by intermediate host
Sporulated oocysts
Contaminated food and water
Intermediate hosts

Toxoplasma



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Toxoplasma

- The term "**tachyzoite**" refers to the asexual proliferative forms responsible for cell invasion and clinical disease, but they are not infective on ingestion but transmitted from mothers to their fetus through placenta.
- **Tissue cyst**: The contained organisms, referred to as **bradyzoites**, are similar to tachyzoites, but are smaller and divide more slowly. like oocysts, are infectious to the animal that ingests them.
- The **oocyst** is ovoid, and possesses a thick wall that makes it resistant to most environmental challenges. This form is responsible for the spread of the parasites from felines to other animals and human via the fecal–oral route

Toxoplasma

- **<u>Clinical disease & clinical finding:</u>**
- *Toxoplasma gondii* causes toxoplasmosis.
- Symptomatic toxoplasmosis may be classified as acute, subacute, chronic, or congenital.
- Most primary infections in **immunocompetent patients** are asymptomatic or produce a Mild, and nonspecific illness.

Toxoplasma

- **Clinical disease & clinical finding:**

1. The most common symptoms of acute toxoplasmosis are painful, swollen, lymph glands frequently accompanied by fever, headache, anemia, muscle pain, and sometimes pulmonary complications.

2. **Congenital toxoplasmosis** can result in abortion, stillbirth, or neonatal disease with encephalitis, chorioretinitis, and hepatosplenomegaly. Fever, jaundice, and intracranial calcifications are also seen.

Most infected newborns are asymptomatic, but chorioretinitis or mental retardation will develop in some children months or years later.

3. In the **immunocompromised host**, toxoplasmosis is a serious, often fatal disease.

(e.g., AIDS patients), life-threatening disseminated disease, primarily encephalitis, occurs

Toxoplasma

- **<u>Laboratory diagnosis:</u>**
- Serologic procedures are the primary method of diagnosis.
- For the diagnosis of acute and congenital infections, an immunofluorescence assay for **IgM antibody** is used.

Toxoplasma

- **Treatment:**
- Acute toxoplasmosis in an immunocompetent individual is usually self-limited.
- Congenital toxoplasmosis, whether symptomatic or asymptomatic and disseminated disease in immunocompromised patients should be treated with a combination of **sulfadiazine** and **pyrimethamine**.

Toxoplasma

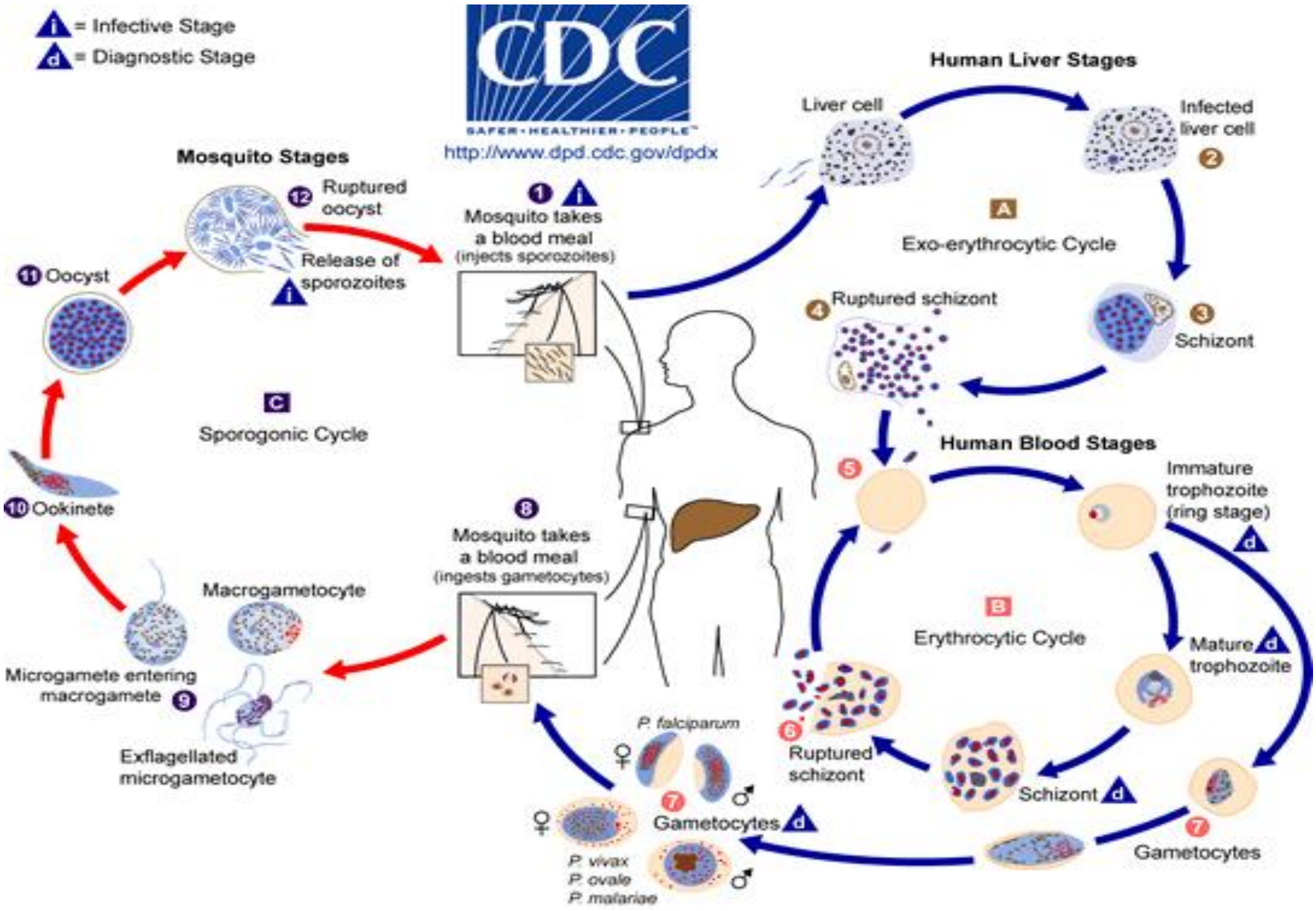
- **Prevention:**
- The most effective means of preventing toxoplasmosis is to cook meat thoroughly to kill the cysts. Pregnant women should be especially careful to avoid undercooked meat and contact with cats.
- Cysts in meat can be destroyed by proper cooking (56°C for 15 minutes) or by freezing to –20°C.
- Drinking water from lakes and rivers should be boiled.

Plasmodium

- The vector and definitive host for plasmodia is the **female *Anopheles* mosquito** (only the female takes a blood meal).
- There are two phases in the life cycle: the **sexual cycle**, which occurs primarily in mosquitoes, and the **asexual cycle**, which occurs in humans, the intermediate hosts.
- The sexual cycle is called **sporogony** because sporozoites are produced.
- Asexual cycle is called **schizogony** because schizonts are made.

- **Distribution:** Malaria is endemic in over 100 countries in the tropics and subtropics and was also formerly present in many temperate regions, including United States and Europe.

- **Transmission:** Females of over 60 species of mosquitoes of the genus Anopheles are the vectors of *Plasmodium*, Human infection commences when sporozoites are injected along with mosquito saliva during blood feeding.


i = Infective Stage
d = Diagnostic Stage
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Human Liver Stages
Liver cell
Infected liver cell
2
A
Exo-erythrocytic Cycle
3
Schizont
4
Ruptured schizont
Human Blood Stages
5
Immature trophozoite (ring stage)
d
Mature trophozoite
d
B
Erythrocytic Cycle
6
Ruptured schizont
Schizont
d
7
Gametocytes
Gametocytes
d
P. falciparum
P. vivax
P. ovale
P. malariae
8
Mosquito takes a blood meal (ingests gametocytes)
Macrogametocyte
Microgamete entering macrogamete
9
Exflagellated microgametocyte
10
Ookinete
11
Oocyst
12
Ruptured oocyst
Release of sporozoites
Mosquito Stages
1
Mosquito takes a blood meal (injects sporozoites)
C
Sporogonic Cycle

Plasmodium

- **Life cycle:**
- The life cycle in humans begins with the introduction of sporozoites into the blood from the saliva of the biting mosquito.

➢ **Exo-erythrocytic cycle in human:**

- The sporozoites enter the circulatory system and are carried to the liver, where penetrate hepatocytes.
- Over the next 6-14 days, each parasite, now a trophozoite, grow and divides into numerous merozoites, which form a cluster (schizoint) within an infected cell.

Plasmodium

- **Life cycle:**

➢ **Erythrocytic cycle in human:**

- Merozoites are released from the liver cells and infect red blood cells. During the erythrocytic phase, the organism differentiates into a ring-shaped trophozoite.
- The ring form grows into an ameboid form and then differentiates into a schizont filled with merozoites. After release, the merozoites infect other erythrocytes. This cycle in the red blood cell repeats at regular intervals typical for each species.
- The periodic release of merozoites causes the typical recurrent symptoms of chills, fever, and sweats seen in malaria patients.

Plasmodium

- **Life cycle:**
- The sexual cycle begins in the human red blood cells when some merozoites develop into male and others into female gametocytes. The gametocyte-containing red blood cells are ingested by the female *Anopheles* mosquito.

Plasmodium

- **Life cycle in mosquito:**
- The gametocyte-containing red blood cells are ingested by the female *Anopheles* mosquito and, within her gut, produce **a female macrogamete** and eight sperm like **male microgametes**.
- After fertilization, the diploid zygote differentiates into a motile **ookinete** that burrows into the gut wall, where it grows into an **oocyst** within which many haploid **sporozoites** are produced.
- The sporozoites are released and migrate to the salivary glands, ready to complete the cycle when the mosquito takes her next blood meal.

Plasmodium

- **Pathogenesis:**
- Ten to fourteen days after the erythrocytic cycle begins, the parasite numbers reach a density that induces the onset of symptoms.. Fever, chills, diarrhea, headache, and sometimes pulmonary and cardiac symptoms are typical.

Plasmodium

- **Pathogenesis:**

a. **Fever.** The pathogenesis of fever in malaria is unclear. Fever coincides with red blood cell lysis, and is likely to be caused by the release of interleukin-1 (IL-1) and tumor necrosis factor-alpha (TNF-α) by macrophages activated during the processing of red blood cell debris.

- In the early stages of infection, the febrile episodes are irregularly timed because red blood cells are lysed almost.
- with time, the erythrocytic asexual cycle becomes synchronous and periodic febrile episodes become obvious, coinciding with the lysis of infected red blood cells.
- The periodicity is **48 hours** for *P. falciparum*, *P. vivax* and *P. ovale* infections (tertian malaria) and 72 hours for *P. malariae* infection (quartan malaria) continuously .

Plasmodium

- **Pathogenesis:**

b. Anemia: Destruction of erythrocytes leads to anemia and enlargement of the liver and spleen

- **Massive hemoglobinuria (blackwater fever):** a consequence of intravascular hemolysis, can lead to acute tubular necrosis and renal failure

c. Cerebral malaria. Occur In *P. falciparum* malaria, late stage schizonts elaborate proteins that are expressed on the erythrocyte surface. The proteins promote aggregation to other non-infected erythrocytes and adhesion to capillary endothelial cells, constricting capillary blood flow and causing anoxia, ischemia and numerous small hemorrhages. When this happens in the brain, it can be rapidly fatal, depending on the extent of the ischemic lesions.

Plasmodium

- **Clinical disease:**
- Malaria is caused by four plasmodia species:
- *Plasmodium vivax*,
- *Plasmodium ovale*,
- *Plasmodium malariae, and*
- *Plasmodium falciparum.*
- Worldwide, malaria is one of the most common infectious diseases and a leading cause of death.

Plasmodium

- **Clinical disease:**

➢ Malaria presents with abrupt onset of **fever** and chills, accompanied by headache, myalgia, and arthralgia, about 2 weeks after the mosquito bite. The fever spike, which can reach 41°C, is frequently accompanied by shaking chills, nausea, vomiting, and abdominal pain.

➢ **Splenomegaly** and **hepatomegaly** are seen in most patients,.

- **Anemia** is prominent.
- Untreated malaria caused by ***P. falciparum*** is potentially life-threatening as a result of extensive brain (cerebral malaria) and kidney (black water fever) damage.
- However, relapses of ***P. vivax*** and ***P. ovale*** malaria can occur up to several years after the initial illness as a result of hypnozoites latent in the liver.

Plasmodium

- **Laboratory diagnosis:**

➢ Diagnosis rests on **microscopic examination** of blood, using both **thick** and **thin** Giemsa-stained smears.

- The thick smear is used to screen for the presence of organisms, and the thin smear is used for species identification.
- **Ring-shaped trophozoites** can be seen within infected red blood cells.
- The gametocytes of *P. falciparum* are **crescent-shaped** ("banana-shaped"), whereas those of the other plasmodia are spherical .

➢ If blood smears do not reveal the diagnosis, then a PCR-based test for *Plasmodium* nucleic acids can be useful.

Plasmodium

- **Treatment:**
- The complete treatment of malaria requires the destruction of three parasitic forms:

➢ the erythrocytic schizont,

➢ the hepatic schizont, and

➢ the erythrocytic gametocyte.

Plasmodium

- **Treatment:**

➢ **Chloroquine** is the drug of choice for acute malaria. Chloroquine kills the merozoites, thereby reducing the parasitemia, but does not affect the hypnozoites of *P. vivax* and *P. ovale* in the liver. These are killed by **primaquine**, which must be used to prevent relapses.

Plasmodium

- **Control & prevention:**

- insecticide spraying, improvements in land drainage, and removal of standing water, particularly in inhabited areas.
- **Chemoprophylaxis** of malaria for travelers to areas where chloroquine-resistant *P. falciparum* is endemic consists of mefloquine or doxycycline. Travelers to areas where the other three plasmodia are found should take chloroquine starting 2 weeks before arrival and continuing for 6 weeks after departure.
- Several **vaccines** are under development.