# *Plasmodium vivax* (Malarial parasite)

## Systematic Position

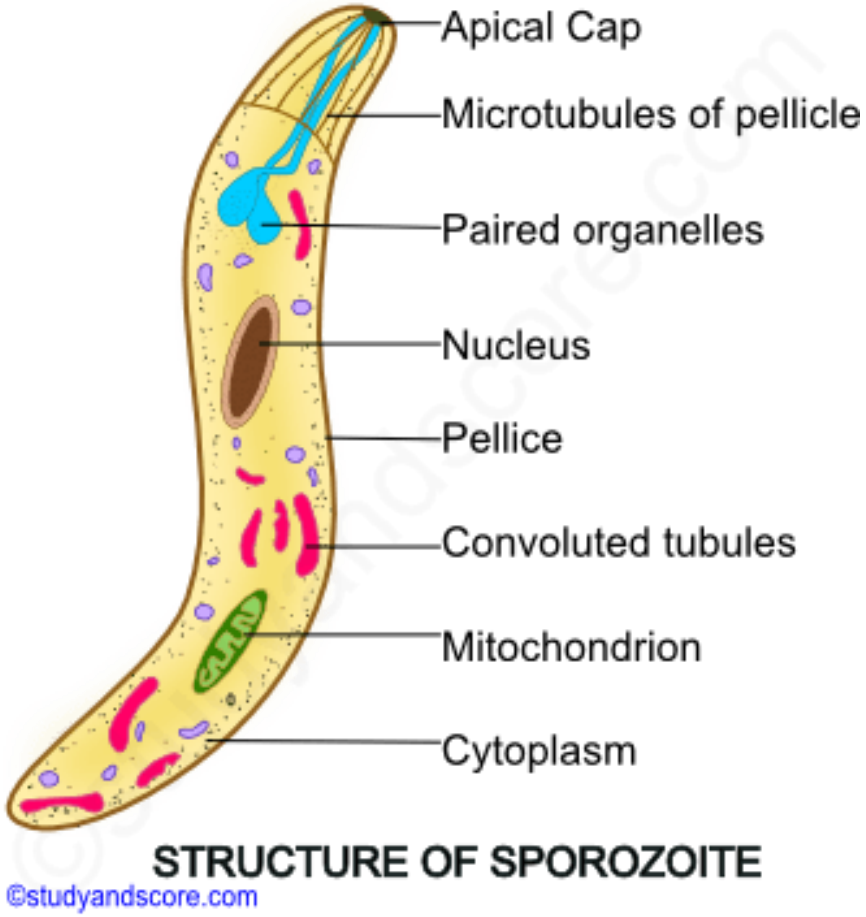
Kingdom: Protista

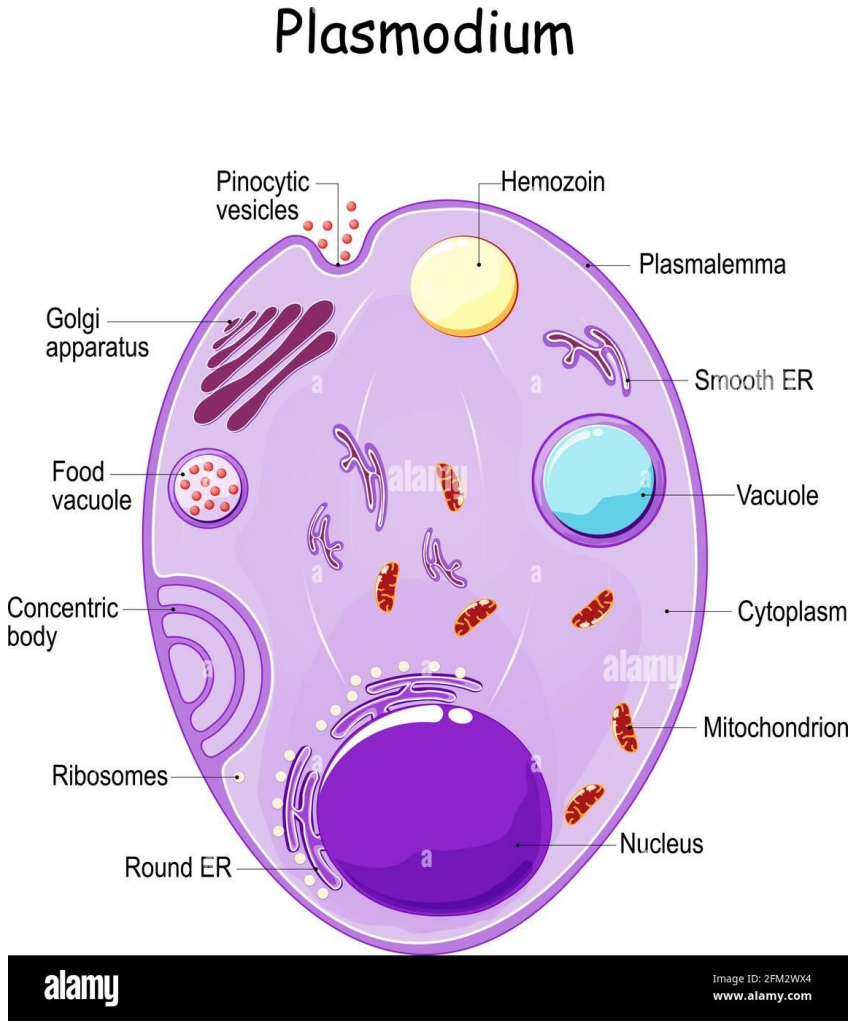
Phylum: Protozoa

Class: Sporozoa

Genus: *Plasmodium*

Species: *vivax*



# *Habit and Habitat*

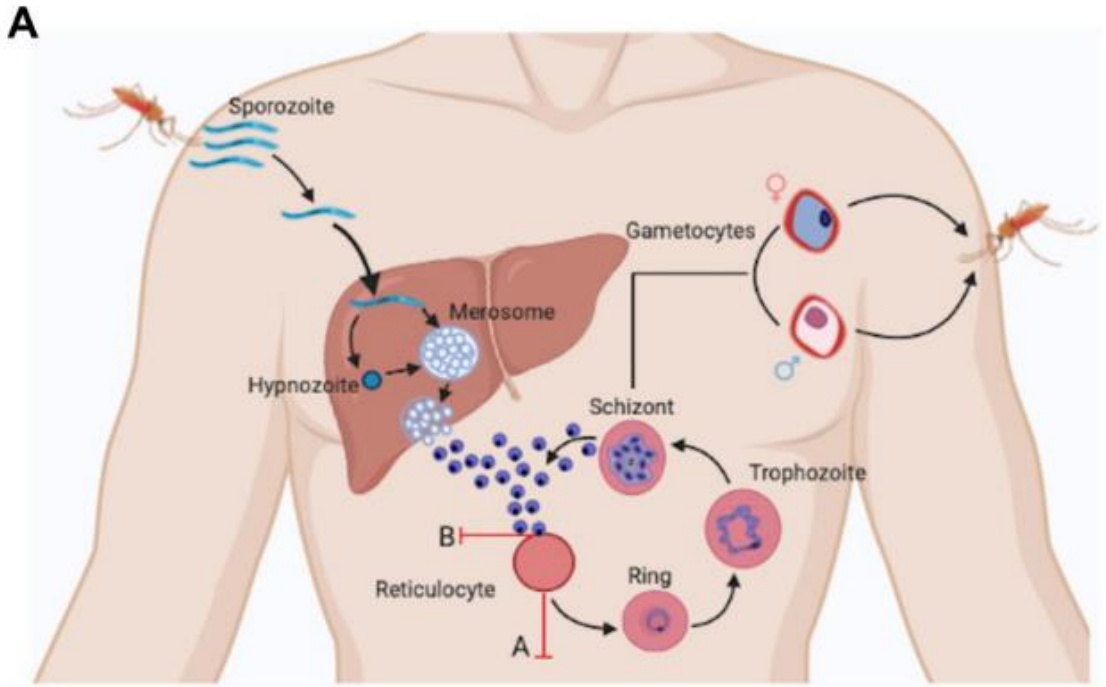
- Intracellular parasite

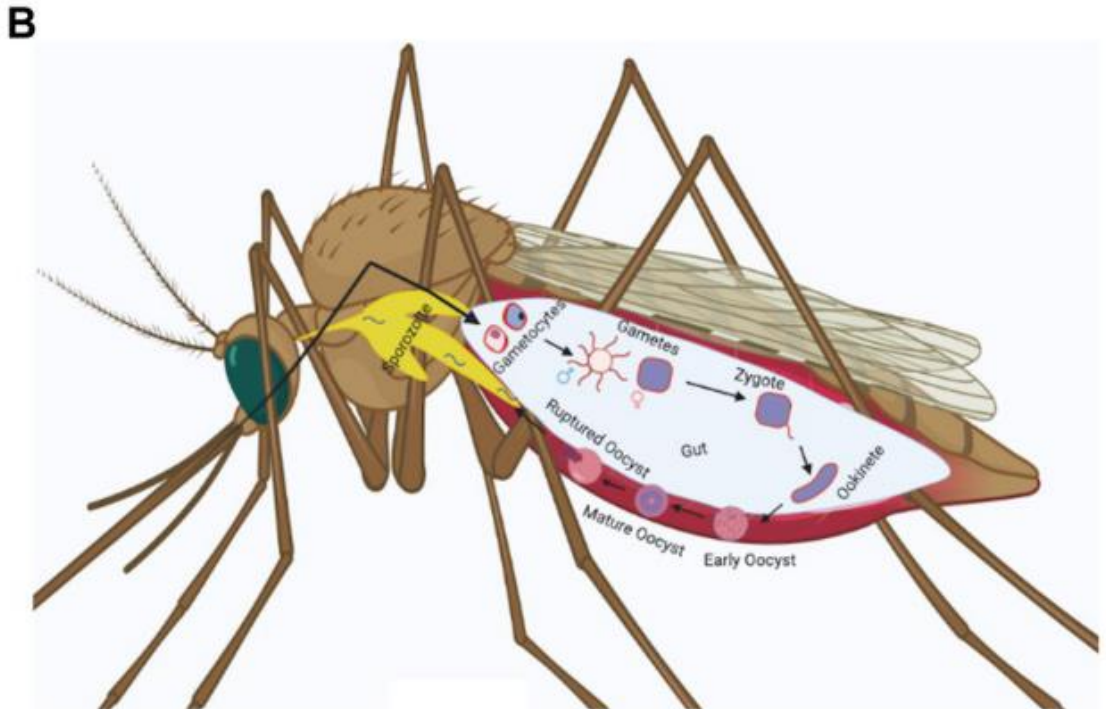
**Habitat:** where does it live?

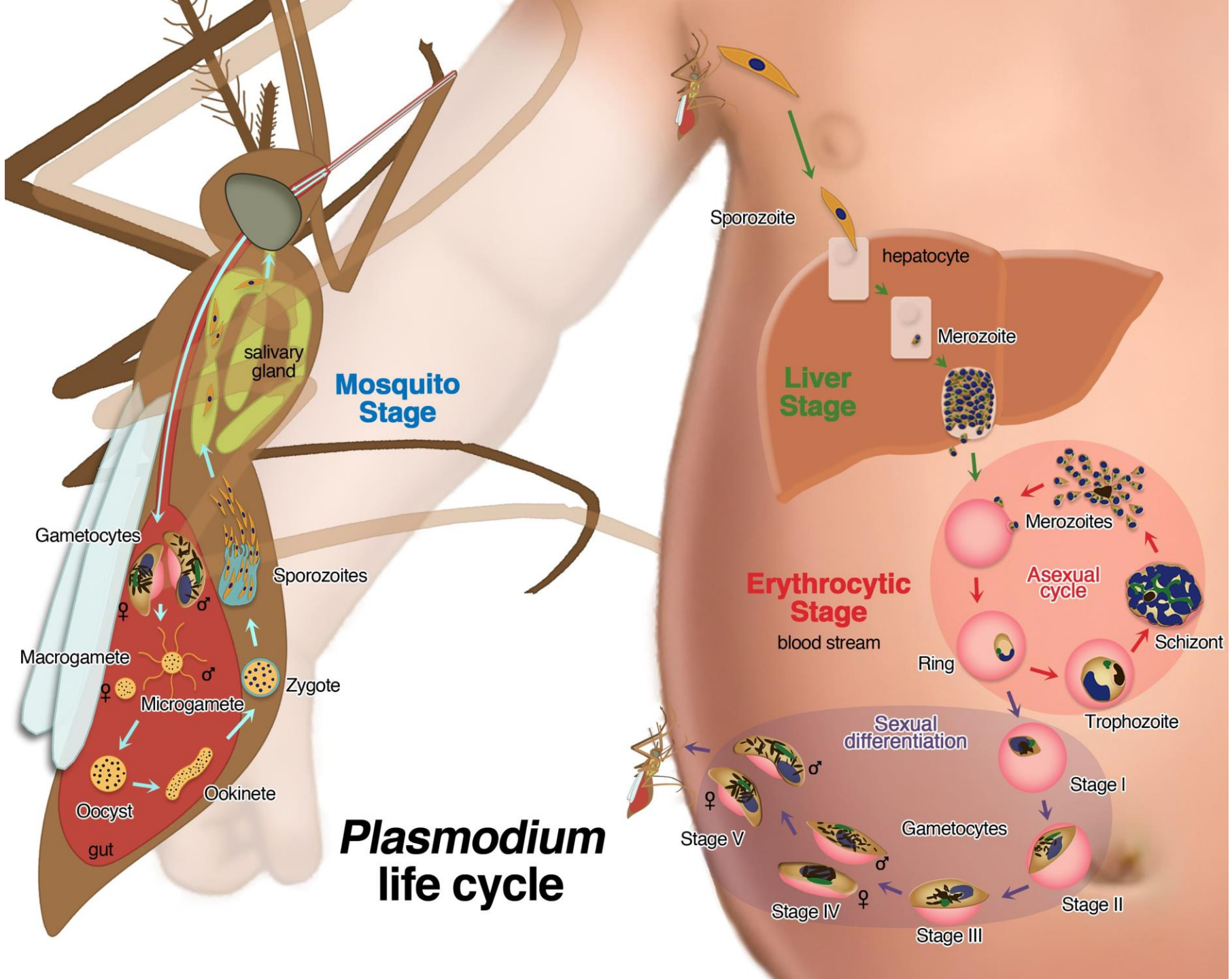
  - Stomach and salivary glands of the female *Anopheles* mosquito
  - Hepatocyte and erythrocyte of the human

**Digenetic pathogen (Two host)**

- Primary host → Female *Anopheles* mosquito, where sexual reproduction occurs
- Secondary host → Human, where sexual reproduction occurs




Sporozoite
hepatocyte
Merozoite
Liver Stage
Mosquito Stage
salivary gland
Gametocytes
Sporozoites
Macrogamete
Microgamete
Zygote
Ookinete
Oocyst
gut
Merozoites
Asexual cycle
Erythrocytic Stage
blood stream
Ring
Schizont
Trophozoite
Sexual differentiation
Stage I
Stage II
Stage III
Stage IV
Stage V
Gametocytes
Plasmodium life cycle

# Morphology and Structure: Polymorphic

**Polymorphic:** The morphology of P. vivax changes significantly during its development, which includes:

a. Sporozoites

b. Trophozoites

c. Schizonts

d. Gametocytes

e. Merozoites

# Sprozoites

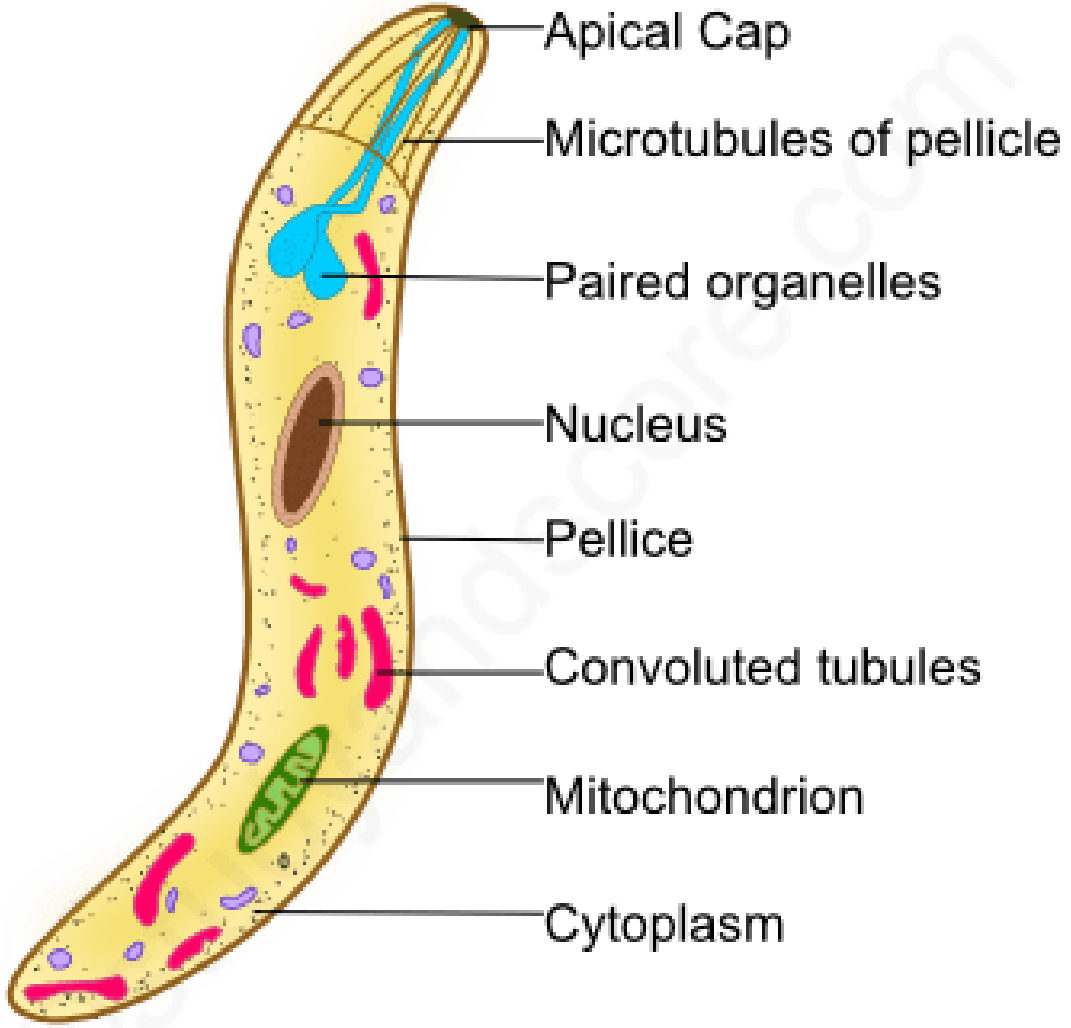
**Shape:** Elongated and spindle-shaped.

- Bounded by elastic pellicle.
- Uninucleate and non vacuolated.
- Infective stage to human.

**Size:** 10–15 µm in length.

**Key Features:**

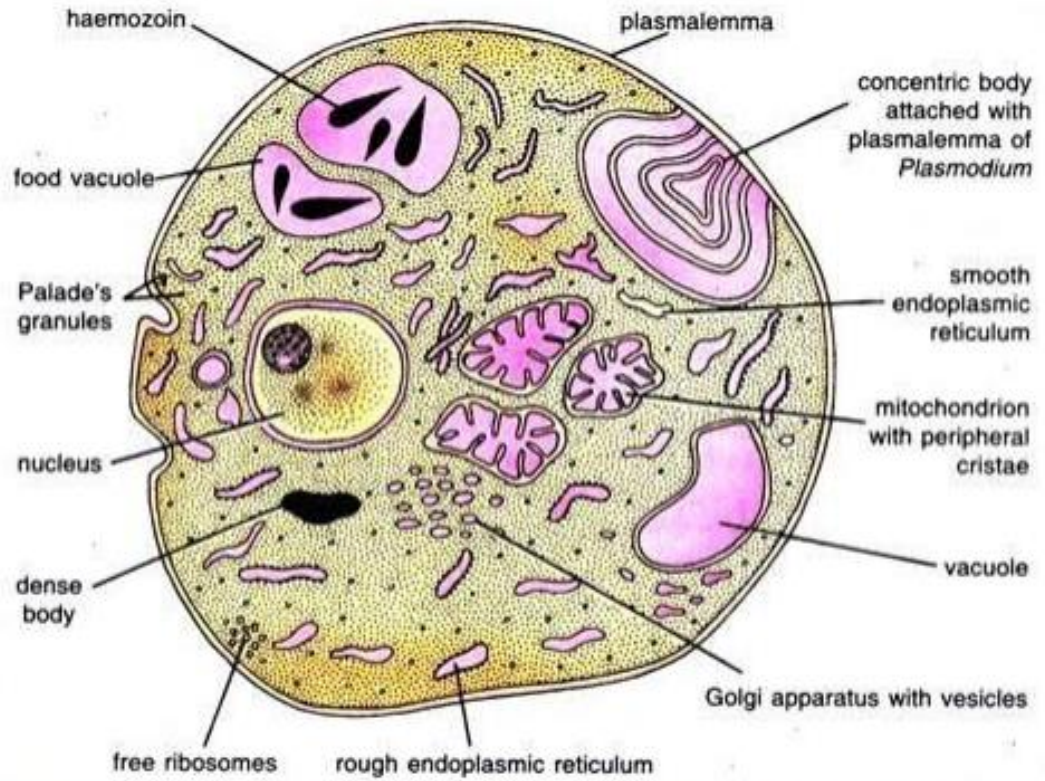
- Pointed anterior end with an apical complex (rhoptries and micronemes) for liver cell invasion.
- Motile (shows wriggling movement) and found in mosquito saliva, injected into humans during a bite, so infective stage for the human.



*P. vivax*

# Trophozoites

- Amoeboid, uninucleated, vacuolated, active feeding stage with granular cytoplasm.
- Located inside RBCs; bounded by double membrane (plasma lemma)
- Cytoplasm contains dense ribonucleoprotein particles
- Golgi body: small vesicles arranged in rows
- Mitochondria: double-membraned with peripheral cristae.
- Concentric body attached to plasma lemma; may serve mitochondrial functions
- Large nucleus with granular/fibrillar nucleoplasm and central nucleolus
- Pinocytotic vacuoles common; act as food vacuoles. Food vacuoles may contain toxic hemozoin.




*Plasmodium*. Ultrastructure of trophozoite in R.B.C. as seen in electron microscope.

# Schizont

- Found in liver and RBCs.

**Immature Schizont:**

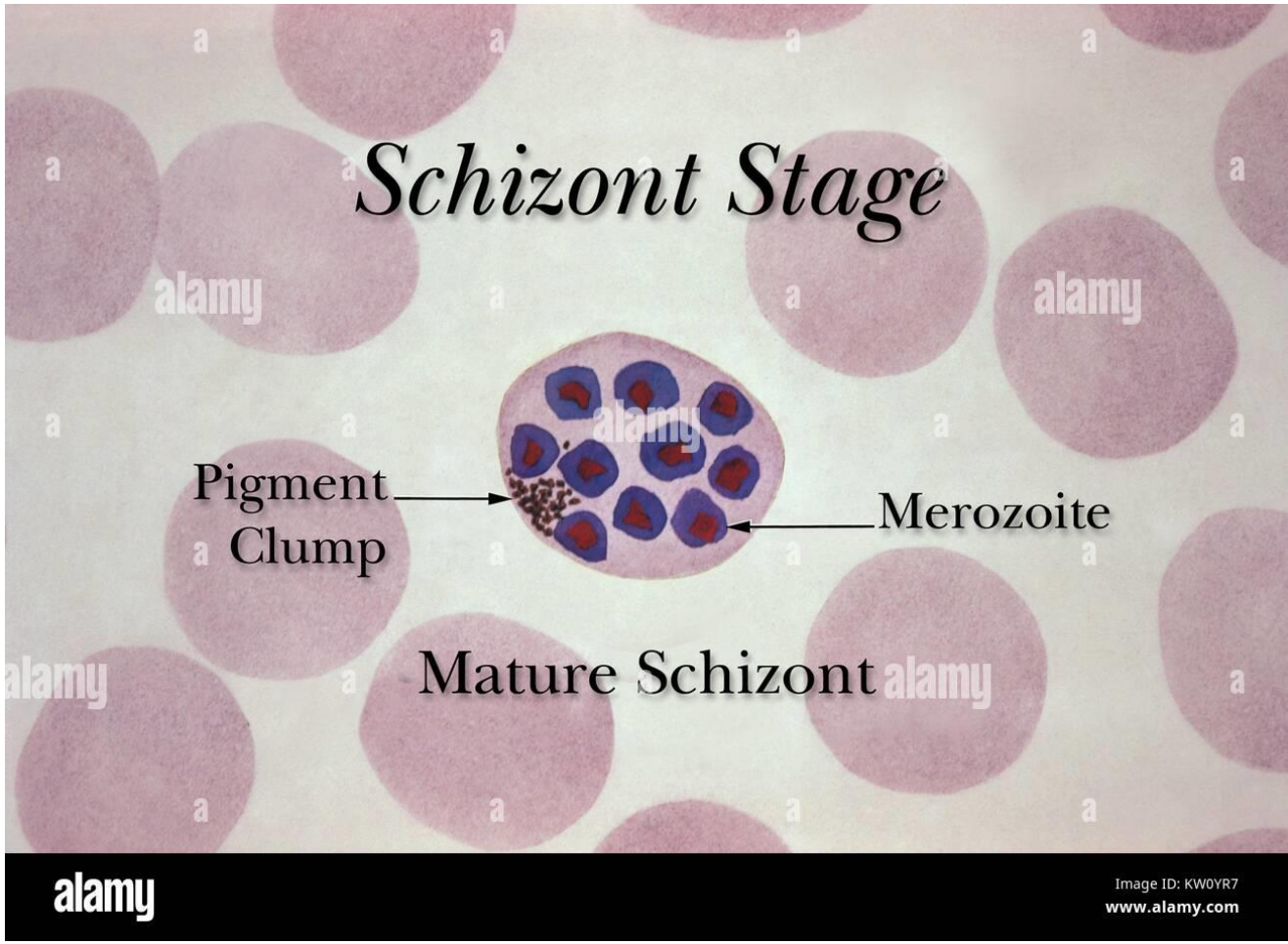
- Cytoplasm grows, and the nucleus begins to divide.

**Mature Schizont:**

- Contains several merozoites arranged loosely in the cytoplasm.

**Key Function:**

- Undergoes the asexual reproduction by multiple fission called **schizogony** to produce multiple merozoites.
- Schizonts rupture to release merozoites into the bloodstream.



*P. vivax*

# Merozoites

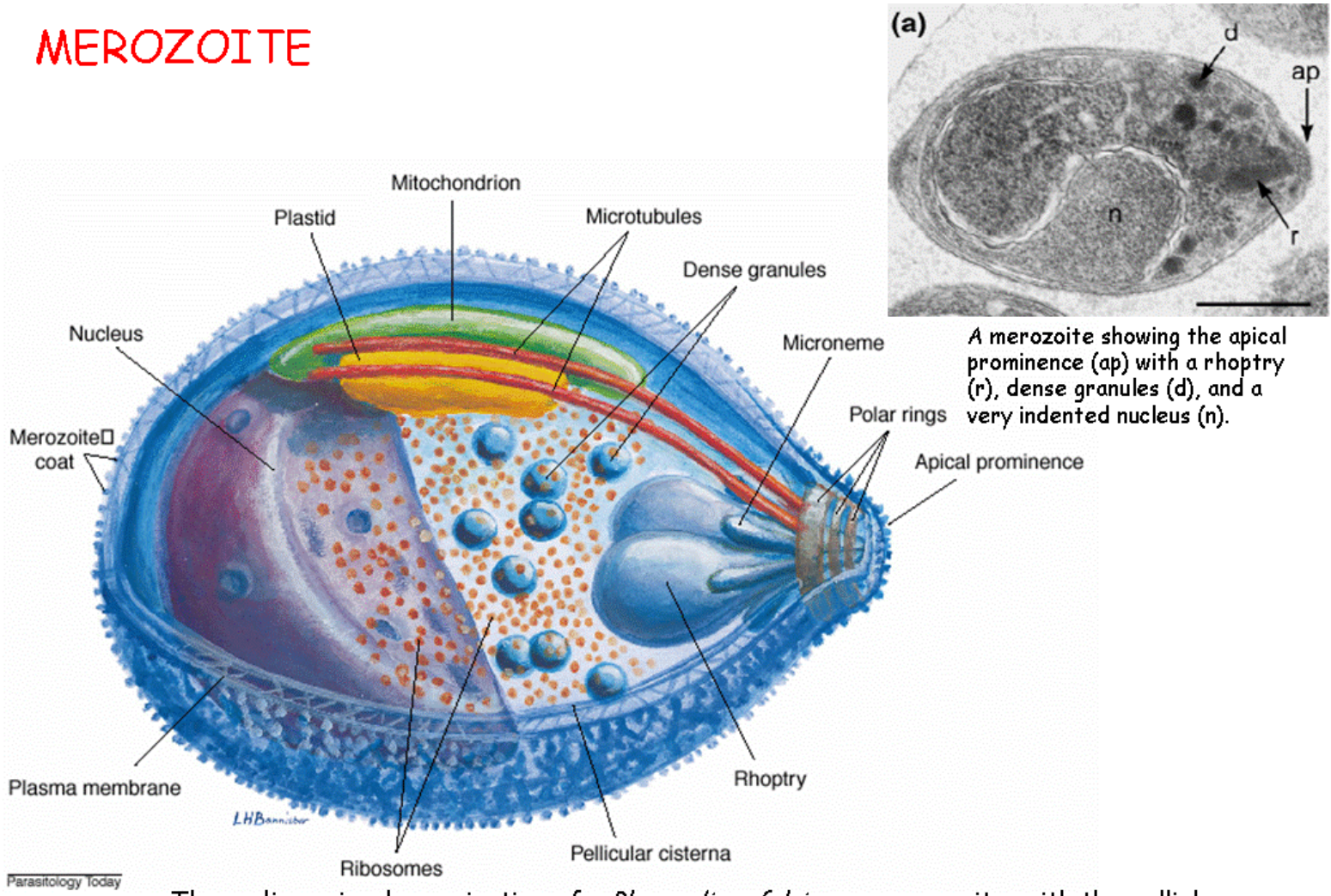
**Shape:** Oval or crescent-shaped.

**Size:** 1–1.5 µm.

**Key Features:**

- Contains an apical complex for RBC invasion.
- Rapidly invades new RBCs to continue the erythrocytic cycle.

**Surface Proteins:** Uses Duffy binding proteins to attach to the Duffy antigen receptor on RBCs.




A merozoite showing the apical prominence (ap) with a rhoptry (r), dense granules (d), and a very indented nucleus (n).

Three-dimensional organization of a *Plasmodium falciparum* merozoite, with the pellicle partly cut away to show the internal structure.

# Gametocyte

**Shape:** Round to oval.

**Male Gametocyte (Microgametocyte):**

- Smaller and has a diffuse nucleus.
- Numerous in number

**Female Gametocyte (Macrogametocyte):**

- Larger with dense chromatin and granular cytoplasm.
- less in number

**Schüffner's Dots:** Prominent in gametocytes.

**Function:** Taken up by mosquitoes for sexual reproduction.

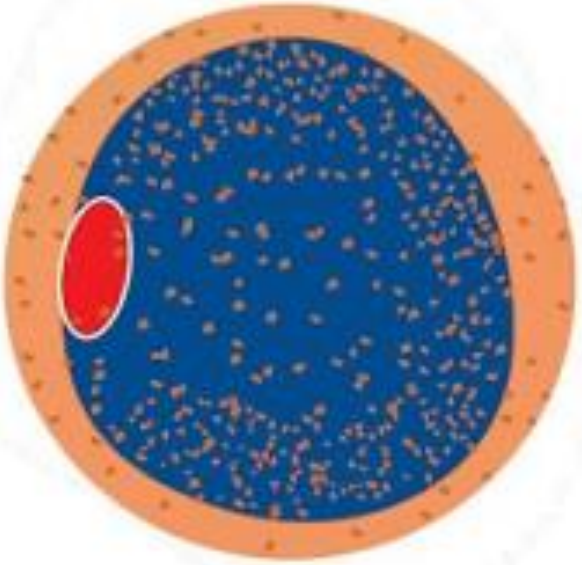


Fig: *Female gametocytes*

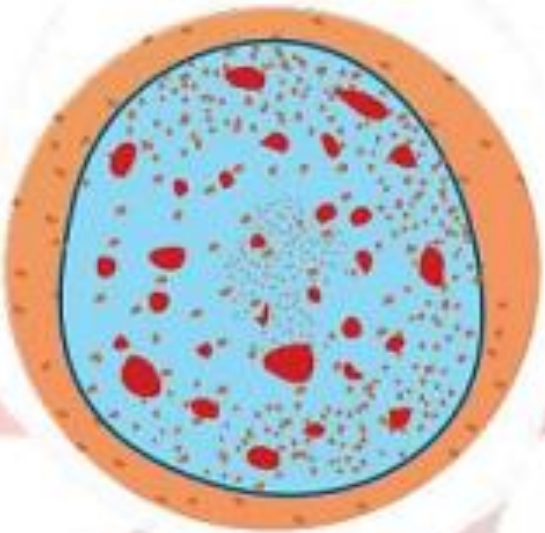


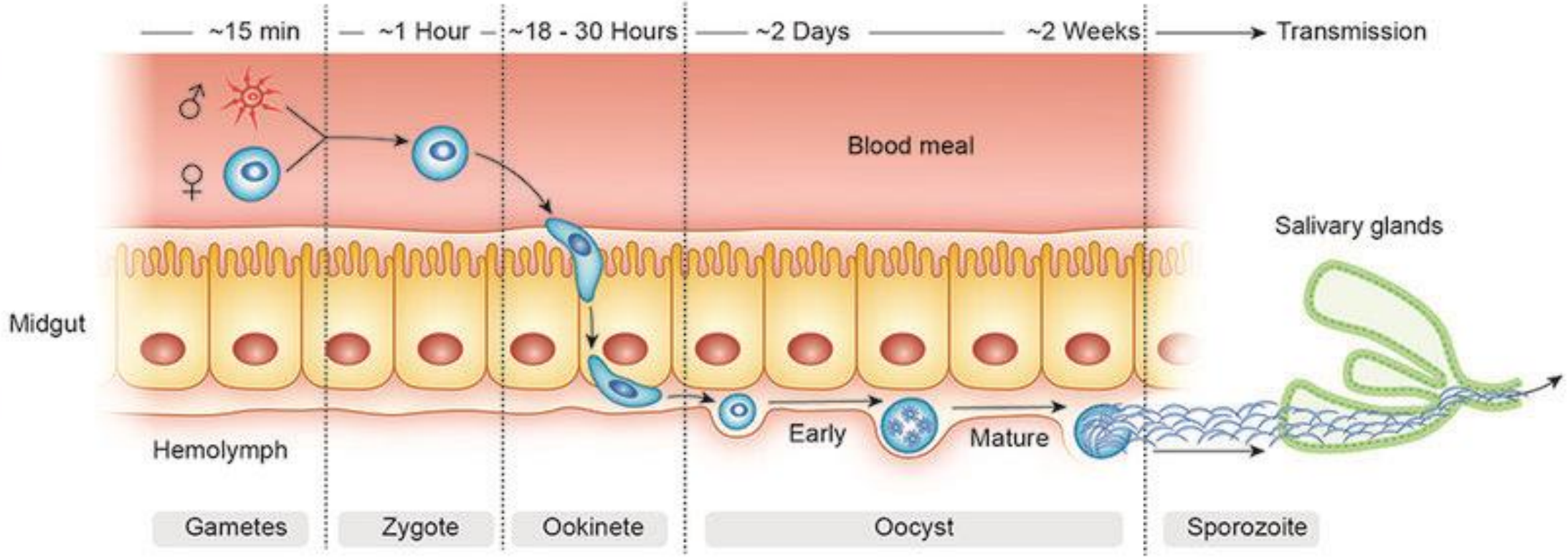
Fig: *Male gametocyte*

# Oocyst in mosquito

**Shape:** Spherical structure bounded by cyst wall.

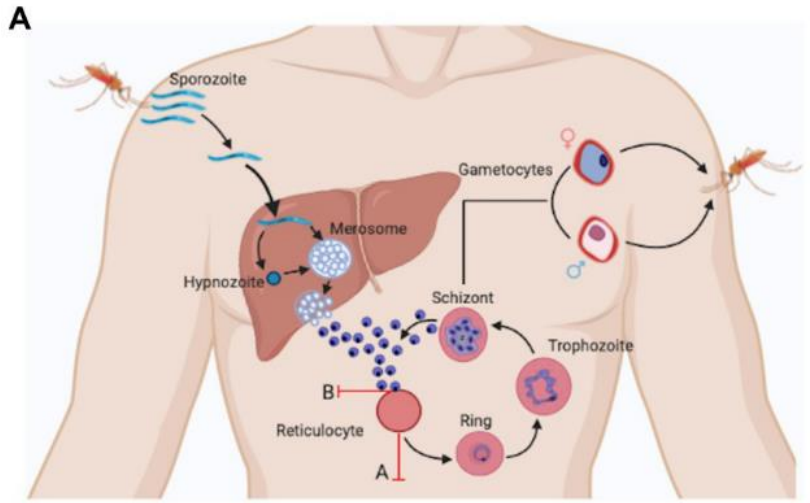
**Location:** Found on the mosquito's midgut wall.

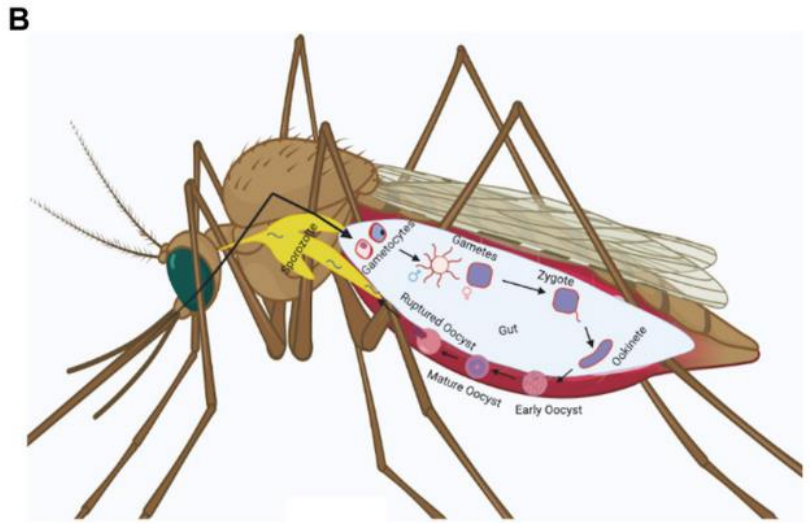
**Function:** Produces thousands of sporozoites, which migrate to the salivary glands.

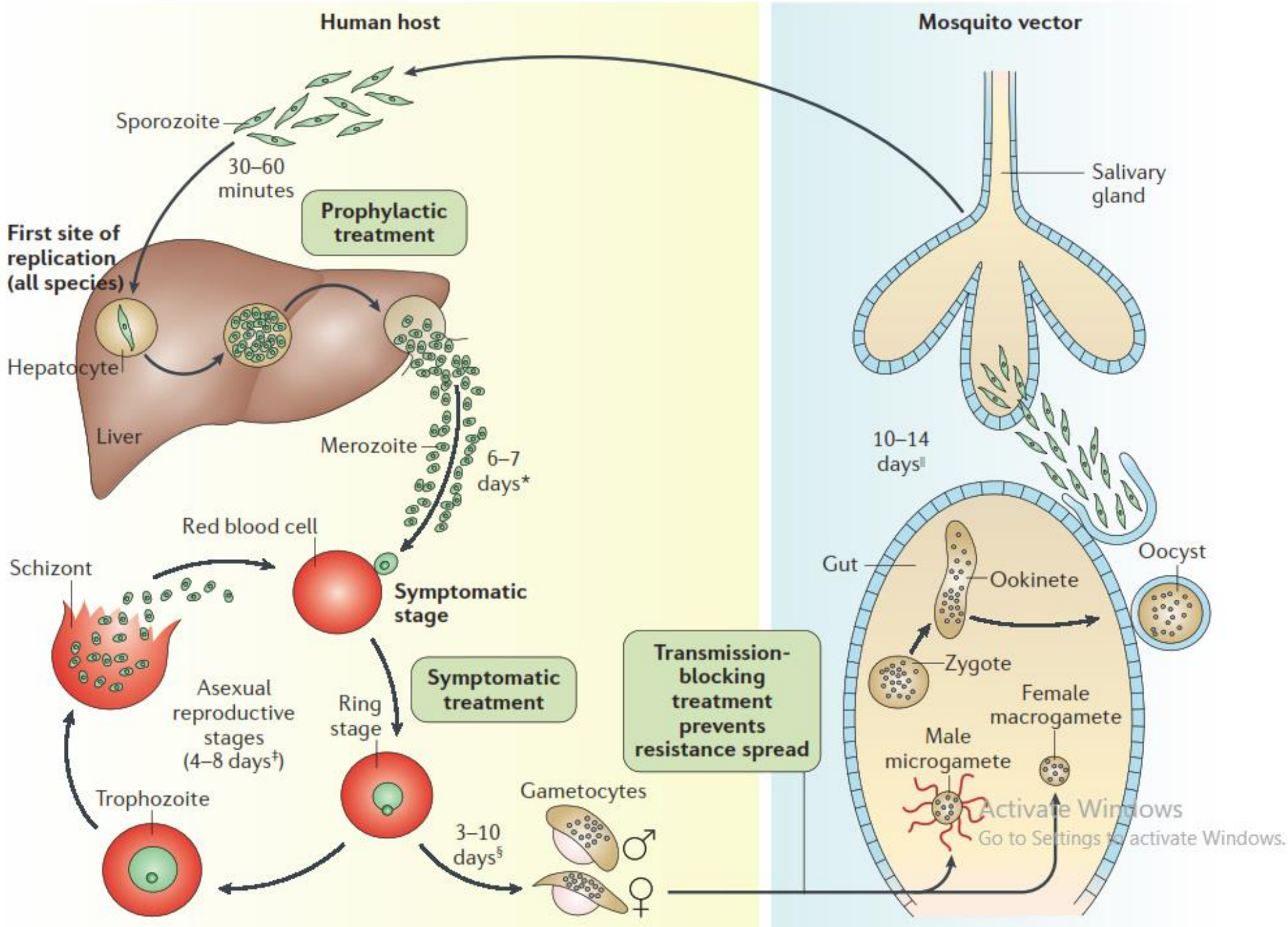


# Life cycle

- Plasmodium is the digenetic parasite i. e. they complete their life cycle in two hosts:
  - **Primary or definitive host:** Female *Anopheles* mosquito
  - **Secondary or intermediate host:** Human
- Life cycle of Plasmodium vivax is divided into three phases:
  - Schizogony: Asexual reproductive phase of multiple fission in liver cells and RBCs of humans.
  - Gamogony: Sexual reproductive phase in stomach of mosquito.
  - Sporogony: Formation of sporozoites in the wall of stomach of mosquito through multiple fission.




Human host
Mosquito vector
Sporozoite
30–60 minutes
Prophylactic treatment
First site of replication (all species)
Hepatocyte
Liver
Merozoite
6–7 days*
Red blood cell
Schizont
Symptomatic stage
Symptomatic treatment
Asexual reproductive stages (4–8 days‡)
Ring stage
Trophozoite
Gametocytes
3–10 days§
Transmission-blocking treatment prevents resistance spread
Salivary gland
10–14 days‖
Gut
Ookinete
Oocyst
Zygote
Female macrogamete
Male microgamete
Activate Windows
Go to Settings to activate Windows.

# A. Asexual cycle or Schizogony in man

## 1. Entry of sporozoites into human body: Inoculation

- The asexual cycle of *Plasmodium* begins when an infected female *Anopheles* mosquito bites a healthy human to suck blood.
- During the bite, the mosquito injects salivary fluid containing sporozoites into the wound through its needle-like mouthparts; this process is termed inoculation..
- The saliva also contains anticoagulants that prevent blood clotting to facilitate the blood sucking.

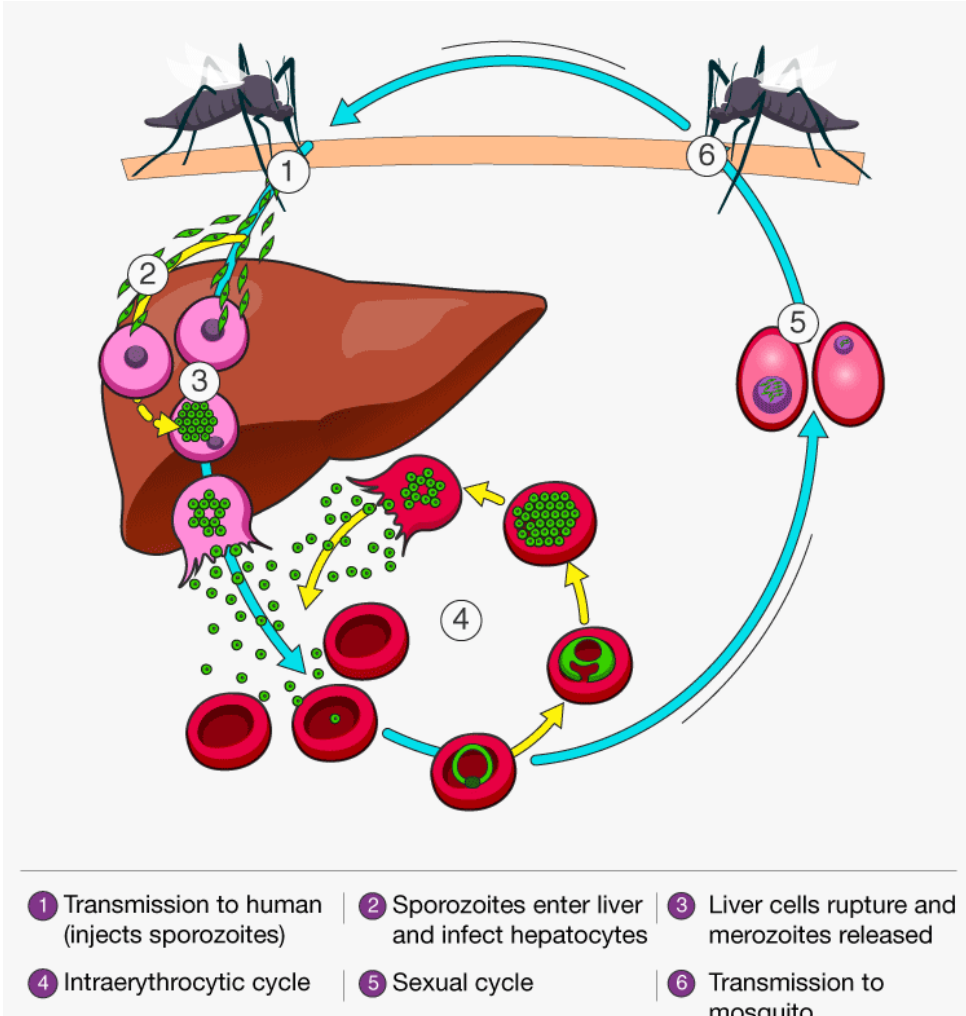
## 2. Invasion of liver cells

- Within 30 minutes, the sickle-shaped **sporozoites** leave the bloodstream and enter the **parenchymatous cells of the liver (hepatocytes)**.
- The **apical cap** of the sporozoite, along with **lytic enzymes secreted by rhoptries**, facilitates the penetration into liver cells.
- This marks the **beginning of the asexual life cycle** in the human host.

# A. Asexual cycle or Schizogony in man.....

- It occurs in human liver cells (liver schizogony) and in RBC (erythrocytic schizogony)
- Asexual cycle or schizogony in human is completed in following phases:

1. Pre-erythrocytic cycle (1st liver schizogony)
2. Exo-erythrocytic cycle (2nd liver schizogony)
3. Erythrocytic cycle
4. Post-erythrocytic cycle
5. Formation of gametocytes

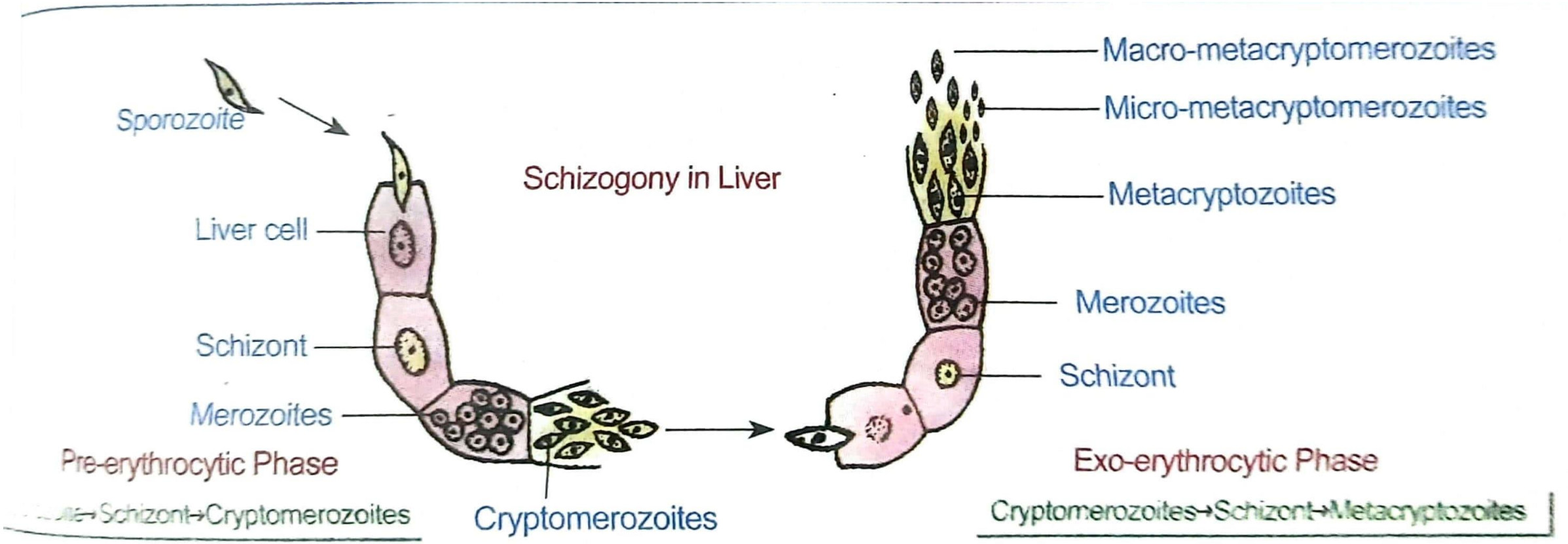


# 1. Pre-erythrocytic Cycle (1st liver schizogony)

- A single **sporozoite** enters one liver cell and grows into an amoeboid, spherical structure called a **schizont**.
- The **schizont undergoes multiple fission** (schizogony) to form numerous spindle-shaped merozoites.
- The host liver cells rupture, so merozoites are liberated in the sinusoids (spaces in the liver filled with blood) of the liver. These liberated merozoites are called **cryptomerozoites.**
- This entire process is known as **pre-erythrocytic schizogony** and it is completed within **8 to 10 days**.
- The cryptomerozoites released from liver cells may invade new liver cells, thereby initiating the exo-erythrocytic cycle (2nd liver schizogony).

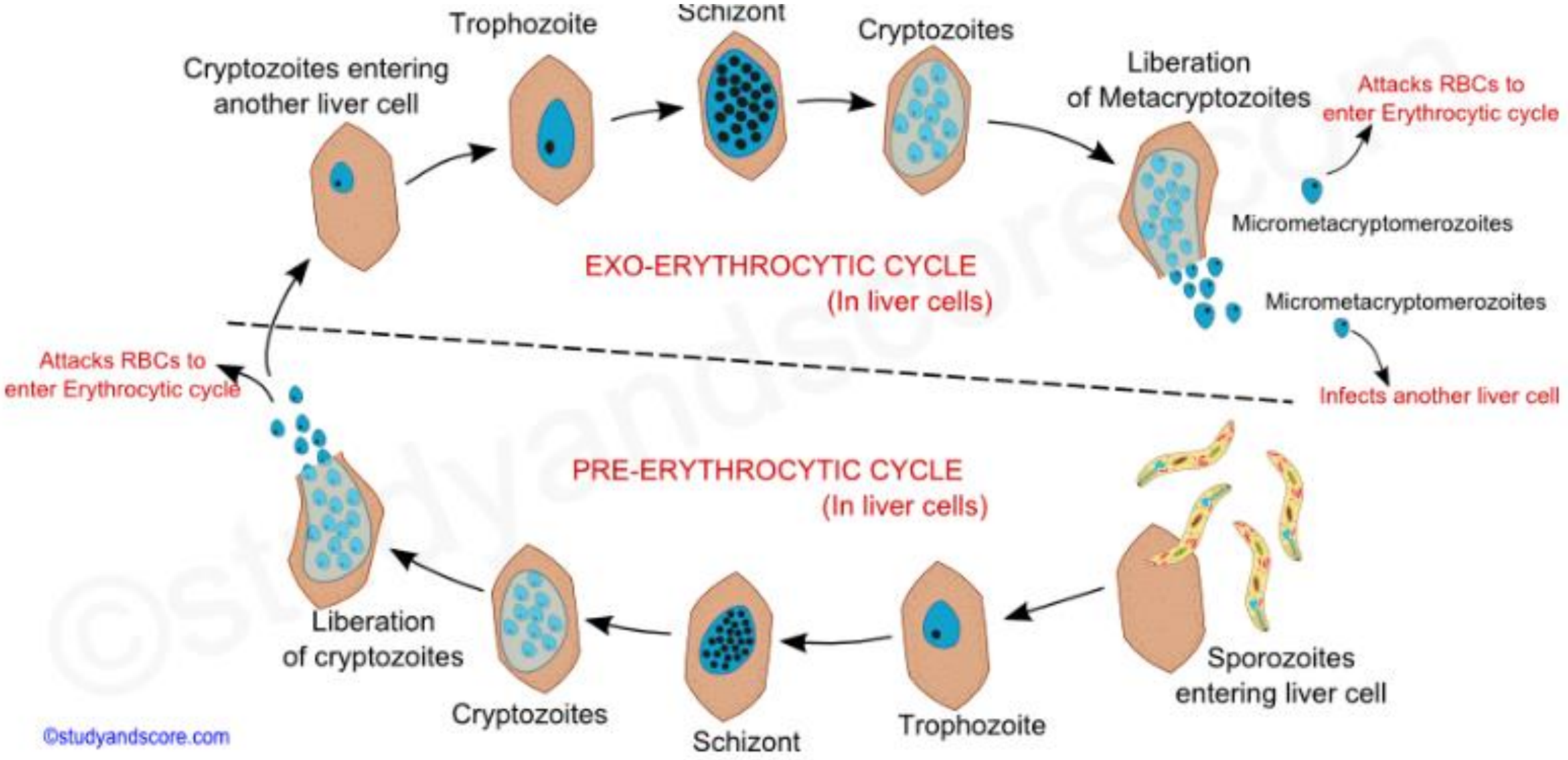
*P. vivax*

# 1. Pre-erythrocytic Cycle (1st liver schizogony)....



*P. vivax*

# 1. Pre-erythrocytic Cycle (1st liver schizogony)....



# 2. Exo-erythrocytic cycle (2nd liver schizogony)

- After completing pre-erythrocytic schizogony, the cryptomerozoites invade new liver cells (hepatocytes).
- Inside these new liver cells, the cryptomerozoites feed on cytoplasm and grow into schizonts again.
- The newly formed schizonts divide by multiple fission to produce the second generation of merozoites, called **metacryptomerozoites**, which are of two types:
  - **Micro-metacryptomerozoites** are small and numerous which invade red blood cells and initiate the erythrocytic cycle.
  - **Macro-metacryptomerozoites** are larger and fewer which reinfect liver cells to continue the exo-erythrocytic cycle, forming a reservoir of infection.
- This second phase of asexual reproduction in the liver is termed the **exo-erythrocytic schizogony** and it is completed in **10-12 days.**

# 3. Erythrocytic cycle

- This cycle starts when the micro-metacryptozoites enter into erythrocytes.
- Single micro-metacryptozoite enters into single RBC and passes through:

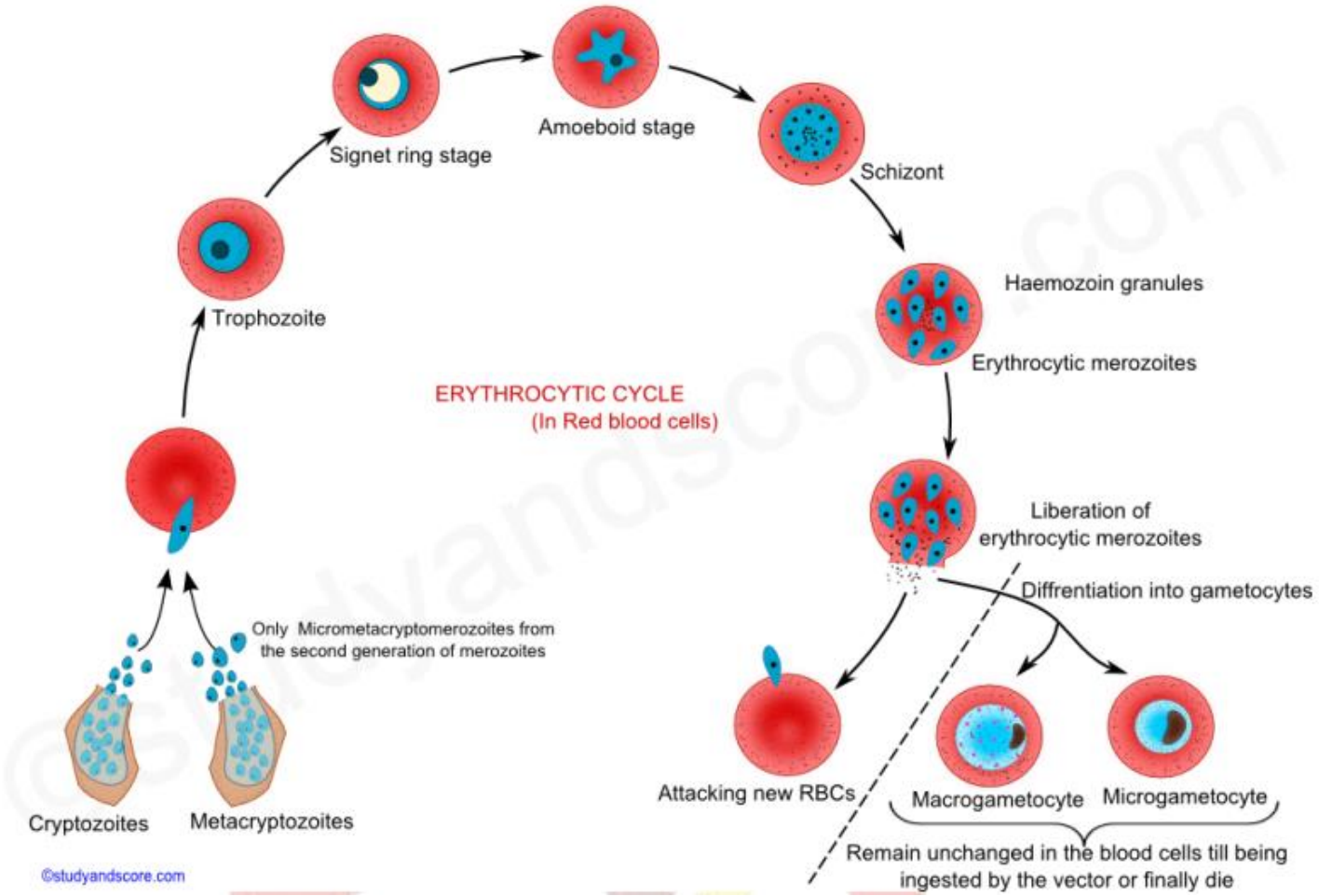
  a. Trophozoite stage,

  b. Signet ring stage,

  c. Amoeboid stage,

  d. Schizont stage and

  e. Rosette stage



# 3. Erythrocytic cycle….

- When miro-metacryptomerozoites invade the RBC it becomes rounded with large nucleus and grows in size by ingesting hemoglobin of corpuscles. This stage of parasite is called **trophozoite stage.**
- Inside the trophozoite, a large non-contractile vacuole appears which pushes the nucleus towards periphery and forms a ring like structure known as **signet ring stage.**
- Trophozoites enlarges and vacuole starts disappearing and develops pseudopodial processes in the cytoplasm and changed into **amoeboid stage.**
- The amoeboid feeds on and breakdown hemoglobin into hematin and globin.
- The globin is absorbed by the cell and hematin is deposited in the form of **hemozoin** (toxic malarial pigment).

## 3. Erythrocytic cycle....

- The amoeboid trophozoites after feeding, becomes rounded, grows in size and becomes **erythrocytic schizont.**
- Asexual multiplication by multiple fission takes place in schizont and forms numerous merozoites and the process is called **erythrocytic schizogony.**
- The merozoites are arranged towards the periphery due to the presence of hemozoin at the center. The arrangement is just like the arrangement of petals in rose flowers. So this stage is called **rosette stage.**
- Merozoites give pressure to the wall of weak RBC and liberated out in the form of erythrocytic merozoites.
- Many merozoites enter the fresh RBC and repeat the erythrocytic cycle.

## 4. Post-erythrocytic cycle

- Sometimes, some merozoites produced after erythrocytic cycle invade the liver cell And undergo another schizogonic development in the liver cell. This is called post-erythrocytic cycle.

# 5. Formation of gametocytes

- After some generation of erythrocytic cycle, some of the merozoites invade the new RBC.
- They grow in size but do not develop into schizonts instead they develop into gametocytes.
- The gametocytes are of two types:

**a. Macrogametocytes or female gametocytes**

- Larger with dense chromatin and granular cytoplasm.
- Numerous in number

**b. Microgametocytes or male gametocytes**

- Smaller and has a diffuse nucleus.
- Few in number

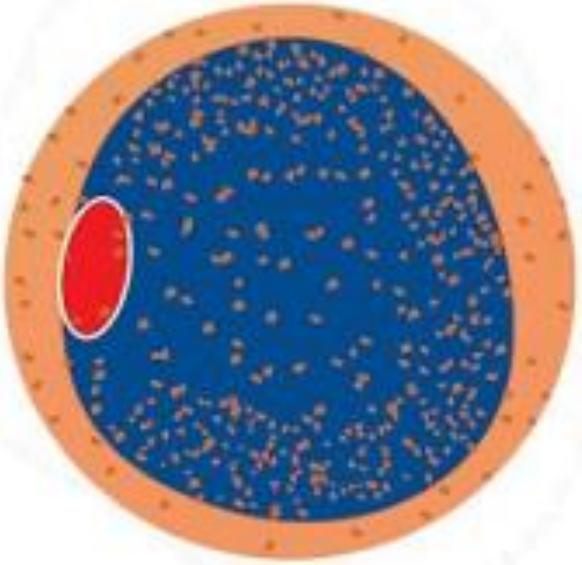


Fig: *Female gametocytes*

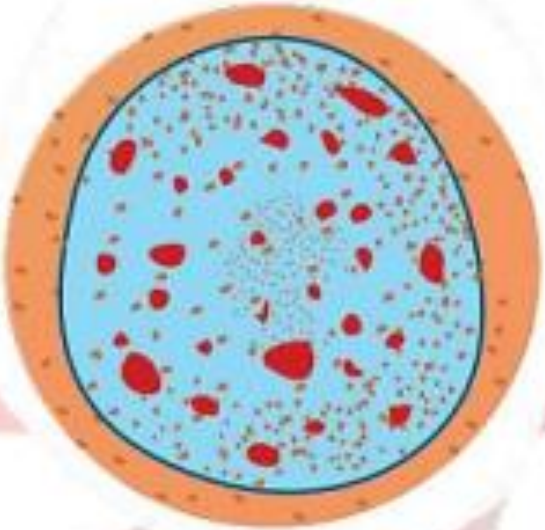


Fig: *Male gametocyte*

# B. Sexual cycle in mosquito

- When female *Anopheles* mosquito bites an infected persons, they suck the gametocytes and other stages of erythrocytic cycle (e.g. erythrocytic merozoite) along with blood.
- They reach the stomach where all the stages along with RBCs are digested except gametocytes.

## 1. Gametogony/Gametogenesis (Formation of gametes)

### i. Formation of microgametes

- Microgametocytes undergo ex-flagellation process in the mid-gut of mosquito.
- The nucleus of microgametocytes divides mitotically to form 6-8 daughter nuclei.
- These nuclei move to periphery along with cytoplasm, forming flagella like structure.
- Thus 6-8 flagella like male gametes are formed from each microgametocyte.

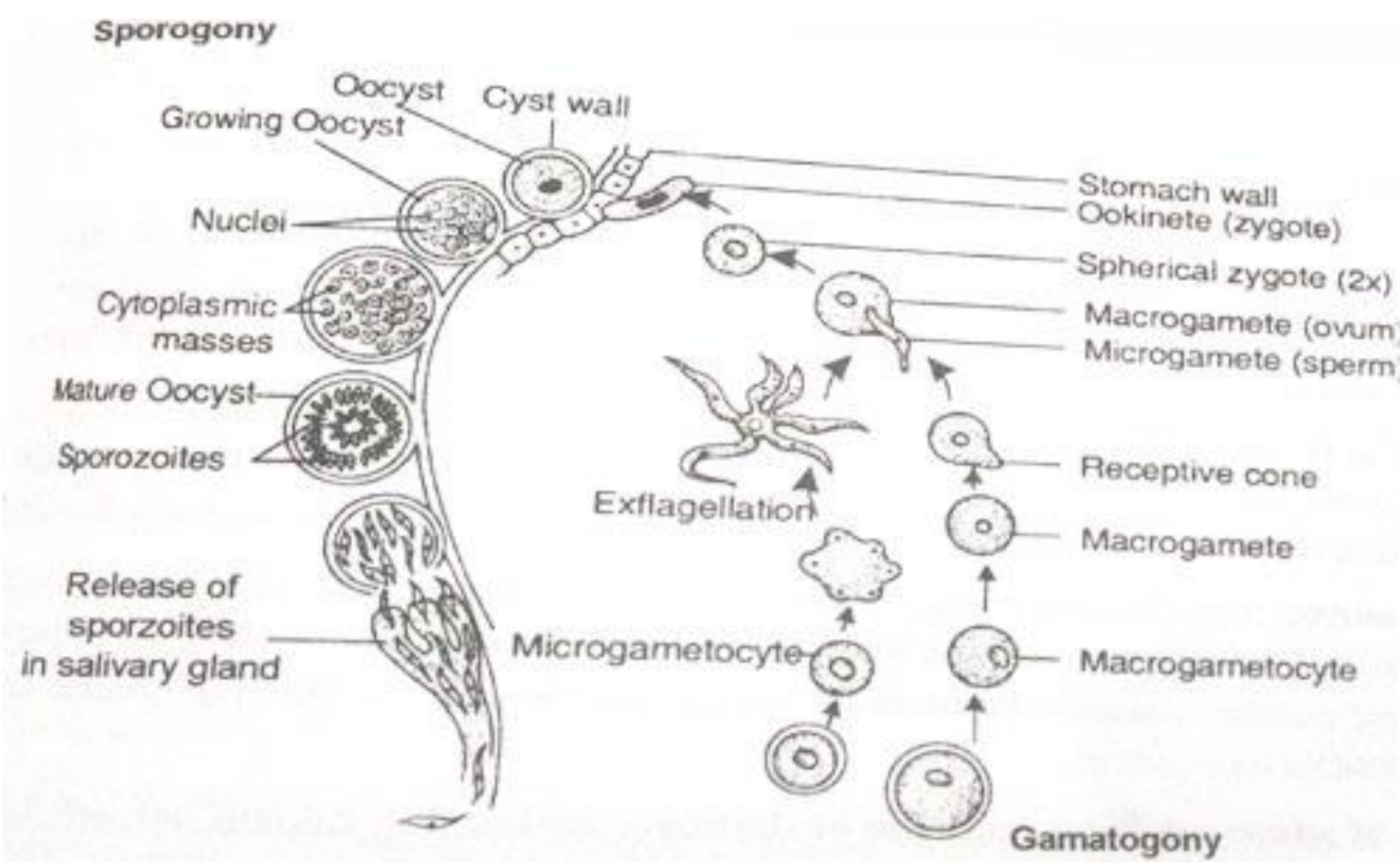
# 1. Gametogony…

**ii. Formation of macrogametes**

- Macrogametocyte undergo some reorganization and become female gametes or macrogametes or megagametes.
- The female gamete is non-motile and develops a cytoplasmic projections called cone of reception or fertilization cone on one side.

# 2. Fertilization

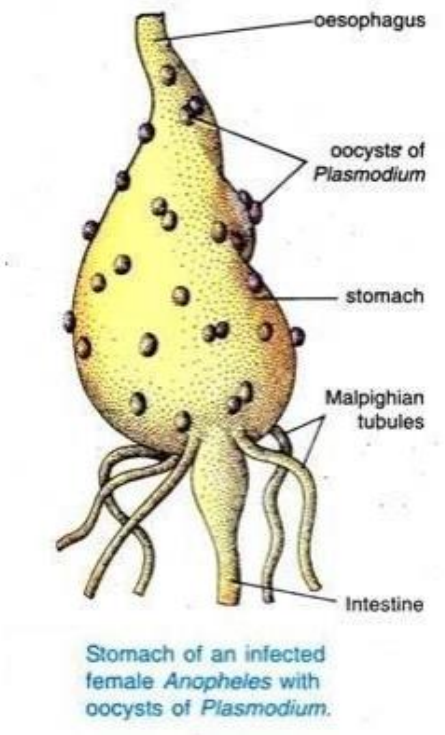
- One microgamete penetrates into macrogamete through the cone of reception and fertilization takes place known as **syngamy.**
- Syngamy is anisogamous due to the dissimilar structure of gametes. Hence, their fusion is called **anisogamy.**
- A complete fusion of nuclei and cytoplasm of the two gametes occurs, resulting in the formation of diploid zygote or **synkaryon.**
- Zygote form in stomach of mosquito about 9 to 10 days after the blood meal.


Sporogony
Oocyst
Cyst wall
Growing Oocyst
Nuclei
Cytoplasmic masses
Mature Oocyst
Sporozoites
Release of sporzoites in salivary gland
Stomach wall
Ookinete (zygote)
Spherical zygote (2x)
Macrogamete (ovum)
Microgamete (sperm)
Exflagellation
Receptive cone
Macrogamete
Microgametocyte
Macrogametocyte
Gamatogony

*P. vivax*

## 3. Formation of ookinete

- After fertilization, the zygote remains rounded and non-motile for some time.
- Then it becomes elongated and vermiform known as **ookinete.**
- Ookinete is motile and has pointed ends.
- It penetrates the wall of stomach with the help of lytic secretion.
- It settles into the inner portion of stomach wall.



Stomach of an infected female *Anopheles* with oocysts of *Plasmodium*.

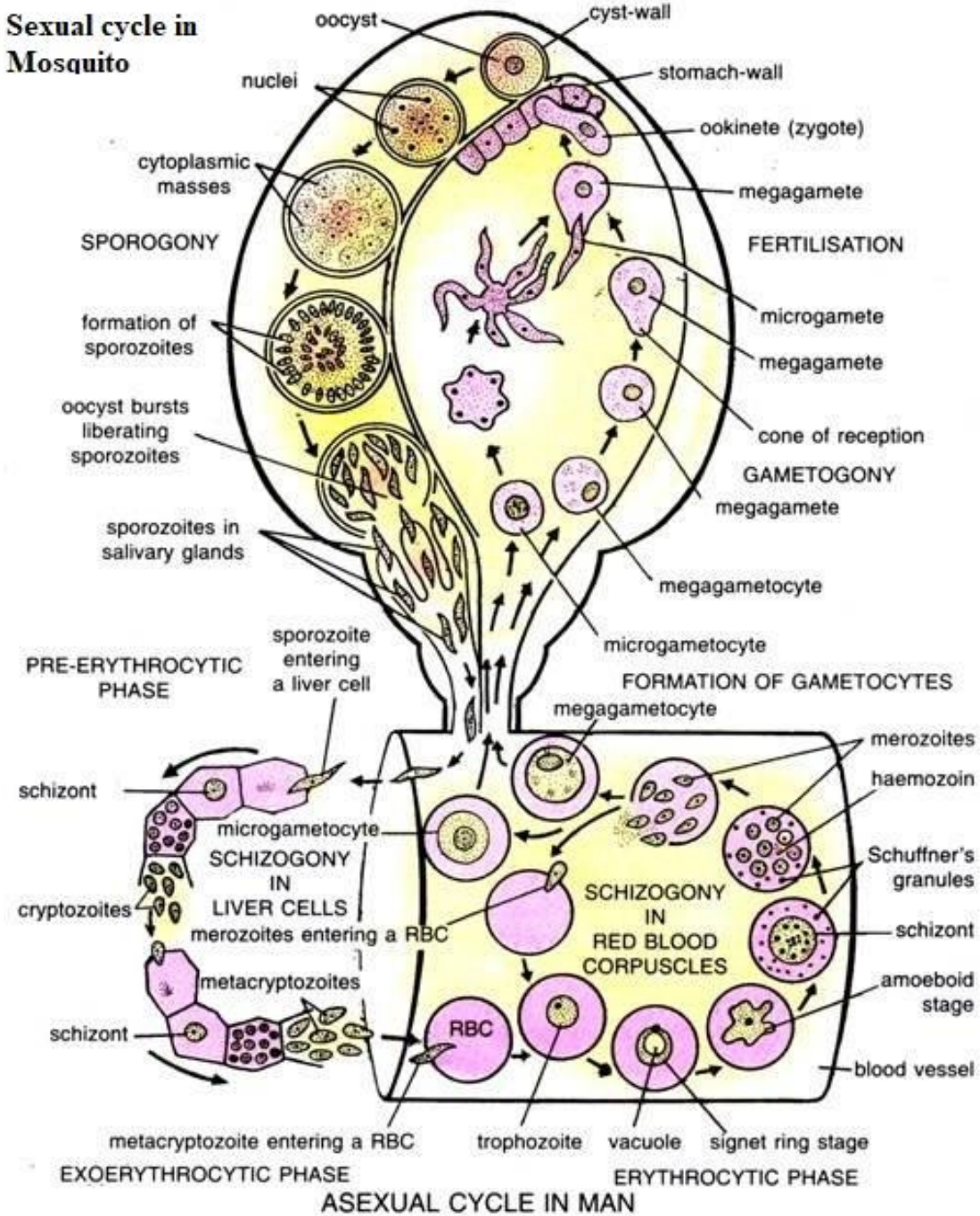
## 4. Formation of oocysts

- The ookinete changes into spherical shape, take nutrition from the wall of stomach and get enclosed in a thin, elastic and permeable cyst wall, such stage is called **oocyst stage or sporont**.

# 5. Sporogony

- It is the **process of formation of numerous sporozoites from the oocyst by asexual multiple fission.**
- The nucleus of oocyst divides first by meiosis and then by mitosis, forming large number of haploid nuclei (2-3 days) and forms sporozoites forming cell known as sporoblasts.
- The nuclei of sporoblast again multiply and cytoplasm gets constricted around them.
- Thus the resultant structures in the sporoblasts elongate to form slender or sickle shaped **sporozoites**.
- Each oocyst fills with numerous sporozoites. These sporozoites give pressure to the oocyst and due to which the oocyst burst or rupture and thousands of sporozoites are released in the body cavity (hemocoel) of mosquito.
- The sporozoites are very active and motile, then they reach to the salivary glands of the mosquito.
- Then the sporozoites are ready to infect the healthy person after each bite.
- So when the infected mosquito bites a healthy man, thousands of sporozoites are injected into his blood along with saliva.

**Sexual cycle in Mosquito**




ASEXUAL CYCLE IN MAN

# Comparison among different *Plasmodium spp.*

| ***Plasmodium spp.*** | **Disease** | **Staining granules or dot** | **Erythrocytic cycle** | **Pre-patent period** | **Incubation period** |
|---|---|---|---|---|---|
| ***P. vivax*** | Benign tertian malaria | Schuffner's dot | ~48 hrs | 8 days | 14 days |
| ***P. ovale*** | Benign sub-tertian malaria | James's dot | ~48 hrs | 8 days | 14 days |
| ***P. falciparum*** | Malignant tertian malaria or cerebral malaria or black water fever | Maurer's dot | ~24-48 hrs | 6 days | 12 days |
| ***P. malarie*** | Benign quartan malaria | Ziemann's dot | ~72 hrs | 20 days | 28 days |

# Malaria

- Malaria is one of the major life-threatening infectious diseases caused by *Plasmodium spp.* And transmitted to people through the bites of an infected female *Anopheles* mosquito.
- It is particularly prevalent in tropical and subtropical low-income regions of the world.
- According to the WHO, 219 million malaria cases and 435,000 deaths worldwide were reported in 2017.

## Mode of transmission

- The main mode of transmission is by the bite of infected female *Anopheles* mosquitoes.
- Occasionally, transmission can occur by
    - Blood transfusion
    - Organ transplantation
    - Needle-sharing
    - Congenitally from mother to foetus

# Pathogenic effects

**Incubation period:** The time interval between the bite of infective mosquito and the first appearance of clinical symptoms 12- 17 days

- **Fever and Chills:**
  - The cyclic rupture of infected RBCs releases merozoites, hemozoin toxin, and immune-stimulating products into the bloodstream.
  - This stimulates the immune system, causing paroxysms of fever, chills, and sweating in 48-hour cycles.
- **Anemia:**
  - Destruction of infected and uninfected RBCs results in a significant loss of erythrocytes.
  - Decreased oxygen-carrying capacity leads to fatigue, pallor, and weakness.
- **Splenomegaly:**
  - The spleen becomes enlarged due to its role in filtering out infected RBCs and immune complex deposition.
  - This may lead to abdominal discomfort or pain in the left upper quadrant.

# Pathogenic effects….

- **Hepatomegaly:** Liver involvement due to parasite metabolism and immune responses can cause liver enlargement, leading to discomfort and mild jaundice.
- **Thrombocytopenia:** Platelet destruction can occur, increasing the risk of bleeding and bruising.
- **Hypoglycemia:**
  - Parasites consume glucose for energy, depleting glucose levels in the host, particularly in severe cases.
  - Hypoglycemia can cause confusion, seizures, or even coma in extreme situations.
- **Immune Suppression:** Chronic P. vivax infections can suppress the immune system, predisposing the host to secondary infections.
- **Relapses:** Hypnozoites in the liver can reactivate periodically, leading to recurrent infections even after apparent recovery. Relapses are a hallmark of P. vivax malaria and complicate treatment and management.
- **Pregnancy-Related Complications:**
  - Infected pregnant women may experience low birth weight, preterm delivery, and maternal anemia.
  - Parasites can sequester in the placenta, reducing nutrient and oxygen transfer to the fetus.

# Diagnosis

1. **Demonstration of parasites by simple light microscopy**
   - Malaria diagnosed by detecting parasites in blood.
   - Two types of peripheral blood smears: Thin smear (1–1.5 µL); Thick smear (3–4 µL)

- **Thin Smear**
  - Made from capillary blood (finger prick)
  - Consists of a single layer of unbroken RBCs
  - Air dried, fixed with alcohol
  - Stained using Romanowsky stains:Leishman, Giemsa, Field's, or JSBb.
- **Thick Smear**
  - Usually 3 drops of blood spread over ~10 mm area
  - Dried and placed in Koplin jar for 5–10 min for dehemoglobinization.

2. **Fluorescence Microscopy and Kawamoto Technique**
   - Differential staining method
   - Uses dyes: acridine orange or benzothiocarboxy purine
   - Stains parasites in RBCs

# Prophylaxis (Preventive measures)

➢ Malaria prophylaxis encompasses measures to prevent infection and disease progression. These include **chemoprophylaxis, vector control strategies, and vaccine development.** Each method targets different aspects of the malaria transmission cycle to reduce disease burden, particularly in endemic regions.

**1. Chemoprophylaxis**

❖ Chemoprophylaxis involves the use of antimalarial drugs to prevent infection. It is particularly recommended for:

- Travelers visiting malaria-endemic areas.
- Short-term measures for personnel like soldiers or police in high-risk regions.

## 1. Chemoprophylaxis….

❖**Drugs for Chemoprophylaxis**

**a. Weekly Regimens:**

- **Chloroquine:** 300 mg weekly.
- **Proguanil:** 400 mg weekly.
- **Mefloquine:** 250 mg weekly.

**b. Daily Regimen:**

- **Doxycycline:** 100 mg daily.

❖**Usage Recommendations**

- **Chloroquine and Mefloquine:** Start 1–2 weeks before travel.
- **Doxycycline:** Start 1 day before travel.
- Continue the regimen during travel and for 4 weeks after leaving the endemic area.

# 2. Vector Control Strategies

- Vector control remains a cornerstone of malaria prevention, aimed at reducing mosquito populations and preventing mosquito-human contact.

- **Anti adult Measures**

**a. Residual Spraying:**

- Use of residual insecticides like DDT, malathion, and fenitrothion.
- Highly effective against adult mosquitoes when sprayed in houses.

**b. Space Application of Pesticides:**

- Dispersion of pesticides as fog or mist using ultra-low volume (ULV) methods.

**c. Individual Protection:**

- Insecticide-treated bed nets (ITNs).
- Use of repellents (e.g., DEET-based).
- Wearing protective clothing to reduce exposure.

# 2. Vector Control Strategies…

➢ **Antilarval Measures**

**a. Larvicides:**

- Use of mineral oil or Paris green to kill mosquito larvae and pupae.

**b. Source Reduction:**

- Environmental sanitation to eliminate mosquito breeding sites. o
- Improved water management and drainage systems.

**c. Biological Control:**

- Use of *Gambusia affinis* (mosquito-eating fish).
- Application of *Bacillus thuringiensis* (a bacterial larvicide).

# 3. Vaccination for Malaria

- Although intensive research is underway, no licensed malaria vaccine for widespread human use exists yet.
- Vaccine development focuses on targeting various stages of the malaria parasite life cycle.

# Control and preventive measures (Summary)

- **Early Diagnosis and Treatment:**
  - Rapid detection and treatment with appropriate antimalarial drugs reduce disease progression and transmission.
- **Public Health Education:**
  - Awareness campaigns to promote the use of ITNs, repellents, and environmental sanitation.
- **Integrated Vector Management (IVM):**
  - Combination of anti-adult, antilarval, and source reduction measures for sustainable control.
- **Monitoring and Surveillance:**
  - Continuous tracking of malaria cases and mosquito populations to detect outbreaks early.