

# Protozoa: الجداول مهمة كثير

- unicellular eukaryotes.

Classes:

I. Sarcodina, e.g. Amoeba (pseudopods).

II. Flagellates (Mastigophora), e.g. Giardia, Leishmania.

III. Ciliates (Ciliophora), e.g. Balantidium.

IV. Sporozoites: e.g. plasmodium.

→ adults are (non-motile).

→ alternate between sexual & asexual phases.

## Malaria:

- intracellular protozoal infection.

- The no.1 killer of parasitic diseases.

- Vector- borne (female anopheline mosquito).

- Tropism (favorite cell target): RBCs.

- **Plasmodium** (the cause of malaria):

- a sporozoan.

- A genus of parasitic alveolates (has a fluid sacs under the cell membrane).

- Has 2 hosts: Dipteran insect host (sexual cycle) & a vertebrate (in humans/asexual).

- Has 2 phases

1- In the mosquito, sexual reproduction (sporogony → sporozoites).

2- In the human, ASEXUAL reproduction (schizogony).

## ●● All plasmodia are intracellular ●●

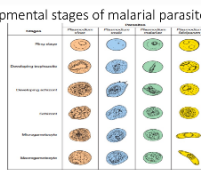
- **Exo-erythrocytic cycle:**

→ - In malaria not babesiosis.

→ - **dormant schizogony** in **liver** may occur in *P. vivax* & *P. ovale*. Called **hypnozoites** (sleeping plasmodium) & they lead to a true relapse if not killed.

- Once in RBCs & reticulocytes it feeds on hemoglobin → hemolysis

- In extra-erythrocytic cycle



- plasmodium species cause malaria:

## 1) *P. vivax*

- (benign tertian malaria).



- Tertian: the fever cycle repeats itself every 48 hrs → 1 day of fever followed by 2 days of feeling ok.

- Infects only reticulocytes → benign.

- Forms dormant schizogony (hypnozoites) in liver.

- Symptoms: headache, photophobia, muscle aches, anorexia, nausea, & sometimes vomiting

- In patients with prior exposure to malaria, the parasites can be found in bloodstream several days before symptoms.

Type of Malaria	Characteristics
<i>Plasmodium vivax</i> (benign tertian malaria)	<ol style="list-style-type: none"> <li>1. 48-hour cycle</li> <li>2. Tends to infect young cells</li> <li>3. Enlarged RBCs</li> <li>4. Schüffner's dots (true stippling) after 8-10 hours</li> <li>5. Delicate ring</li> <li>6. Very ameboid trophozoite</li> <li>7. Mature schizont contains 12-24 merozoites</li> </ol>

## 2) *P. ovale*

- (benign tertian malaria).

- Infects only reticulocytes → benign.

- Forms dormant schizogony (hypnozoites) in liver.

- Less common, less severe than vivax.

- vivax & ovale have the same treatment.



<i>Plasmodium ovale</i>	<ol style="list-style-type: none"> <li>1. 48-hour cycle</li> <li>2. Tends to infect young cells</li> <li>3. Enlarged RBCs with fimbriated edges (oval)</li> <li>4. Schüffner's dots appear in the beginning (in RBCs with very young ring forms, in contrast to <i>P. vivax</i>)</li> <li>5. Smaller ring than <i>P. vivax</i></li> <li>6. Trophozoite less ameboid than that of <i>P. vivax</i></li> <li>7. Mature schizont contains an average of 8 merozoites</li> </ol>
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## 3) *P. malariae*

- Quartan/classic malaria.

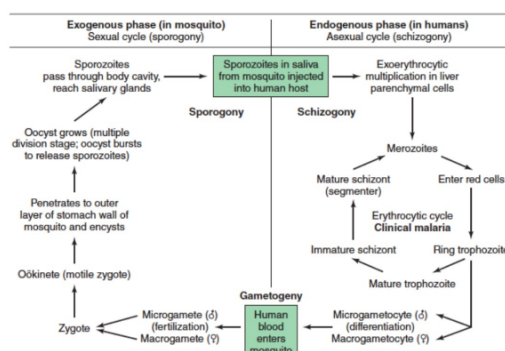
- Quartan: 72 hrs for the cycle to be repeated.

- Infects all RBCs.

- No cytoplasm stippling (no Schüffner's dots).

<i>Plasmodium malariae</i> (quartan malaria)	<ol style="list-style-type: none"> <li>1. 72-hour cycle (long incubation period)</li> <li>2. Tends to infect old cells</li> <li>3. Normal size RBCs</li> <li>4. No stippling</li> <li>5. Thick ring, large nucleus</li> <li>6. Trophozoite tends to form "bands" across the cell</li> <li>7. Mature schizont contains 6-12 merozoites</li> </ol>
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## Malaria life cycle



- *P. malariae* causes **proteinuria** & with clinical signs of **nephrotic syndrome**.
- With a chronic infection, kidney problems result from deposition within the glomeruli of circulating antigen antibody complexes.
- The most common lesion seen in quartan malaria: **membrane proliferative type of glomerulonephritis**.

#### 4) *P. falciparum*

- Malignant Tertian malaria.
- Most fatal plasmodium worldwide.
- Ring stage: double rings, each ring is double chromatin dotted & shows **Applique'/Accole' forms** (rings attach themselves to erythrocytes edges).



- Infects all RBCs.
- Causes **cytoadherence** (RBC membrane becomes sticky & adhere to the capillaries endothelial lining of the internal organs).
- Causes **cerebral malaria** (the major cause of death with *P. falciparum*).
- Causes **blackwater fever** (results from RBCs lysis → hemoglobin into bloodstream & urine → discoloration).
- **Childhood febrile convulsions** may occur with **any** of the malarias.
- But **generalized seizures** are specific for *falciparum* malaria & may cause **encephalopathy**.
- **Maurer's dots** (Large, single, bluish dots).
- Gametocytes are **crescent 'banana' in shape**.
- Extreme fever, 41.7° C (107° F) or higher.

#### *Plasmodium falciparum* (malignant tertian malaria)

1. 36-48-hour cycle
2. Tends to infect any cell regardless of age, thus very heavy infection may result
3. All sizes of RBCs
4. No Schüffner's dots (Maurer's dots: may be larger, single dots, bluish)
5. Multiple rings/cell (only young rings, gametocytes, and occasional mature schizonts are seen in peripheral blood)
6. Delicate rings, may have two dots of chromatin/ring, appliqué or accolé forms
7. Crescent-shaped gametocytes

#### 5) *P. knowlesi*

- Simian/5th human malaria.
- Infects any RBC regardless of age.
- Resembles **falciparum** in its early blood stage.
- Resembles **malariae** in its late blood stage & gametocytes.
- Faint, clumpy dots.
- Can be fatal.

#### *Plasmodium knowlesi* (simian malaria)\*

1. 24-hour cycle
  2. Tends to infect any cell regardless of age, thus very heavy infection may result
  3. All sizes of RBCs, but most tend to be normal size
  4. No Schüffner's dots (faint, clumpy dots later in cycle)
  5. Multiple rings/cell (may have 2-3)
  6. Delicate rings, may have two or three dots of chromatin/ring, appliqué forms
  7. Band form trophozoites commonly seen
  8. Mature schizont contains 16 merozoites, no rosettes
  9. Gametocytes round, tend to fill the cell
- Early stages mimic *P. falciparum*; later stages mimic *P. malariae*

Characteristic	Finding for Indicated Species*			
	<i>P. falciparum</i>	<i>P. vivax</i>	<i>P. ovale</i>	<i>P. malariae</i>
Duration of intrahepatic phase (days)	5.5	8	9	15
Number of merozoites released per infected hepatocyte	30,000	10,000	15,000	15,000
Duration of erythrocytic cycle (hours)	48	48	50	72
Red cell preference	Younger cells (but can invade cells of all ages)	Reticulocytes and cells up to 2 weeks old	Reticulocytes	Older cells
Morphology	Usually only ring forms; banana-shaped gametocytes	Irregularly shaped large rings and trophozoites; enlarged erythrocytes; Schüffner's dots	Infected erythrocytes, enlarged and oval with tufted ends; Schüffner's dots	Band or rectangular forms of trophozoites common
Pigment color	Black	Yellow-brown	Dark brown	Brown-black
Ability to cause relapses	No	Yes	Yes	No

#### Clinical features of all malaria:

- First symptoms are nonspecific:
- Lack of a sense of wellbeing, headache, fatigue, abdominal discomfort, & muscle aches followed by fever (all are similar to minor viral illness symptoms).
- Symptoms like prominence of headache, chest pain, abdominal pain, cough, arthralgia, myalgia, or diarrhea may suggest another diagnosis. But we exclude the others by their specific symptoms.
- The fever that comes on the third to fourth day has 3 stages (**cold** stage with chills & rigors -**hot** stage- **sweating** stage) then there are two days of feeling well, then the fever attacks again.
- Anemia can show (due to hemolysis) but mostly in **falciparum** due to high parasitemia.



## - Diagnosis:

- Definitive diagnosis: seeing plasmodium in peripheral blood.

### 1. Routine Methods:

o Thick & thin **blood films**.

o **Stains**: 1. Giemsa 2. Wright 3. Fluorescent nucleic acid stains like acridine orange.

- The Blood is collected using **EDTA** anticoagulant.

### 2. Serologic Methods:

o **Rapid malaria tests (RMTs)**:

1. Some use monoclonal antibodies against the histidine-rich protein 2 (HRP2).

2. Others detect species-specific parasite lactate dehydrogenase (pLDH).

o These procedures are based on an **antigen capture** approach in dipstick or cartridge formats.

### 3. Molecular Diagnostics:

• PCR for detection of specific genes.

### 4. Automated Instruments.

## - Therapy:

- Quinolones for malaria **EXCEPT falciparum**.

- **Quinolones** are used with **primaquine** to kill **hypnozoites**.

- Artemisinin (mainly for *P. falciparum*) & Quinolones.

## CONTROL

Type of control	Measures
Personal protection	Insecticide treated mosquito nets; Mosquito proofing of dwellings; Repellents; Site selection
Environmental management	Drainage & water management; Land reclamation by filling and drainage
Chemical (Insecticides) control	Residual house spraying; larviciding; space spraying
Other measures	Biological control, Genetic control, Zoophylaxis



- Avoid the feeding time of the mosquito from dusk till dawn.

- Quinolones for prophylaxis.

## Babesiosis:

- *Babesia microti* (the deer tick (*Ixodes scapularis*)), worldwide & in the USA.

- *B. divergen* (*Ixodes dentatus*) in Europe.

- *B. duncani*.

- Reservoir: **white footed mouse**.

- Infection through **blood transfusions**.

- ASEXUAL reproduction in humans, sexual reproduction in the definitive host.

- Symptoms & signs resemble malaria but no pattern in fever (NO CYCLES), they go directly to RBCs → hemolysis.

- Symptoms: gradual onset of malaise, fatigue, & weakness. Fever can reach 40.9°C & is accompanied by one or more of: chills, sweats, headache, myalgia, arthralgia, nausea, anorexia, & dry cough. [non specific].

- Symptoms develop following 1–4 weeks incubation after tick bite & 1–9 weeks after blood transfusion.

- Complications following RBC hemolysis: anemia, jaundice, hepatomegaly, splenomegaly

- Severe *B. microti* illness (Severe babesiosis) occurs in: patients with age >50 years, neonatal prematurity, male gender, asplenia, HIV/AIDS, malignancy, hemoglobinopathy, & immunosuppressive therapy takers.

- Differences with malaria:

- Extra cellular merozoites unlike malaria.

- Merozoites tend to arrange in tetras (maltese cross) (pathognomonic)

- Treatment:

- Quinolones, artemisin-based combination.

- **Atovaquone + azithromycin** (for mild to moderate babesiosis).

- **Clindamycin + quinonesis** (for severe infections).

- Prevention: Wear clothing that covers the lower part of the body, apply tick repellents (such as DEET) to clothing, & limit outdoor activities where ticks may abound.

