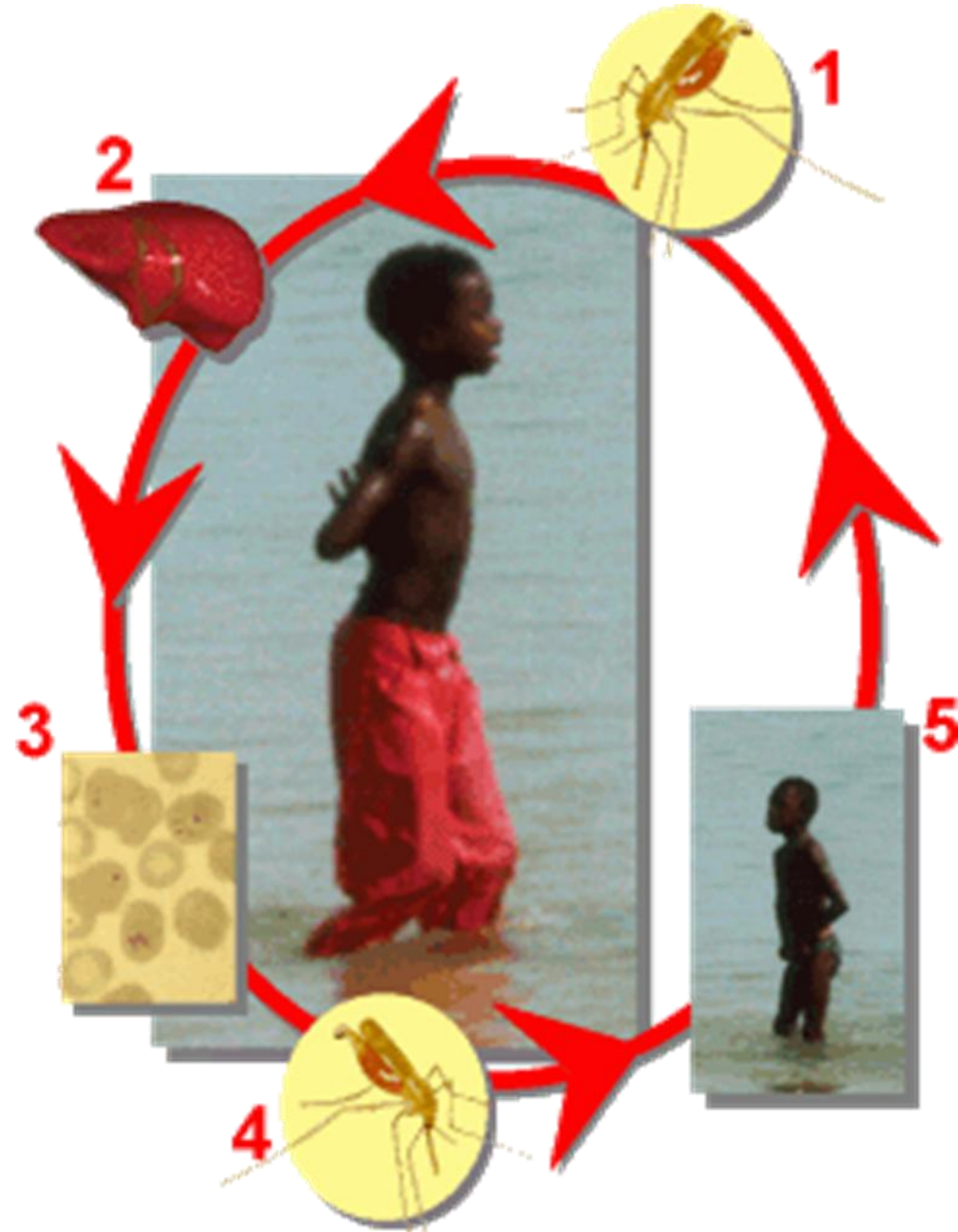


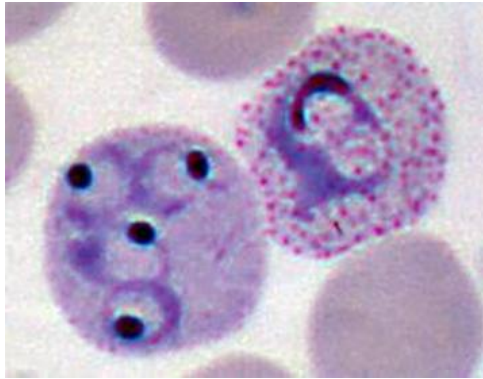
Infectious  
Diseases  
Lecture -  
Malaria



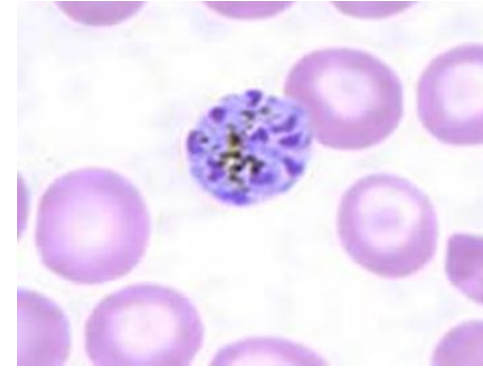
## Definition:

- Malaria is an infectious disease caused by four species of parasites of the genus *Plasmodium*, and transmitted by the bite of mosquitoes of the genus *Anopheles*.
- Clinically, the disease is characterized by malarial attacks (periodic attacks of fever), anemia, and splenomegaly.

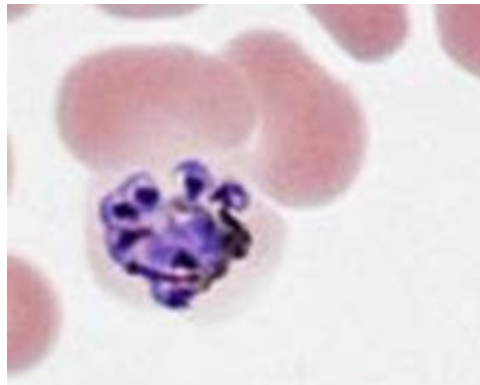
# Etiology



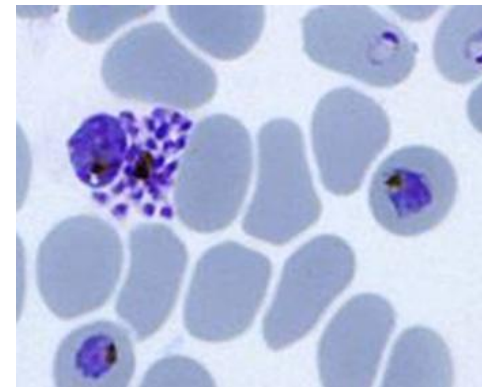
*Plasmodium vivax*  
causative agent M.  
terciane



*Plasmodium malariae*  
causative agent M.  
quartane



*Plasmodium ovale*  
causative agent M. ovale



*Plasmodium falciparum*  
causative agent M. tropica

# Anopheles

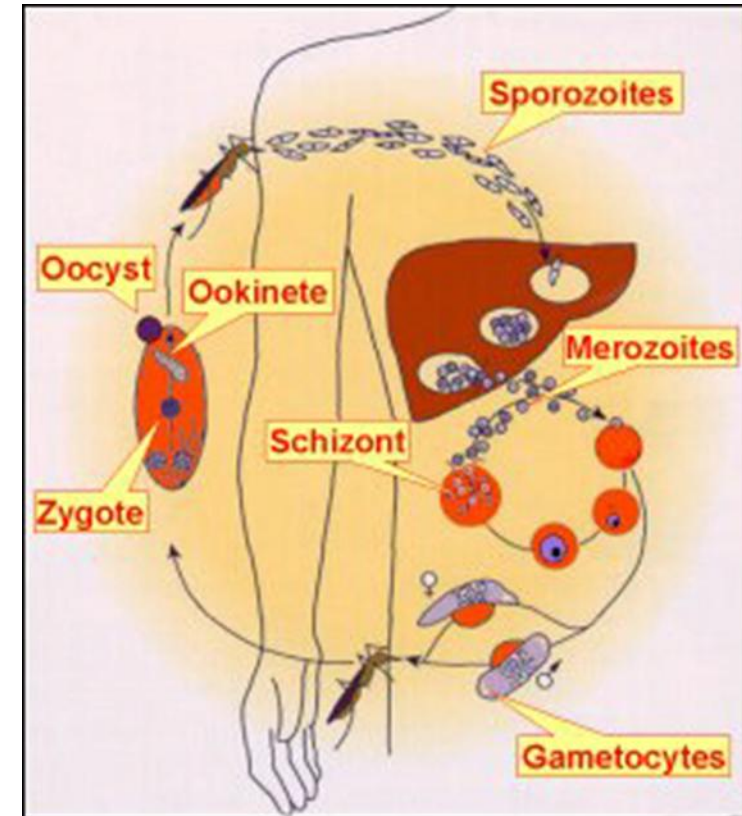


# Life cycle of Plasmodium

## I Asexual cycle ("schizogony")

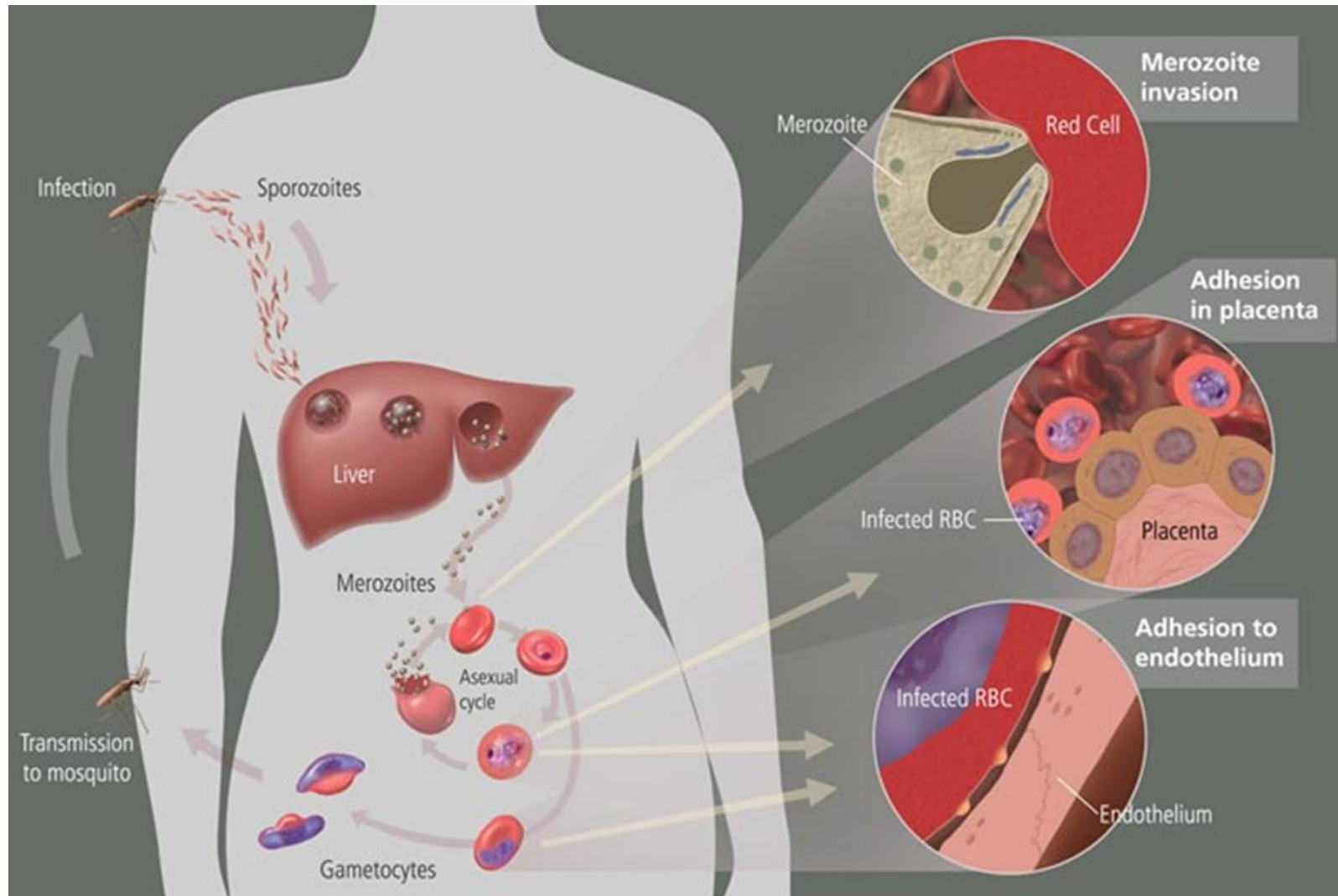
- preerythrocytic phase
- erythrocyte phase
- exoerythrocytic phase

## II Sexual cycle ("sporogony")

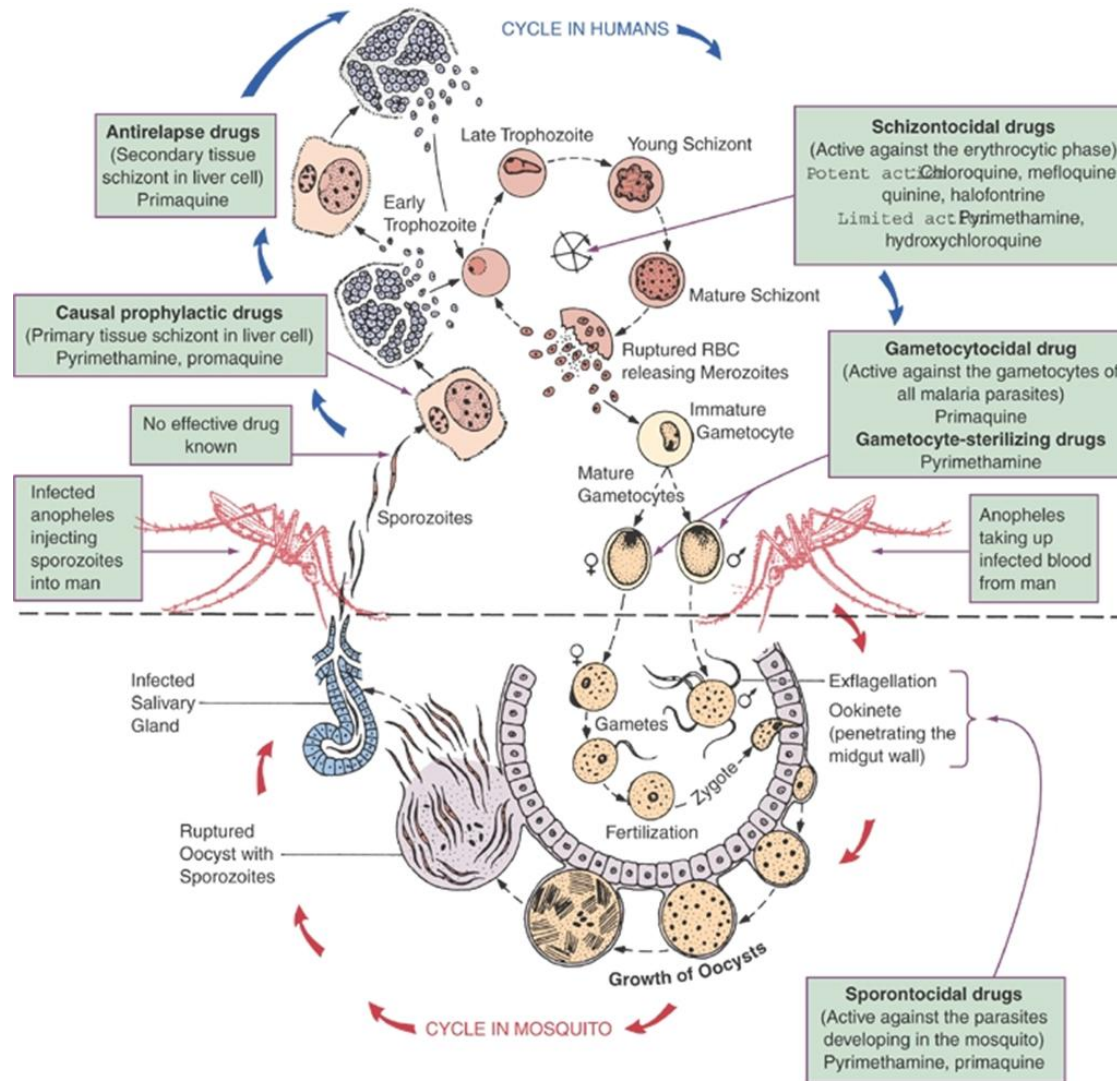




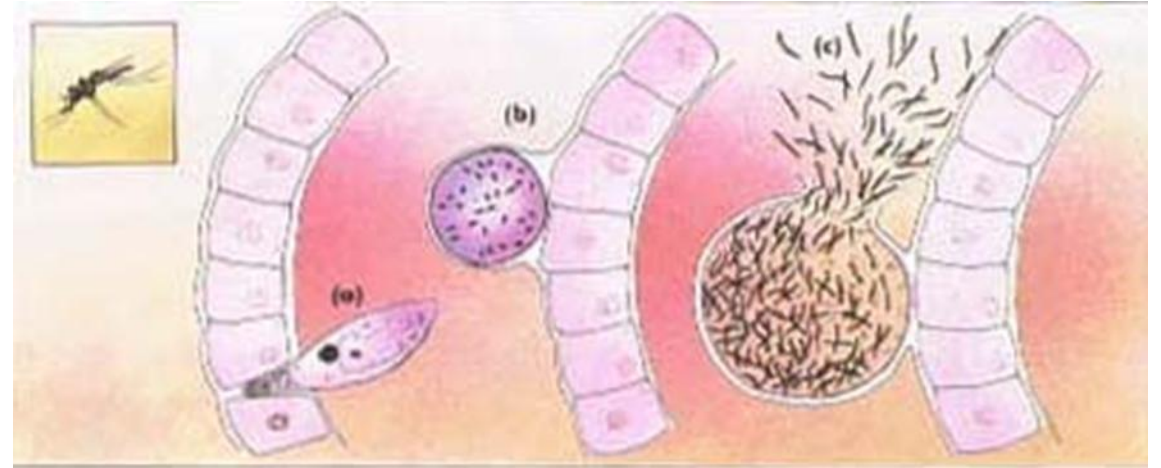
# Life cycle of Plasmodium



# Plasmodium life cycle



# Oocist



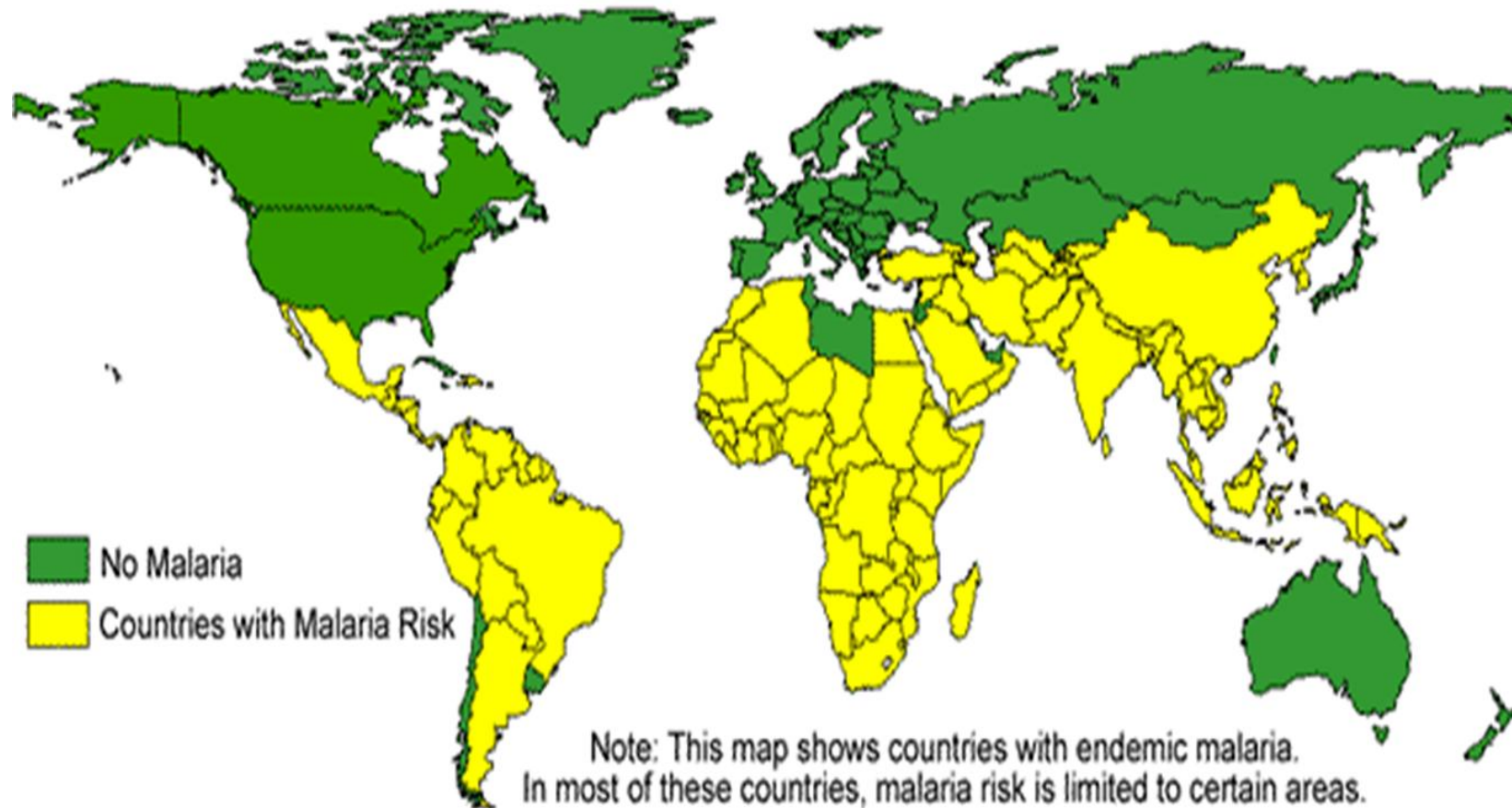


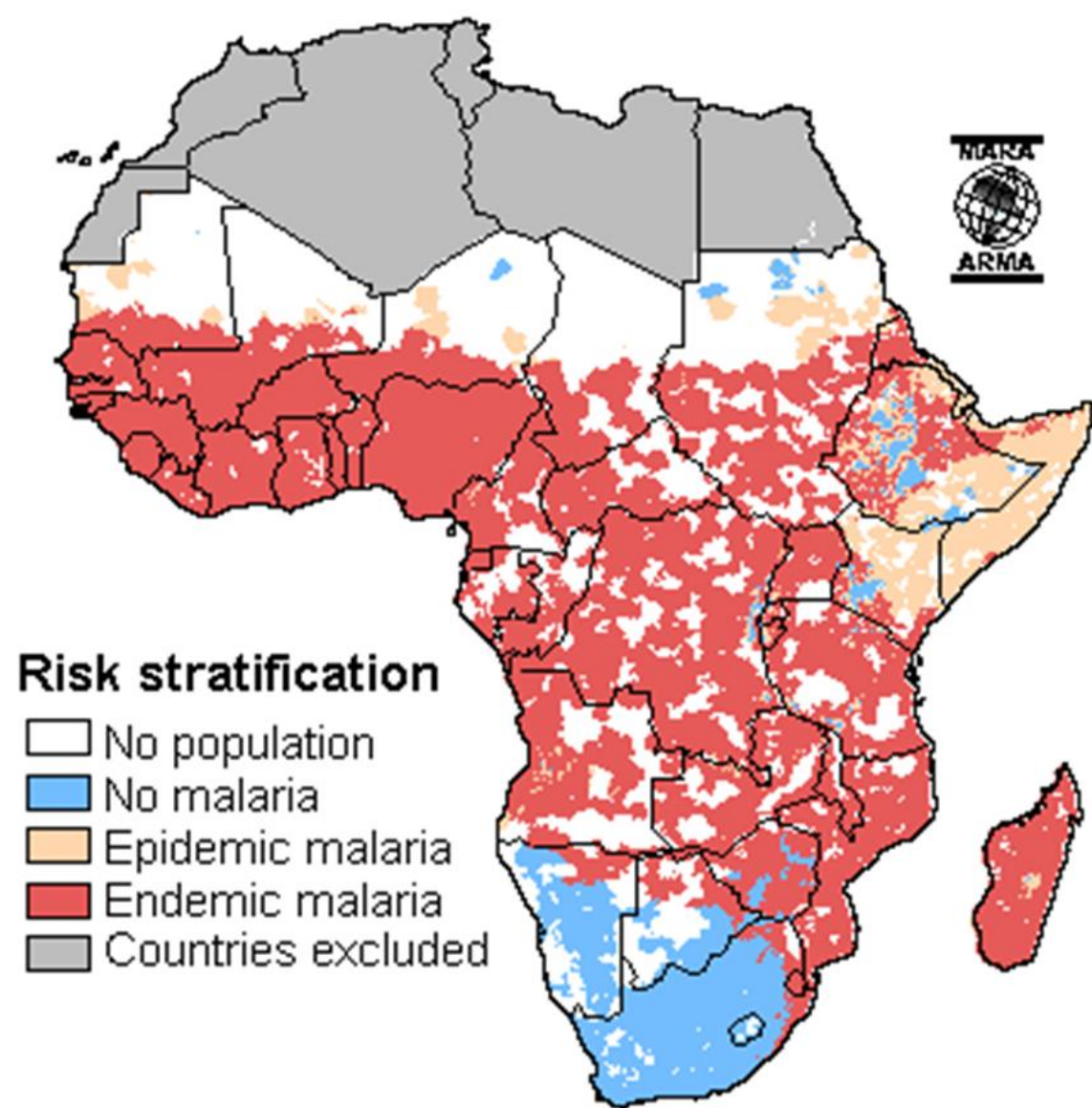
# Epidemiology

- It is the most important human parasite, spread in 103 countries, which annually affects about a billion people and kills more than 2 million
- There are no indigenous cases of malaria in Serbia (the last case was in 1964, Yugoslavia), but imported cases do occur
- Three factors are necessary for the development and maintenance of malaria: parasite, vector and human
- In addition, other factors are also necessary: atmospheric, climatic, terrain
- Malaria is most widespread in tropical and subtropical regions where it has an endemic-epidemic character

## Geographical distribution of malaria

### Malaria Endemic Countries, 2003





# Pathogenesis

- ❑ The pathogenesis of the disease coincides with the asexual cycle of parasite development in humans
- ❑ Basic pathogenetic mechanisms
  - ✓ Hemolysis of erythrocytes
  - ✓ Toxic damage to various tissues
  - ✓ Release of cytokines (TNF- $\alpha$ , INF- $\gamma$ , ...)
  - ✓ Cytoadherence and the “rosette” phenomenon
  - ✓ Microvascular (capillary) occlusions in various organs



# Clinical picture

- Incubation - 10-12 days (8-23 days)
- ✓ Primary malaria attack stage
- ✓ Latency stage
- ✓ Relapse stage

## STAGE I OF PRIMARY MALARIA ATTACKS

- Invasive stage: temperature up to 40°C, headache, malaise, muscle pain, ...
- Malaria attacks go through three stages: the shivering stage, the hyperpyrexia stage and the sweating stage
- Malaria attacks last 5-10 hours
- In tertian and oval malaria, malaria attacks recur every 48 hours, in quartan malaria every 72 hours, in tropical malaria every 24-48 hours
- In untreated tertian and oval malaria, malaria attacks recur for 2-4 weeks, in quartan malaria for 1-2 months, and then spontaneously stop
- With each new malaria attack, anemia progresses, the spleen becomes increasingly enlarged, and patients become increasingly exhausted

- Clinical and laboratory signs of severe malaria include:

- ✓ High parasitemia (>5% of infected erythrocytes),
- ✓ Hyperpyrexia (body temperature > 40°C),
- ✓ Signs of nervous system involvement (“cerebral malaria”),
- ✓ Anemia (hematocrit < 20),
- ✓ Glycoregulation disorder (hypoglycemia < 2.2 mmol/l),
- ✓ Spontaneous bleeding,
- ✓ Acidosis (pH < 7.25; bicarbonate < 15 mmol/l),
- ✓ Renal failure (creatinine > 265 mmol/l; diuresis < 400 ml),
- ✓ Hyperbilirubinemia (bilirubin > 50 mmol/l),
- ✓ Cardiovascular collapse,
- ✓ Lung infections and/or pulmonary edema,
- ✓ Diarrhea and/or vomiting (which makes oral medication difficult).

## II LATENCY PERIOD

- In treated patients, it occurs due to the destruction of the erythrocyte phase in the development of the parasite, and in untreated patients due to the development of partial immunity.
- In this period, there are no subjective complaints, the objective finding is dominated by splenomegaly.
- The latency period in tropical malaria is short (1-6 weeks), while in *m. tertiana* and *m. ovale* it can last several weeks to several months.



### III STAGE OF RECURRENCE

- Relapses can be early and late
- Early relapses can occur in all forms of malaria; late relapses, also in all except *M. tropica*
- Relapses are clinically presented by typical malarial attacks, which are periodically repeated at a certain time interval; the only difference is that over time, malarial attacks in relapse become milder, and the period between individual relapses is increasing
- In *M. tertianum*, *M. quartanum* and *M. ovale* relapses occur due to the exoerythrocytic phase in the development of the parasite, and in *M. tropica* due to the maintenance of the erythrocytic phase

# Malaria complications

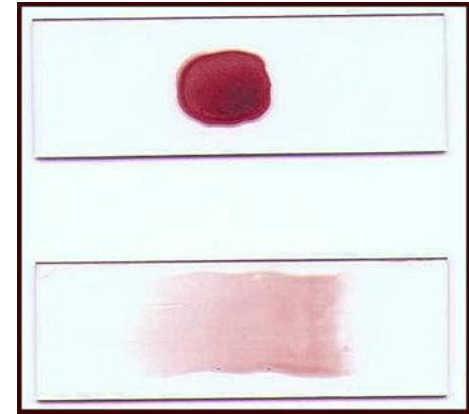
- Splenic rupture or torsion,
- Miscarriage or premature birth,
- Black blood fever.

# Diagnosis

- Clinical picture,
- Epidemiological data,
- Laboratory tests:
  - accelerated SE,
  - normocytic, normochromic anemia,
  - normal leukocyte count (rarely leukocytosis),
  - thrombocytopenia,
  - slightly elevated transaminase activity.

- Exact diagnosis:

- Identification of Plasmodium in blood (smear or thick drop),
- Detection of parasite antigen (fluorescence microscopy),
- Serological analyses,
- PCR.





# Treatment



- The main goal of treatment is to terminate the acute malarial attack and prevent relapse.
- Today, we have a large number of antimalarial agents that act on different developmental forms of Plasmodium.

Quinolone derivatives	quinine, quinidine, chloroquine, mefloquine, halofantrine, primaquine
Artemisin derivatives	artemisinin, artemether, artesunate
Antifolates	pyrimethamine, proguanil, chlorproguanil, trimethoprim
Antibacterial drugs	tetracyclines, clindamycin, macrolides, sulfonamides
Newly synthesized naphthaquinone drugs	atovakon

- Malaria chemoprophylaxis

- Antimalarial prophylaxis should be taken 2 weeks before departure, during stay and 4 weeks after return from endemic areas
- ZONE A (endemic areas where plasmodium is sensitive to chloroquine)

✓ **CHLOROQUINE**, tablets 300 mg, one tablet weekly, children: 5 mg/kg body weight

✓ Contraindications: hypersensitivity to chloroquine, epilepsy, psoriasis.

❑ **ZONE B** (endemic areas with chloroquine-resistant Plasmodium)

- **CHLOROQUINE + PROGUANIL**, 100 mg 200 mg
- One combined tablet daily.
- Contraindications: hypersensitivity to chloroquine and/or proguanil, hepatic and renal insufficiency, epilepsy, psoriasis.
- The tablet size is not adequate for persons weighing less than 50 kg.
- Take 1 day before departure, throughout the stay and for 4 weeks after returning from the malarial area. **ZONE C** (endemic areas with high chloroquine-resistant Plasmodium falciparum)
- **MEFLOQUINE** (Lariam), 250 mg tablets,
- one tablet weekly
- Children: 5 mg/kg body weight weekly

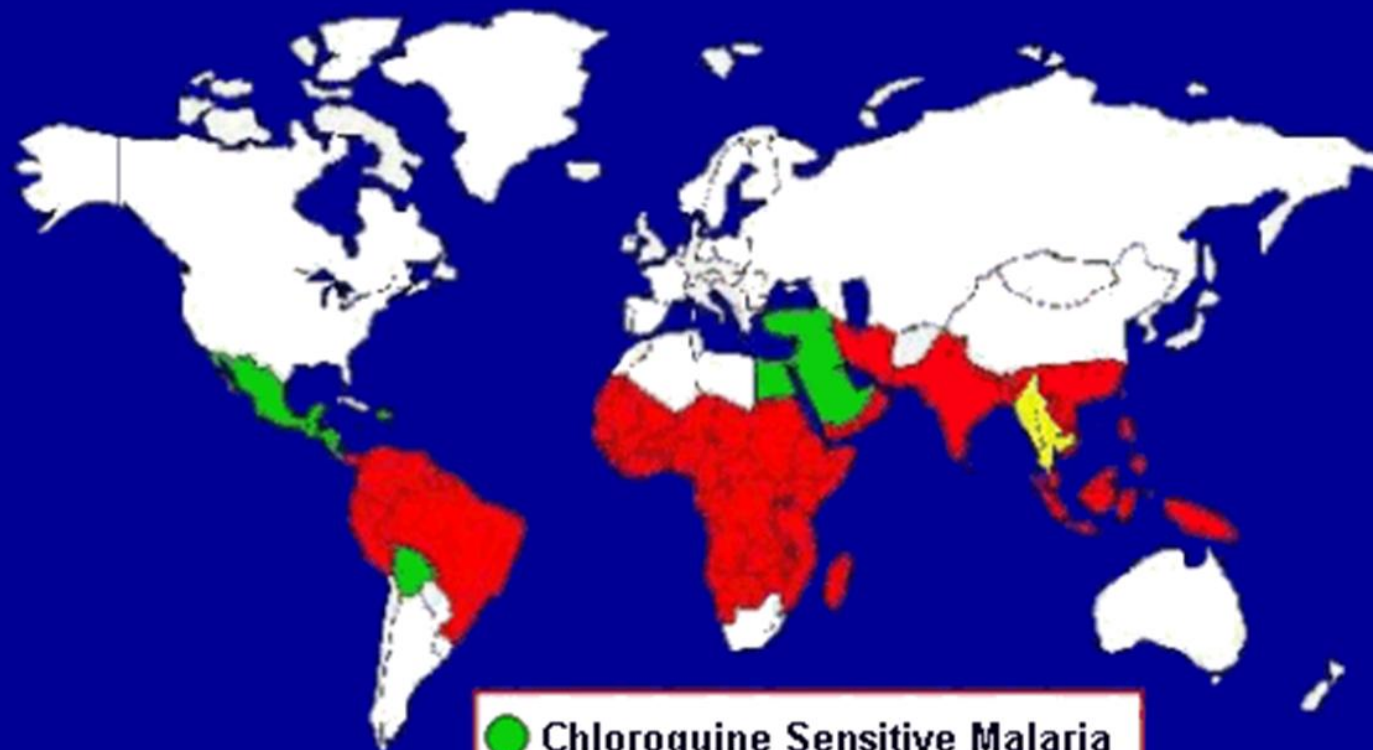
- **Contraindications:** body weight below 5 kg, pregnancy, hypersensitivity to mefloquine, neuropsychiatric disorders (including depression), epilepsy, convulsions, mefloquine therapy in the previous 4 weeks, not recommended for people whose profession requires fine motor coordination and spatial orientation (pilots, drivers...).
- **Note:** do not take mefloquine within 12 hours of quinine administration and within 3 days of live bacterial vaccines (typhoid and cholera vaccines)
- Ampicillin and tetracycline, if administered simultaneously, may increase the level of mefloquine in the blood.



- DOXYCYCLIN, 100 mg tablets, one tablet daily

- Contraindications: pregnancy and lactation, children under 8 years of age, hypersensitivity to tetracyclines, liver dysfunction.
- Note: doxycycline increases the skin's sensitivity to sunlight, so people with sensitive skin should use UVA protection and avoid direct exposure to sunlight.
- Take 1 day before departure, throughout the stay and for 4 weeks after returning from a malarious area.
- In case you are unable to obtain the recommended medications, as well as for any other information related to the type and method of use of antimalarial drugs, contact the health service of the country you are in.

# Malaria Endemic Areas



- Chloroquine Sensitive Malaria
- Chloroquine Resistant Malaria
- Multi-Resistant Malaria

# Infectious Diseases Lecture

## Amebiasis



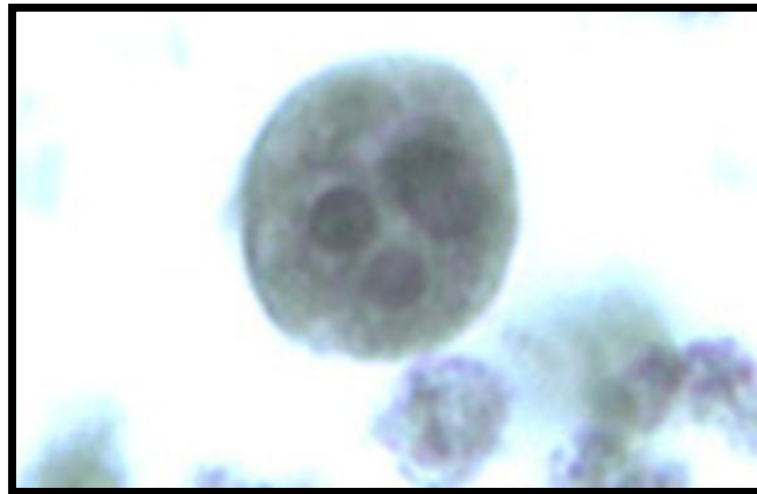
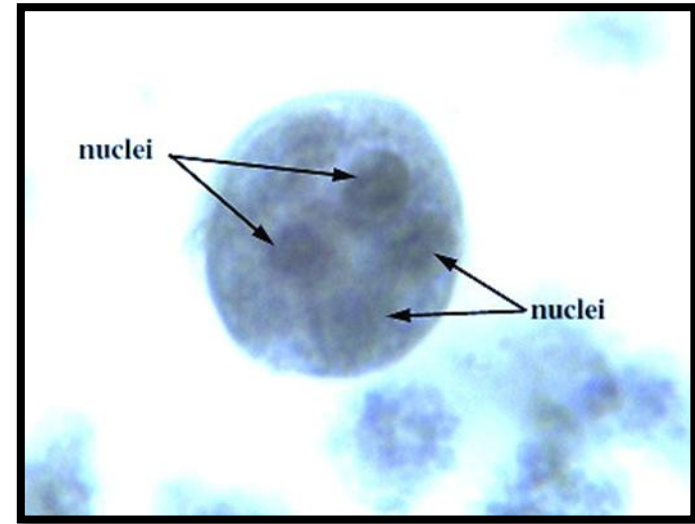
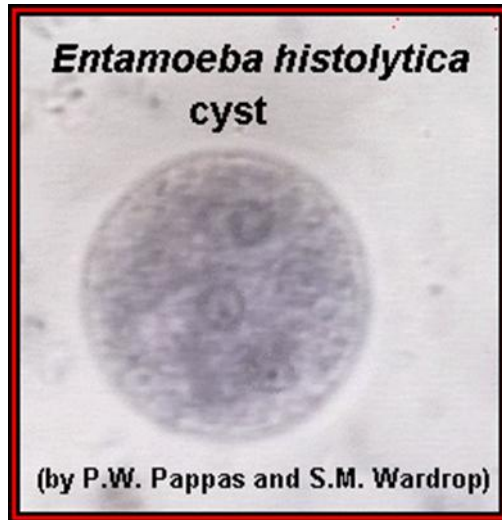
# Definition

Amebiasis refers to infestation of the body with the protozoan *Entamoeba histolytica*, which manifests clinically in a wide spectrum - from asymptomatic, through amoebic colitis to invasive forms with the formation of abscesses, primarily in the liver.

# Etiology

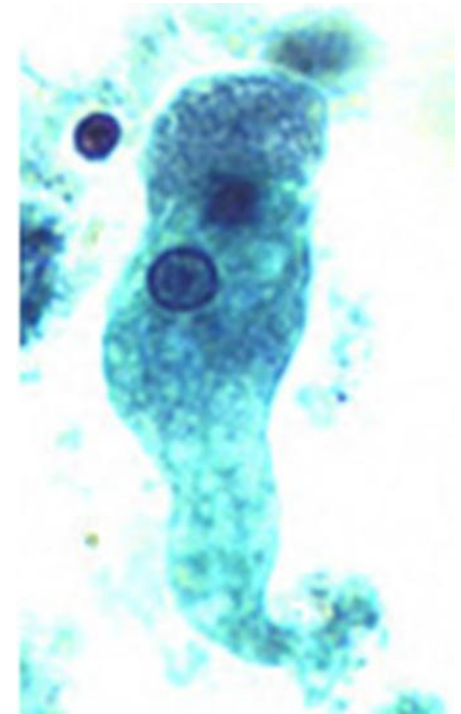
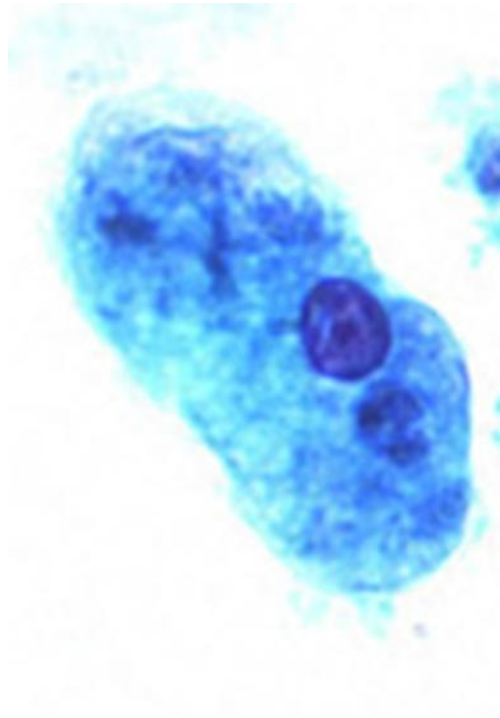
- Entamoeba histolytica is primarily a parasite of the large intestine,
- It occurs in three forms:
  - ✓ cystic form,
  - ✓ transient form (minute)
  - ✓ histolytic form (trophozoite).
- The trophozoite is the pathogenic form of the parasite (produces proteolytic enzymes).

# Cystic form of *Entamoeba histolyticae*



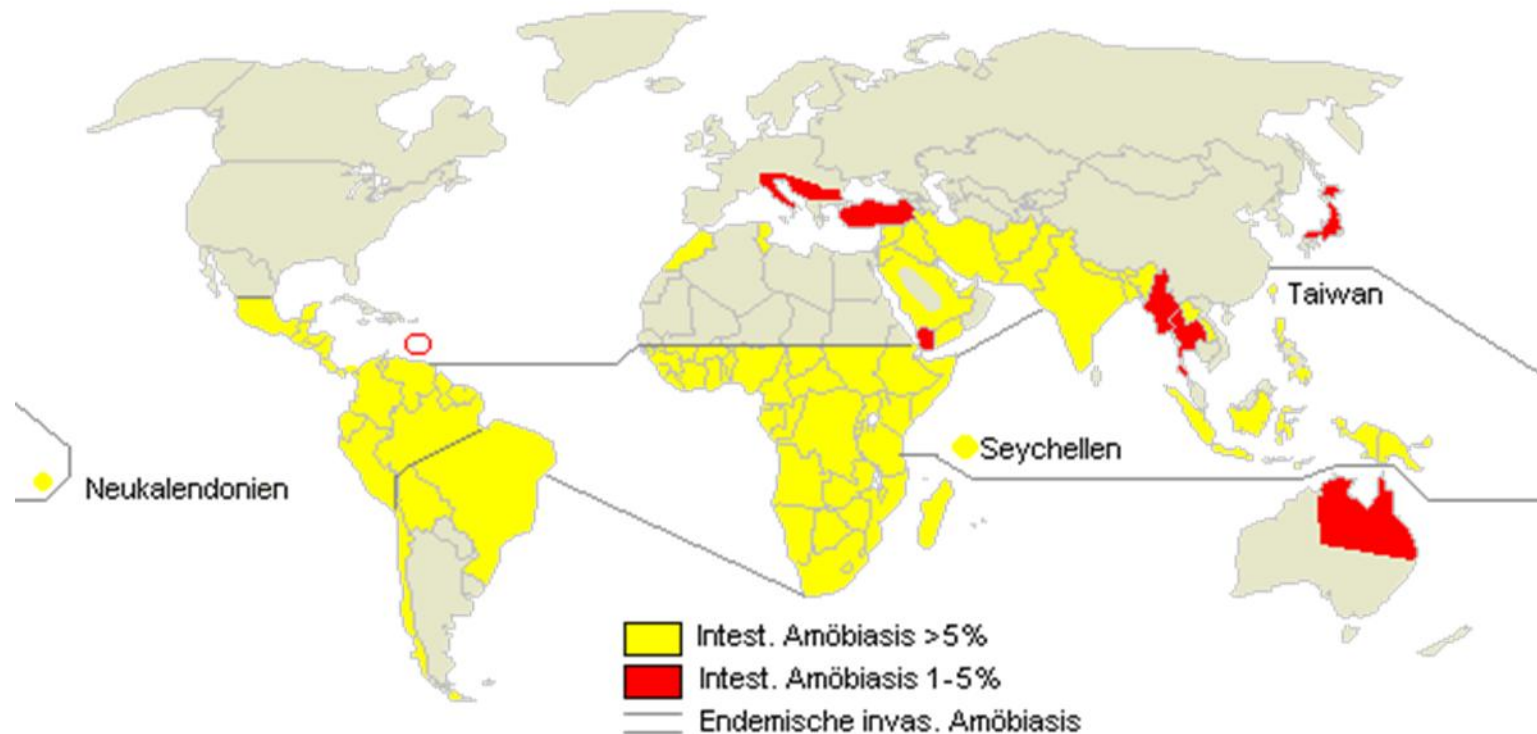


Histolytic form (trophozoite)



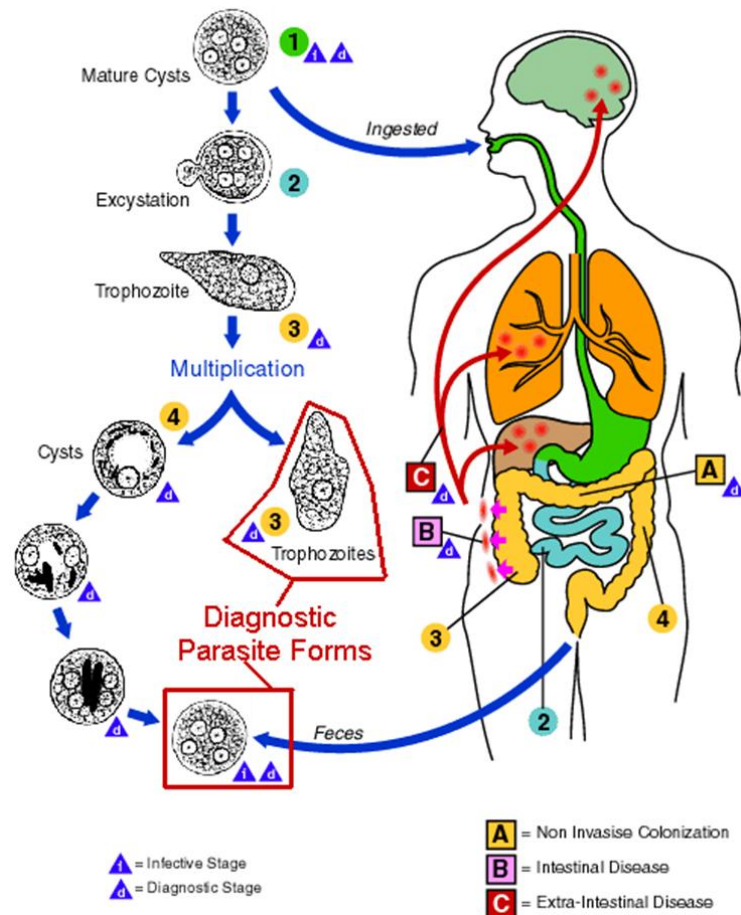
# Epidemiology

- There are about 500 million people in the world infected with amoeba
- Amebiasis is a cosmopolitan disease, but it is most prevalent in tropical and subtropical regions



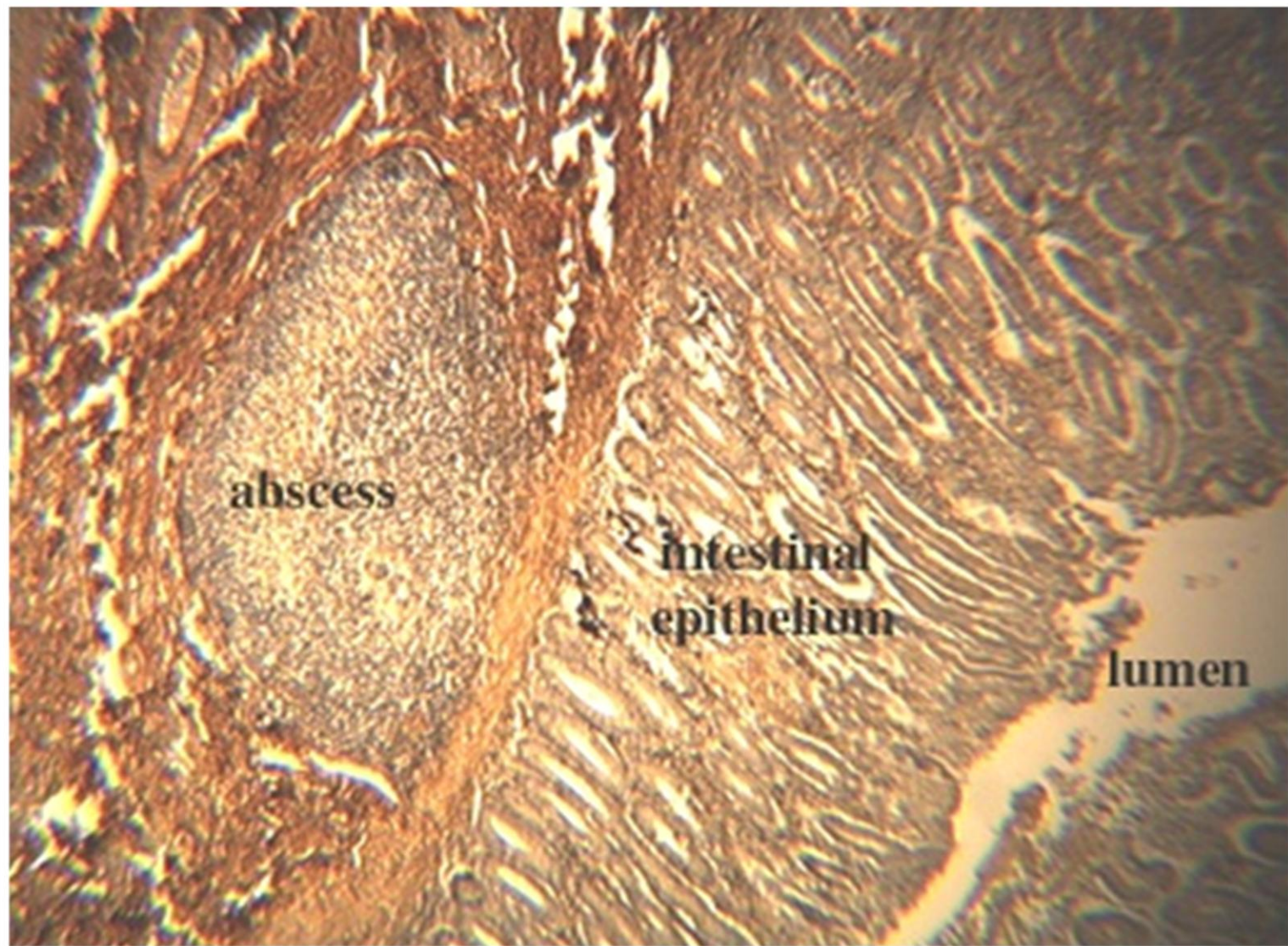
- Amebiasis is a typical fecal-oral infection; the source of infection is a patient or an amoeba carrier who excretes cysts into the external environment with their stool; a person becomes infected by introducing cysts into the body (dirty hands, water, food).

# Pathogenesis



- After ingestion, the cysts pass through the stomach and small intestine, reaching the large intestine where, under favorable conditions, they transform into trophozoites.
- Thanks to their proteolytic enzymes (cysteine proteases), they can penetrate the intestinal mucosa, causing necrotic-inflammatory changes in the submucosa, which ultimately results in the formation of ulcers.
- Lesions in amebiasis are usually localized to the cecum and ascending colon, but the rectum and sigmoid colon are often affected.
- Lesions in amebiasis are usually localized to the cecum and ascending colon, but the rectum and sigmoid colon are also often affected.
- Less rarely, trophozoites can also penetrate the blood vessels (intestinal wall) and the portal blood flow to the liver, where they form amoebic abscesses.





## Clinical picture

- Incubation in amebiasis is variable
- Amoebiasis can be clinically manifested in several forms:
  - asymptomatic amebiasis,
  - acute intestinal amoebiasis (amoebic dysentery),
  - chronic intestinal amoebiasis,
  - extraintestinal amoebiasis.

## ACUTE INTESTINAL AMEBIASIS (AMEBIC DYSENTERY)

- Rare in our climate,
- Symptoms: abdominal pain, frequent mucous-bloody stools ("rectal sputum"), tenesmus and false urges to defecate,
- Unlike bacillary dysentery, amoebic dysentery does not have more pronounced signs of fever, dehydration, and intoxication of the body.

# Complications

- Perforation with subsequent peritonitis,
- Stenosis,
- Amoebomas (chronic granulomatous proliferations in the intestinal wall),
- Bleeding (most often occult),
- Extraintestinal amebiasis (hepatic, cerebral, peritoneal, ...).



# Diagnosis

- Clinical picture
- Microbiological examinations:
  - direct microscopic examination of stool preparations,
  - stool cultivation on Leffler-Simić medium,
  - serological reactions (RVK, RIH, ELISA),
  - molecular method (PCR)
- Rectoscopic examination with mucosal biopsy (for histological examination of the mucosa for trophozoites!).

# Therapy

- Division of amebicides

Luminal amebicides	Diloxanide furoate, cefamide, paromomycin, teclosan, etofamide, diiodohydroxyquinoline, nitazoxanide, tetracyclines
Tissue or systemic amebicides	Emetine, dihydroemetine, chloroquine, miltefosine, arsenic derivatives (carbazone and milibis)
Mixed amoebicides	5-nitroimidazoles (metronidazole, ornidazole, tinidazole)



- Asymptomatic carriers (luminal agents)
  - Iodoquinol (650 mg tab.) – dose: 3×650 mg/day, 20 days
  - Paromomycin (250 mg tab.) – dose: 3×500 mg/day, 10 days
- Acute colitis
  - Metronidazole (250 mg tab.) – dose: 3×750 mg/day, 10 days + luminal agent
- Amebic liver abscess (one of):
  - Metronidazole (250 mg tab.) – dose: 3×750 mg/day, 14 days
  - Tinidazole – dose: 2gr/day, 5 days
  - Ornidazole – dose: 2gr/day, 5 days
  - + luminal agent.

Infectious Diseases  
Lecture -  
Leishmaniasis







# Definition

Leishmaniasis is a chronic infectious disease caused by parasites of the genus *Leishmania* and transmitted by insects of the genus *Phlebotomus*. Clinically, it occurs in three forms: visceral, cutaneous and mucosal.