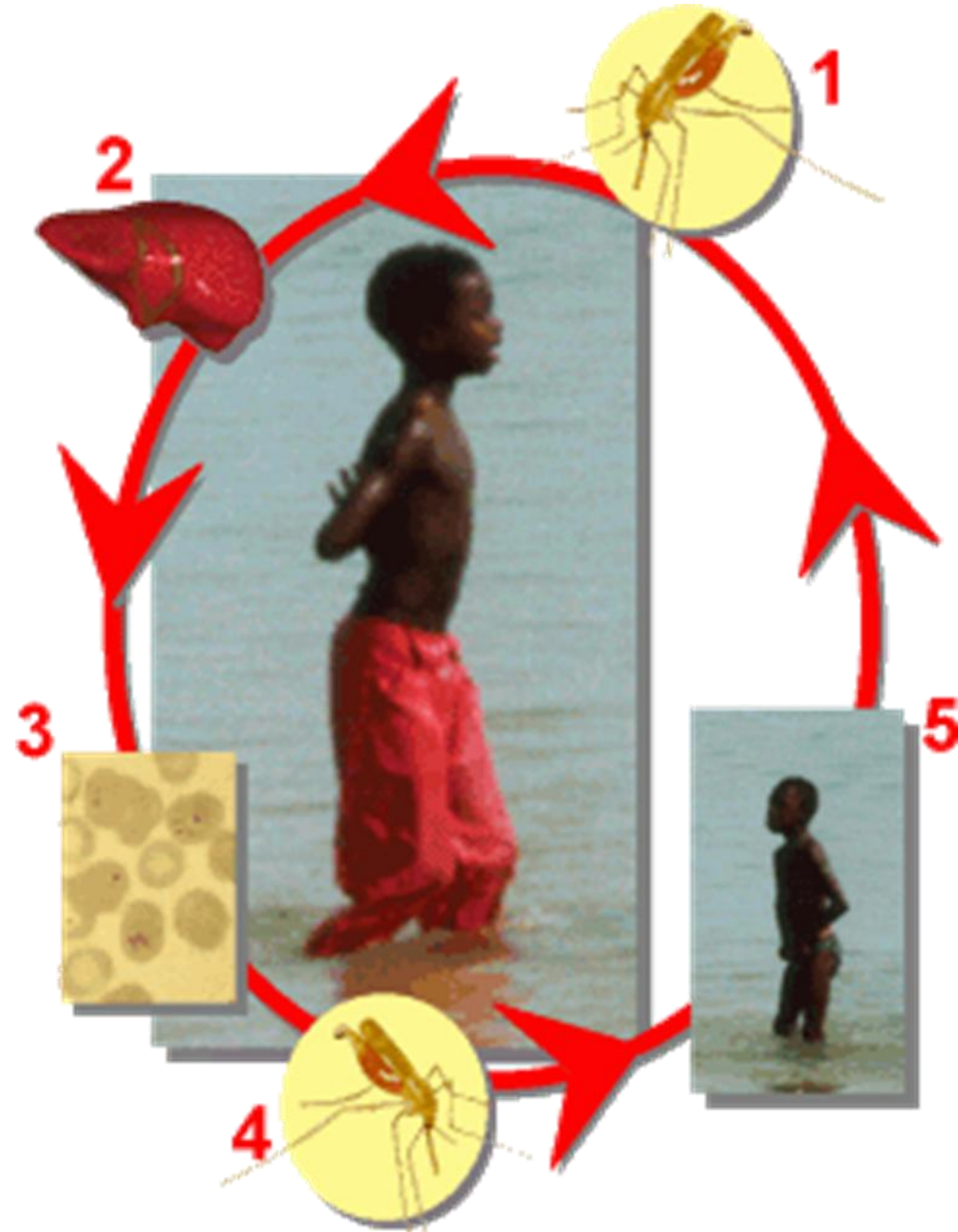


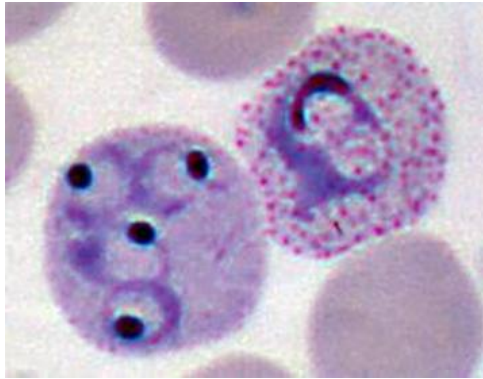
Infectious
Diseases
Lecture -
Malaria



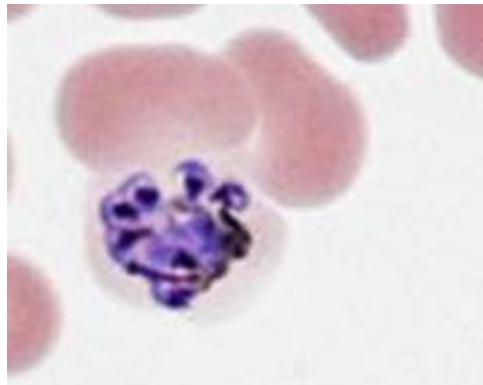
Definition:

- Malaria is an infectious disease caused by five 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.

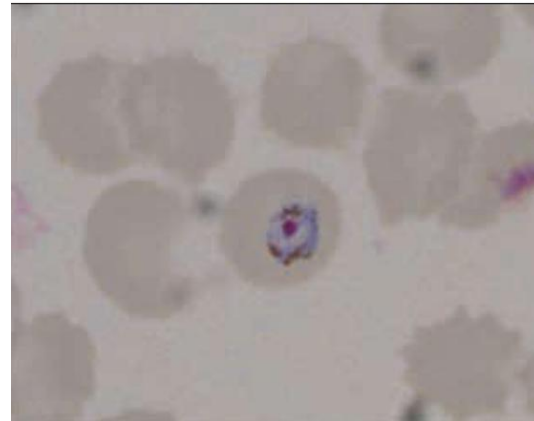
Etiology



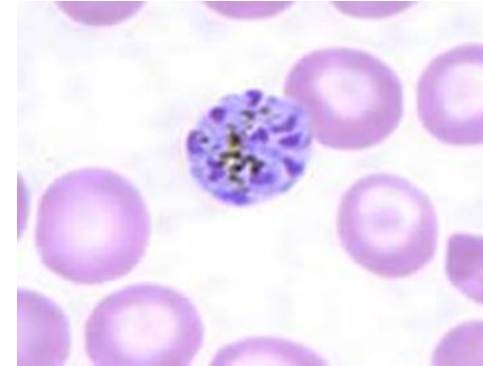
Plasmodium vivax
causative agent M.
terciane



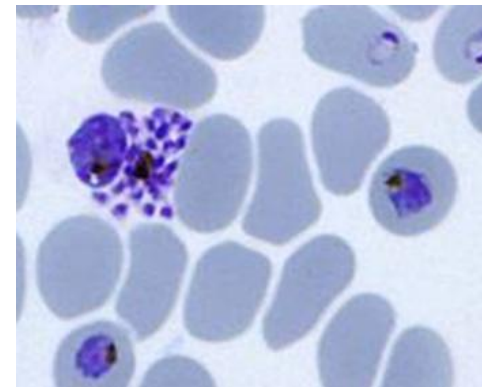
Plasmodium ovale
causative agent M. ovale



Plasmodium knowlesi



Plasmodium malariae
causative agent M.
quartane



Plasmodium falciparum
causative agent M. tropica

Anopheles

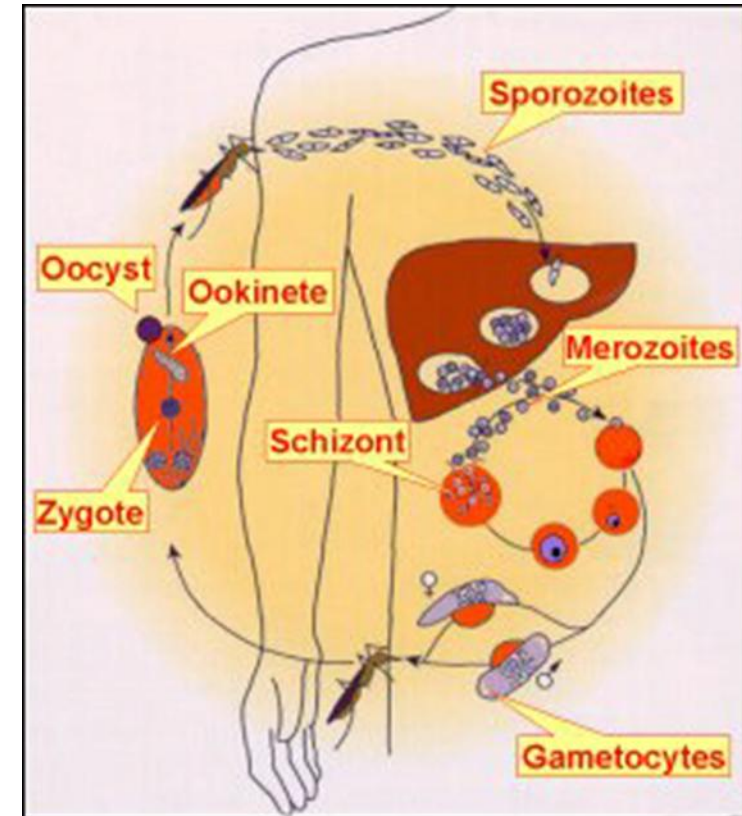


Life cycle of Plasmodium

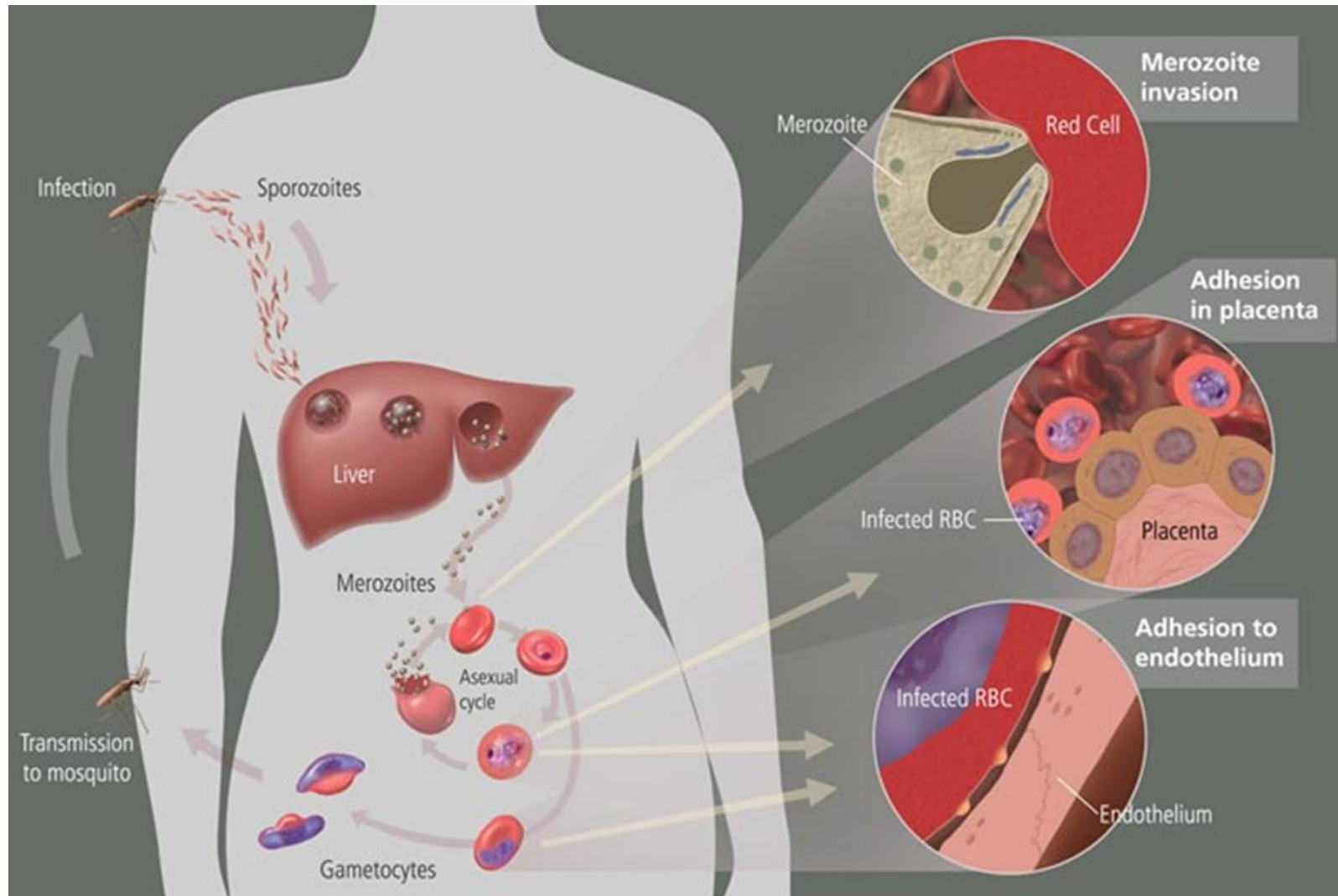
I Asexual cycle ("schizogony")

- preerythrocytic phase
- erythrocyte phase
- exoerythrocytic phase

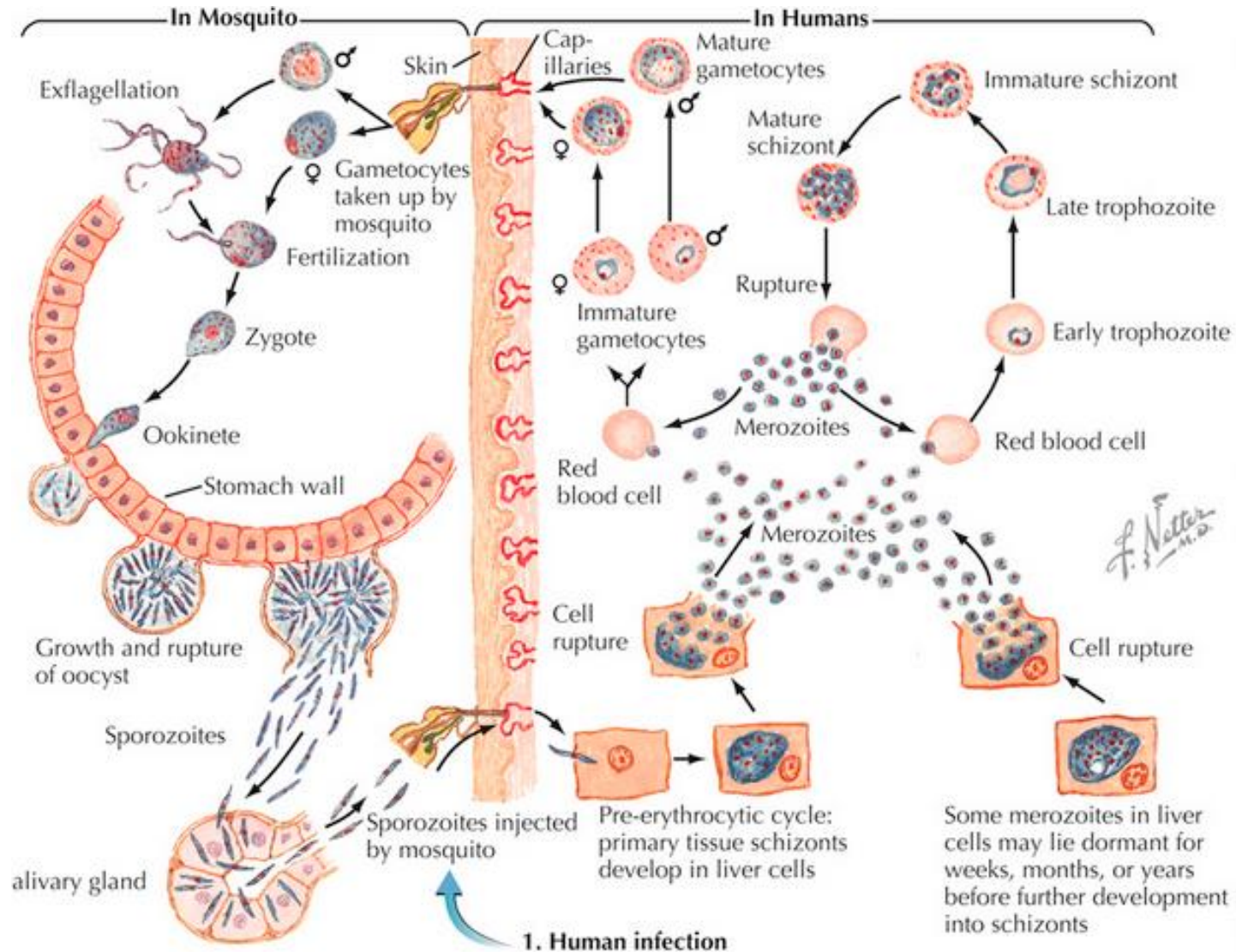
II Sexual cycle ("sporogony")



Life cycle of Plasmodium

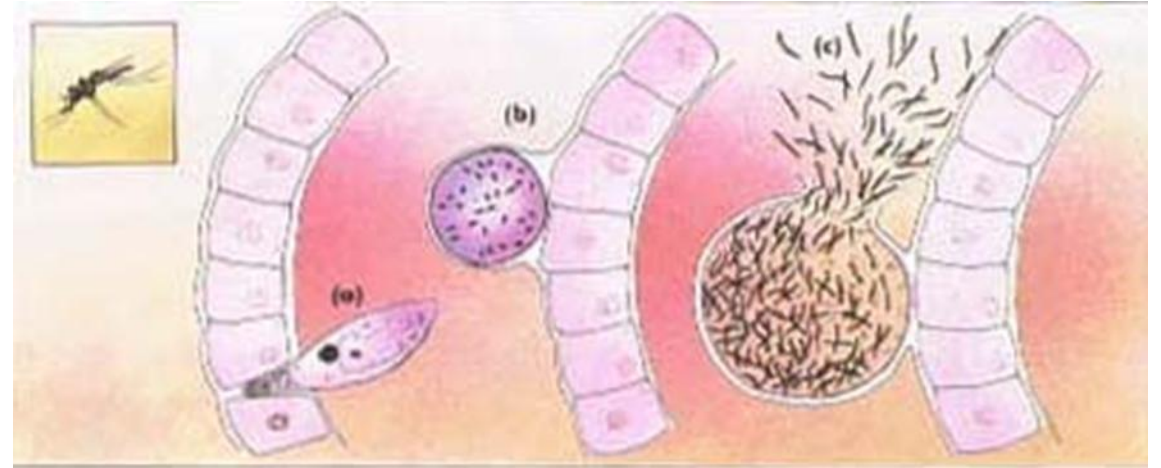


Plasmodium life cycle



- After entering the human body through an infected mosquito bite, the malarial sporozoites reach the liver, where they infect hepatocytes, incubate, and multiply
- After the parasites multiply, each infected hepatocyte ruptures, releasing hundreds to thousands of malarial merozoites into the bloodstream
- The merozoites released by the hepatocytes infect circulating RBCs, subsequently developing into early trophozoites, which appear as ring-shaped forms within RBCs on Giemsa-stained peripheral blood smears
- The intraerythrocytic trophozoites subsequently progress through the schizont phase to ultimately produce merozoites that are released on rupture of the infected RBCs
- After release, these second-generation merozoites rapidly infect other circulating RBCs and the infection is amplified, with the subsequent completion of new erythrocytic cycles resulting in the release of new generations of infective merozoites.

Oocist

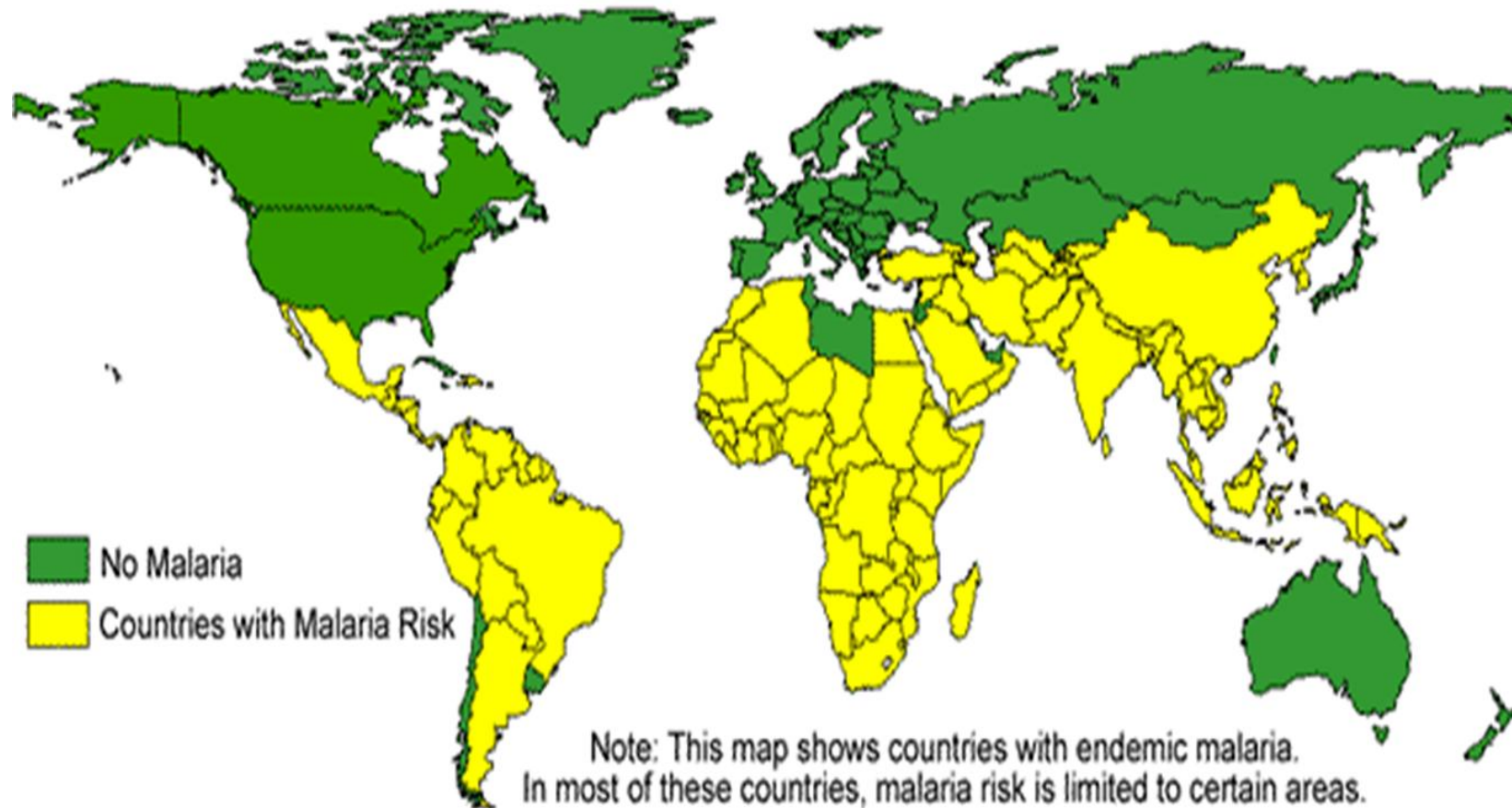


Epidemiology

- 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



A. Malaria-endemic countries in the Eastern Hemisphere¹



Boundary representation is not necessarily authoritative.

¹In this map, countries with areas endemic for malaria are shaded completely even if transmission occurs only in a small part of the country.

B. Malaria-endemic countries in the Western Hemisphere¹



Boundary representation is not necessarily authoritative.

¹In this map, countries with areas endemic for malaria are shaded completely even if transmission occurs only in a small part of the country.

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- α , **INF-g**, ...)
 - ✓ 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 forms except for *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

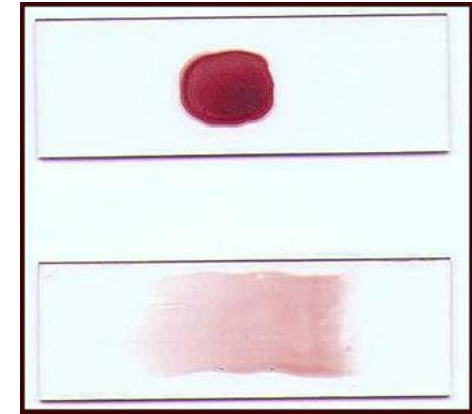
- Splenic rupture or torsion,
- Miscarriage or premature birth,
- Black blood fever.

Diagnosis

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

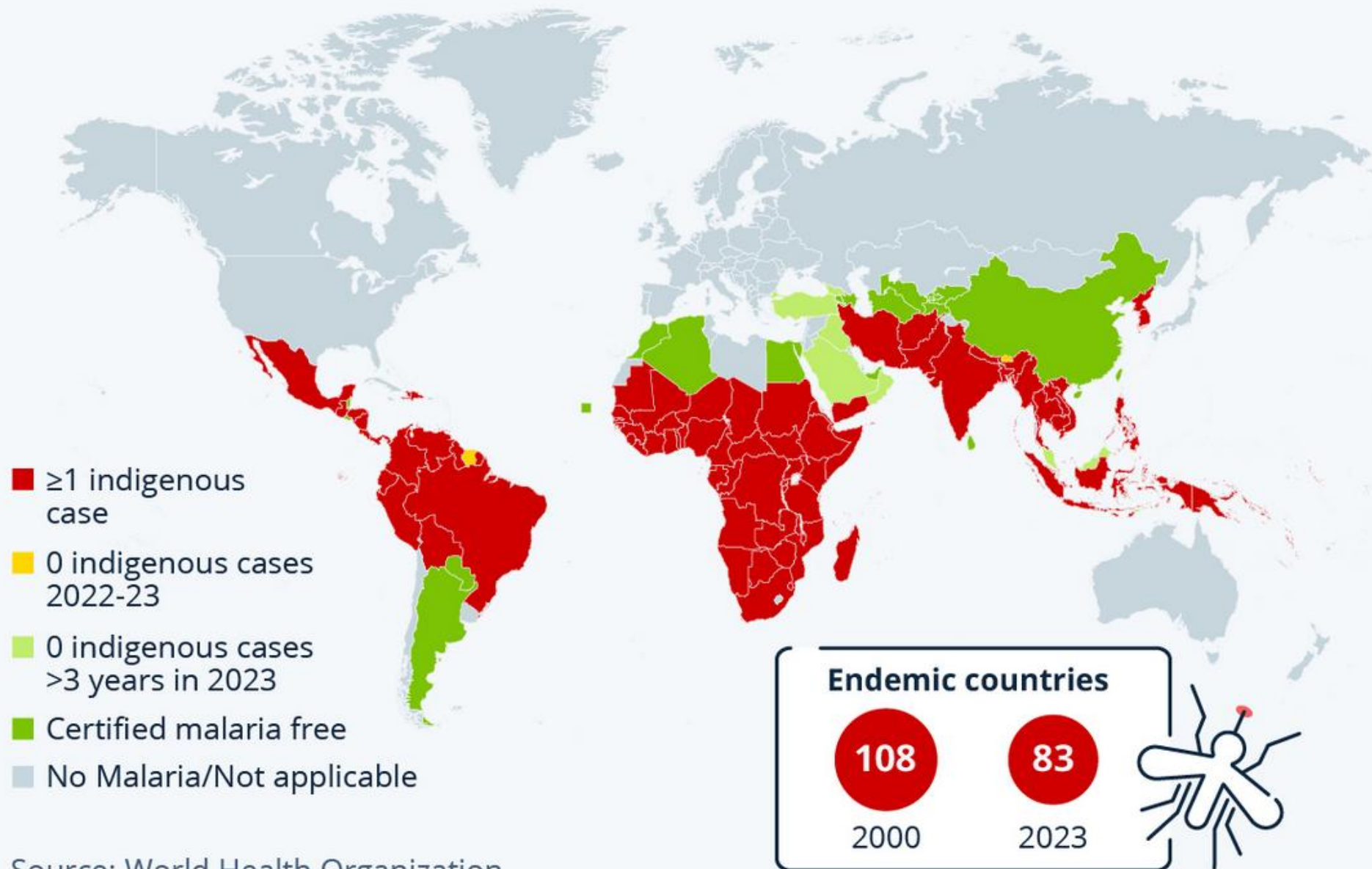
- Exact diagnosis:

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



Rapid Diagnostic Test

Status of indigenous malaria cases in 2023 in countries which had at least one case in 2000



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

Drugs for the Treatment of **Uncomplicated Malaria** in Travelers Returning to Nonendemic Countries: Malaria Caused by **Chloroquine-Sensitive** *Plasmodium falciparum*, *Plasmodium vivax*, *Plasmodium ovale*, *Plasmodium malariae*, or *Plasmodium knowlesi*

Drug-Drug Combination	Adult Treatment Regimen
Chloroquine phosphate (Aralen and generics)	First dose: 600 mg base (1000 mg salt) PO, followed by 300 mg base (500 mg salt) PO at 6, 24, and 48 h Total dose: 1500 base (2500 mg salt)
Hydroxychloroquine (Plaquenil and generics)	First dose: 620 mg base (800 mg salt) PO, followed by 310 mg base (400 mg salt) PO at 6, 24, and 48 h Total dose: 1550 mg base (2000 mg salt)
Primaquine phosphate (used to decrease the risk of relapses of <i>P. vivax</i> and <i>P. ovale</i> infections)	30 mg base PO qd for 14 days. Give the first dose of primaquine phosphate with the last dose of chloroquine phosphate or hydroxychloroquine used for treatment of <i>P. vivax</i> or <i>P. ovale</i>
Tafenoquine (similar use as Primaquine)	300 mg once with the last dose of chloroquine phosphate or hydroxychloroquine used for treatment of <i>P. vivax</i> or <i>P. ovale</i>

Drugs for the Treatment of **Uncomplicated Chloroquine-Resistant Plasmodium falciparum** Malaria in Travelers Returning to Nonendemic Countries

Drug-Drug Combination	Adult Treatment Regimen
Atovaquone-proguanil combination tablet (Malarone)	Adult tablet: 250 mg atovaquone and 100 mg proguanil Adult dose: 4 adult tablets as a single oral dose daily for 3 consecutive days
Artemether-lumefantrine combination tablet (Coartem)	One tablet: 20 mg artemether plus 120 mg lumefantrine 3-day course of six doses total taken at 0, 8, 24, 36, 48, and 60 h Adult dose ≥35 kg: four tablets per dose
Quinine sulfate plus doxycycline or tetracycline or clindamycin	Quinine sulfate: 542 mg base (650 mg salt) 8 mg base/kg tid for 3 days (or 7 days for infections acquired in Southeast Asia)
	Doxycycline: 100-mg tablet Adult >50 kg: 1 tablet PO bid for 7 days
	Tetracycline: 250-mg tablet Adult: 250-mg tablet PO qid for 7 days
	Clindamycin: 300-mg base tablet Adult >60 kg: 20-mg base/kg/day divided into 3 doses/day for 7 days
Mefloquine (Lariam and generics)	Total dose: Five (250 mg salt) tablets
Dihydroartemisinin-piperaquine (Eurartesim)	One dose daily for 3 consecutive days Adults >50 kg: 3 tablets daily for 3 days

- 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.

Duration of Therapy for Malaria Chemoprophylaxis Regimens

Drug	Chloroquine-Sensitive Malaria	Chloroquine-Resistant Malaria	Pretravel Administration: Time Before First Potential Exposure to Begin Medication	Posttravel Administration: Time After Last Known Exposure to Continue Medication
Atovaquone-proguanil (daily dose)	Yes	Yes	1–2 days	7 days
Tafenoquine (daily for 3 days pre exposure) then once a week till one week after exposure	Yes	Yes	3 days	1 week
Primaquine (daily dose)	Yes	Yes	1–2 days	7 days
Doxycycline (daily dose)	Yes	Yes	1–2 days	4 weeks
Chloroquine (weekly dose)	Yes	No	1 week	4 weeks
Mefloquine (weekly dose)	Yes	Yes	1–3 weeks	4 weeks

❑ **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.

- DOXYCYCLINE, 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.

Infectious Diseases Lecture

Amebiasis



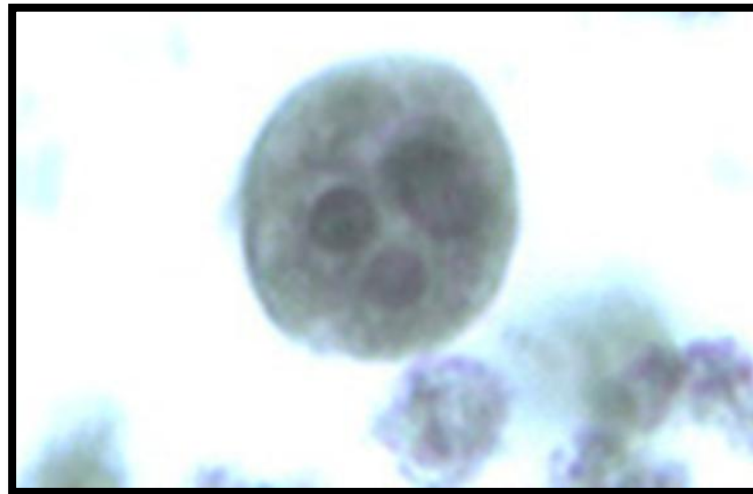
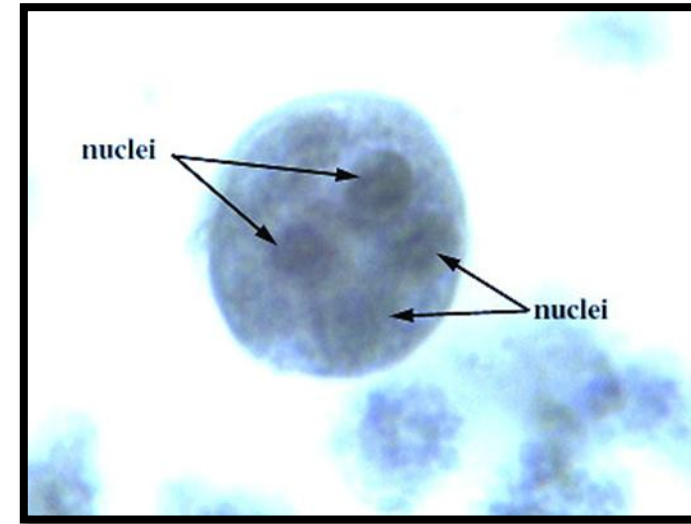
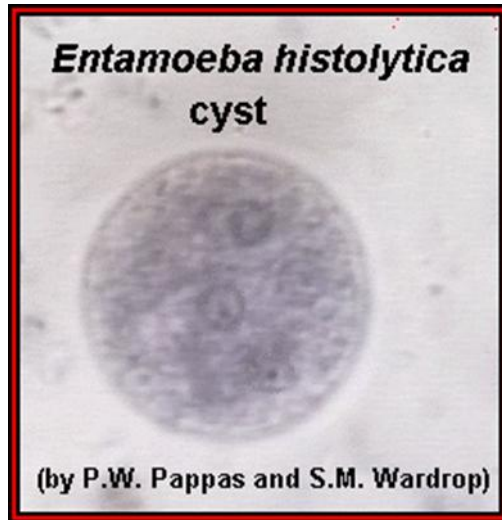
Definition

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.

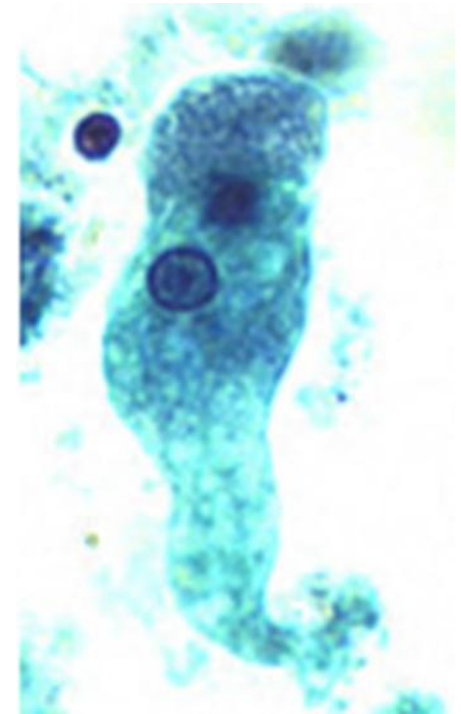
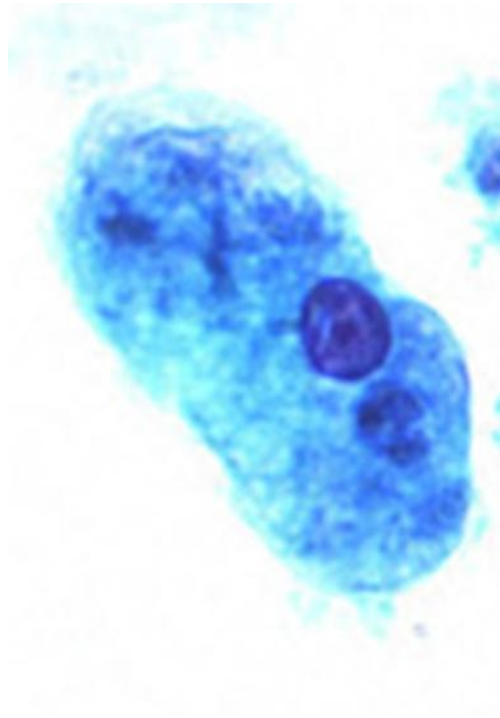
Etiology

- 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 histolytica*

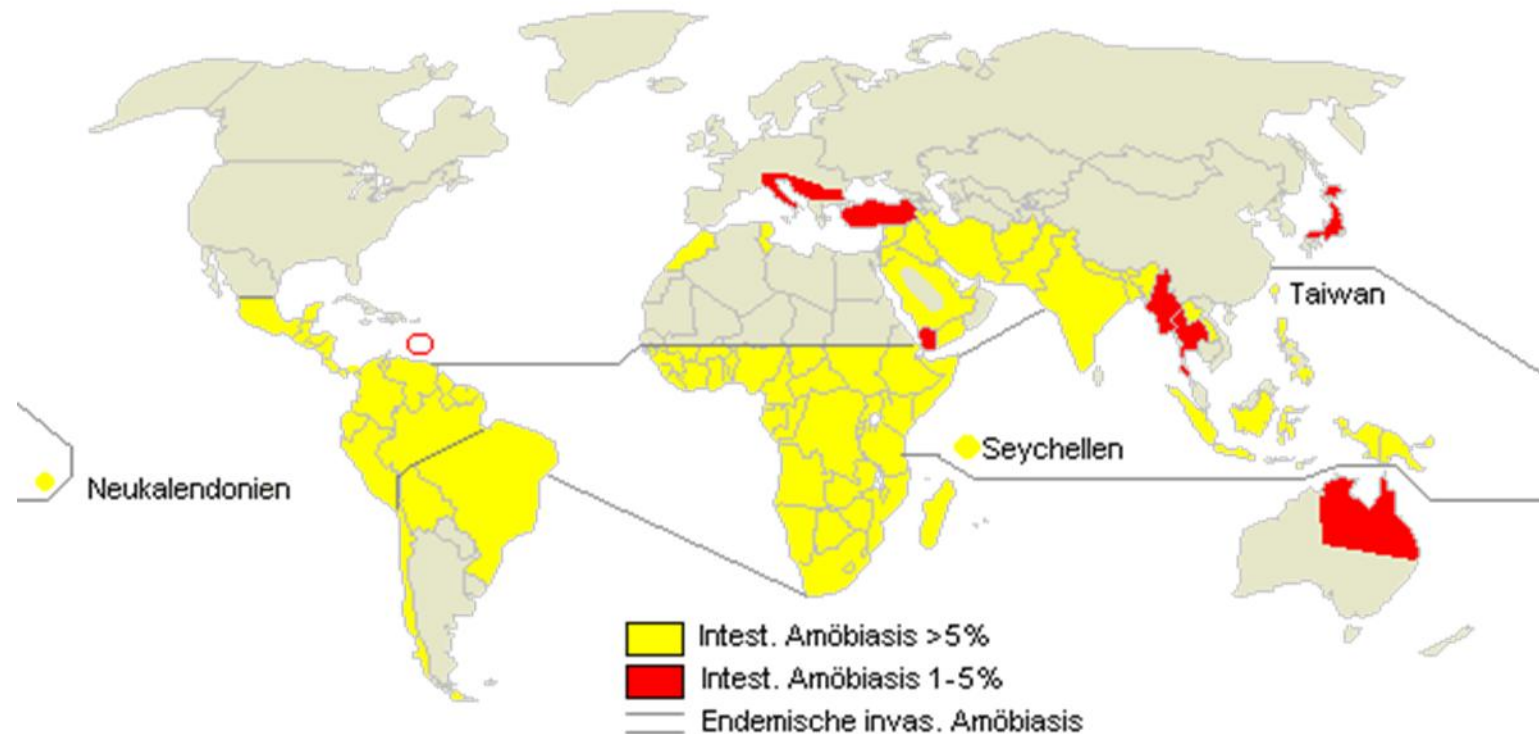


Histolytic form (trophozoite)



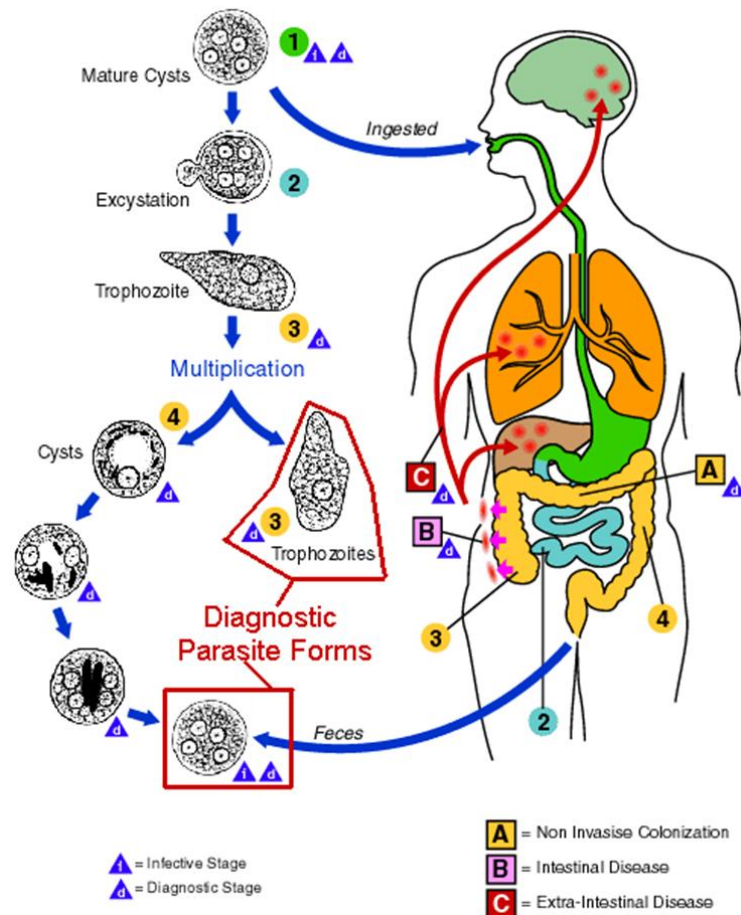
Epidemiology

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

Drug Therapy for Amebiasis

Drug	Adult Dose
Asymptomatic Cyst Passer	
Paromomycin	25–35 mg/kg/day by mouth in 3 divided doses × 7 days
Iodoquinol	650 mg by mouth tid ^a × 20 days
Mild to Moderate Intestinal Disease	
Either metronidazole or tinidazole followed by either iodoquinol or paromomycin as described	
Metronidazole	500–750 mg by mouth tid × 7–10 days
Tinidazole	2 g once daily by mouth × 3 days
Severe Intestinal Disease, Amebic Liver Abscess, and Other Extraintestinal Infection	
Either metronidazole or tinidazole followed by one of the luminal drugs used for asymptomatic	
Metronidazole	750 mg tid by mouth or IV × 7–10 days
Tinidazole	2 g once daily by mouth × 5 days



- 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

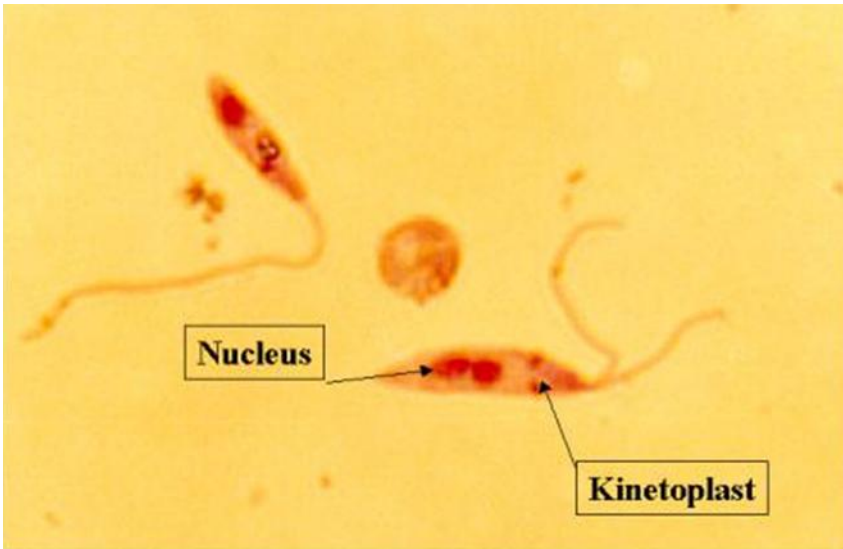
Leishmaniasis is a chronic infectious disease caused by parasites of the genus *Leishmania* and transmitted by insects of the genus *Phlebotomus*. Clinically, it occurs in three forms: visceral, cutaneous and mucosal.

Etiology

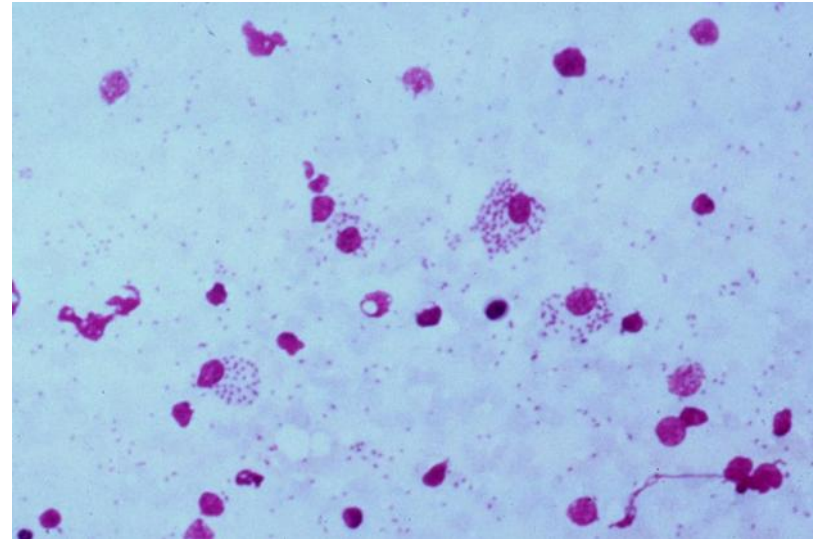
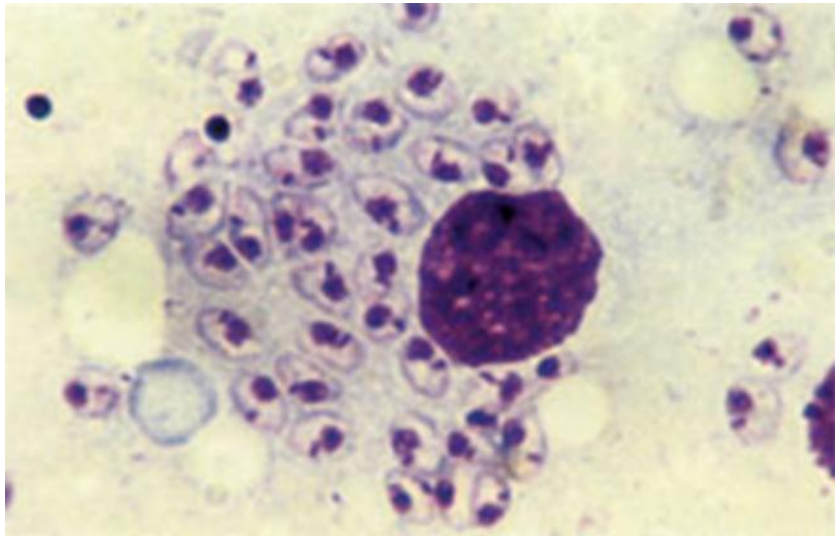
- Leishmania (genus Leishmania, family Trypanosomatidae, class Mastigophora, phylum Protozoa)
- Visceral leishmaniasis is caused by: *L. donovani*, *L. infantum* and *L. shagasi*
- Cutaneous leishmaniasis in the Old World is caused by: *L. tropica*, *L. infantum*, *L. major*, *L. eatiopica*
- Cutaneous and mucosal leishmaniasis in the New World is caused by: *L. mexicana*, *L. braziliensis*, *L. peruviana*, *L. guyanensis*, *L. amazonensis*

- ❑ Leishmania occurs in two morphological forms:
 - promastigote (leptomonans)
 - amastigote

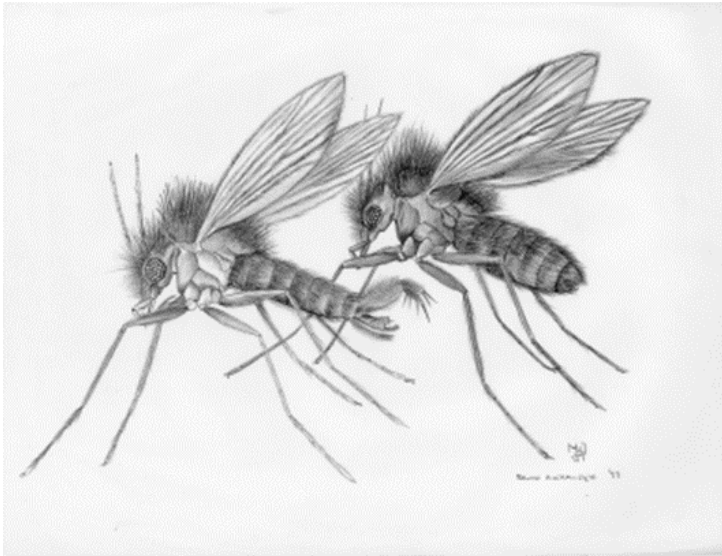
Promastigot



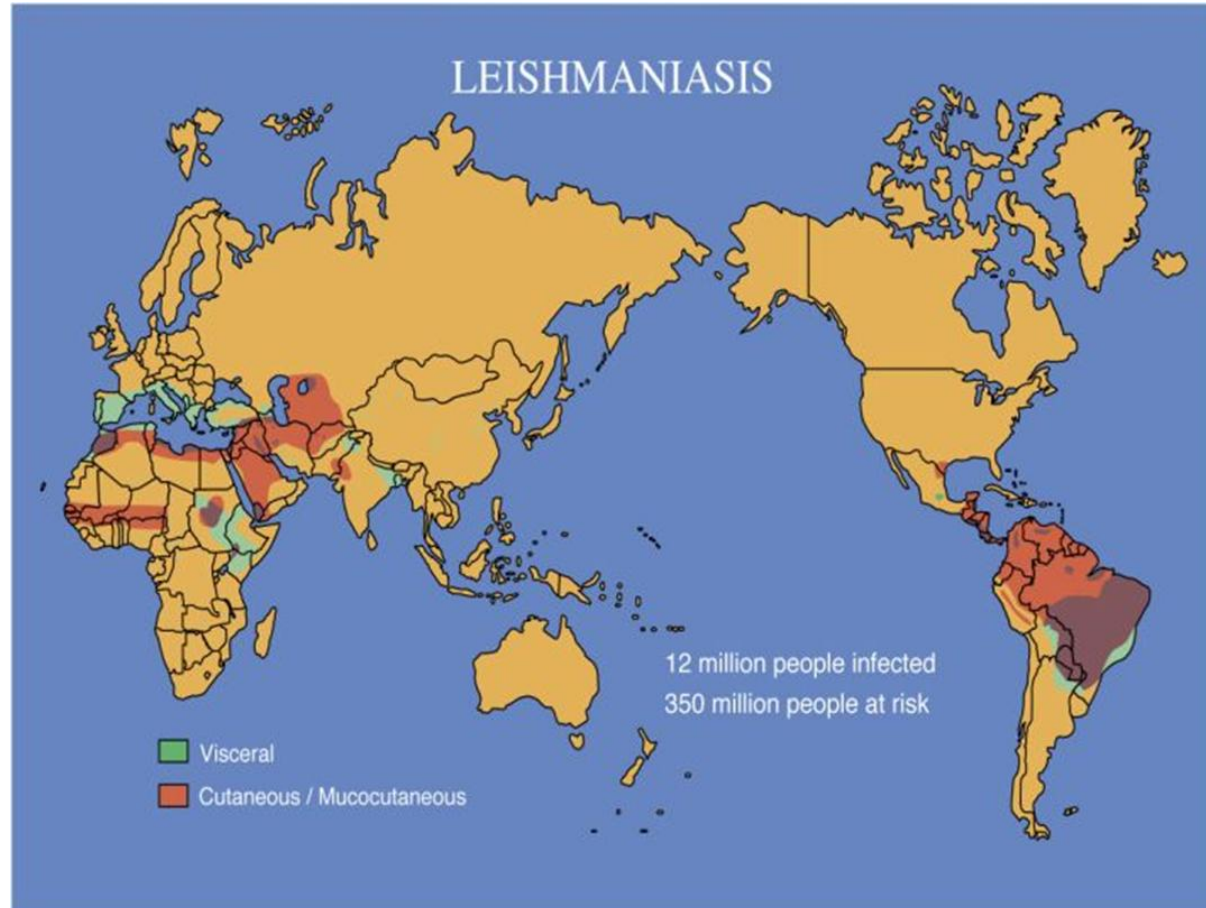
Amastigot



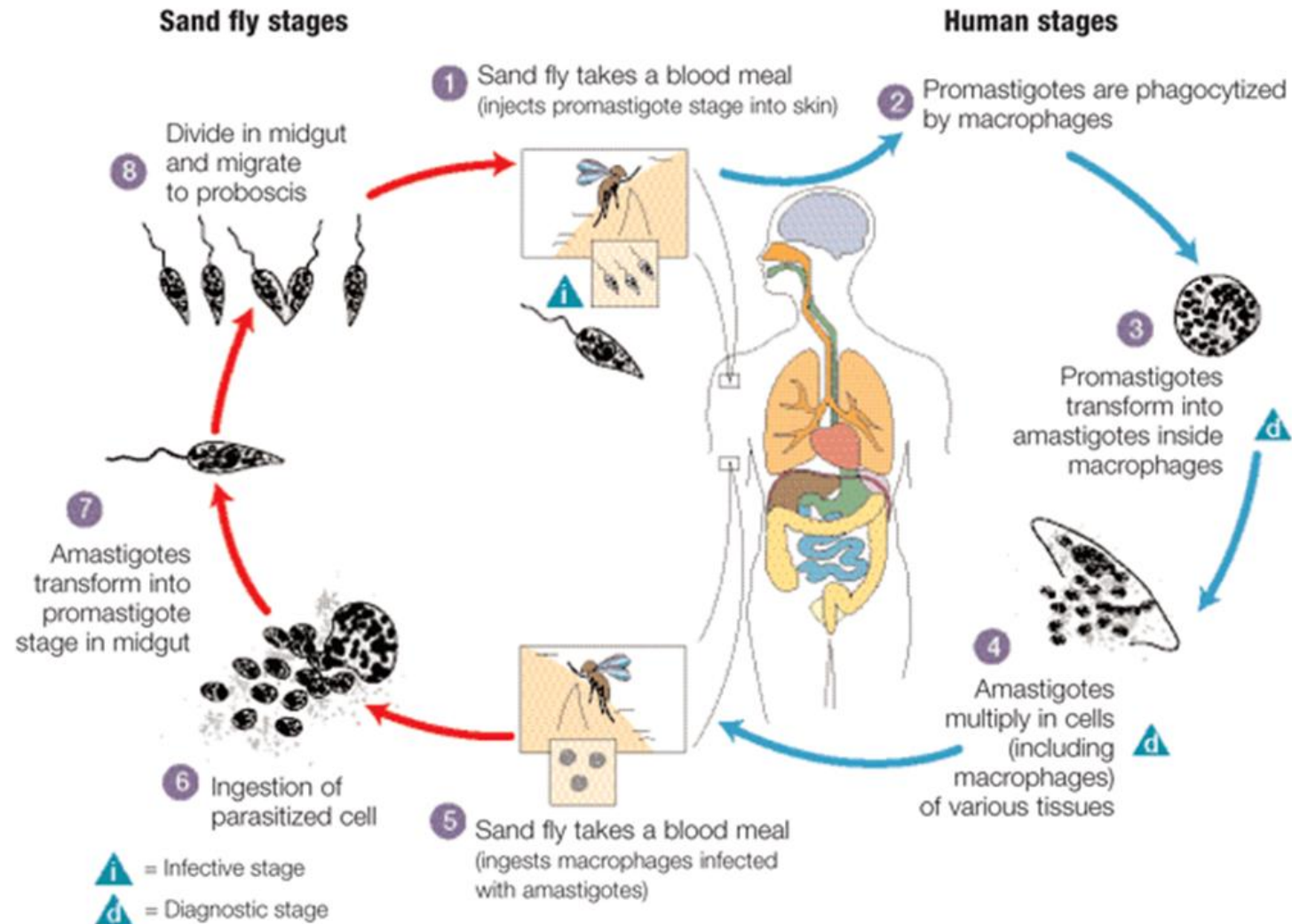
- ❑ The reservoir of infection is humans and various species of domestic and wild animals
- ❑ The disease is most often transmitted by the bite of insects of the genus *Phlebotomus*, less often it can be transmitted by blood transfusion and sexual contact



Leishmaniasis most commonly occurs in tropical countries in Asia, Africa, and South America, and in Europe, mainly around the Mediterranean Sea



Phlebotomine....promastigote....RES...amastigote..... RES (lymph glands, spleen, liver, bone marrow).

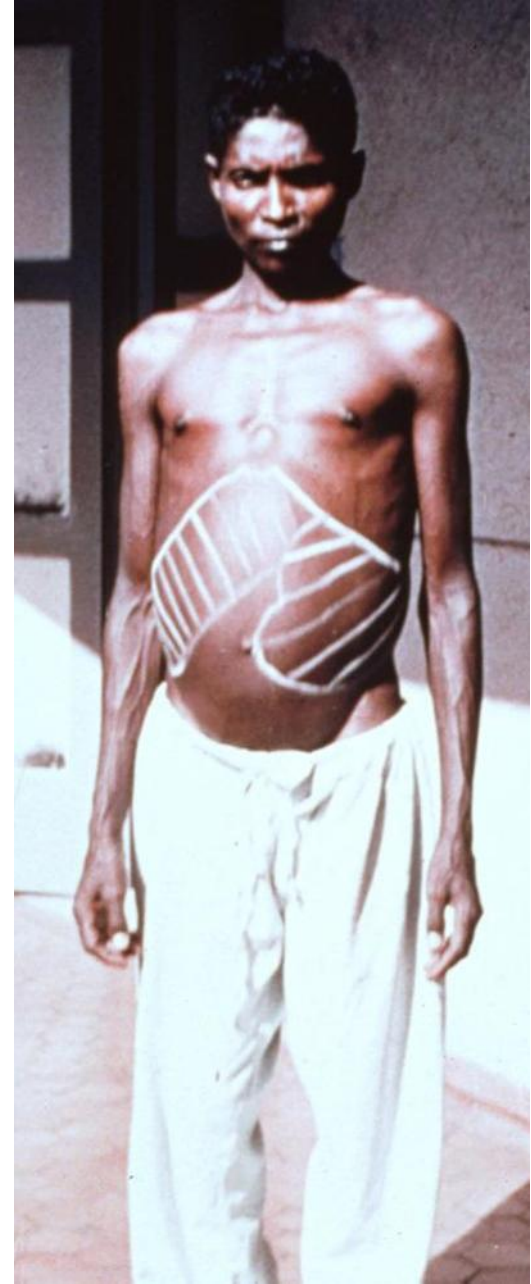


Clinical picture

- The disease manifests itself in three clinical forms:
 - ✓ Visceral
 - ✓ Cutaneous
 - ✓ mucosal

Visceral leishmaniasis (Kala Azar)

- Incubation varies from 3 days to 8 months
- The disease begins gradually: fever, sweating, loss of appetite, malaise, weight loss
- Physical findings: pale skin and mucous membranes, lymphadenopathy, splenomegaly, hepatomegaly, interstitial pneumonia, hemorrhagic syndrome
- Untreated visceral leishmaniasis ends in death.



Cutaneous leishmaniasis

- Incubation varies from 2 weeks to several months
- Changes occur on exposed parts of the body: at the site of the bite, a **macule** first appears, which quickly turns into a **papule**, and this into a subcutaneous **nodule**, which can persist for months and spontaneously disappear or exulcerate (painless ulceration)
- Skin changes are accompanied by regional lymphadenitis.

Cutaneous leishmaniasis

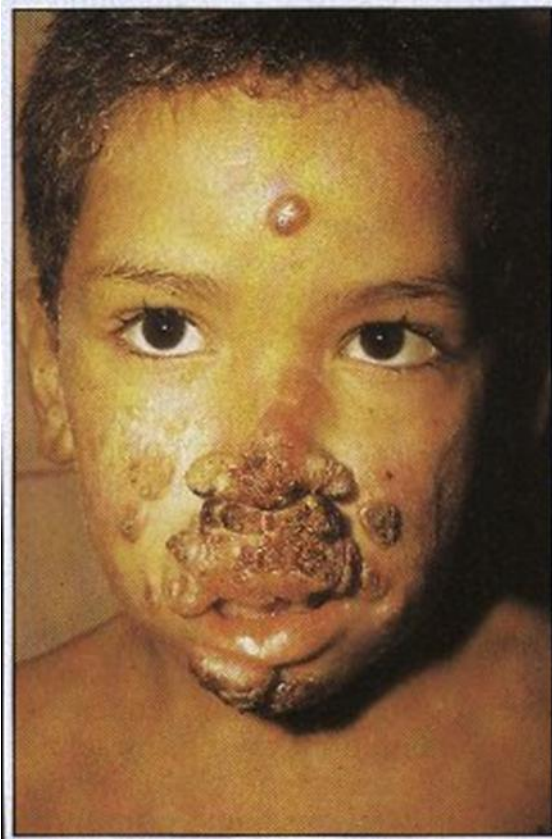


Diffuse cutaneous leishmaniasis



Mucosal leishmaniasis

- It is characterized by extensive, destructive changes in the mucous membrane of the nose, mouth, pharynx or larynx (local deformities).



Diagnosis

- The diagnosis is made on the basis of:
 - ✓ Clinical picture
 - ✓ Epidemiological data and
 - ✓ Laboratory analyses

Laboratory diagnostics

- Hematological analyses

- ✓ Pancytopenia (anemia, leukopenia, thrombocytopenia).

- Biochemical analyses

- ✓ hypoalbuminemia,

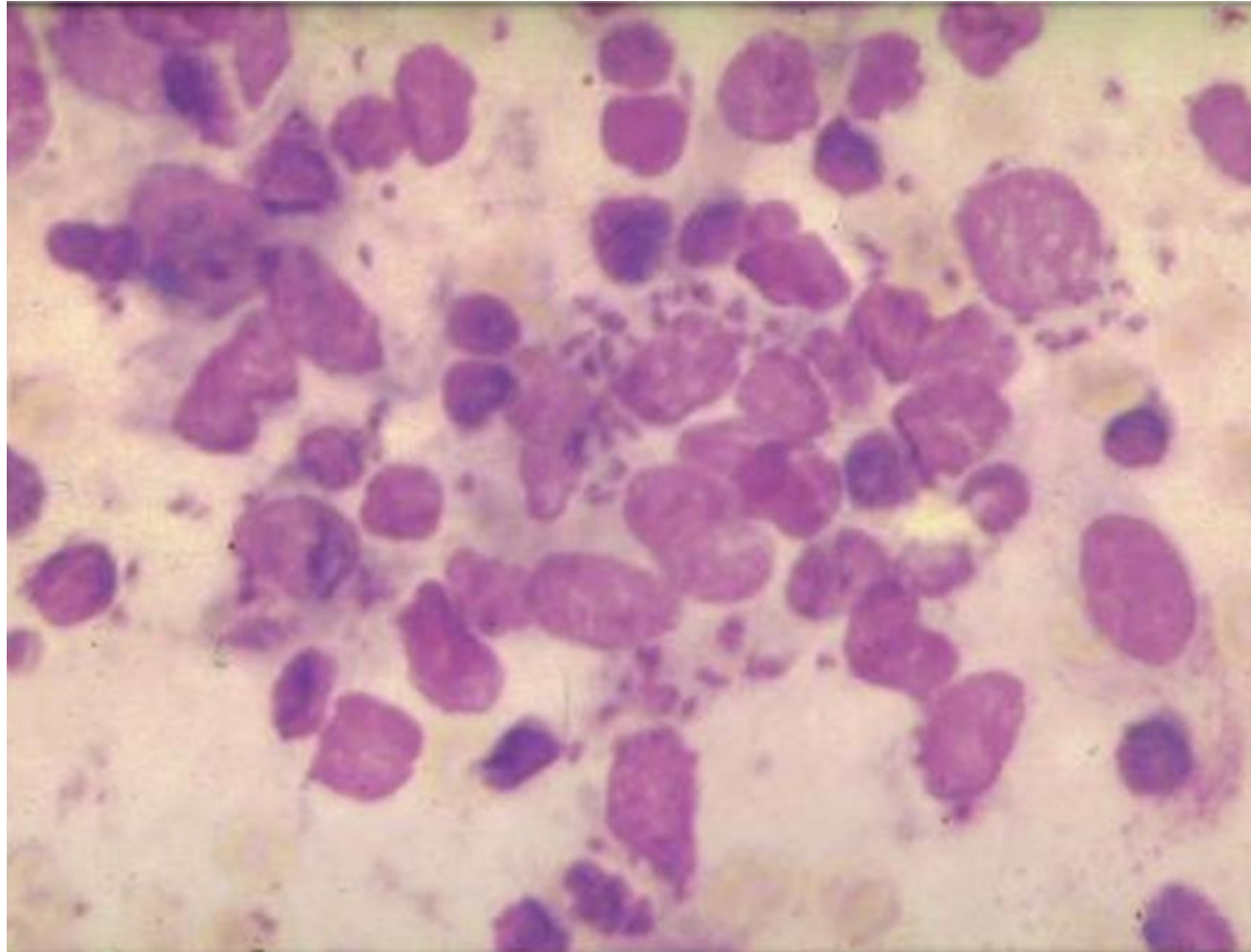
- ✓ hypergammaglobulinemia,

- ✓ increased transaminase activity.

Etiological diagnosis

- Identification of the causative agent in the tissue, most often bone marrow (microscopic examination of punctate)
- Isolation of the causative agent from blood, bone marrow and other tissues (cultivation on NNN media)
- Detection of specific antibodies to Leishmania (IF, ELISA)
- Detection of parasitic DNA (PCR)

Amastigote in a skin biopsy



Therapy

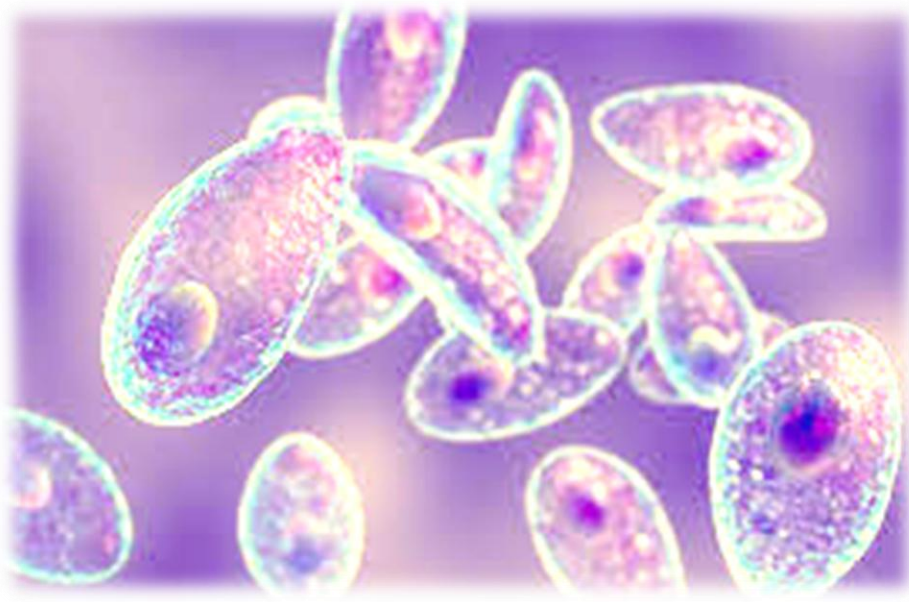
- **Antiparasitic therapy**

- ✓ antimony preparations,
- ✓ aromatic diamides,
- ✓ amphotericin B.

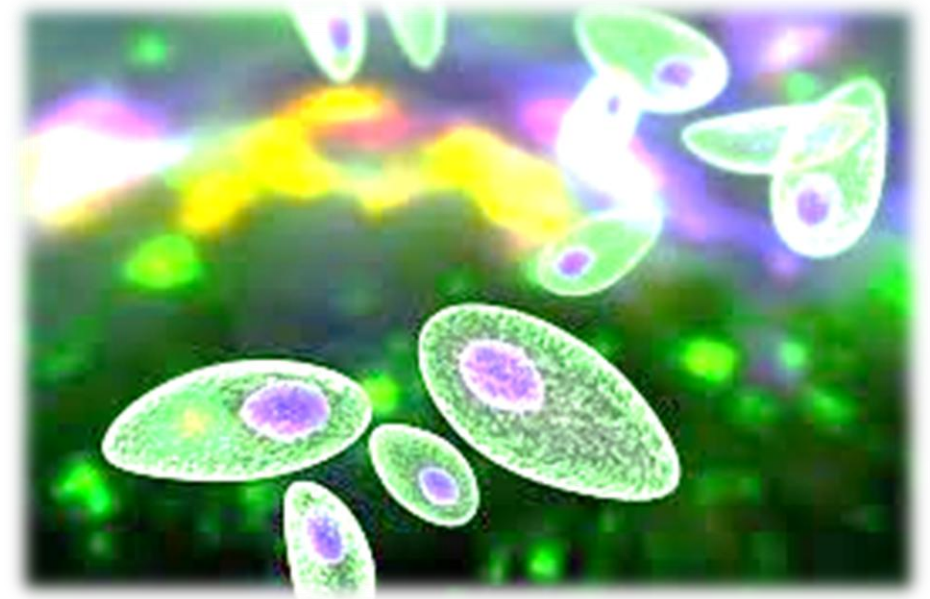
- **Symptomatic-substitution therapy**

- ✓ treatment of anemia (blood transfusions, iron, vitamin B12),
- ✓ treatment of hypoproteinemia (20% albumin),
- ✓ high-calorie diet.





Infectious diseases - Lecture –
TOXOPLASMOSIS/TOXOPLASMOSIS



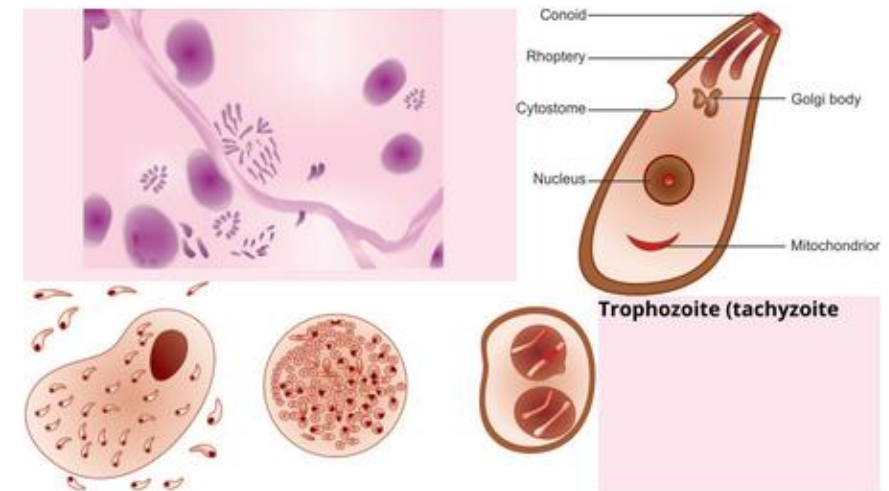
ETIOLOGY

- Protozoa-TOXOPLASMA GONDII
- Trophozoite (tachyzoite)
- CYST (bradyzoite)
- Oocyst-infective form in the cat's intestine

Life cycle

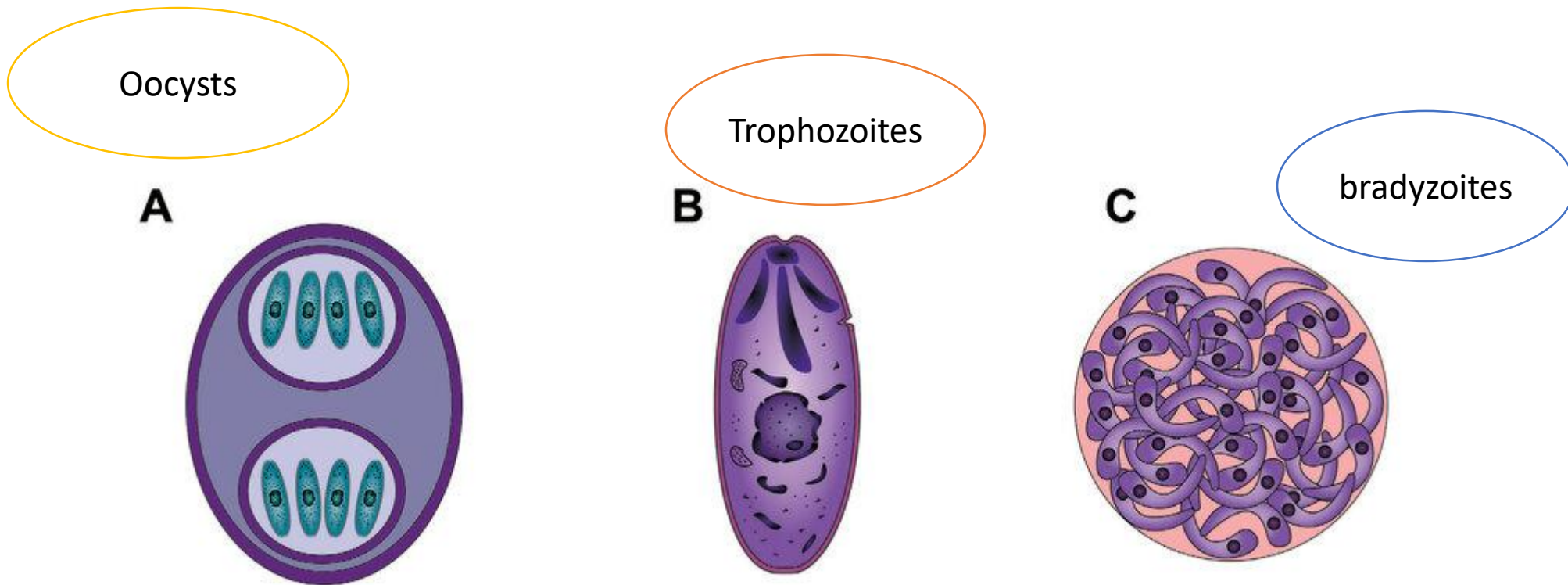
Trophozoites

- Trophozoites-infection of cells (all cells with a nucleus)
- Pushing of the nucleus to the periphery-pseudicyst
- Splashing of infected cells-infection of naive cells
- Due to the development of immunity-prevention of further development and multiplication of trophozoites



Life cycle

- **Cystic forms** (surrounded by a membrane) - latent phase
- Division of trophozoites within the cyst is significantly slower - **bradyzoites** (infectious form - CNS, myocardium)



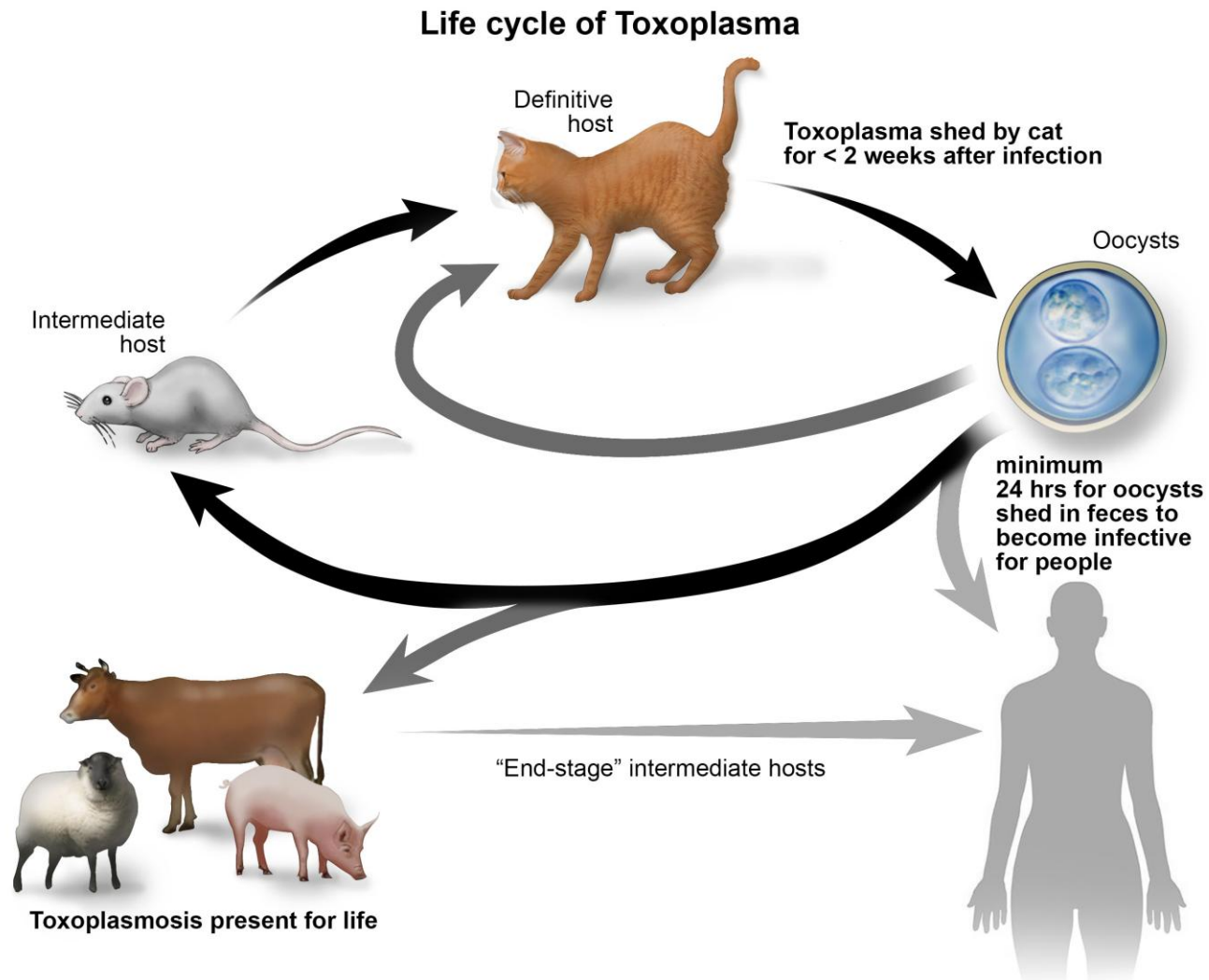
Life cycle

Oocyst

- Oocyst-intestinal epithelium of cat (infectious form, sporozoite)
- Excretion into the external environment-contamination
- Human infection→trophozoite→cyst, pseudocyst

- Cat infection-oocyst, tissue forms
- Cat intestine-oocyst→sporozoite→intestinal epithelium
↓
- Schizonts→spindle merozoites→occupation of new cells
- Some of the merozoites→gametocytes→gametes
↓
- Zygote→oocyst→external environment

Life cycle



EPIDEMIOLOGY

- The most widespread zoonosis in the world
- The prevalence of tissue cysts in edible meat is very high! (they can also be found in eggs, milk - especially goat's milk, on vegetables)
- Reservoir: cats (1% of cats worldwide excrete oocysts)
- Numerous animals - carriers of cysts
- Routes of spread:
- Consumption of raw, i.e. thermally unprocessed meat and organs (contain cysts)- 25% of pork and beef

Routes of spread

- Contaminated water, food and hands (with oocysts)
- Parenteral infection of laboratory workers (accidental)
- Blood and blood product transfusion
- Organ transplantation
- Transplacental transmission

PATHOGENESIS

- Multiplication at the site of entry



- Regional LGL→parasitemia



- Infection of susceptible cells (focal necrosis)



- Development of immunity (up to 3rd week)→cysts (myocardium, CNS, lungs, liver, uterus, intestinal wall, spleen, eye, muscles, LGL)
- Cysts are inactive throughout life in most people (most common)-asymptomatic cyst carriage
- **Immunosuppression** (cytostatics, corticosteroids, AIDS)→massive necrosis (brain, heart, lungs)

CLINICAL PICTURE

Acquired toxoplasmosis in immunocompetent individuals

Acquired toxoplasmosis in immunodeficient individuals

Congenital toxoplasmosis

Ocular toxoplasmosis

Acquired toxoplasmosis in immunocompetent individuals

- The most common clinical manifestation
- In 80-90% of cases, it is asymptomatic
- Generalized lymphadenopathy (lymphoglandular form) - predominates in the neck region
- Symptoms (mild or absent): weakness, night sweats, myalgia, sore throat, headache, subfebrile temperature, abdominal pain (abdominal lymphadenopathy)
- Rash, hepatosplenomegaly (sometimes)
- Less common: disseminated form, chorioretinitis (unilateral), meningoencephalitis, hepatitis, myocarditis, pneumonia
- Lasts several months, has a benign course

Acquired toxoplasmosis in immunodeficient individuals

- Severe clinical course (most common in patients with AIDS)
- ✓ CNS infection
- ✓ Myocarditis
- ✓ Pneumonitis
- ✓ Myositis
- ✓ Chorioretinitis
- ✓ Orchitis

CONGENITAL TOXOPLASMOSIS

- Acute maternal infection during pregnancy (much less common, reactivation of chronic infection in pregnant women, due to severe immunosuppression)
- 1st trimester → 25% fetal infection (spontaneous abortion, fetal death, generalized neonatal disease)
- 2nd and 3rd semester → 50-65% fetal infection (80% of infected children are born without symptoms)

Clinical picture

- **Chorioretinitis** (bilateral), blindness, epilepsy, psychomotor and mental retardation, anemia, jaundice, encephalitis, microcephaly, intracranial calcifications, pneumonitis
- Most children are born healthy in appearance
- **Premature babies** → signs of eye and CNS damage (in the first 3 months of life)
- **Term children** → milder clinical picture, in the first 2 months lymphadenopathy, hepatosplenomegaly (although CNS damage and ocular symptoms may occur later)

OCULAR TOXOPLASMOSIS

- Common manifestation of congenital toxoplasmosis
- Progressive necrotizing retinitis (bilateral)
- Visual impairment
- Blindness
- Most commonly manifests in the 2nd or 3rd decade of life
- Diff.dg: TB, syphilis, leprosy, ocular histoplasmosis

DIAGNOSIS (not simple)

- EPIDEMIOLOGY AND CLINICAL DATA ARE NOT RELIABLE
- HISTOPATHOLOGICAL MATERIAL: staining, cultivation, inoculation of susceptible animal (most reliable)
- SEROLOGY
 - SABIN-FELDMAN test (“dye test”)
 - Complement fixation reaction
 - Indirect immunofluorescence test (IgM, IgG)
 - ELISA (IgM, IgG)

THERAPY

- Mild forms (lymphoglandular) in immunocompetent individuals→NO NEED TO BE TREATED!
- Visceral manifestations (severe) in immunocompetent individuals→2-4 months
- Acute forms in immunodeficient individuals→6 months and longer
- Chronic, latent forms are not treated

- **PYRIMETHAMINE** 1 mg/kg bw for 15 days and then 0.5 mg/kg bw for another 15 days
- **SULFADIAZINE** 100 mg/kg/24h in two doses for 20 days (with Na-bicarbonate, due to crystallization in urine)
- **FOLIC ACID**
- **ROVAMYCIN** 3gr/24h throughout pregnancy
- **SPIRAMYCIN** (not suitable for the treatment of encephalitis)
- **ROXITROMYCIN, AZITROMYCIN, CLARITROMYCIN**
- **CLINDAMYCIN**
- **CORTICOSTEROIDS** - ocular form

- Pregnant women with acute infection
- Spiramycin 3g/day-until the end of pregnancy
- After 1st trimester→pyrimethamine, sulfadiazine (especially if the diagnosis of fetal infection is confirmed, prenatally)
- Congenital infection, without clinical symptoms (after birth):
 - Pyrimethamine 1mg/kg (every 2 days)+Sulfadiazine 100mg/kg (in two doses)+Folic acid. 5mg (on the 2nd day)-21 days
 - Then continue with spiramycin or sulfadiazine for up to 6 months (if there are no signs of the disease), and if clinical picture develops, up to a year.

Q FEVER / Q FEVER

Definition

- Q fever (in Anglo-Saxon literature "Q fever") is an acute infectious disease, which most often occurs under the guise of atypical pneumonia.

Etiology

- The causative agent of the disease is *Coxiella burnetii*, which belongs to the Rickettsia family,
- It produces spores in a dry environment, so it can survive for several months in the external environment,
- It is pathogenic for humans, it is believed that one microorganism is sufficient to cause the disease.

Epidemiology

- **Q fever** is a classic zoonosis, the source of infection is sick animals (sheep, cattle, goats) that excrete coxiella in feces, urine and milk, especially during calving,
- humans are mainly infected by inhaling dust containing rickettsiae, less often by consuming milk or by being bitten by an infected tick (interhuman transmission is rare),
- the disease occurs sporadically or in epidemics, most often in spring.

Pathogenesis

- After inhalation of contaminated aerosol, *C. burnetii* reaches the lungs where it multiplies in alveolar macrophages; then it enters the blood and disseminates to various organs (systemic disease)
- the causative agent can be found in the blood, pleural effusion, cerebrospinal fluid, pericardium, endocardium, liver, spleen and kidney
- pulmonary infiltrates are primarily located in the interstitium (consisting of macrophages, lymphocytes and plasma cells), and similar inflammatory changes, in the form of granulomatous foci, can also be found in other organs such as the liver, spleen, heart, brain, testicles and kidneys

Clinical picture

- The incubation period is usually 2 to 3 weeks.
- General symptoms of infection
- The disease begins abruptly with typical symptoms of infection: fever, severe headache, retrobulbar pain, myalgia, the headache may be accompanied by photophobia, meningism and somnolence, a quarter of patients may experience vomiting and diarrhea.

Pneumonia



In half of patients with Q fever, along with general symptoms of infection, atypical pneumonia occurs; by the end of the first week of the disease, a dry, irritating cough appears, accompanied by dyspnea and chest pains; physical findings on the lungs are usually scanty, and radiographs reveal interstitial infiltrates in the lungs.

Other clinical forms of Q fever

The disease can also manifest with other clinical manifestations

Izvanplućne manifestacije Q-groznice	
Organski sustav	Kliničke manifestacije
Kardiovaskularni	Miokarditis, endokarditis, perikarditis, tromboflebitis, arteritis
Hepatobilijarni	Hepatitis, pankreatitis
Središnji živčani	Serozni meningitis, encefalitis, cerebelarna ataksija, Guillain-Barréov sindrom
Oko	Upala optičkog živca, iridociklitis, uveitis
Ostali organi	Artritis, hemolitična anemija, otitis, nefritis, orhitis, epididimitis, nodozni eritem, tireoiditis, osteomijelitis

- **Diagnosis**

- ✓ clinical picture (non-specific),
- ✓ epidemiological data (contact with domestic animals),
- ✓ blood count (non-specific).

- **Exact diagnosis**

- ✓ isolation of the causative agent from blood, sputum, urine, cerebrospinal fluid and pleural effusion,
- ✓ serological reactions (RVK, IIF, ELISA).

Therapy

- Antibiotic therapy (tetracyclines, macrolides, chloramphenicol, quinolones), 10-14 days
- Symptomatic therapy.

