Lesson 21

Introduction to medical parasitology. Parasitic infections, pathogenesis and principles of microbiological diagnosis of parasitic infections.

Classification of protozoa

- The simplest are single-celled microorganisms, eukaryotes ranging in size from 2 to 100 microns. They belong to the Kingdom of Animalia (animals), the Sub-kingdom of Protozoa
- Sarcomastigophorae (sarcodynes and flagellates)
- Apicomplexa (sporozoans),
- Ciliophora (ciliary ciliates)
- Representatives of Microspora types cause parasitic diseases (infestations) in humans.

Protozooses

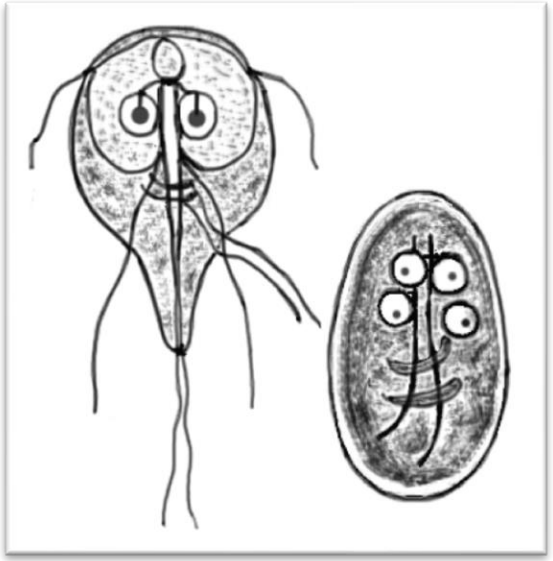
- The branch of microbiology that studies **protozoa** is called protozoology, and the diseases caused by protozoa are called **protozooses or parasitic diseases (infestations).**
- **Protozooses found in humans are divided into two large groups according to localization:**

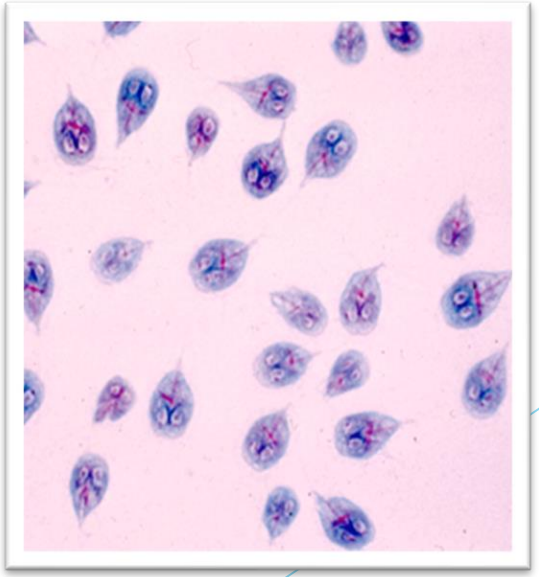
1) ***Intestinal and urogenital protozoosis - giardiasis, amoebiasis, balantidiasis, cryptosporidiosis, microsporidiasis, trichomoniasis;***
2) ***Blood and tissue protozoosis - malaria, toxoplasmosis, leishmaniasis, trypanosomiasis.***

Causative agents of intestinal and urogenital protozoosis

The causative agent of giardiasis (*Giardia lamblia*)

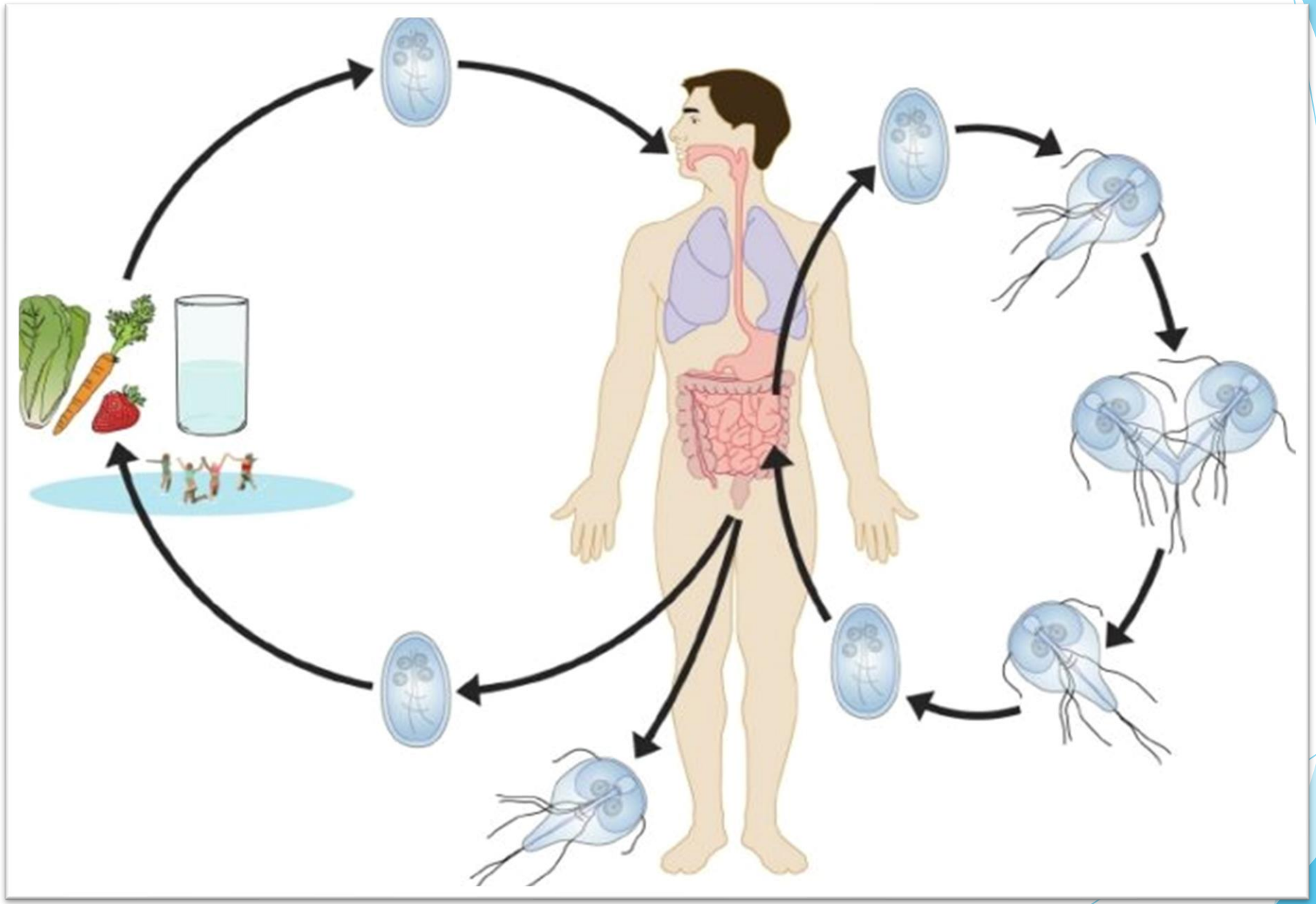
- There are two morphological forms of G. lamblia: trophozoite and cyst
- The trophozoite (vegetative) form found in the small intestine is 10-20 microns long, flat, pear-shaped and has two nuclei. In the center of the nuclei are karyosomes. Movement in the form of oscillations or swimming is carried out by four pairs of flagella. The support function is performed by two axostyles. On the anterior surface of the body there are two suction discs that provide attachment of the parasite to intestinal epitheliocytes. Propagated by longitudinal division.
- When it enters the large intestine, the trophozoite turns into an oval, thick-walled, large **cystic form**, 8-14 microns in size, very resistant to the environment. Immature cysts have two nucleoli, while mature cysts have four.





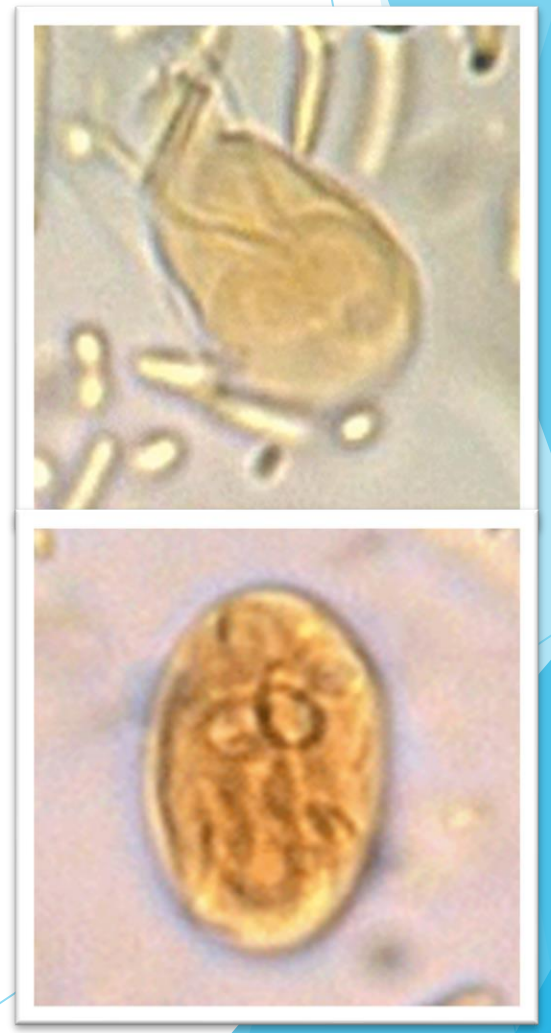
Features of the pathogenesis and clinic of giardiasis

- The source of infection is mainly patients who excrete a large number of cysts with feces. The mechanism of infection is fecal-oral, as in intestinal infections.
- Penetrated into the small intestine with food and water, cysts pass into a vegetative form. Manifestations of the disease depend on the resistance of the organism, possibly asymptomatic. In some people, the intensive reproduction of Giardia in the mucous membrane of the duodenum and jejunum causes symptoms of mild inflammation. The result is damage to intestinal epithelial cells, crypt hypertrophy, fold atrophy.
- Digestion and peristalsis disorders, liquid fetid diarrhea, general weakness, pain in the abdomen, loss of appetite, weight loss, allergic reactions, and so on are possible. The expressed form of the disease is more often observed in children and debilitated persons.



Microbiological diagnosis of giardiasis

- **Microscopic method** - based on the detection of Giardia during microscopy of a smear (preparation of "crushed drop") prepared from feces.
- In the formed feces, mainly cysts can be found, and during diarrhea, both cysts and trophozoites (vegetative forms).
- Sometimes, if cysts are not found, a study of the **duodenal contents is performed**, or three or more samples taken on different days are examined.
- The ELISA method based on the detection of antibodies (IgM and IgG) to giardia in the blood serum makes it possible to identify patients with asymptomatic forms.

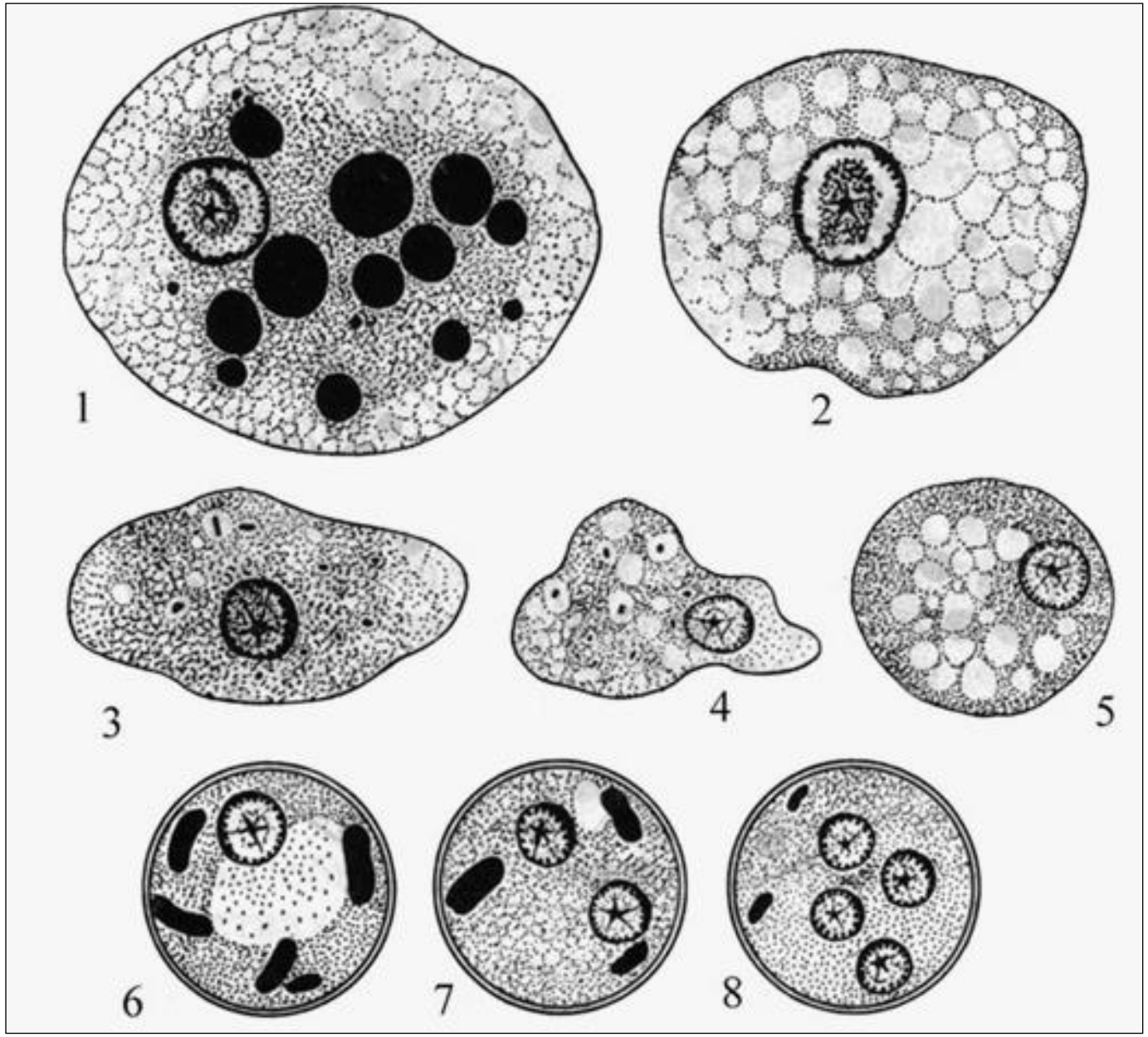


The causative agent of amoebiasis (*Entamoeba histolytica*)

- The causative agent of amoebiasis (Entamoeba histolytica) belongs to the Sarcodina subtype of the Sarcomastigophorae type, is the cause of **amoebiasis (amebic dysentery)**, accompanied by ulcerative lesions of the colon.
- There are three morphological forms of the pathogen: trophozoite, intermediate (pre-cystic) form and cyst**.**
- Trophozoites are found mainly in tissues, but sometimes they are found in diarrhea in the feces. The shape of the cell is variable, its size is 15-30 microns. Two zones are distinguished in the cytoplasm - the outer chromogenic ectoplasm and the inner granular endoplasm. Ingested erythrocytes are often observed in the endoplasm.
- They move with the help of the so-called **pseudopodia** (Greek, amoibe - changeable). They reproduce asexually (by dividing in half).

Entamoeba histolytica

- In the intestinal lumen, E.histolytica is often found in a small vegetative **pre-cystic form**.
- In the intestinal lumen forms rounded **cysts** 10-20 microns in size. Thick-walled hyaline cysts, depending on the stage of maturity, have from 1 to 4 nuclei. Initially, they have one nucleus, glycogen vacuoles and chromatoid bodies. As a result of nuclear division, a cyst with four nuclei is formed, during this process, glycogen vacuoles and chromatoid bodies disappear. Thus, mature cysts have four nuclei, which are distributed inside the cyst along the periphery like wheels (the non-pathogenic intestinal inhabitant Entamoeba coli has 8 nuclei).

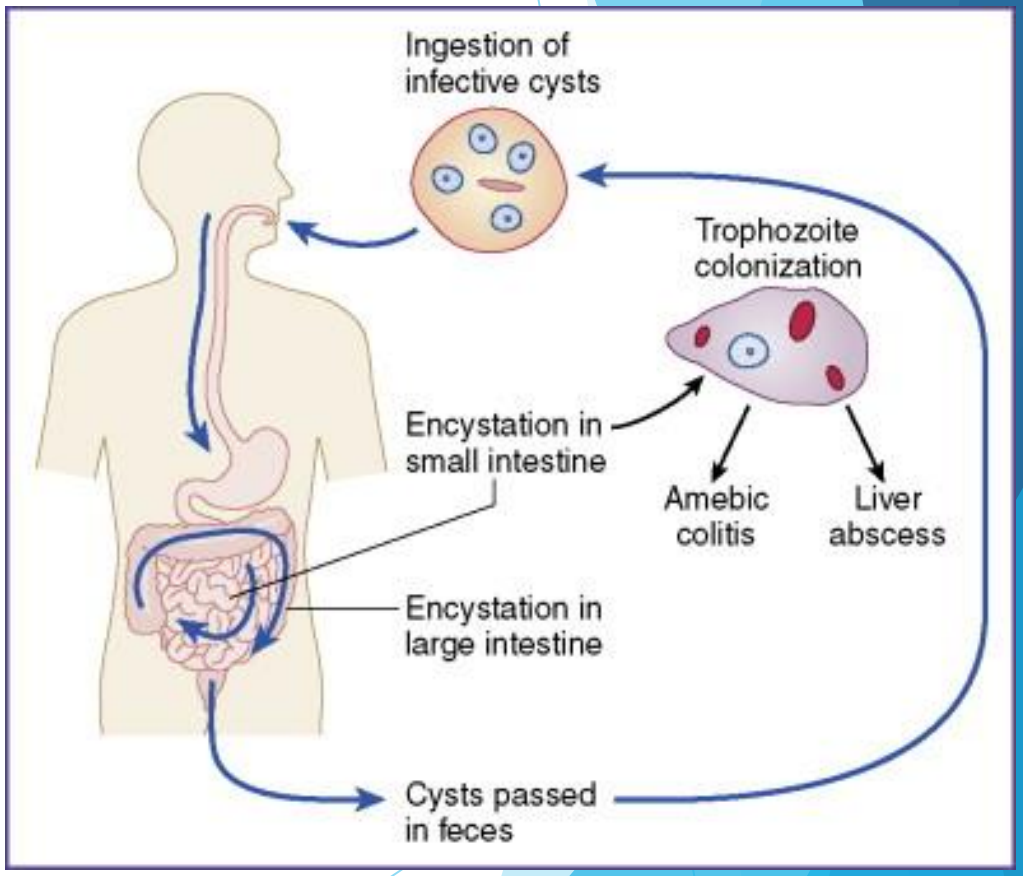


Entamoeba histolytica

(1,2-trophozoite forms; 3,4,5-intermediate forms; 6,7,8-one, two- and four-core cysts)

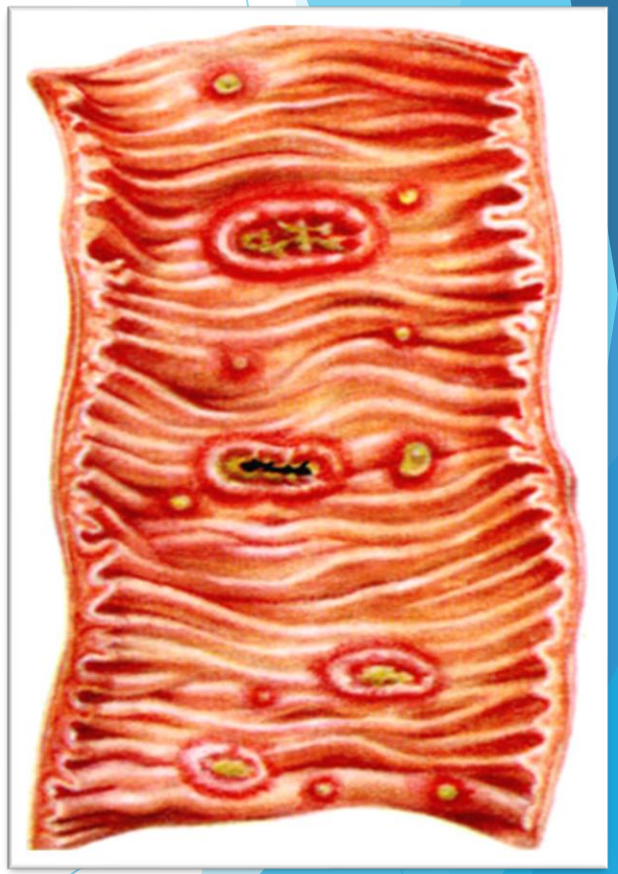
Features of the pathogenesis of amebiasis

- Infection occurs when eating food (mainly fruits and vegetables) and water containing cysts, sometimes by the fecal-oral route through household items.
- From the cysts in the stomach and duodenum that have entered the body, metacystic forms are released. Four metacysts released from the cyst divide and thus 8 trophozoites are formed. They move up to the caecum and populate it. In most cases, trophozoites, feeding on bacteria, secrete cysts into the intestinal lumen, which is accompanied by the onset of the disease. Asymptomatic carriage of *E.histolytica* is widespread.



Features of the pathogenesis of amebiasis

- Under the influence of certain factors, invasion and reproduction of trophozoites in the intestinal epithelium lead to the formation of areas of necrosis, and then ulcers **(primary ulcers).**
- The trophozoites released from here into the **intestinal lumen** form secondary intestinal ulcers, mainly in the sigmoid and rectum, and are excreted with feces.

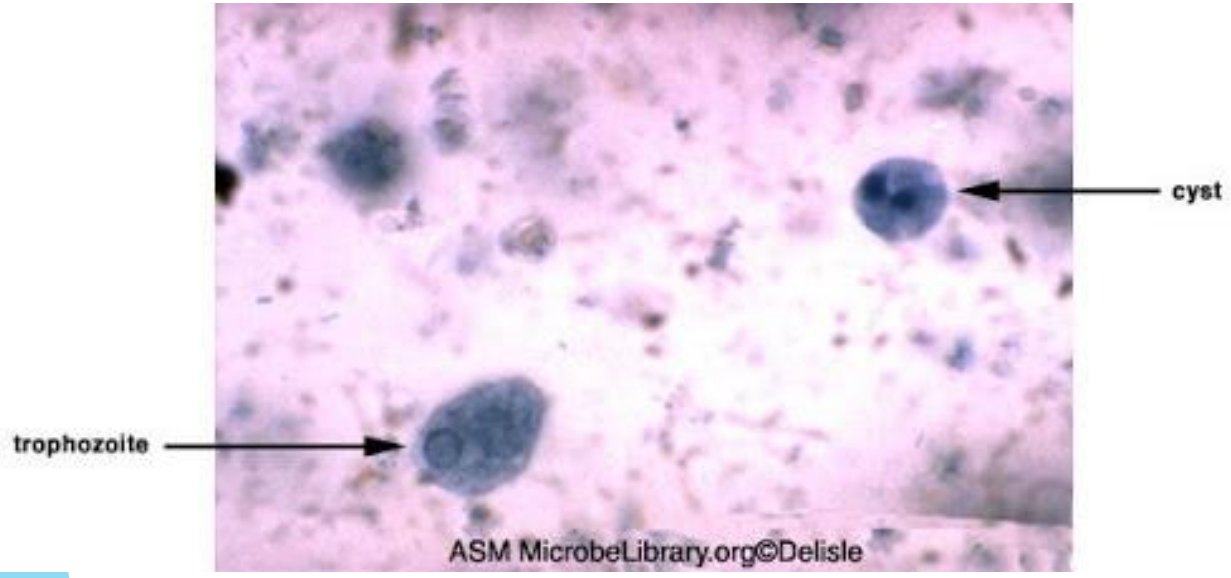


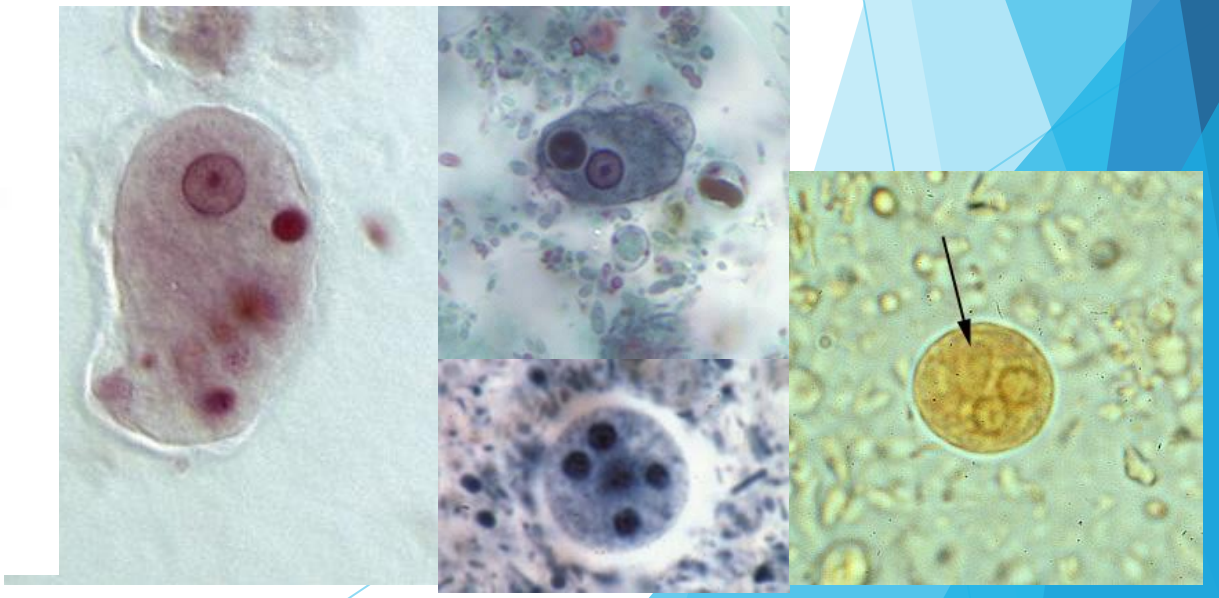
Clinical features of amoebiasis

- Clinically, intestinal amebiasis is manifested by tenesmus, frequent loose stools with blood, pus and mucus. Due to the presence of pus and blood, it resembles “raspberry jelly.” With a long course, dehydration is possible.
- Amoebas can spread through the bloodstream to the internal organs (liver, spleen, lungs and brain), resulting in extraintestinal amoebiasis. Relatively more common amoebic hepatitis and liver abscess (about 4%).

Microbiological diagnostics

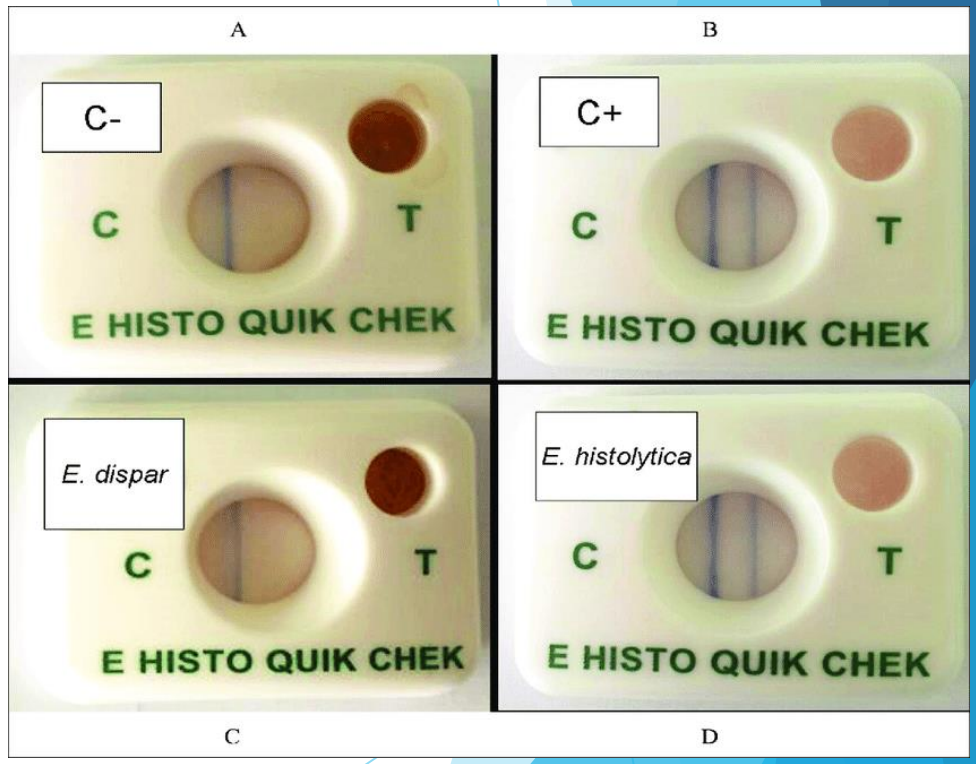
- Basically, a microscopic method is used. In native preparations prepared from fresh unformed feces, mobile trophozoites can be found.
- In the formed feces, cysts are mainly found. For this, native preparations, as well as preparations stained with Lugol's solution, are examined.





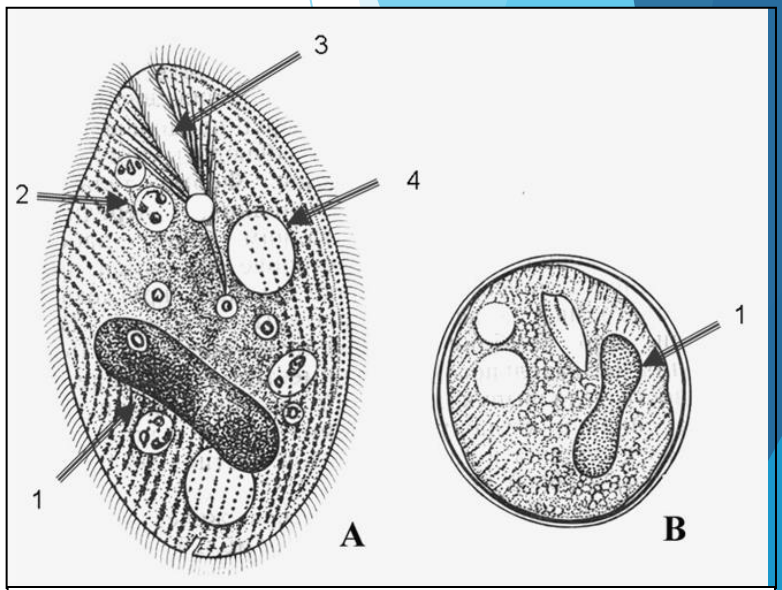
Microbiological diagnostics

- **Serological method.** It is mainly used for extraintestinal amoebiasis. During the method, antibodies to E. histolytica are determined in blood serum using RPGA, RNGA
- The sometimes used enzimeba test is based on the detection of antibodies in the blood serum to E. histolysin histolytica. In fact, this test belongs to the solid-phase **ELISA**, it is very convenient if it is not possible to detect cysts and trophozoites in the material.
- Recently, an **ELISA** test has been developed to detect a specific epitope antigen (galactose adhesin) in feces using monoclonal antibodies.



The causative agent of balantidiasis (Balantidium coli)

- The causative agent of balantidase is Balantidium coli, belongs to the Ciliata class of the Ciliophora type.
- When the parasite reproduces, the vegetative and cystic stages are distinguished.
- The vegetative form of the **trophozoite** is large (45-60 microns and more), oval in shape, the surface is covered with organelles of movement - cilia. At the anterior end there is a semi-oval mouth opening - cytosome and peristome. At the posterior end is the anus, the cytoproce. Inside the trophozoite there is a large kidney-shaped nucleus (macronucleus), a small rounded nucleus (micronucleus) and two contractile vacuoles.
- Large, thick-walled **cysts** with a diameter of 40-70 microns have one nucleus. They come out with feces and persist in the environment for a long time.



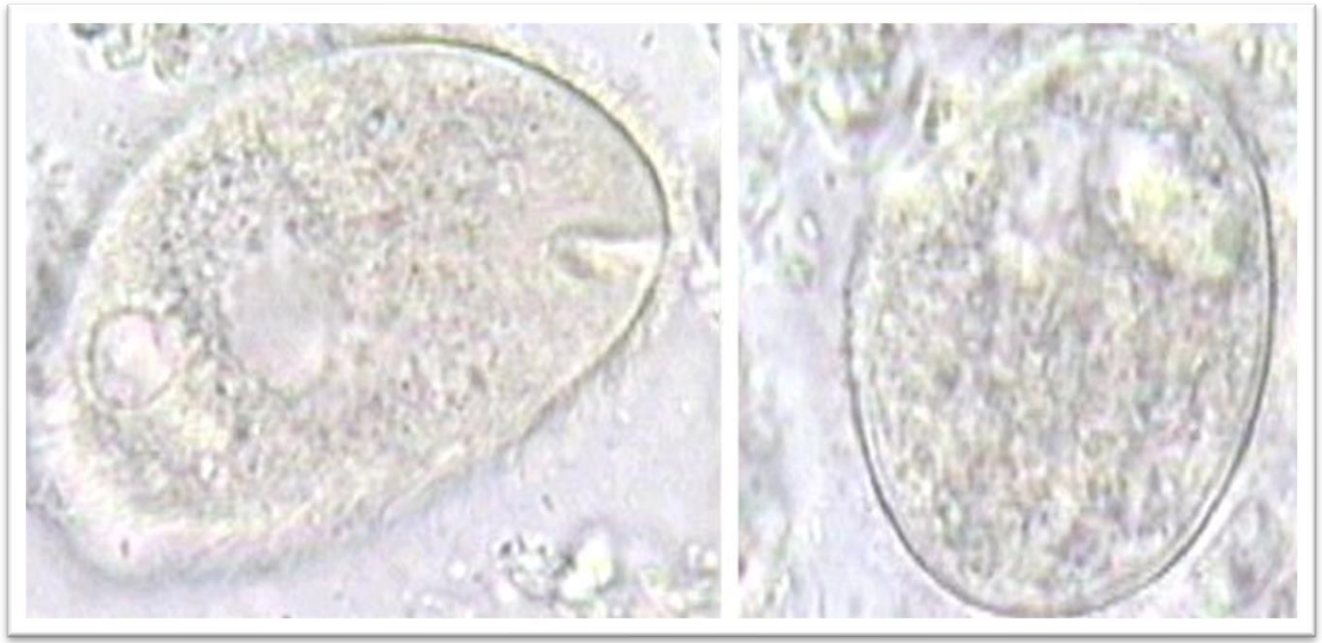
Pic 32.3 *Balantidium coli. A-vegetative form; B-cyst: 1-macronucleus, 2-digestive vacuole, 3-cytostome, 4-contractile vacuole*

Clinical and pathogenetic features of balantidiasis

- In the digestive tract, trophozoites form from the cysts, they feed on the bacteria of the large intestine and form cysts that are excreted in the feces.
- Balantidia often do not cause disease, but sometimes they invade and multiply in the mucous membrane of the large intestine and terminal ileum, leading to the formation of abscesses and ulcers.
- The main clinical signs of balantidiasis are chronic diarrhea or constipation, sometimes severe cases of the disease, accompanied by loose stools with blood and mucus and tenesmus, resemble amoebiasis.

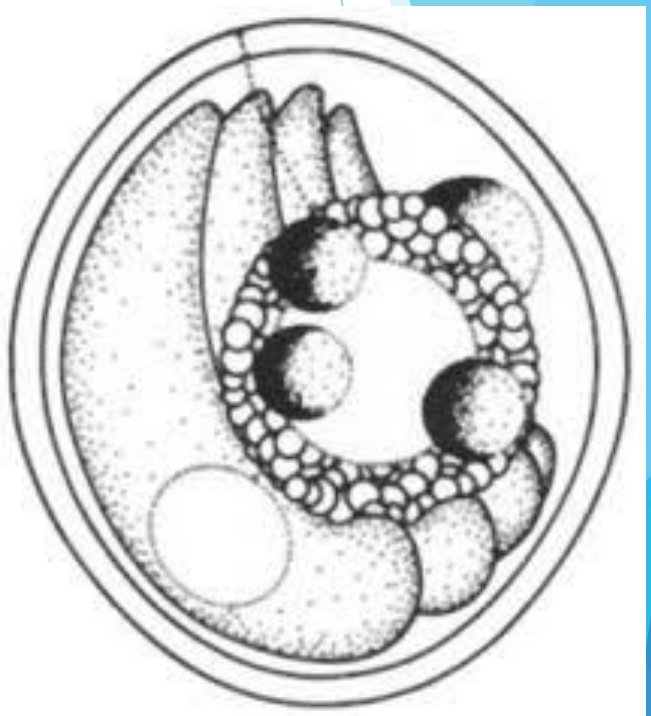
Microbiological diagnostics

- It is carried out using microscopy of a smear prepared from freshly excreted feces.
- In the smear, you can see cysts or active forms of balantidia.



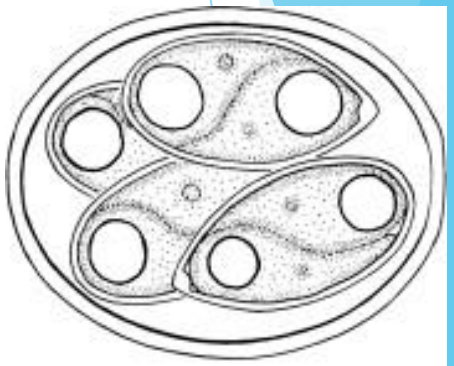
Cryptosporidium (Cryptosporidium genus)

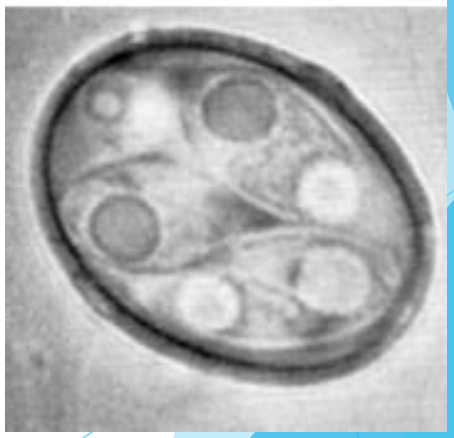
- Cryptosporidium is the causative agent of the disease cryptosporidiosis, which is mainly observed in immunocompromised individuals and *AIDS* and is accompanied by symptoms of gastroenteritis and diarrhea.
- The genus Cryptosporidium belongs to the order *Eucoccidiida* to the class *Sporozoa* of the phylum *Apicocomplexa*. *C.hominis* is a typical representative of this genus.
- In nature, cryptosporidium parasitizes in the body of rodents, birds, large and small cattle and other herbivores.



Cryptosporidium

- **The trophozoite form** of the parasite is small in size (2–5 μm) and round in shape. It reproduces sexually and asexually in the epithelial cells of the gastrointestinal tract.
- During asexual reproduction, trophozoites divide into 8 crescent-shaped merozoites, leave the host cell and invade other cells, continue their development.
- During sexual reproduction, oocysts 4–5 μm in diameter are formed in the intestinal epithelium of the host and excreted with feces. **Oocysts** have a thick cell wall, they are able to independently live in the environment and infect a new host. In the small intestine, 4 sporozoites are released from oocysts, they are introduced into epithelial cells and then form intracellular trophozoites.



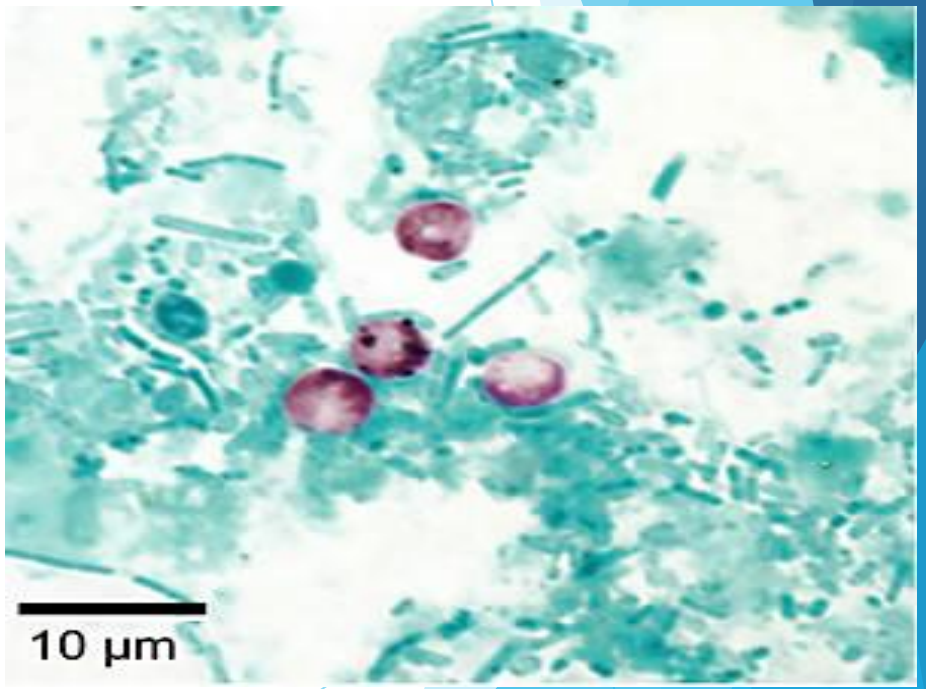


Pathogenesis and clinical features of cryptosporidiosis

- The source of infection are people and animals. Cryptosporidium oocysts enter the body with water and food.
- After ingestion of oocysts in the small intestine, sporozoites are formed from them, which penetrate the epithelial cells and there turn into trophozoites. Trophozoites are located between the cell membrane and the cytoplasm. Thus, cryptosporidium are located intracellularly, **but outside the cytoplasm**. Cryptosporidium mainly damages the cells of the epithelium of the lower parts of the small intestine.
- The main clinical symptom of cryptosporidiosis is diarrhea, which is usually mild and the person recovers within 1-2 weeks even without treatment. But in people with immunodeficiency, children and the elderly, the disease can have a long and severe course.

Microbiological diagnostics

- **A microscopic method** is used to detect oocysts in feces.
- In smears prepared from enriched material and stained with the Ziehl-Neelsen modification (Garcia and Bruckner methods), acid-resistant red oocysts are found, the rest of the microflora is stained blue.
- Recently, **ELISA** has been used to detect parasite antigens in feces.

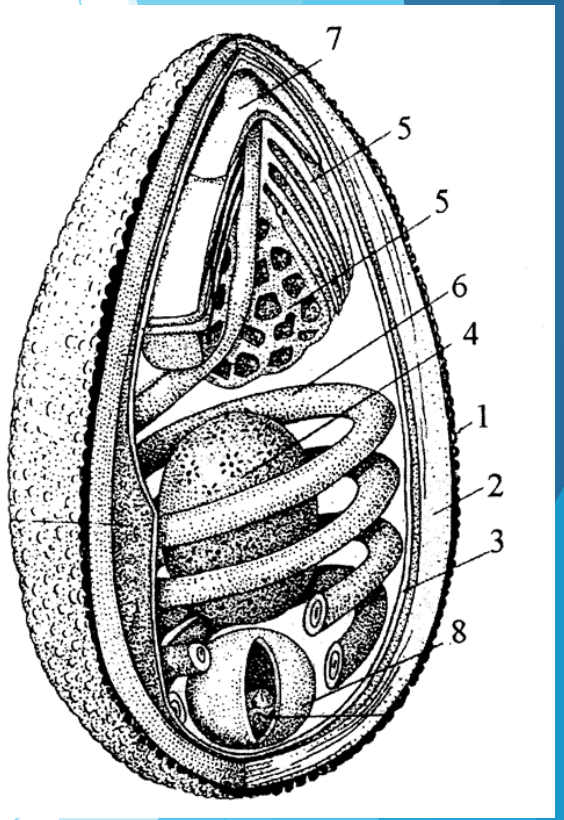


Microsporidia (type Microspora)

- Microsporidia are poorly understood opportunistic parasites. Although these widespread parasites are non-pathogenic for ordinary people, in patients with immunodeficiency, especially AIDS, microsporidia cause **microsporidiosis**, that is, various clinical symptoms - chronic diarrhea, purulent-inflammatory diseases, keratitis, disseminated pathological processes.
- Microsporidia belong to the order Microsporidia of the phylum Microspora. There are many genera and species.
- The genera *Enterocytozoon, Encephalitozoon, Nosema, Pleistophora, Vittaforma, Microsporidium, Brachiola, Trachipleistophora* have a more important etiological significance.

Microsporidia

- Microsporidia have a unique structure, they are small (1-3 microns), round obligate intracellular parasites.
- Inside the infecting form - **sporoplasm** are spores, and at the poles - spiral filaments. These filaments facilitate the introduction of sporoplasm into the host cell.
- After penetration of the sporoplasm into the cell, two-nuclear rounded or elongated schizonts are formed, which pass into merozoites.
- As a result of sexual and asexual reproduction, sporoplasms are formed by numerous divisions. When the cell is destroyed, the released mature sporoplasms again infect other cells and, repeating their development cycle, are released into the environment.



Pathogenetic features of microsporidia

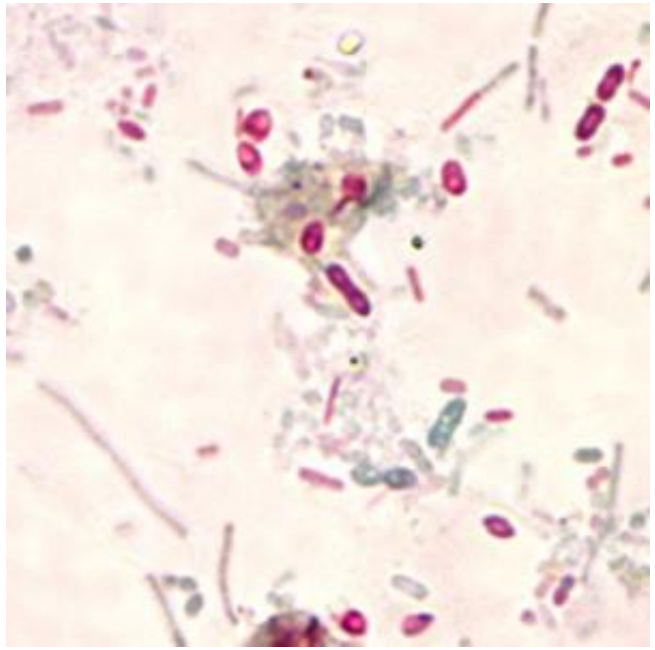
- Microsporidia are widely distributed in vertebrates (mainly fish) and invertebrates (mainly insects).
- Microsporidia spores are excreted in the feces and urine of animals. Infection occurs by the fecal-oral route, usually by ingestion of spores with water and food. Infection is possible by respiratory (with aspiration of intestinal contents), contact (conjunctivitis), and also by the transplacental route.
- Spores that have entered the gastrointestinal tract through the alimentary route are introduced and multiply in the epithelial cells of the small intestine and, as a result, local inflammation develops.

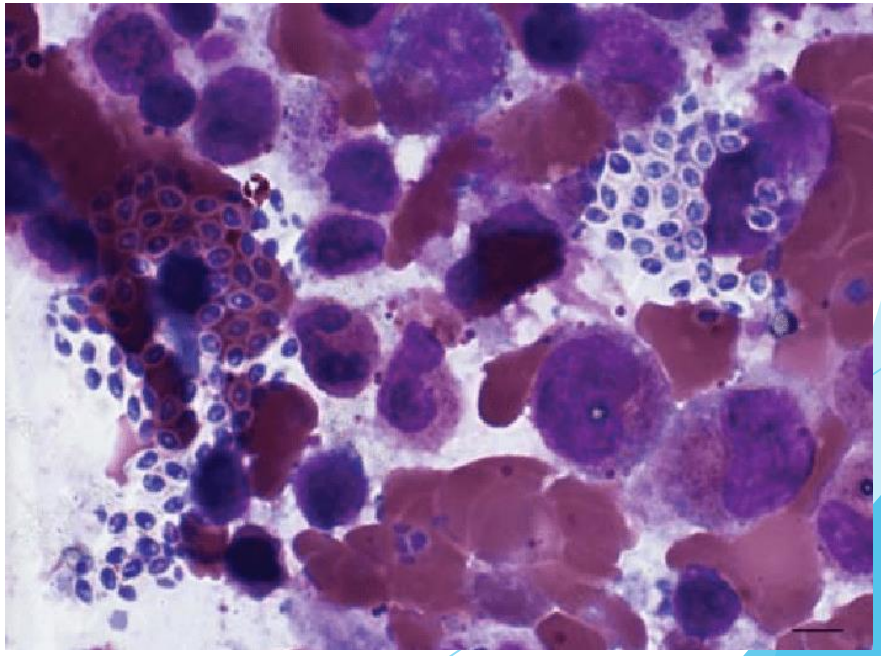
Clinical features of microsporidiosis

- Microsporidia cause infections of the eyes and intestines, as well as disseminated pathological processes.
- **Intestinal infections** Enterocytozoon bieneusi və Enterocytozoon intestinalis in AIDS patients cause chronic diarrhea, and in people with immunodeficiency purulent-inflammatory processes (sinusitis, bronchitis, pneumonia, nephritis, urethritis, cystitis, etc.)
- **Eye infections.** Encephalitozoon hellem, Nosema ocularum and Vittaforma corneae are the cause of conjunctivitis, keratitis and systemic infections.
- **Disseminated infections**. Encephalitozoon hellem, Encephalitozoon cuniculi, Nosema connori, and others cause disseminated infections in people with AIDS.

Microbiological diagnosis of microsporidiosis

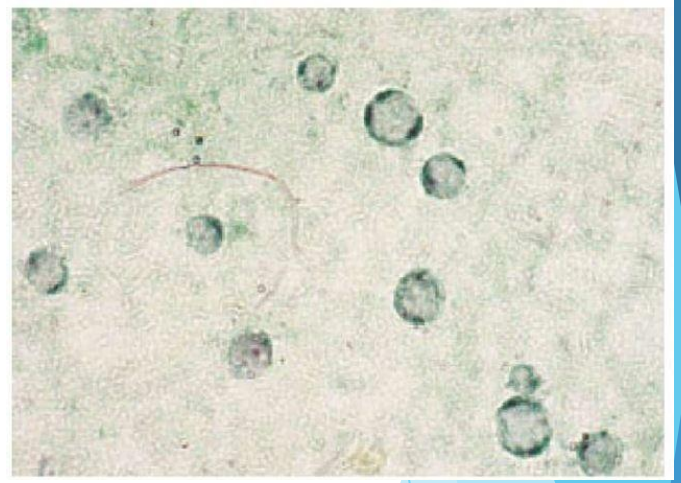
- Conducted by microscopy of smears prepared from feces, urine sediment, nasopharyngeal mucus and cerebrospinal fluid
- Gram-positive spores can be seen on Gram and trichrome blue stains.

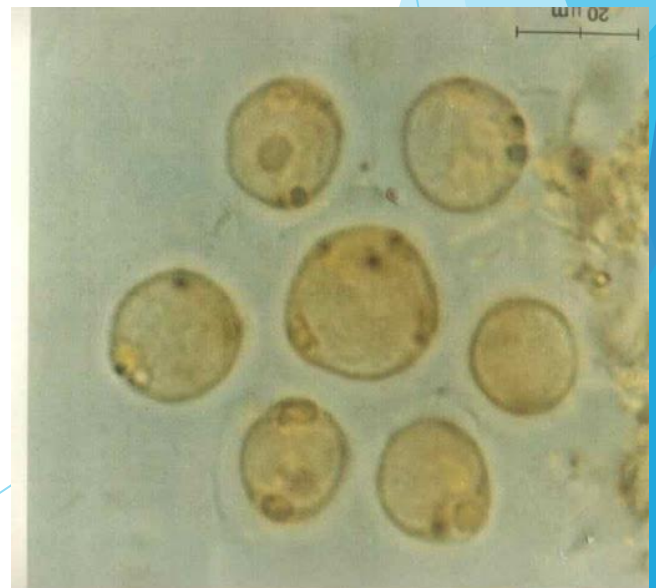




Parasites of the genus Blastocystis (blastocysts)

- It usually causes an asymptomatic carriage, but can cause the disease **blastocystosis** accompanied by diarrhea.
- Blastocysts were previously thought to be yeast fungi. Currently, they are among the simplest.
- Blastocysts are spherical polymorphic protozoa, 5-30 microns in size, similar to amoeba, form pseudopodia. The nucleus of the parasite is displaced by vacuole-like bodies located in the cytoplasm to the periphery. They feed on bacteria and reproduce by binary fission.
- Diagnosis is based on microscopy of smears prepared from feces. In preparations prepared from feces (“crushed drop”), the diagnostic sign is the presence of 5 or more parasites in the field of view.



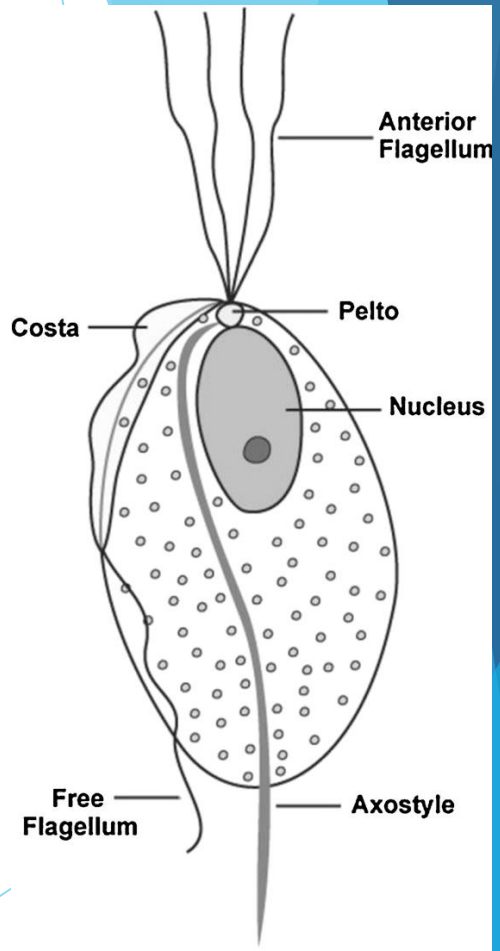


The causative agents of trichomoniasis (genus Trichomonas)

- These protozoa belong to the *Mastigophora* subphylum of the *Sarcomastigophora* type of the Trichomonas genus. The species Trichomonas vaginalis causes **trichomoniasis** in humans, accompanied by an inflammatory process in the genitourinary system.
- In addition, non-pathogenic representatives of the normal microflora *T.tenax* and *T.hominis* belong to this species. *T.tenax* is an inhabitant of the oral cavity, and *T.hominis* is a commensal intestinal microorganism.

Trichomonas vaginalis

- *Trichomonas vaginalis* is a pear-shaped parasite measuring 5-30 microns in length and 2-14 microns in width, with an elongated nucleus at the anterior end. Trichomonas do not form cysts. The parasite is motile, movement is provided by the rotation and swaying of the flagella.
- There are four flagella at the anterior end of the parasite. Another flagellum is connected to the body of the parasite by means of a wavy membrane reaching to the middle of the cell.
- An axial thread passes through the entire body - an axostyle, protruding at the posterior end in the form of a spike



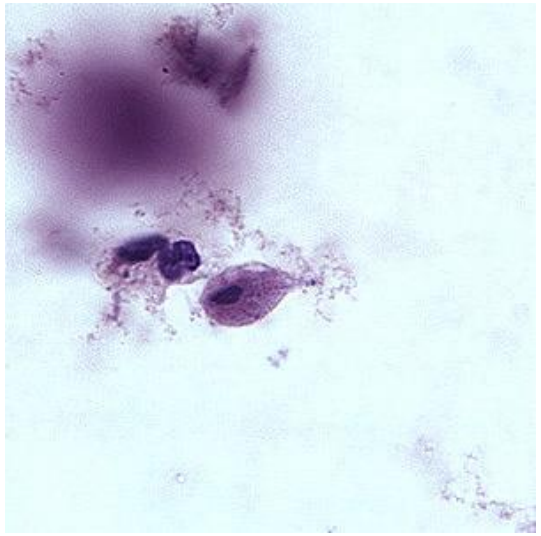
Trichomonas vaginalis
(Trophozoite stage)

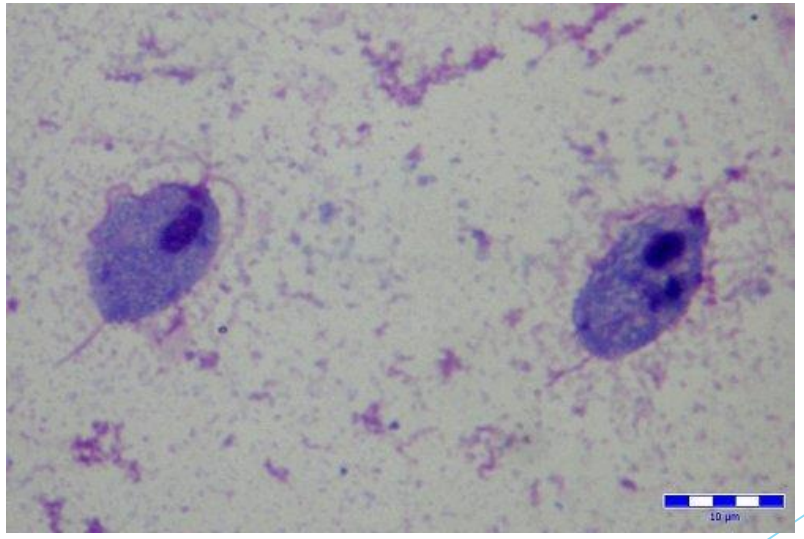
Pathogenesis and clinical symptoms of trichomoniasis

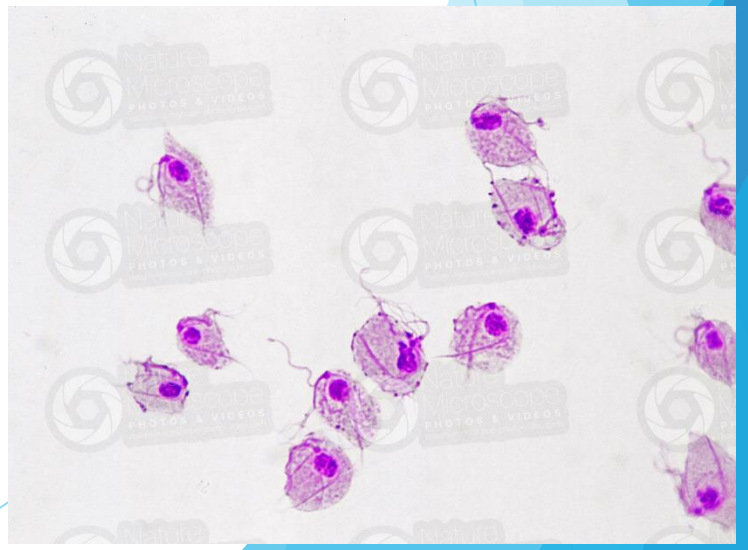
- Trichomoniasis is transmitted mainly through sexual contact. In rare cases, infection is possible through bath equipment and medical examination instruments (indirect contact). It is also possible to infect a child through the birth canal of a sick mother.
- **In women**, the vulva, vagina, and cervix (cervix) are affected. Thus, vulvovaginitis develops, but trichomonas, as a rule, are not able to penetrate into the uterine cavity. The inflammatory process is accompanied by pain, discomfort, purulent-serous discharge, the intensity of this process depends on the physiological state of the vagina. That is, the normal acidity of the vaginal secretion pH (3.8-4.4) prevents the reproduction of Trichomonas.
- **In men**, trichomoniasis is accompanied by inflammation of the urethra, prostate, and seminal sacs (urethritis, prostatitis, and vesiculitis). With urethritis, pain, discomfort, dysuria, and mucopurulent discharge are observed.
- In both women and men, the disease is often mild or asymptomatic.

Microbiological diagnostics

- Trichomonas can be detected microscopically on preparations stained with methylene blue and Giemsa, as well as in native smears prepared in men from urethral secretions, prostate secretions and urine sediment, and in women from vaginal secretions.
- In chronic forms, the detection of Trichomonas by the microscopic method is difficult, therefore the cultural method is more convenient. When cultivating material for research on special nutrient media, you can get a culture of Trichomonas.







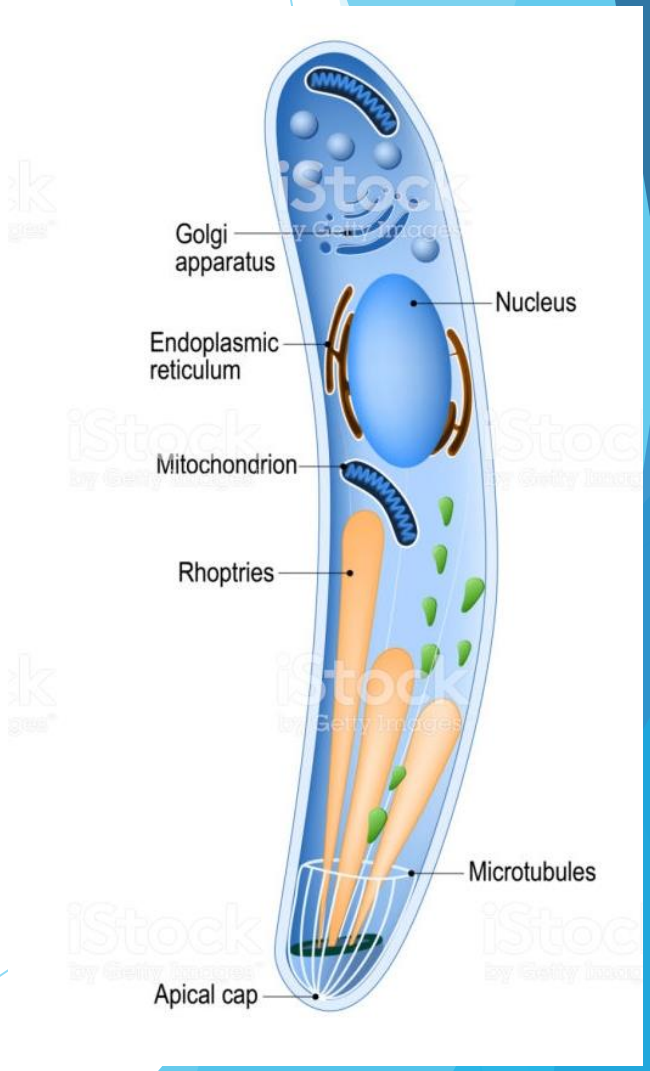
The causative agents of blood and tissue protozoosis

Malaria pathogens (genus Plasmodium)

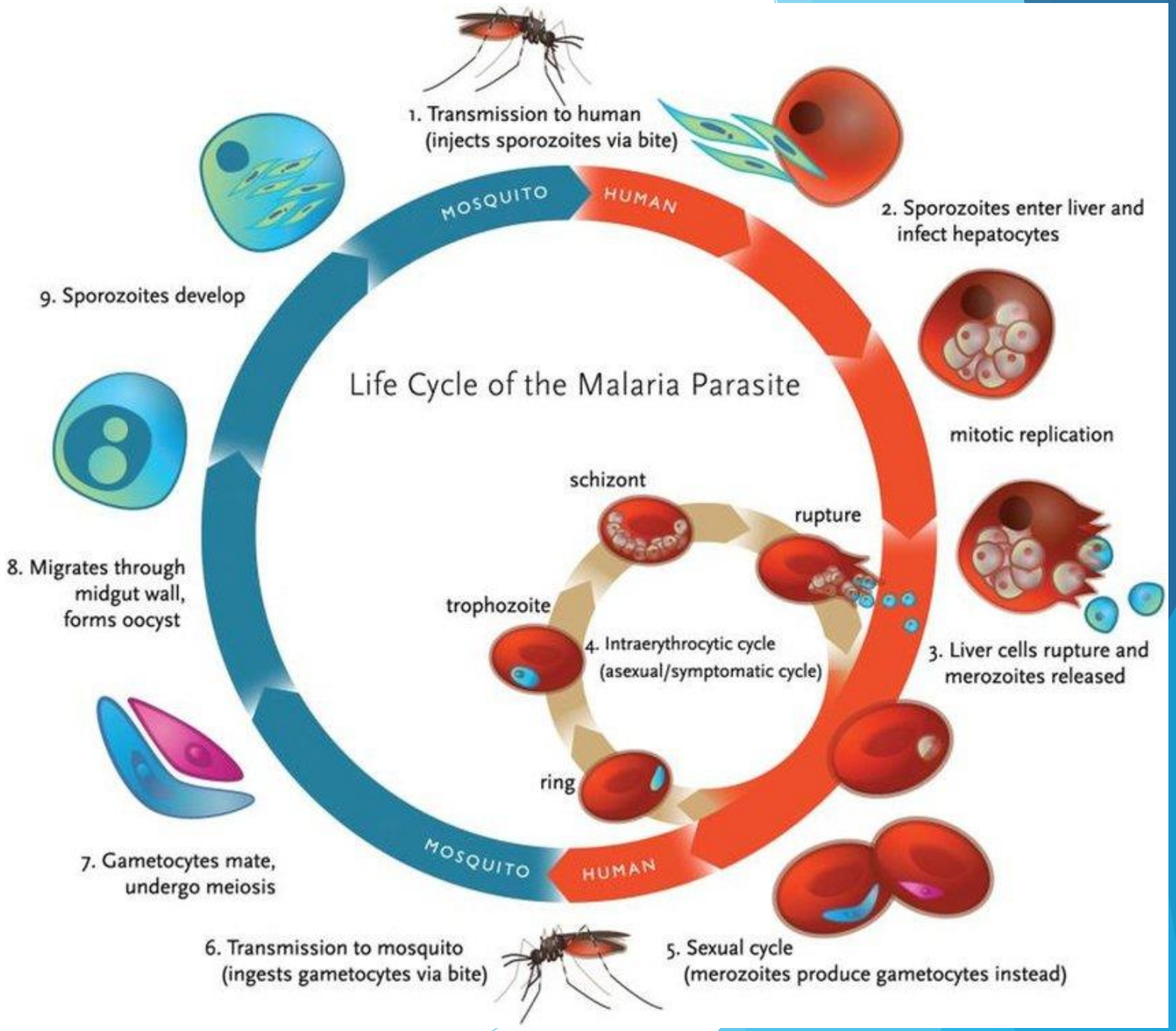
- Some types of parasites of the genus Plasmodium cause **malaria** in humans, which is accompanied by bouts of fever, anemia, enlargement of the liver and spleen. They belong to the order Eucoccidiida of the Sporozoa class of the Apicocomplexa type.
- **P.vivax və P.ovale - is the causative agent of three-day malaria,**
- **P.malariae - four-day malaria,**
- **P.falciparum tropical malaria.**

Malaria pathogens (life cycle)

- The life cycle of Plasmodium occurs with the change of the main and intermediate host.
- In the body of the main host - mosquitoes of the genus Anopheles, sexual reproduction occurs, or **sporogony**
- In the human body, which is the intermediate host, asexual reproduction or the stage of schizogony occurs.



life cycle of malaria pathogens



Sporogony

- When a patient bites during bloodsucking, the sexual forms of pathogens (micro- and macro-gametocytes) enter the mosquito's stomach with blood.
- Here, micro- and macro-gametocytes, when combined, form zygotes, which then turn into elongated mobile ookinetes.
- Ookinetes, passing through the wall of the stomach, form an oocyst containing thousands of sporozoites.
- As a result of the destruction of the oocyst, sporozoites enter the hemolymph, and from there into the salivary glands of the mosquito.

Schizogony

Sporozoites penetrate from the salivary glands of the mosquito into the bloodstream, quickly enter the liver cells.

In the liver, the first phase of schizogony begins **- tissue (exoerythrocyte schizogony)**. At this time, in hepatocytes, sporozoites turn into tissue schizonts (trophozoites) that can multiply.

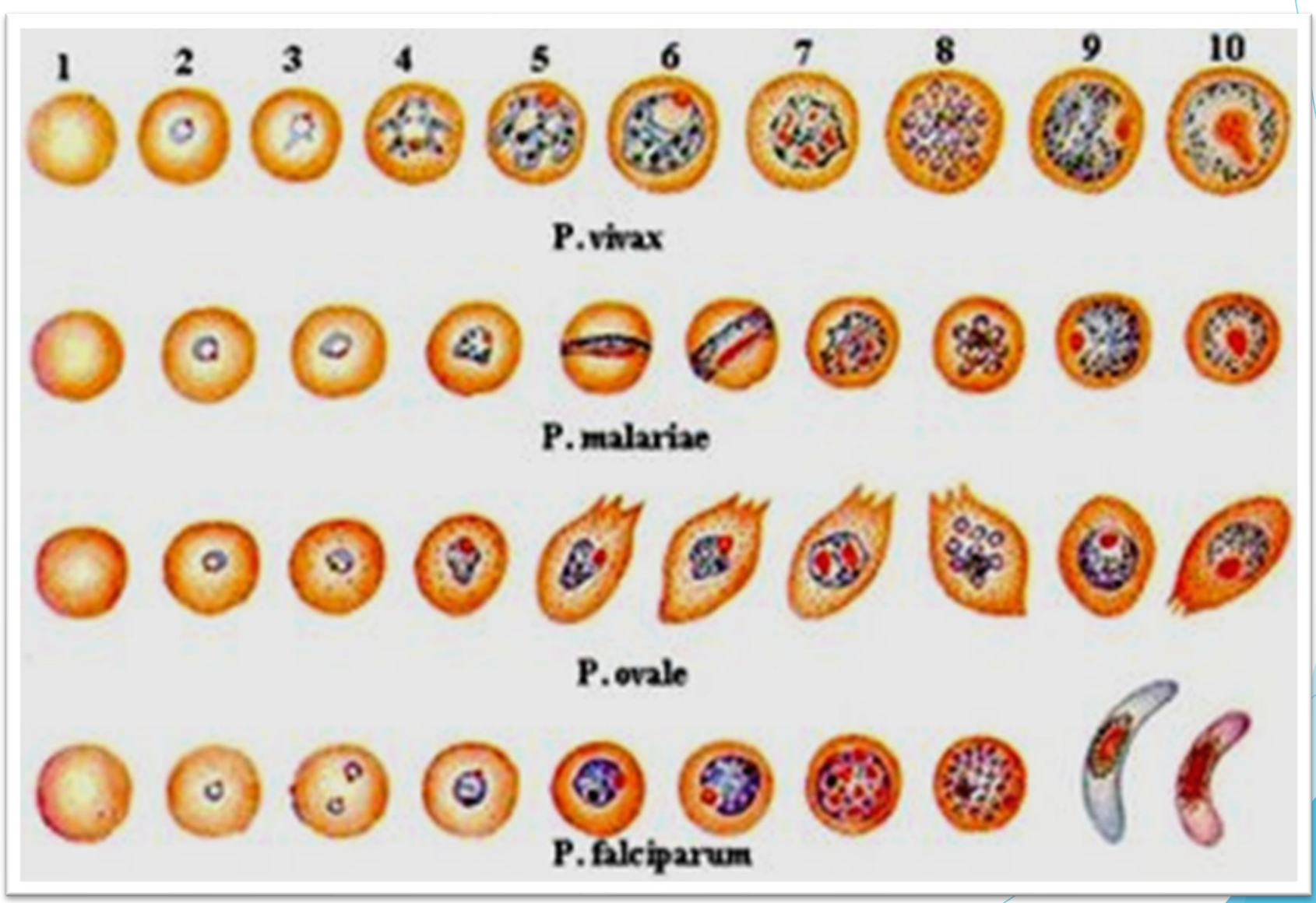
Tissue schizonts divide during the process of merulation to form merozoites. A single sporozoite produces thousands of merozoites.

After the destruction of liver cells, these merozoites enter the bloodstream and are introduced into erythrocytes by endocytosis. Then erythrocyte **schizogony** begins.

Erythrocyte schizogony

- Inside erythrocytes, merozoites form growing forms of parasites - trophozoites. They, depending on the degree of development, are called young and mature trophozoites. Trophozoites grow by feeding on the hemoglobin of erythrocytes.
- Young schizonts in preparations of erythrocytes stained according to Giemsa resemble a ring with a red pebble: two vacuoles located in the center displace the nucleus of the parasite to the periphery, the central part with vacuoles is not stained, and the cytoplasm, staining blue, looks like a ring.

Erythrocyte schizogony

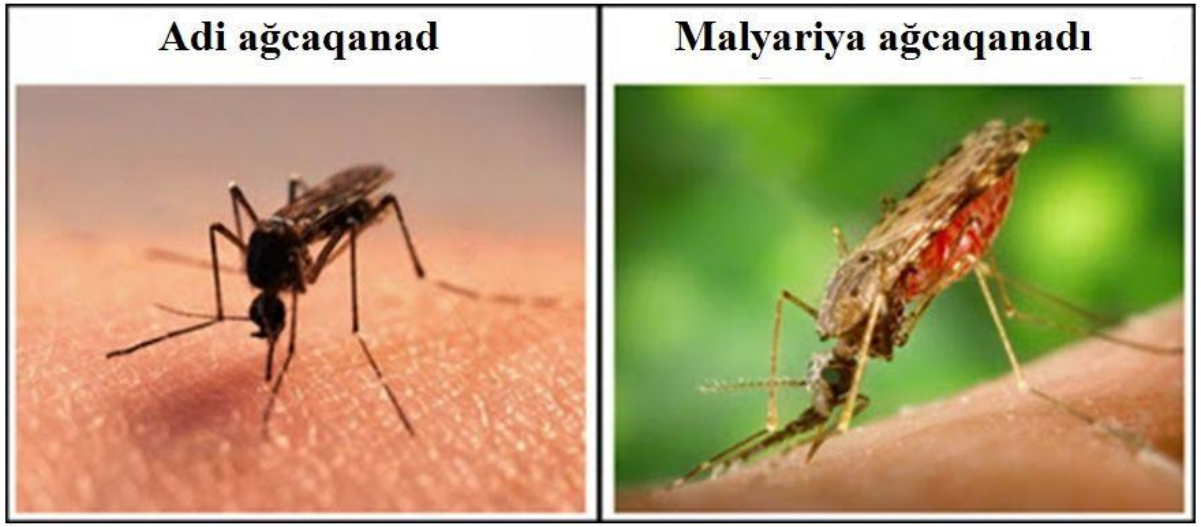


Erythrocyte schizogony

- Mature trophozoites turn into multinuclear schizonts, in the process of merulation, mature merozoites schizonts are formed, and after the destruction of erythrocytes, they pass into other erythrocytes and repeat their development cycle.
- For *P.vivax*, *P.ovale*, *P.falciparum* erythrocyte schizogony lasts 48 hours, and for P.malariae 72 hours.
- In erythrocytes, merozoites also form immature sex cells - male and female gametes (gametocytes). The gametes are oval in shape, only the gametes of P. falciparum are crescent-shaped (this is the name of the species). The latter give the ability to cause malaria to a blood-sucking mosquito when bitten by a sick person.

Source of infection and mechanism of transmission

- The source of infection in malaria are patients or parasite carriers. Infection occurs transmissible by blood absorption by mosquitoes of the genus Anopheles.
- Possible parenteral infection through blood transfusion.
- The disease is mainly widespread in countries with tropical and subtropical climates.
- **In Azerbaijan**, malaria occurs mainly in the Kura-Araz lowland.



Features of the pathogenesis and clinic of malaria

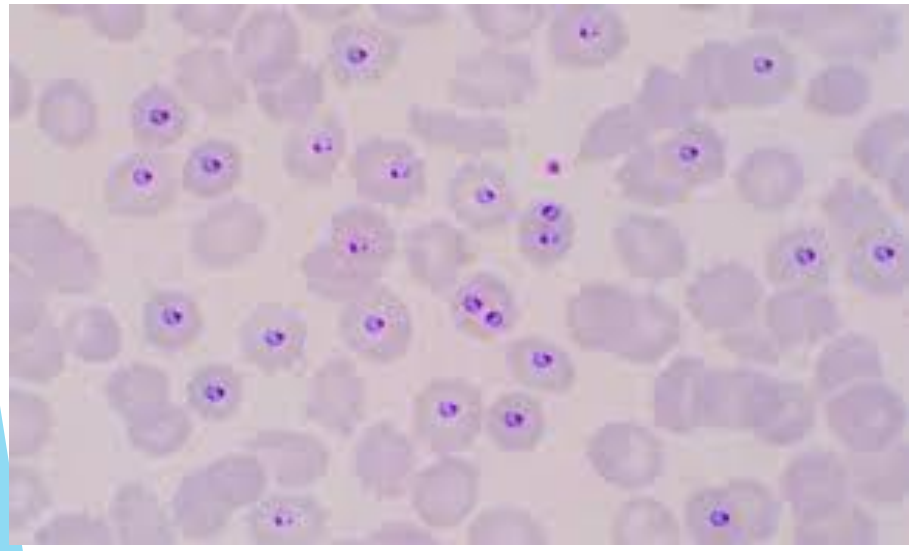
- With various forms of malaria, the incubation period can last from one week to a year.
- The main clinical manifestations are **paroxysms (attacks) of malaria**, which are an alternation of fever, sweating and a decrease in temperature. The cause of malarial paroxysms is the destruction of erythrocytes and the release of pyrogenic substances, consisting of products secreted by merozoites and their metabolites.
- Paroxysms change depending on the type of pathogen, or rather, on the period of erythrocyte schizogony: with three-day malaria caused by P.vivax and P.ovale, they repeat every two days, and with four-day malaria caused by P.malariae, they repeat every three days.
- In endemic foci, as a result of multiple infection, paroxysms can be repeated daily.

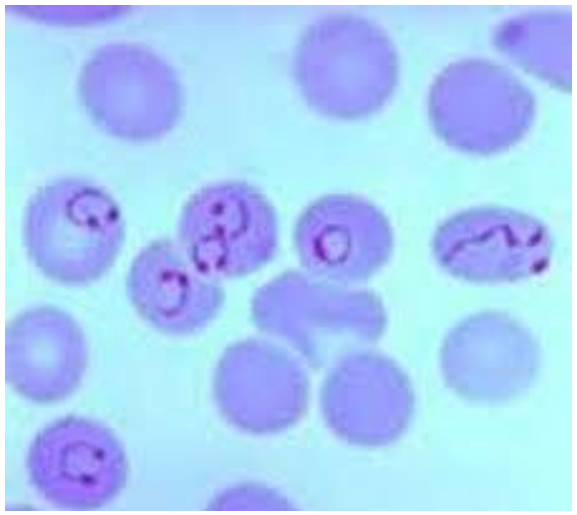
Immunity

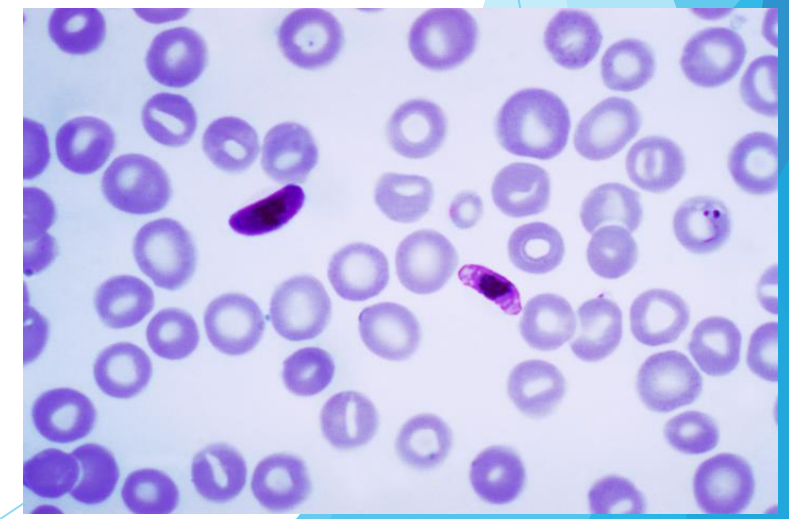
- During the disease, due to the gradual development of the pathogen, an unstable, species-specific non-sterile immunity is formed. **Possible recurrence of the disease.**
- In children with hemoglobinopathies (for example, in the form of sickle cell anemia, thalassemia), as well as congenital insufficiency of 6-phosphate dehydrogenase, there is **a natural resistance to malaria**.
- Many black people in West Africa, a malaria endemic area, have a natural resistance to P. vivax due to their lack of the Duffy (FyFy) group antigen. Since this antigen, located on erythrocytes, is a receptor for P. vivax, the pathogen cannot penetrate into such erythrocytes.

Microbiological diagnosis of malaria

- **Microbiological diagnostics** is based on microscopy of preparations of "thin" and "thick" blood drops stained by the Giemsa method.
- In preparations of a “thick” drop, pathogens are easy to detect, they are stained without prior fixation, therefore, erythrocytes and plasmodia do not undergo deformation, the possibility of detecting a pathogen increases to a large extent.
- In preparations of a “thin” drop, it is possible to establish the type of pathogen.







Microbiological diagnosis of malaria

- Recently, immunochromatographic strip tests have been developed for faster diagnosis of malaria. The method is based on the detection of trophozoite antigens using monoclonal antibodies in lysed blood. This test is called **the Rapid diaqnostic test (RDT**) and distinguishes *P. falciparum* from the other three species.

Negative

All Plasmodium Species

P.falciparum

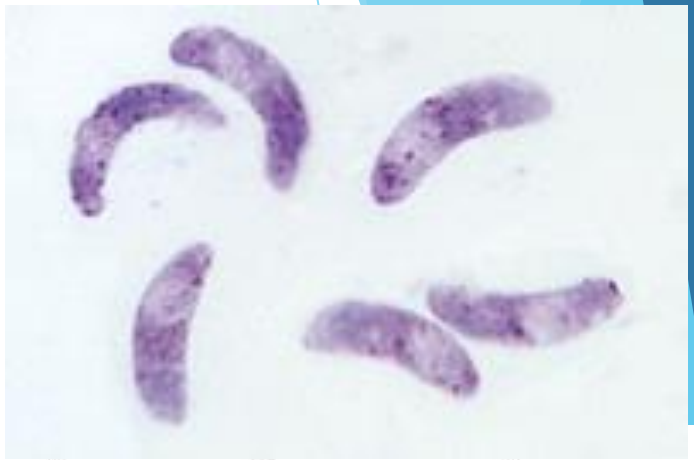
Prevention and treatment of malaria

- **Treatment** is carried out with antimalarial etiotropic drugs **- quinine, chloroquine (chingamine), quinine, primaquine, bigumal, pyrimethamine, etc.**
- There are preparations of **schisontotropic** and **gamototropic** action.
- **Prevention**. Preventive measures are based on removing the source of malaria infection by curing patients and parasite carriers, destroying mosquitoes and using mosquito repellents.

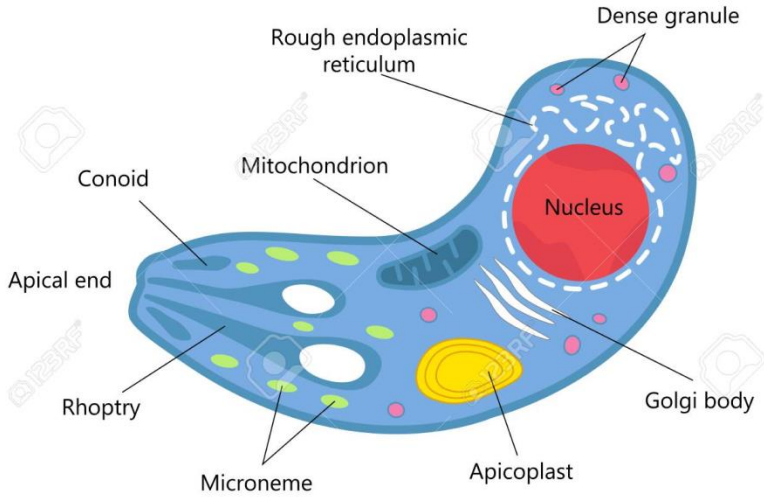
Chemoprophylaxis in endemic areas antimalarial etiotropic drugs..

The causative agent of toxoplasmosis (Toxoplasma gondii)

- Toxoplasma gondii belongs to the order Eucoccidiida, the class Sporozoa of the type Apicocomplexa.
- It causes parasitaemia and **toxoplasmosis** in humans, which is characterized by polymorphic clinical manifestations and is accompanied by symptoms of damage to various organs.
- T. gondii is an obligate intracellular parasite. Its life cycle consists of sexual and asexual reproduction with the change of the main and intermediate host. Sexual reproduction occurs in the intestines of felines, which are the primary host. And asexual reproduction occurs in the body of intermediate hosts - some birds, rodents and other mammals, including humans.

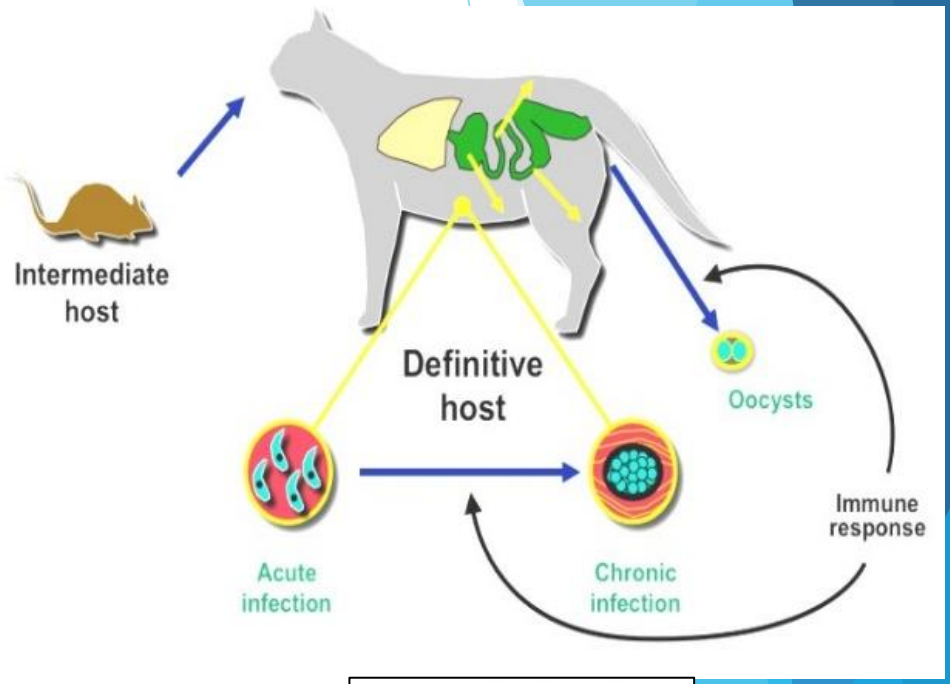


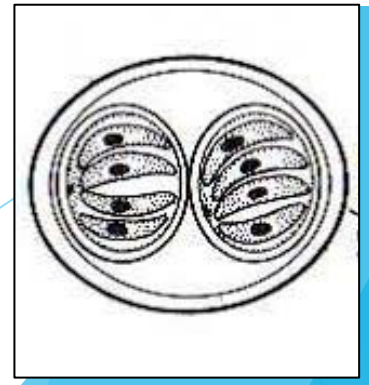
Toxoplasma Gondii



Toxoplasma gondii (sexual reproduction)

- Oocysts, as well as bradyzoites of T. gondii tissue cysts, penetrating into the intestinal epithelium of a cat, reproduce sexually, forming schizonts and gametocytes.
- Gametocytes, connecting, form an oval-shaped oocyst (10-12 microns). Oocysts are excreted in the cat's feces and, after maturing in the environment for two days, remain viable for up to one year.
- A mature oocyst contains two sporocysts, each containing 4 sporozoites.



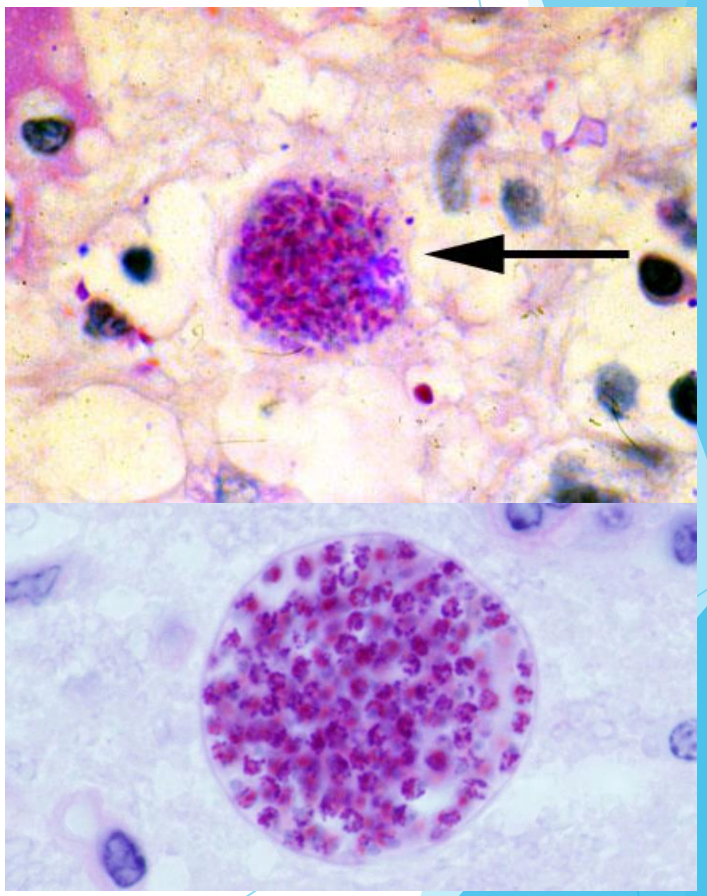


Toxoplasma gondii (sexual reproduction)

- Sporosites are released from oocysts that have fallen in the alimentary way (for example, with unwashed fruits and vegetables) into the intestines of intermediate hosts, including human oocysts.
- They circulate with the blood, invade various cells, especially macrophages, and, reproducing asexually, turn into trophozoites, then enter the lymph nodes and other organs. This condition coincides with the acute period of infection.
- Trophozoites have a characteristic orange slice or crescent shape (size 3-7 µm). Giemsa staining stains the cytoplasm blue and the nucleus bright red.

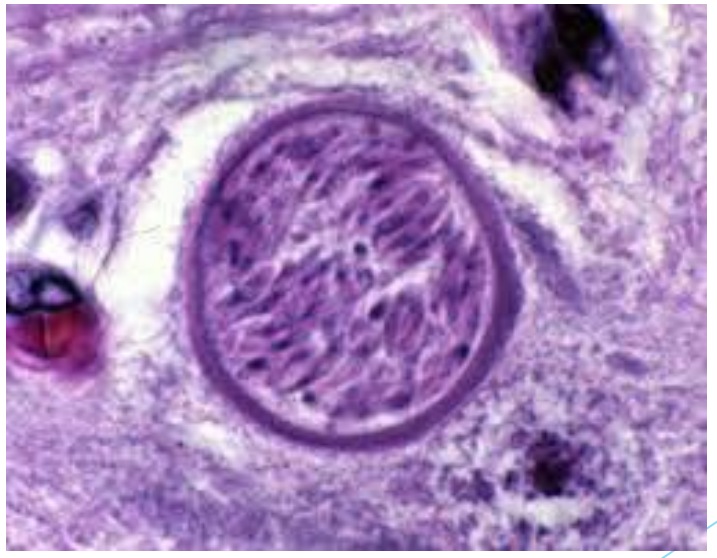
Toxoplasma gondii (sexual reproduction)

- Then the parasites, penetrating into the nervous tissue, especially the brain and eyes, multiply, forming bradyzoites, which secrete **tissue cysts** (formerly called **pseudocysts).** This process coincides with the period of chronic infection.
- Tissue cysts consist of an accumulation of trophozoites that do not have a separate membrane. They enter the body of a cat, reproduce sexually and form oocysts, which, when they enter the body of other animals and people who eat meat, reproduce asexually and cause the formation of tissue cysts.



Toxoplasma gondii (asexual reproduction)

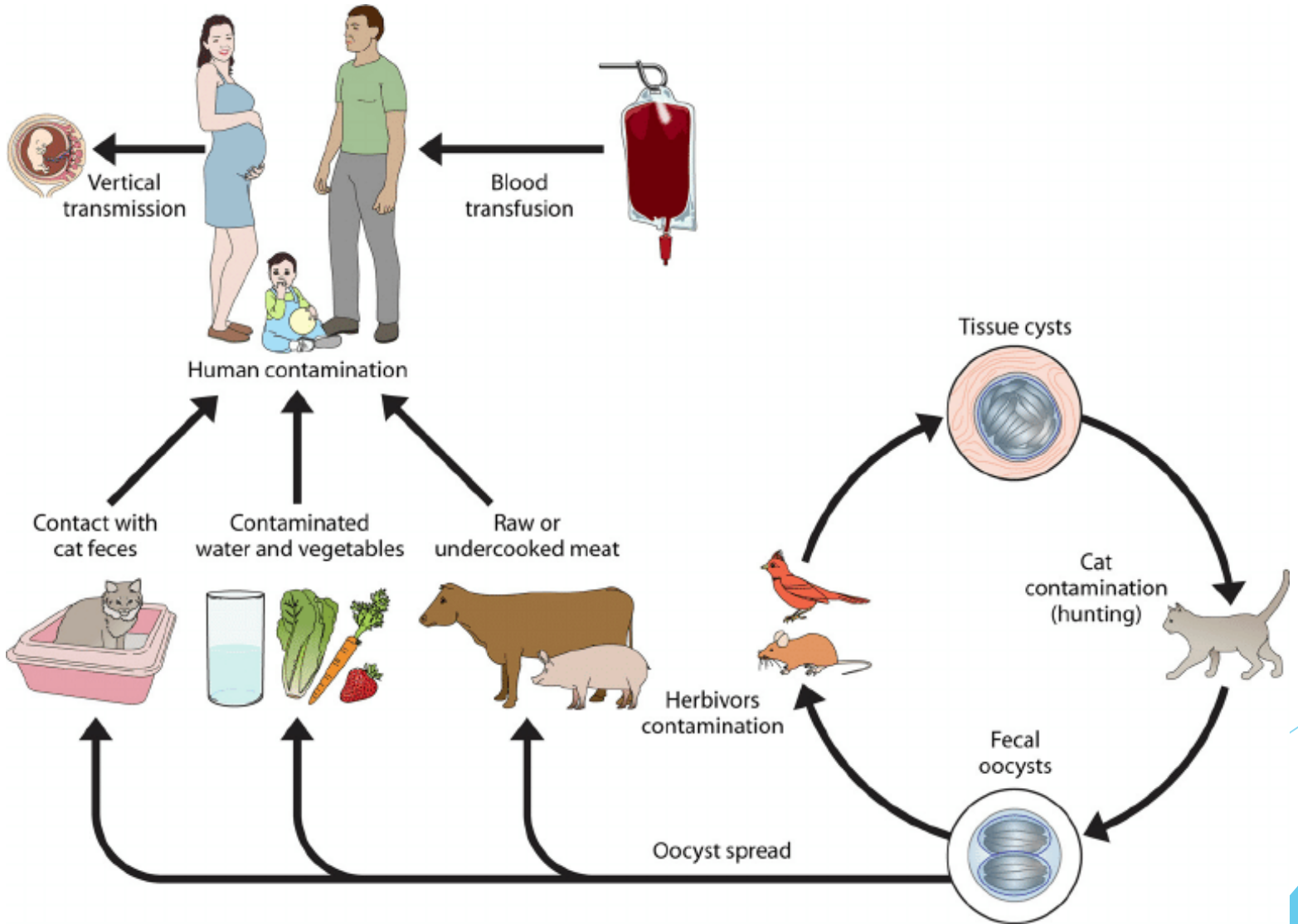
- Toxoplasma also form **true cysts** hundreds of microns in size in the brain and other tissues.
- They have a dense shell and contain thousands of spore-like bradyzoites. Like other cysts, true cysts are contagious.



Source of infection and routes of transmission

- The source of infection is mainly domestic animals and many species of wild mammals, as well as birds.
- Infection occurs in the alimentary way when using insufficiently thermally processed livestock products (meat, milk, eggs) containing parasites, and their tissue and true cysts.
- Humans and animals can also become infected with oocysts excreted by cats.
- In congenital toxoplasmosis, the pathogen enters the fetus through the placenta. Sometimes infection occurs as a result of blood transfusion, organ transplantation.

Toxoplasmosis
Source of infection and routes of transmission

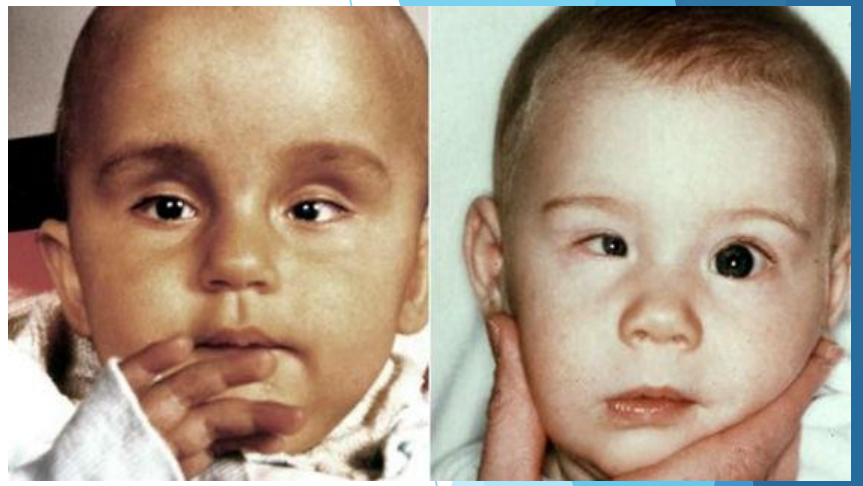


Pathogenesis and clinical manifestations of toxoplasmosis

- Toxoplasma enters the body with the lymph flow to the regional lymph nodes, multiply here (tachyzoites), penetrate the bloodstream, spread throughout the body and, penetrating into almost all reticuloendothelial cells, form tissue and true cysts.
- The incubation period for toxoplasmosis is approximately 10-15 days. Clinical manifestations are varied. As with infectious mononucleosis, there may be mild signs of adenopathy (especially of the cervical lymph nodes). Depending on the location and affected organs, fever, rash, hepatosplenomegaly, pharyngitis, meningoencephalitis, pneumonia, and other symptoms are possible.
- In people with immunodeficiency, including AIDS, toxoplasmosis causes severe disorders in the form of necrotizing encephalitis, endocarditis, pneumonia, and is often fatal.

Congenital toxoplasmosis

- Infection with toxoplasmosis in the first trimester of pregnancy leads to **congenital toxoplasmosis**.
- In this case, fetal death is possible (miscarriage or stillbirth), or the child may be born with malformations (chorioretinitis, blindness, macro- and microcephaly, and other neurological symptoms).
- When infected at the end of pregnancy, neurological symptoms in children are not expressed and they appear later.

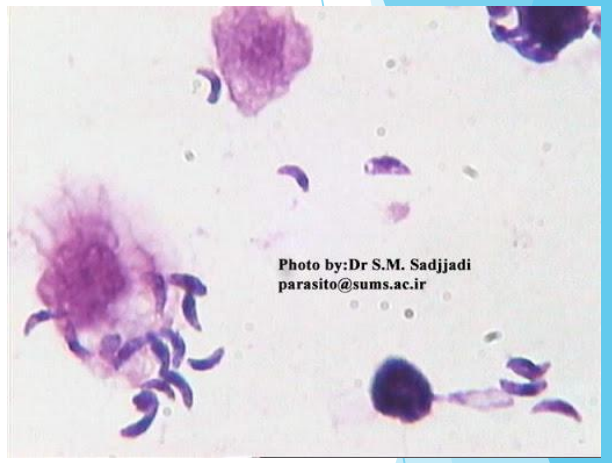


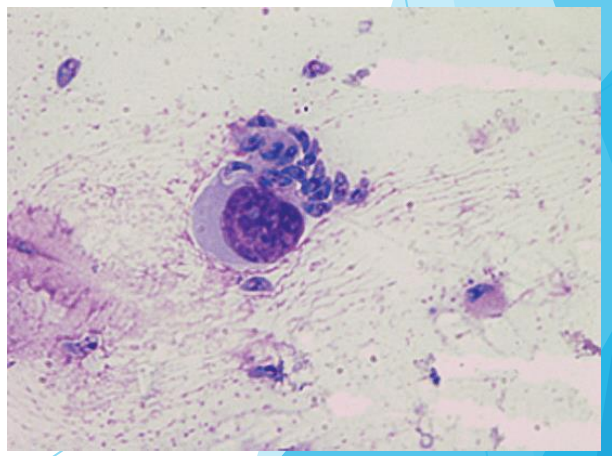
Immunity

- **Immunity** is provided by cellular and humoral factors. Specific antibodies have a certain protective effect.
- With congenital toxoplasmosis, high titers of specific antibodies (IgM and IgG) are found in the blood serum of a newborn.

Microbiological diagnostics

- In acute infection, **microscopy** of smears prepared from blood, cerebrospinal fluid, sputum, spinal cord, various exudates and stained with the Giemsa method helps to detect parasites. In chronic infection, it is possible to detect cysts in biopsies of lymph nodes and other organs.
- **The biological method** consists in the study of the blood and internal organs of white mice infected parenterally with pathological material. Infected animals usually die in 7-10 days, otherwise blood from the heart cavity is examined by serological method. Cysts are found in the brains of animals.





Microbiological diagnostics

- Based on the detection of specific antibodies, **the serological method** is considered the main method for the diagnosis of toxoplasmosis. Currently, ELISA is mainly used for this purpose.
- The detection of IgM antibodies indicates the initial period of the disease.
- The resulting IgG antibodies are determined in the blood serum one month after the onset of the disease and remain for a long time.
- In some cases, an intradermal reaction to toxoplasmin is performed. **A positive skin-allergic test (Frenkel test)** appears a month after the onset of the disease and remains positive for a long time.

Treatment and prevention of toxoplasmosis

- **Treatment**. The most effective is the combination of pyrimethamine with sulfonamides. Alternative drugs such as spiramycin, clindamycin, sulfamethoxazole trimethoprim are also used. During pregnancy, the appointment of spiramycin (rovamycin) is recommended.
- **Prevention**. It is important to avoid contact with cats (especially those who do not have an owner), to heat-treat animal products. Pregnant women are advised to thoroughly wash their hands after cutting raw meat, and periodically be examined for the presence of specific IgM and IgG antibodies.

The causative agents of leishmaniasis (genus Leischmania)

- Parasites of the genus Leischmania (leishmania) are the causative agents of leishmaniasis in humans and animals. There are several forms of leishmaniasis.
- **Cutaneous leishmaniasis** (New and Old World cutaneous leishmaniasis),
- **Visceral leishmaniasis** (kala azar),
- **Leishmaniasis of the skin and mucous membranes** (mucocutanosis or naso-oral leishmaniasis, or espundia).
- These forms can be caused by various types of pathogens, but some types cause certain clinical forms.
- The causative agents of leishmaniasis belong to the Mastigophora subtype of the Sarcomastigophora type.

The causative agents of leishmaniasis (genus Leischmania)

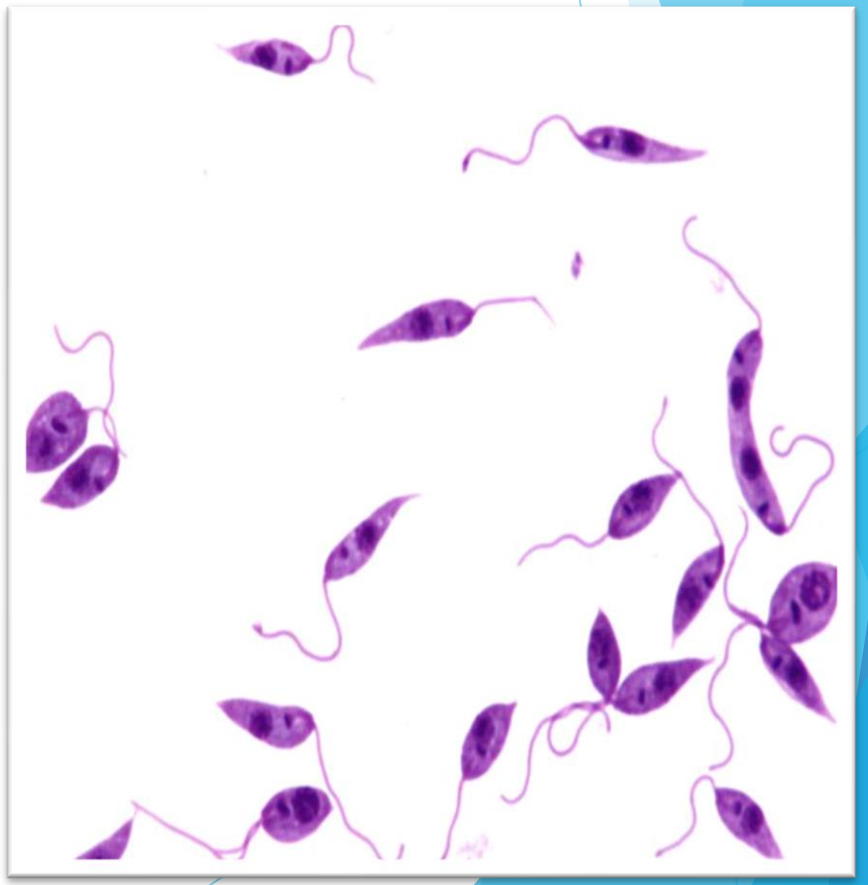
- Of the numerous types of Leishmania among pathogenic for humans, 4 complexes can be distinguished:
- **L. tropica complex** (Subspecies tropica and mayor species L. tropica and species L. aethiopica) - are the causative agents of cutaneous leishmaniasis of the Old World (in Africa and Asia);
- **Complex L. mexicana** (Subspecies mexicana, amazonensis, venesuelensis and pifanoi species L. mexicana and species L. peruviana and L. uta) - are the causative agents of cutaneous leishmaniasis of the New World (in America);
- **Complex L. braziliensis** (Subspecies braziliensis, guyanensis and panamensis species L. braziliensis) - are the causative agents of leishmaniasis of the skin and mucous membranes;
- **Complex L.donovani** (Subspecies donovani, infantum, chagasi and archibaldii of the species L.donovani) - are the causative agents of visceral leishmaniasis;

Leishmaniasis pathogens (genus Leischmania)

- Different types of leishmaniasis do not differ morphologically. But they are differentiated using molecular methods and monoclonal antibodies. Depending on the stage of development, leishmania has two forms:
- Flagellated form - **promastigote**
- Flagellaless form - **amastigote**

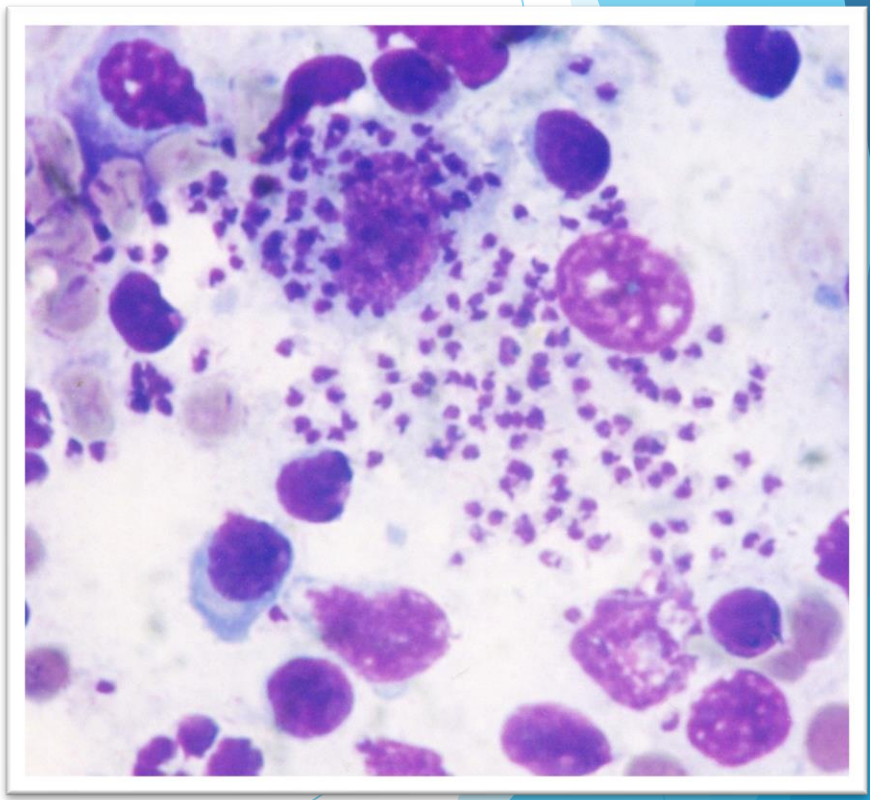
The causative agents of leishmaniasis (genus Leischmania)

- On nutrient media and in the body of mosquitoes-carriers develop in the **form of promastigotes.**
- The length of the promastigote is 10-20 microns, the width is up to 5 microns, the shape is elongated spindle-shaped. The flagellum extending from the rounded end ensures the movement of Leishmania. At the base of the flagellum is an organoid - the kinetoplast, which provides the flagellum with energy for movement and contains mitochondrial DNA.



Leishmaniasis pathogens (genus Leischmania)

- In infected human and animal tissues (bone marrow, spleen, liver, lymph nodes, macrophages), Leishmania occur in the **form of amastigotes**.
- The size of an amastigote is 2-6x1-3 microns, it is round in shape, without flagella. When stained according to Giemsa, the cytoplasm becomes blue, and the nucleus and kinetoplast become red-violet.



Leishmaniasis pathogens (cultivation)

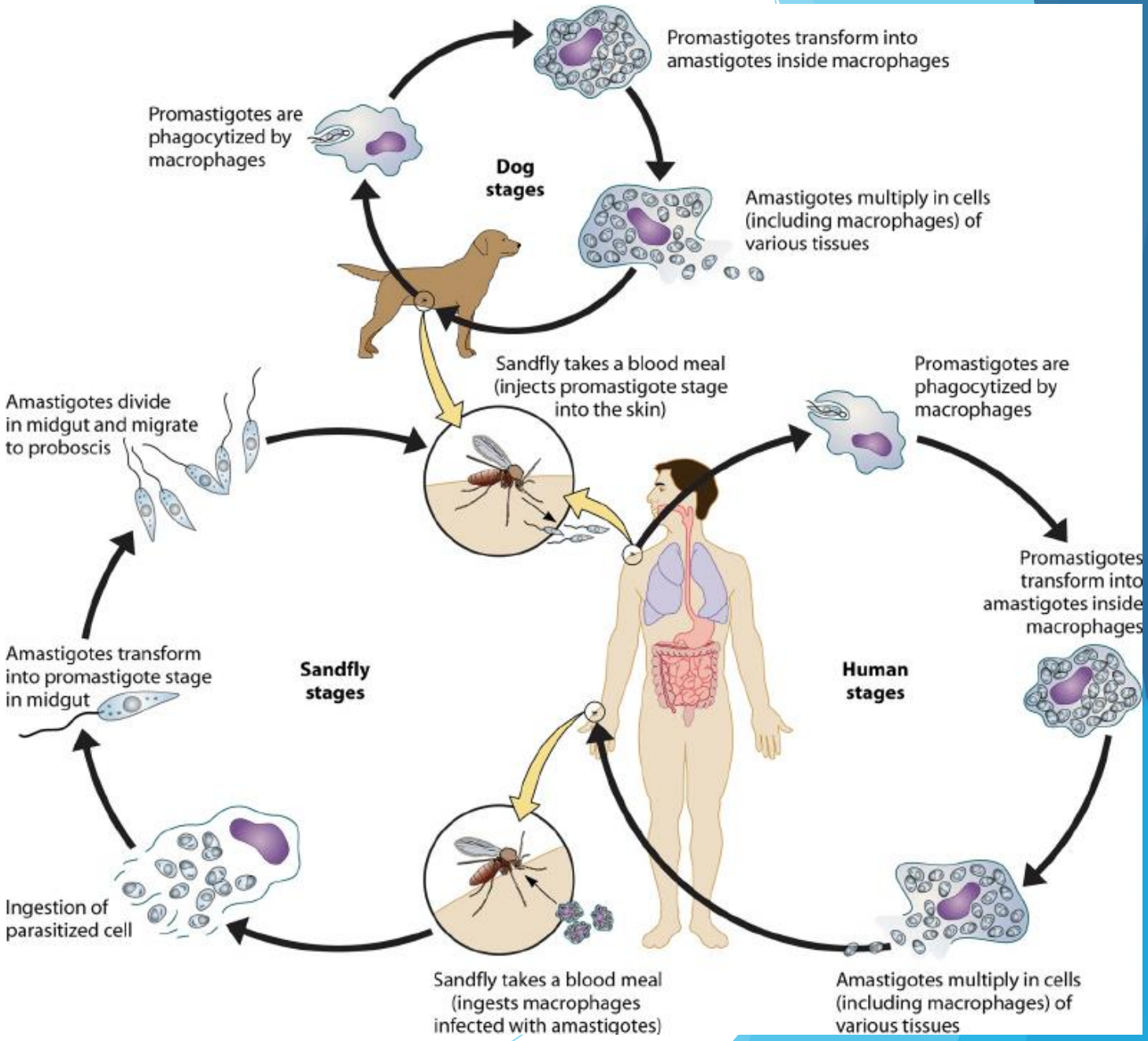
- Leishmania are cultivated at a temperature of 26-280C in NNN medium (Novy, Neal, Nicole) or in RPMI media (Roswell Park Memorial Institute), Tobie, Schneider, etc.
- Parasites on the NNN medium for 21 days, and on the RPMI and Schneider media in just 4-5 days multiply in the form of **promastigotes.**
- Leishmania can also be cultivated in cell cultures (macrophages and fibroblasts), in which case the parasites reproduce as **amastigotes..**

NNN mühiti

Source of infection and routes of transmission

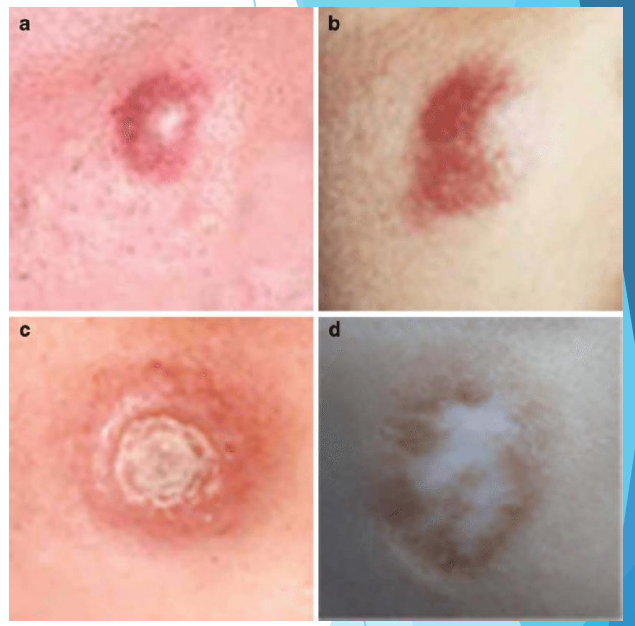
- Transmission occurs through the bite of mosquitoes or mosquitoes. The carrier of leishmaniasis in the Old World is mosquitoes of the genus Phlebotomus, and in the New World - of the genus Lutzomyia.
- According to epidemiological features, **anthroponotic** and **zoonotic leishmaniasis** are distinguished.
- **The source of infection** in anthroponotic leishmaniasis is a person and various animals, and in zoonotic only animals.
- The endemic foci of leishmaniasis in Azerbaijan mainly include the northwestern regions.

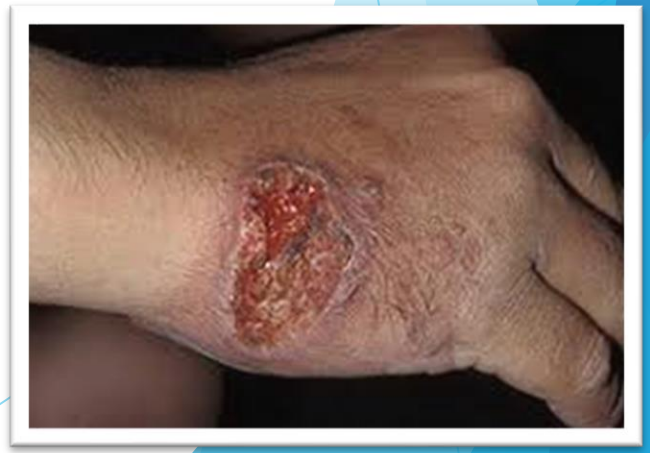
Source of infection and routes of transmission



Pathogenesis and clinical features of leishmaniasis

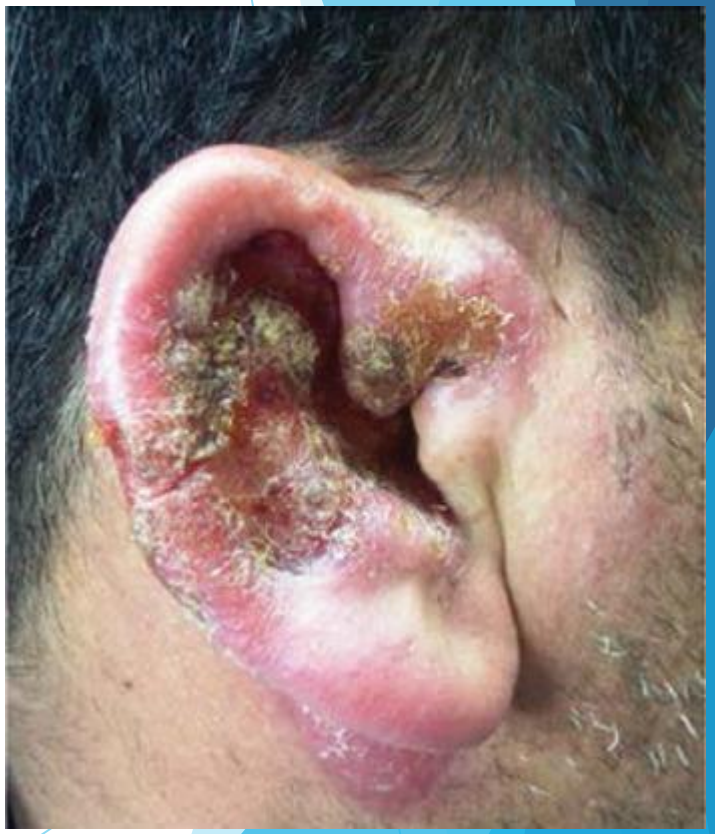
- **Cutaneous leishmaniasis of the old world.**
- With anthroponotic (late ulcerative, urban type) cutaneous leishmaniasis, at the end of the latent period, itchy nodules form at the site of the mosquito bite, which subsequently increase and turn into ulcers.
- With zoonotic (early ulcerating, rural type) cutaneous leishmaniasis, the latent period is shorter, the course is more acute. Nodules at the site of inoculation quickly turn into moist (watery) ulcers.





Pathogenesis and clinical features of leishmaniasis

- **Cutaneous leishmaniasis of the new world** L. mexicana is caused by the leishmania complex and is found mainly in the Americas. The genus Lutzomyia is transmitted by mosquitoes. Clinically similar to Old World cutaneous leishmaniasis.
- But the “rubber ulcer” caused by the species L. mexicana subspecies mexicana is somewhat different. The disease is mainly common among rubber gatherers and lumberjacks.
- Painless, chronic, long-term (years) persisting and non-spreading ulcers of the ear and neck, as a rule, lead to gross deformities of the ear.

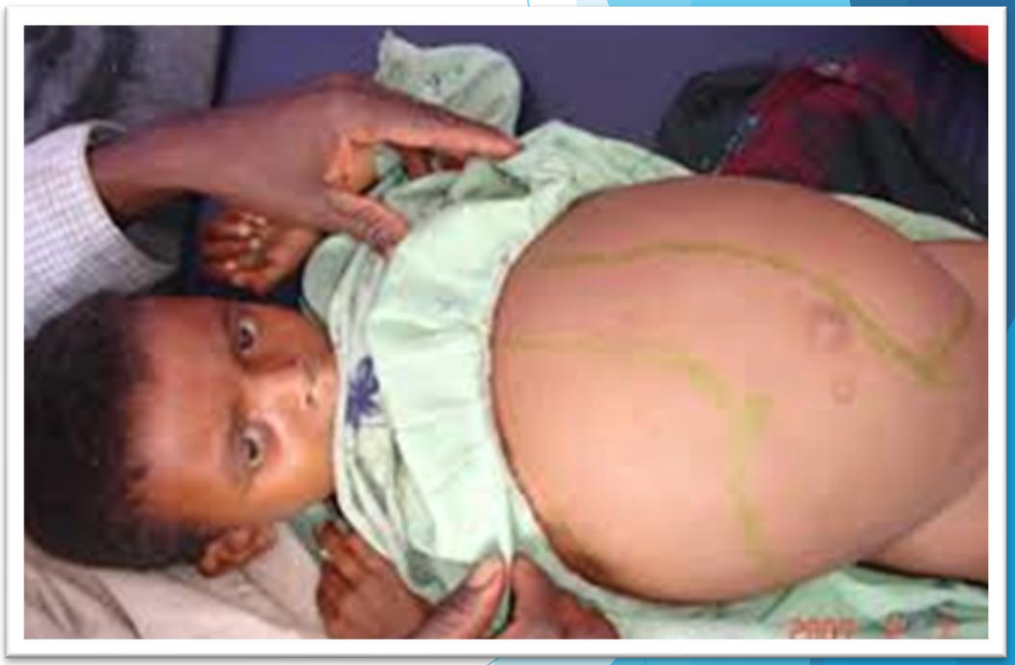


Pathogenesis and clinical features of leishmaniasis

- **Leishmaniasis of the skin and mucous membranes (espundia**) is caused by a complex of leishmania L. braziliensis, mainly found in Central and South America.
- The incubation period lasts 1-4 weeks. The first signs resemble cutaneous leishmaniasis. But in most cases, slowly progressing over months and years, leads to a painless deformity of the mouth and nose.
- Erosive ulcers form on the mucous membrane of the tongue, cheeks and in the nasal cavity, destruction of the nasal septum, pharynx and palate occurs

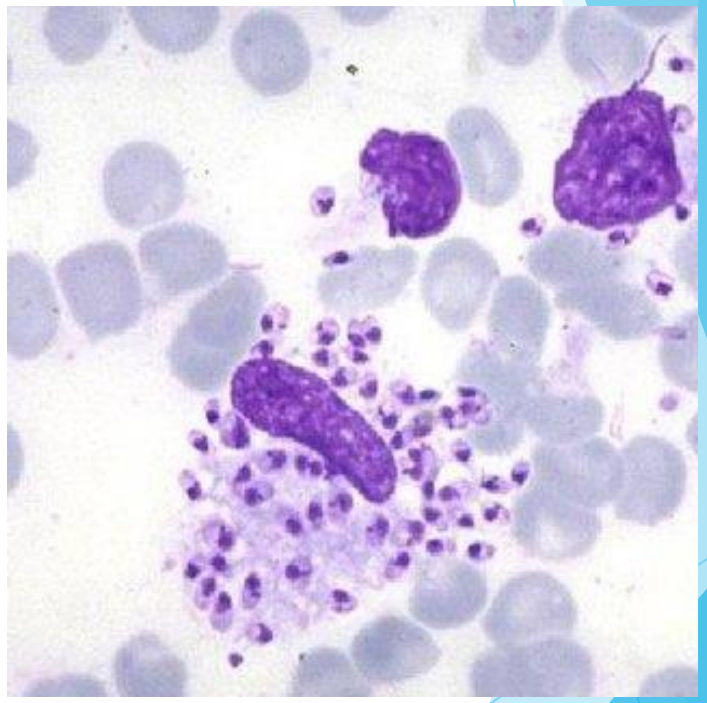
Pathogenesis and clinical features of leishmaniasis

- **The cause of visceral leishmaniasis (kala azar**) is a complex of leishmania L.donovani.
- In Eurasia and Latin America, the source of infection is rodents, jackals, foxes and dogs, and in Southeast Asia (India, Bangladesh) it is humans.
- There are symptoms of temperature, enlargement of the liver and, especially, of the spleen, lymphadenopathy, diarrhea. Organ dystrophy and necrosis develops. The skin takes on a dark, earthy color. (adisonism)
- The visceral leishmaniasis of the Mediterranean Sea (children's kala-azar) caused by the species L.infantum from the L.donovani complex has a similar clinic, but more often affects children..



Microbiological diagnostics

- For the diagnosis of cutaneous leishmaniasis, scrapings and aspirates from nodes and skin lesions serve as the material for research, and in case of visceral leishmaniasis, mainly bone marrow punctate is examined.
- **Microscopic method**. Small, oval-shaped amastigotes are visible in smears stained according to the Giemsa method.
- The pathogen can also be detected in pathological material by PCR.

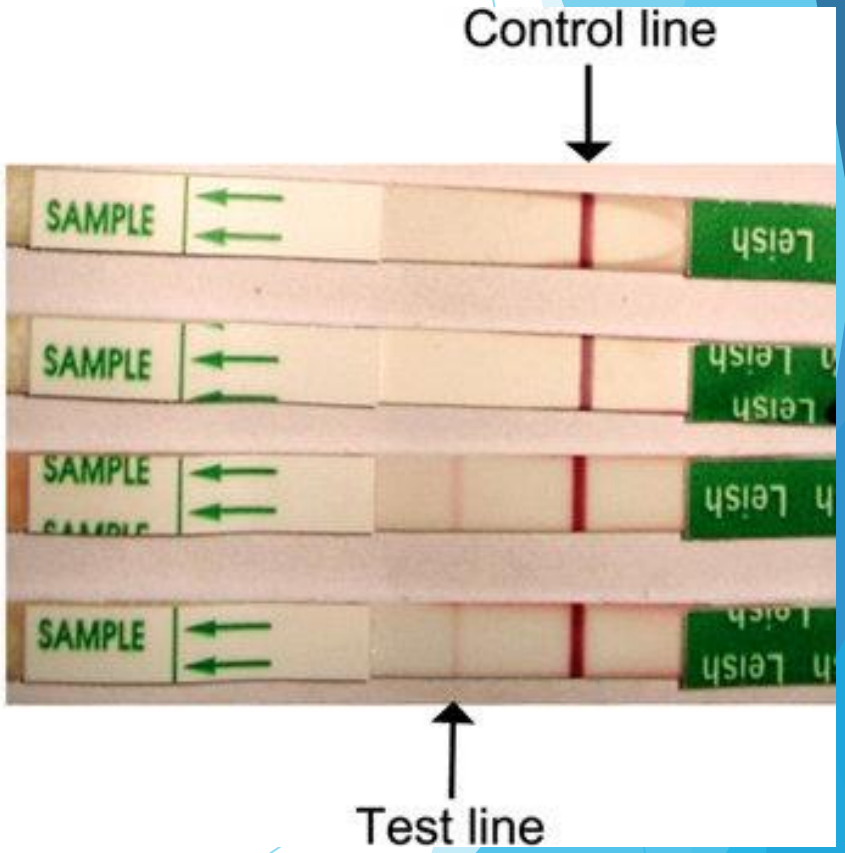


Microbiological diagnostics

- **Cultural studies.** To obtain a culture of the pathogen, the material is incubated at a temperature of 270C in a special nutrient medium (NNN medium, etc.) for 15-20 days.
- Recently, a microculture method has been developed to quickly obtain a culture of the pathogen. The **microculture method** consists in the fact that for cultivation, the pathological material, after being added to a liquid nutrient medium, is taken into a hematocrit capillary in a volume of 50-100 μl. Then both ends of the capillary are closed with paraffin and incubated at 270C for 2-7 days.

Microbiological diagnostics

- Diagnosis of visceral leishmaniasis is carried out mainly by the serological method. The detection of antibodies to the pathogen using **serological methods** of ELISA and RIF in the blood serum of patients is not sufficiently specific.
- Recently, the detection of specific antibodies to the causative agent of visceral leishmaniasis is carried out using the qualitative method "**leishmania dipstick rapid test**". The principle of the method is based on the determination of antibodies to Leishmania antigens in the blood serum of patients by immunochromatographic method.
- **Allergic test (Montenegro test).** Based on a skin-allergic reaction to the killed promastigote form (HRT). The method is used more often for epidemiological studies and gives a positive reaction after 4-6 weeks.



Leishmaniasis treatment

- With minor skin manifestations of leishmaniasis, etiotropic treatment is carried out.
- Previously, large and poorly healing ulcers were treated with pentavalent antimony preparations. Currently, **miltefosine and alkylphosphocholine** are more commonly prescribed.
- For the treatment of recurrent cutaneous leishmaniasis, ketoconazole is prescribed for 4-8 weeks, as well as ultraviolet or infrared radiation 20 minutes a day for a month.
- Miltefosine and amphotericin B are more frequently prescribed for the treatment of visceral leishmaniasis.