

PARASITOLOGY

Introduction to Parasitology

TABLE 51-1 Worldwide Occurrence of Selected Parasitic Infections

A. Prevalence

<i>Infection</i>	<i>Number of Individuals Infected</i>
Ascariasis	1.38 billion
Toxoplasmosis	1–2 billion
Hookworm disease	1.25 billion
Schistosomiasis	200 million
Giardiasis	200 million
Filariasis (skin and lymphatic)	137 million
Pinworm infection	60–100 million
Strongyloidiasis	50–80 million
Trichuriasis	45 million
Trypanosomiasis	15–20 million
Leishmaniasis	12 million

B. Incidence and Mortality

<i>Infection</i>	<i>New Cases per Year</i>	<i>Deaths per Year</i>
Malaria	200–300 million	1–3 million
Amebiasis	48 million	70,000
Leishmaniasis	2 million	80,000
Trypanosomiasis	450,000	145,000

Based on estimates from the 1998 WHO World Health Report.

Protozoa- unicellular eukaryotes

- *Plasmodium species*
- *Toxoplasma*
- *Giardia*
- *Cryptosporidium*
- *Leishmania*
- *Trypanosomes*
- Infections with any of those pathogens can be initiated by relatively small inocula.
- Disease is generally a consequence of the replication of the parasites in large numbers within the host:
 - Intracellularly (*Plasmodium* and *Leishmania species*)
 - Extracellularly (*Giardia* and amebas in lumen of GIT)
- their transmission from one host to another depends on arthropod vectors
- Transition into cyst form, adapted for survival in various environmental extremes.

Protozoa

- **Amebas** (or Sarcodina): formless cells that move purposefully by extending pseudopods toward an attractive stimulus and then streaming their cytoplasm in the desired direction. Amebas are intestinal parasites that alternate between trophozoite and cyst forms.
- **Flagellates**: intestinal and blood protozoa that use one or more flagella for locomotion. Like the amebas, flagellates that infect the gastrointestinal tract form environmentally resistant cysts. Flagellates that infect the tissues or blood are usually transmitted by arthropods.
- **Ciliates**: protozoa covered with tiny cilia that provide locomotion. Pathogenic ciliates are extremely unusual.
- **Sporozoa**: very important pathogens that include the agents of malaria, toxoplasmosis, and several common intestinal parasites.

Helminths (worms)- multicellular organisms

- They reproduce sexually. Productive infections require both, male and female worms. Some tapeworms are hermaphroditic, having both male and female reproductive organs.
- **Roundworms**: circular in cross section. Adult worms of various roundworm species range in size from a few millimeters to 20 cm.
- **Flatworms**: asymmetric in cross section. They comprise two main types:
 - **Flukes** (e.g., *Schistosoma*, *Fasciola*): relatively short flatworms with nonsegmented bodies.
 - **Tapeworms**: segmented worms that vary in size from millimeters to several meters in length. A tapeworm can be thought of more as a colony than as an integrated multicellular organism. The segments are generated from a germinal worm head that contributes to a growing chain of flat segments, each with its own nutritional and reproductive organs.
- Because of their large size, helminths are typically extracellular.

Vectors

- Vectors are living transmitters of disease.
- Most vectors are arthropods.
 - female *Anopheles* mosquito, which transmits malaria
 - tsetse flies, which transmit sleeping sickness
 - black flies, which transmit the tissue roundworm infection called river blindness
 - reduviid (“kissing”) bugs, which transmit Chagas disease
- Arthropods are not simply passive agents that transfer parasites from one mammalian host to another. They also are involved in essential steps of the parasitic life cycle.
- To a large extent, the prevalence of a parasitic disease in a given geographical location may depend on whether the local conditions are favorable to arthropod breeding
- their elimination from the environment can theoretically eradicate the respective diseases they cause in humans

TABLE 51-3 Modes of Spread of Some Parasitic Diseases

Mode of Exit	Mode of Entry	Human-to-Human	Animal-to-Human
Feces	Mouth	Cryptosporidiosis	Cryptosporidiosis
		Amebiasis	Toxoplasmosis
		Giardiasis	Visceral larva migrans
		Strongyloidiasis ^a	Echinococcosis
		Ascariasis ^b	
		Trichuris infection ^b	
		Pork tapeworm	
Feces	Skin	Strongyloidiasis	Creeping eruption (dog or cat hookworm)
		Hookworm	Schistosomiasis ^c
Arthropod bite	Arthropod bite	Lymphatic filariasis	Trypanosomiasis (sleeping sickness, Chagas disease)
		Leishmaniasis	Leishmaniasis
		Malaria	
		Onchocerciasis	
None (parasite encysts in muscle)	Ingestion (inadequately cooked meat)		Trichinosis
			Toxoplasmosis
			Beef tapeworm
			Pork tapeworm
			Fish tapeworm

^aUsually transmitted by fecal–cutaneous route but may also be transmitted by the fecal–oral route.

^bMay require a period outside the human host to be infectious.

^cMode of exit may also be urine; development in an intermediate host is obligatory.

SPREAD AND MULTIPLICATION

- Inoculum Size
 - large inocula are required to cause amebiasis in humans
 - symptomatic cryptosporidiosis can be produced by the ingestion of relatively few cysts
 - In most helminthic infections, the severity of the infection is proportional to the inoculum size
- Parasite Survival Mechanisms in Immunologically Normal Hosts
 - evading the Host Immune Response:
 - adult schistosomes coat themselves with host plasma proteins
 - Trypanosomes are varying their surface antigens
 - Leishmania species, which live in the phagolysosomes of macrophages, secrete a superoxide dismutase that protects them from the toxic superoxide produced in the phagolysosome
 - directing lymphocyte proliferation into the Th2 rather than Th1 pathway
- Species and Tissue Tropisms- specific receptors
- Temperature
 - *Leishmania donovani* replicates well at 37°C and causes visceral leishmaniasis (kala azar), a disease of the bone marrow, liver, and spleen
 - *Leishmania mexicana* grows well at 25°C to 30°C but poorly at 37°C and causes infections of the skin (where temperatures are 25°C to 30°C).

DAMAGE

- the clinical manifestations of parasitic disease may reflect tissue damage by the parasite, the effects of the host immune response, or both:
- amebas → direct cytolytic effect
- schistosomiasis and cutaneous filariasis → Chronic inflammation
- Trichinosis → host inflammatory response → persistent disease even after the parasites have died
- Cysticercosis → asymptomatic for a long period. Dead of the parasite → leakage of parasite antigens into the tissues → hypersensitivity reaction
- Eosinophilia
 - typically accompanied by increased levels of IgE
 - driven by elevated levels of interleukin-5
 - useful in suggesting a helminth diagnosis
 - is not a feature of most protozoal infections nor of helminth infections that do not involve migration through tissue

DIAGNOSIS

- identifying the parasites or their characteristic progeny (cysts, eggs, or larvae) in clinical specimens
- it is important to understand the parasite's life cycle
 - in the life cycle of hookworms, the adult female lives in the lumen of the human intestine→ release her eggs into the stool. Examination of the stool for hookworm eggs is an effective and sensitive method for the diagnosis of hookworm infection.
 - in the life cycle of *Strongyloides* species, the adult female invades the intestinal wall to release her eggs, Intact eggs are rarely seen in the stool. The larvae that emerge from eggs in the intestinal wall can be found in the stool of a person with *Strongyloides* infection.

TREATMENT AND PREVENTION

- Drugs- Chemoprophylaxis
 - Chloroquine- malaria. Today, most of the strains of *P. falciparum* in most malarious areas of the world have become resistant to chloroquine
- Treatment
 - Mass treatment may be an effective control strategy for diseases that depend on humans as a reservoir.
 - Treatment of people with zoonotic and deadend infections will not influence the occurrence of those diseases.
 - If treatment is to be effective in reducing transmission, it must be given to all infectious persons, both symptomatic and asymptomatic.
- Immunity and Immunization
 - Major Problem in Designing Vaccines: Evasion of the Host Immune Response
 - Other Problems in Designing Vaccines: Stage-Specific Antigens

PROTOZOA

TABLE 52-1 Comparison of Major Blood and Tissue Protozoa

Organism	Reservoir	Mode of Transmission	Clinical Manifestations
Blood Protozoa			
<i>Plasmodium</i> species (malaria)	Infected humans	Vectorborne by the female <i>Anopheles</i> mosquito	Fever and chills with red blood cell lysis
<i>Babesia</i> species (babesiosis)	Rodents (voles), deer, mice	Vectorborne by the hard-bodied <i>Ixodes</i> tick	Fever and chills with red blood cell lysis
Tissue Protozoa			
<i>Toxoplasma gondii</i> (toxoplasmosis)	Sheep, pigs, cattle, cats	Foodborne by the ingestion of inadequately cooked beef or lamb Fecal–oral by the ingestion of infectious oocysts in cat feces	Intrauterine (congenital) infection can cause severe retardation in the neonate Mononucleosis-like illness most common Infection of the brain (encephalitis) or heart (myocarditis) in severely immunocompromised patients
<i>Leishmania</i> species (leishmaniasis)	Infected humans, dogs, jackals, foxes, rats, ground squirrels, gerbils	Vectorborne by infected <i>Phlebotomus</i> sand flies	Trivial or mild (self-healing) skin lesions Disfiguring mucocutaneous lesions Systemic illness with involvement of liver, spleen, and bone marrow
<i>Trypanosoma cruzi</i> (Chagas disease, American trypanosomiasis)	Wildlife, domestic animals (zoonosis)	Vectorborne by reduviid bugs followed by rubbing infected feces in the bite wound	Gastrointestinal tract dysfunction from autonomic nerve damage (megacolon, megaesophagus) Cardiac dysfunction from damage to the conducting system (right bundle branch block)
<i>Trypanosoma brucei gambiense</i> or <i>T. brucei rhodesiense</i> (West and East African trypanosomiasis, respectively, or sleeping sickness)	Infected humans, wildlife, cattle	Vectorborne by the tsetse fly	Systemic illness with fever, headache, muscle, and joint pains Progresses to central nervous system involvement with altered speech, gait, and reflexes (encephalitis)

CASE • Ms. M. is a 54-year-old businesswoman from Liverpool who traveled to East Africa (Kenya and Tanzania) on a business trip and then went on a photographic safari. After 1 week in Nairobi, she embarked on a 10-day trip through the wildlife preserves of Serengeti and Ngorongoro, with a final visit to Mombasa on the Indian Ocean. During her flight home, 9 days after leaving the game parks, Ms. M. developed a “flu-like” syndrome, with headache, muscle aches, and a temperature of 38°C. After she returned to Liverpool, she saw a physician, who diagnosed influenza. She had returned to England in February during an outbreak of influenza A.

Ms. M. was given acetaminophen, which initially reduced her fever and muscle aches. However, she felt worse the next day. She suddenly developed an intense chill that lasted for about 30 minutes, followed by a fever to 40.2°C that lasted for 6 hours. As the fever abated, Ms. M. became drenched in sweat and felt exhausted and drained. Her symptoms continued to worsen, and she was brought to the hospital unconscious 2 days later. On examination, she had edema of the lungs. She showed no signs of endocarditis, and a lumbar puncture was negative for bacterial meningitis.

The attending physician, drawing on his experience while serving in the armed services abroad, recognized that Ms. M.’s clinical manifestations were typical of a **malarial paroxysm**. The recent history of travel to endemic areas gave credence to his suspicion of the disease, and the diagnosis was confirmed when a Giemsa-stained smear of Ms. M.’s blood revealed large numbers of parasites within red blood cells. The parasites were identified as

Plasmodium falciparum by their characteristic ring shape. Ms. M.’s hematocrit (packed red cell volume) was 18% (normal is 40 to 45%). Urinalysis revealed dark urine, suggesting extensive hemolysis. Her serum creatinine (a measure of renal function) was 5.4 mg per 100 mL (normal is 1 mg or less per 100 mL).

Because Ms. M. had traveled in Kenya, a country in which drug-resistant malaria is endemic, treatment was begun with intravenous quinidine, which is effective against *P. falciparum* strains resistant to other antimalarial drugs. Ms. M. was also given intravenous glucose as a precaution against hypoglycemia (which can produce coma in patients with severe *P. falciparum* malaria). Hypoglycemia can result both from consumption of glucose by large numbers of parasites and from the direct release of insulin from the pancreas caused by quinidine or quinine. For her pulmonary edema, Ms. M. required artificial ventilation with a respirator. She was given multiple transfusions for her anemia and was put on a dialysis machine because of her kidney failure. She recovered and was discharged after spending 10 days in the intensive care unit.

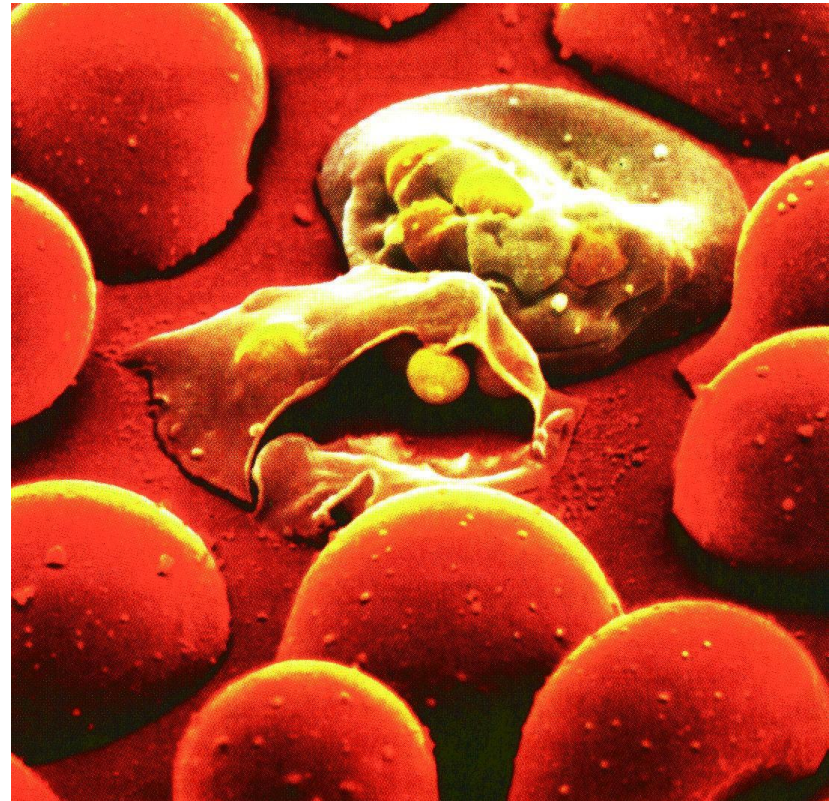
This case raises several questions:

1. Why did Ms. M.’s fevers occur in paroxysms (episodes) of shaking chills followed by fever and then drenching sweats?
2. Why did she have dark urine?
3. Why did she develop edema of the lungs and an elevation of the serum creatinine?

See Appendix for answers.

Parasites of red blood cells (Plasmodium species)

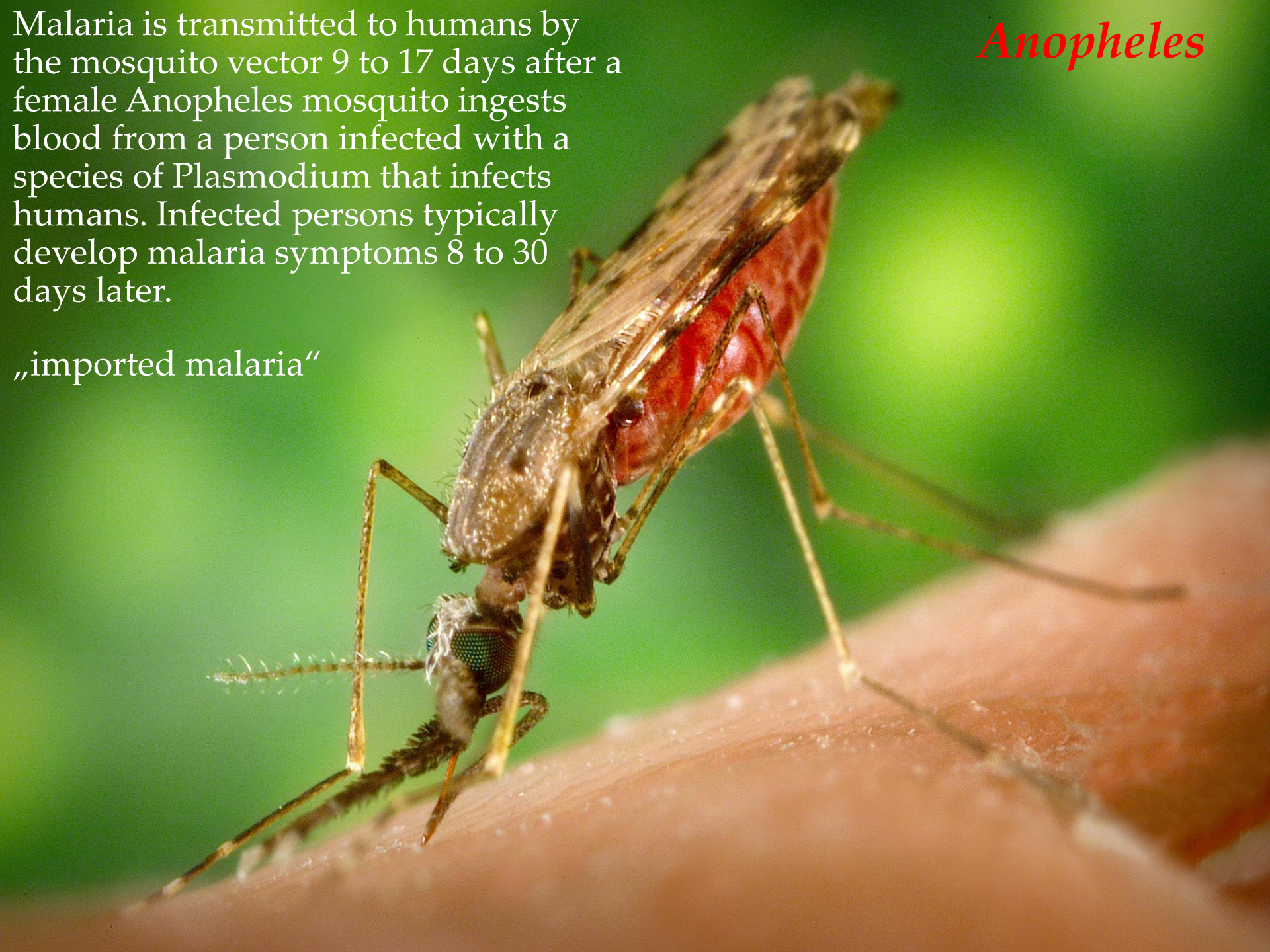
- Malaria is the most important of all protozoal diseases
- It occurs in many tropical and semitropical regions of the world, with approximately 200 to 300 million cases annually
- 2 to 3 million people die of malaria each year, especially malnourished African children
- *P. Falciparum*
- *P. Vivax*
- *P. Ovale*
- *P. malariae*
- Infected humans are the only reservoir for these plasmodial species that infect humans; transmission occurs through the bite of infected female anopheline mosquitoes



Anopheles

Malaria is transmitted to humans by the mosquito vector 9 to 17 days after a female *Anopheles* mosquito ingests blood from a person infected with a species of *Plasmodium* that infects humans. Infected persons typically develop malaria symptoms 8 to 30 days later.

„imported malaria“





Anopheles

Malaria multiplies deaths from war



SPREAD AND MULTIPLICATION

Anopheles (salivary glands)

Sporozoites

bloodstream (after bite)

Sporozoites

Liver (30 min.)

Hepatocellular cycle

(12-14 days)- merozoites

Red blood cells

Erythrocytic cycle

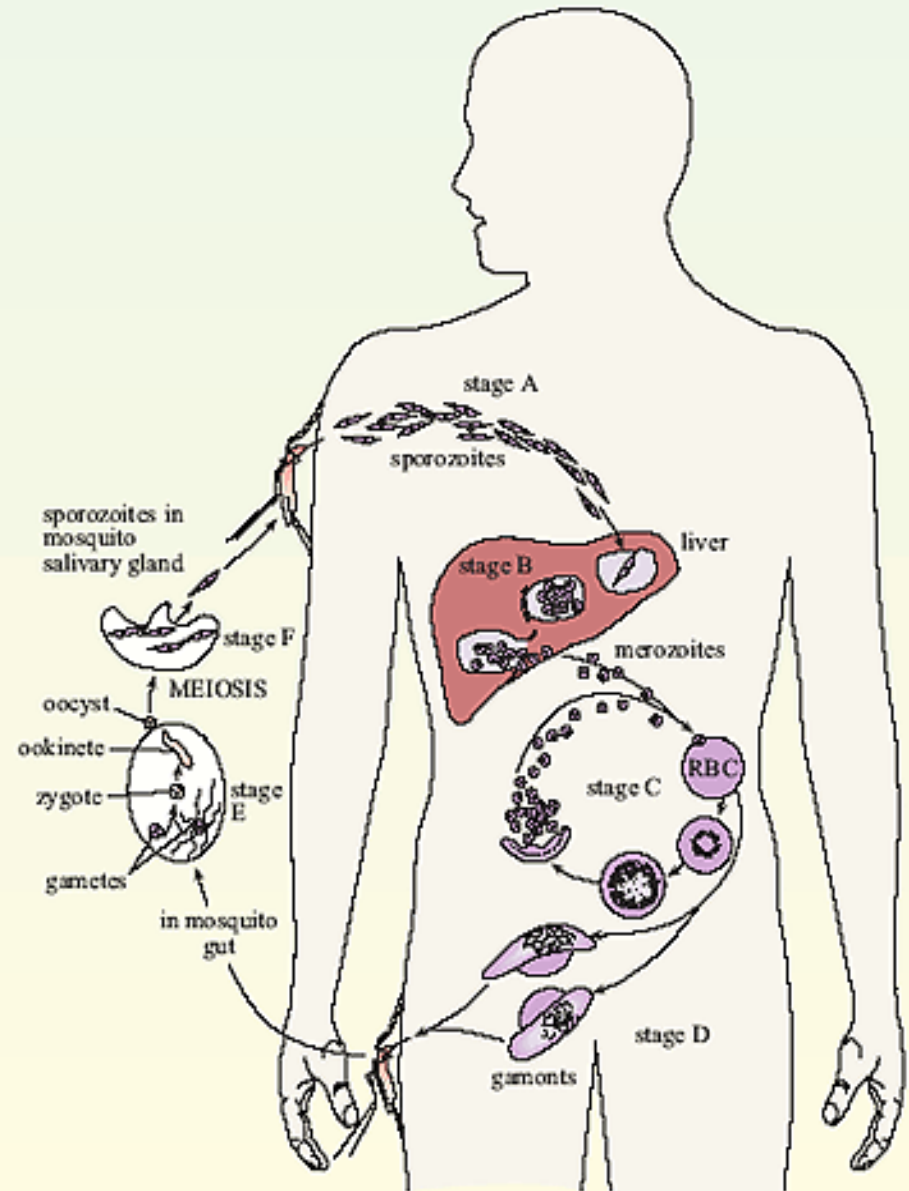
(2-3 days) merozoites,

Gametocytes

Anopheles (mosquito gut)

diploid zygote

Sporozoites



SPREAD AND MULTIPLICATION

- *P. Falciparum* invades erythrocytes of all ages, producing the highest parasitemias and the greatest risk of mortality
- *P. Vivax* prefers reticulocytes and young red blood cells
- *P. malariae* favors older red blood cells
- *P. Vivax* and *P. Malariae* infect only 1 to 2% or less of red blood cells, thus producing less severe disease
- *P. Ovale* is virtually identical to *P. Vivax*, clinically and morphologically
- The presence of *plasmodia* within red blood cells makes the cells less deformable. The spleen recognizes and removes older and less deformable red blood cells from the circulation, thus removing parasitized red blood cells from the circulation (**splenomegaly**)
- Splenectomized people have higher degrees of parasitemia and more-severe infections.
- *P. falciparum*–infected cells are prevented from circulating to the spleen and being removed from the circulation.

PATHOGENESIS

Anopheles

Blood



Egzo- erythrocytic cycle- Hepatocellular cycle

Liver (20.000 multiplications/ first 5 days)

Parasites enter bloodstream. Leukocytes phagocyte parasites.

Parasites are escaping into erythrocytes.

Erythrocytic cycle

Safe from leukocytes, they feed on hemoglobin

Intense proliferation within erythrocytes

Mass excretion of erythrocytes (millions of parasites)

Paroxysm (consequence of immune response)

PATHOGENESIS



- <http://www.youtube.com/watch?v=IVbq2yQH52g&feature=related>
- <http://www.youtube.com/watch?v=WolO-g1hiSo>

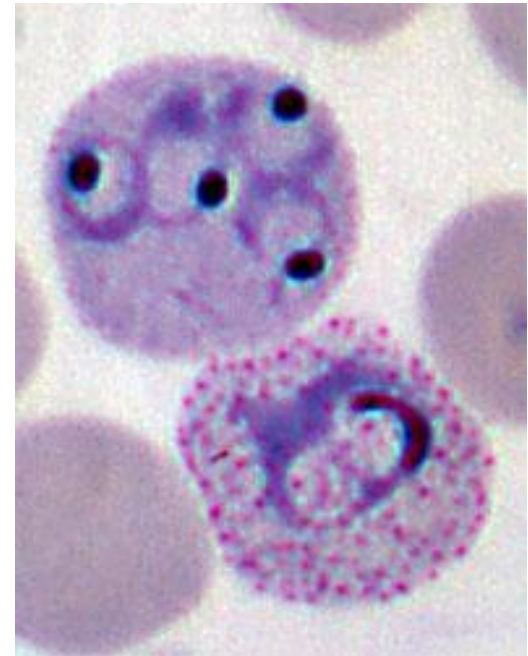
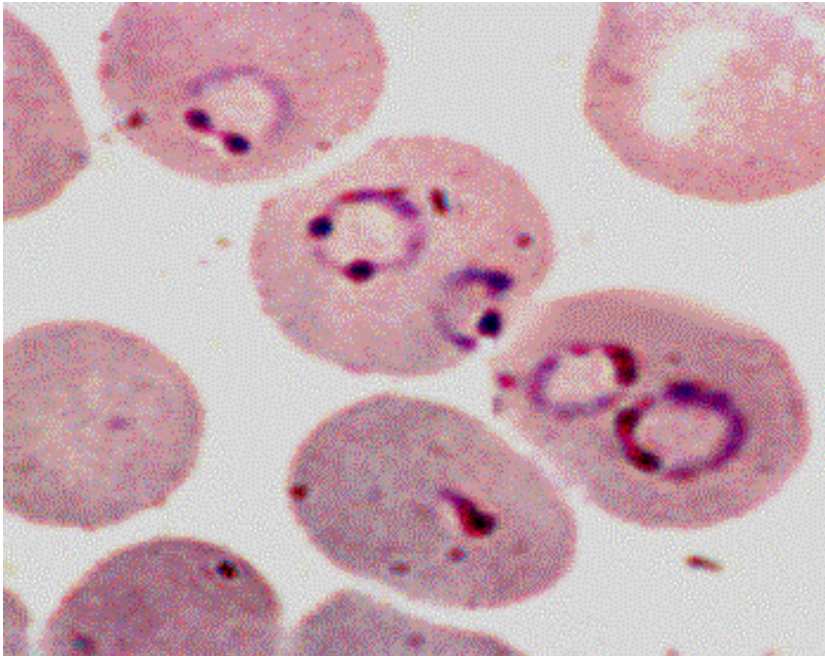
DAMAGE



- The main manifestations:
 - Fever
 - chills
 - anemia
- The typical **malarial paroxysm** (as in Ms. M.'s case) coincides with the lysis of many red blood cells and the release of large numbers of merozoites.
- In the process, parasite molecules, such as membrane molecules, are also released, and some of those molecules stimulate the production of tumor necrosis factor and interleukin-1 in macrophages.
- The surge in those cytokines is the stimulus for the sudden chill and fever characteristic of a malaria paroxysm
- Parasite replication can become synchronized
- Paroxysms occur at specific time intervals:
 - every 2 days for *P. Vivax* and *P. Ovale*
 - every 3 days for *P. malariae*
 - for *P. falciparum* are often not constant intervals

DIAGNOSIS

- Microscopic examination of a Gimza-stained peripheral blood smear.
- In acutely ill patients, the causative agent is usually *P. Falciparum* or *P. Vivax*.
- *P. malariae* usually causes subacute and chronic diseases.
- *P. Ovale* is so clinically similar to *P. Vivax* that distinguishing these causative agents has no practical significance.



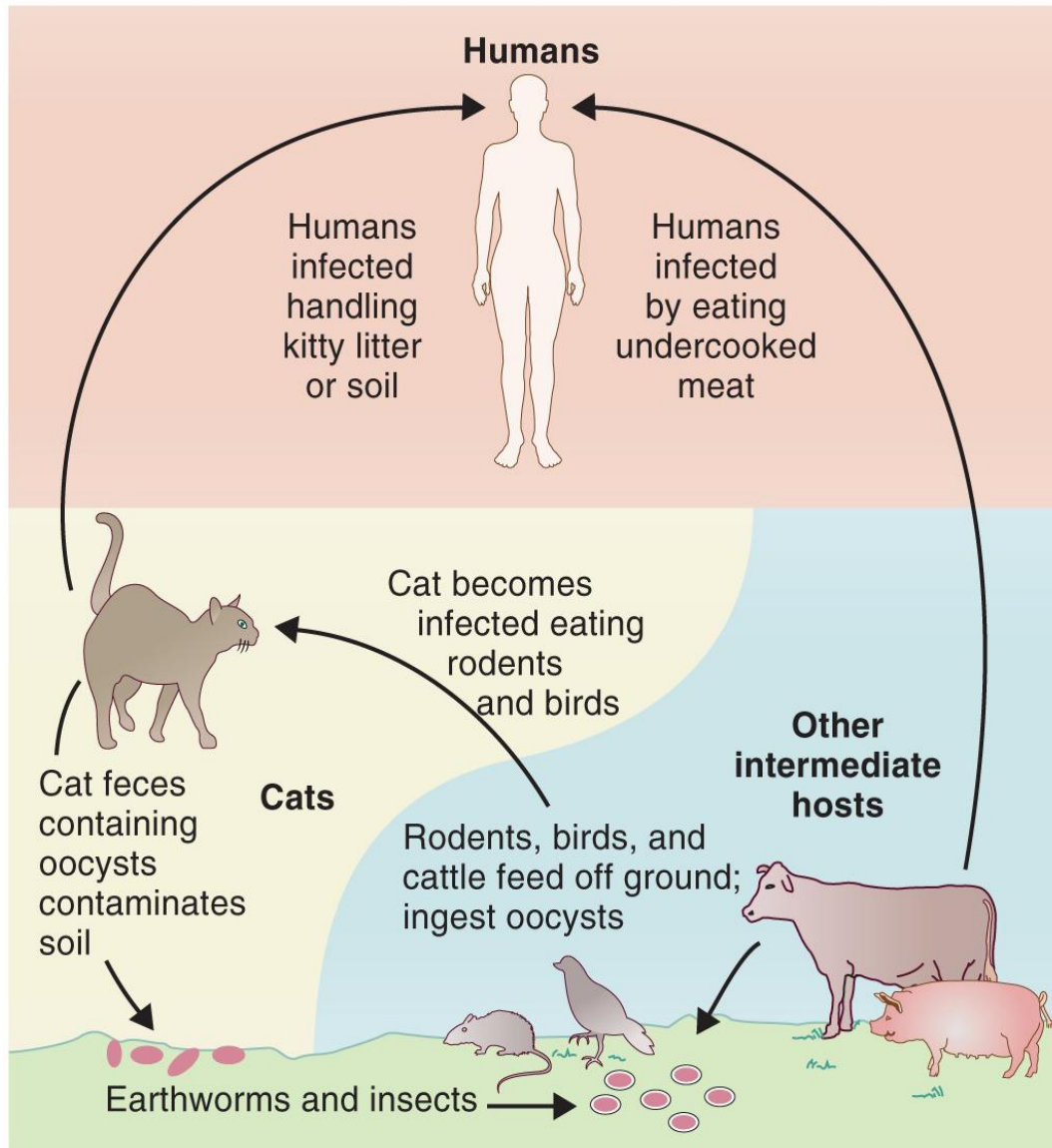
TREATMENT

- The immune response to malaria cannot eliminate parasites.
- Infections of those not immunized are significantly more severe than those previously immunized.
- Protective immune response is characterized by cytotoxic killing of infected hepatocytes and secretion of antibodies against merozoite antigens.
- **Chloroquine** was the most widely used drug for antimalarial hemoprophylaxis and therapy.
- Chloroquine enters the nutrient vacuoles of parasites in which hemoglobin is broken down. Toxic heme released by the breakdown of hemoglobin is detoxified and converted into malarial pigment. Chloroquine blocks the detoxification of heme and thus kills parasites.
- It is not effective in eliminating the hepatocellular stage of the parasite (hypnosis). **Primakin**
- **Prevention:** insecticides, drainage of wetlands, nets ...

Tissue protozoa: *Toxoplasma gondii*

- Infection is common in humans
- Less than 1% of infected people are diagnosed with the disease
- Particularly dangerous in immunocompromised (HIV) and fetuses
- Three different syndromes:
 - Mononucleosis-like syndrome
 - Congenital infection with severe consequences
 - Infection of immunocompromised hosts

Toxoplasma gondii. ENCOUNTER

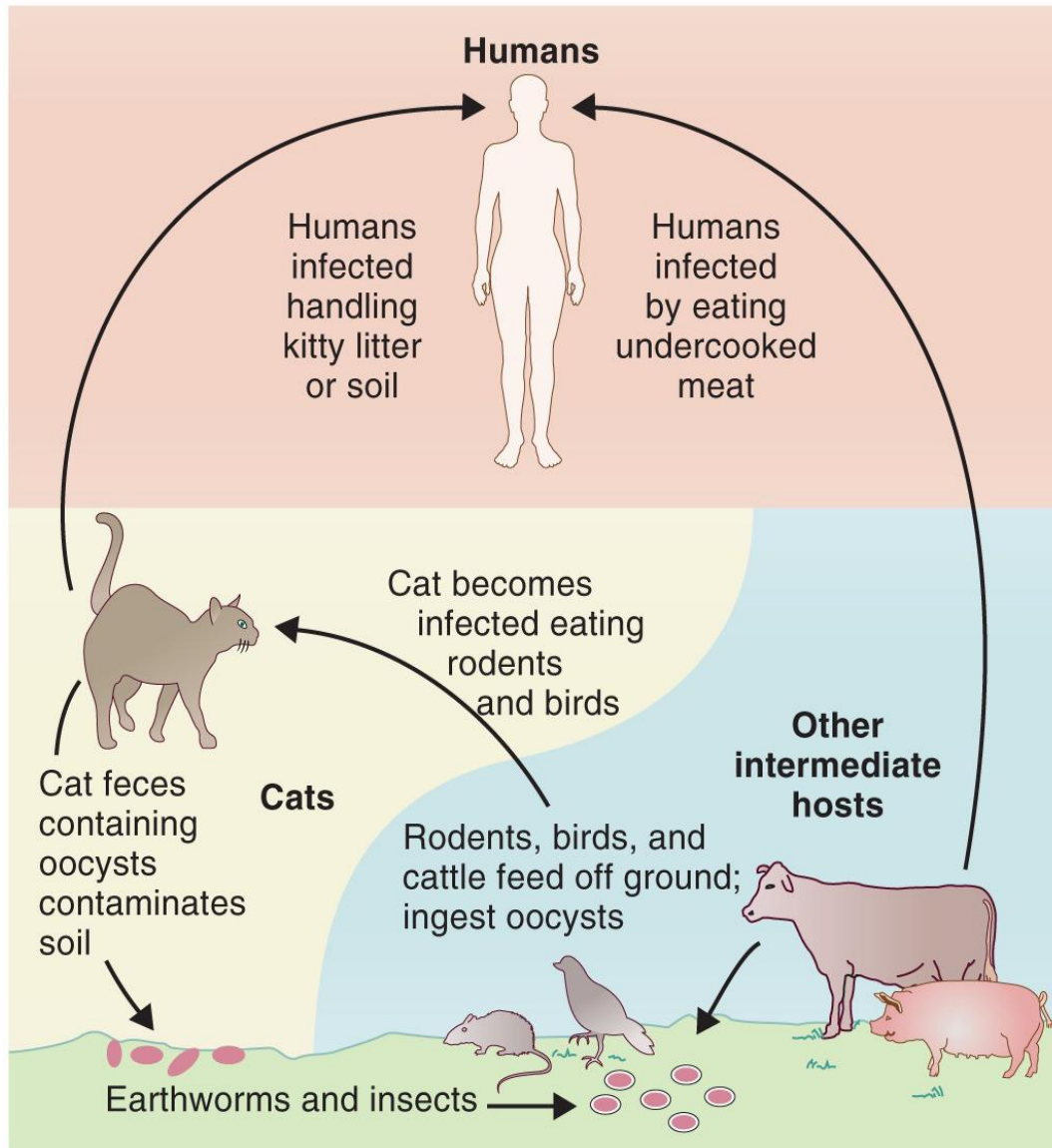


Insufficiently heat-treated meat (lamb, beef) containing tissue cysts *T. Gondii*

by ingestion of infectious oocysts, which are present in the feces of cats.

The first mode of infection is much more common.

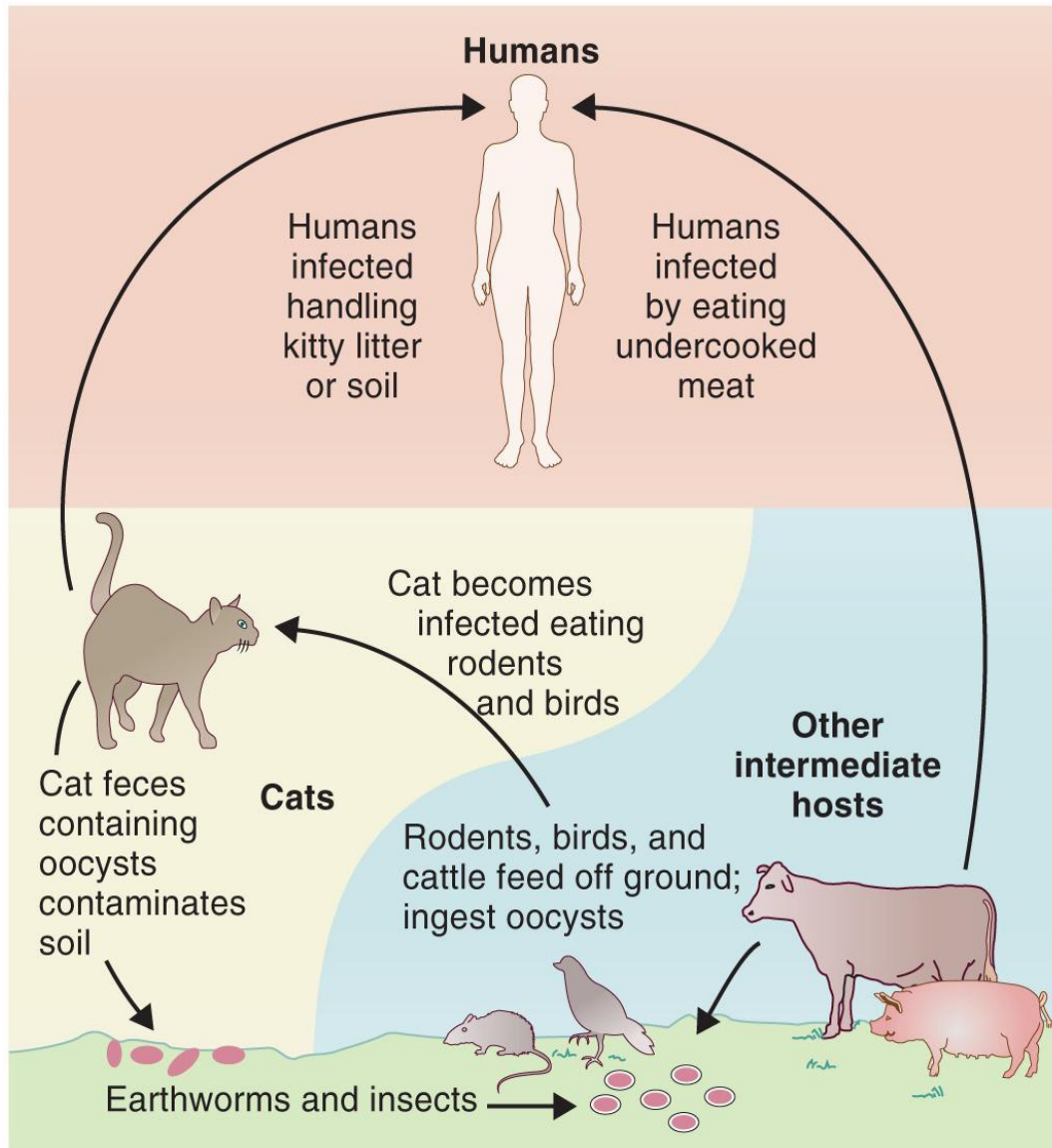
Toxoplasma gondii. ENCOUNTER



Cats are an important carrier. The sexual part of the parasite's life cycle takes place in cats (analogous to the mosquito phase, for malaria). Resistant, infectious oocysts reach the external environment through feces.

The life cycle of the parasite is completed when cats eat small rodents that are infected with oocyst ingestion..

Toxoplasma gondii. ENCOUNTER



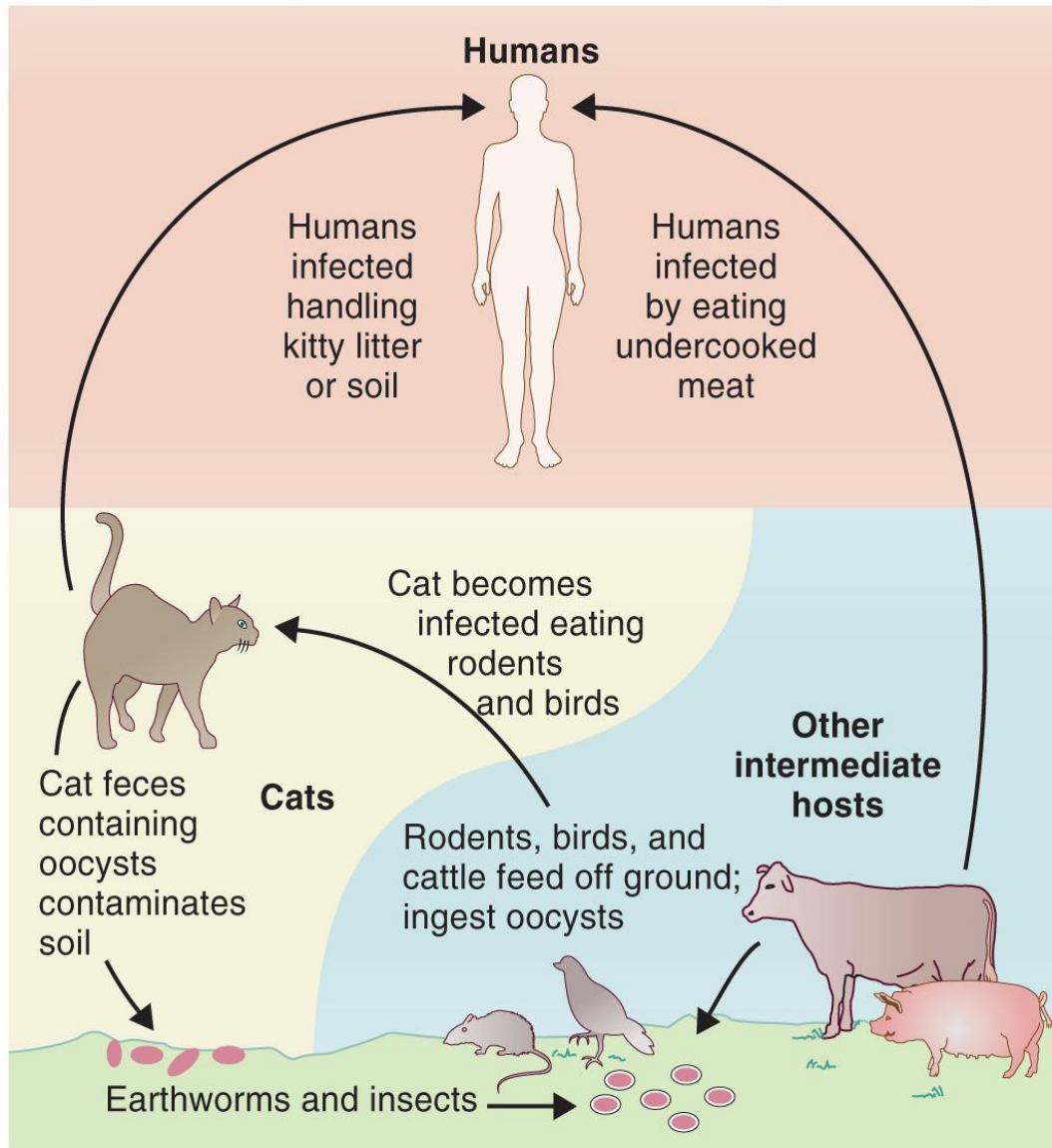
In animals developing toxoplasmosis:

Parasites → small intestine → bloodstream → brain, heart, muscles, and other organs.

first 4 to 6 weeks → immune response of host → controls the infection.

Parasites multiply within the cells of various tissues and organs and enter the latent stage by forming a **tissue cyst**.

Toxoplasma gondii. ENCOUNTER



Cats become infected by ingesting animals that have these tissue cysts in their muscles and organs.

The process of dissemination of parasites in various organs can be accompanied by transient symptoms.

After that, the infection remains inactive, unless the person becomes **immunocompromised**.

Toxoplasma gondii. SPREAD AND MULTIPLICATION

In the active phase of infection, *T. gondii* is found within **macrophages**

Active invasion, enveloped by a cell membrane (which forms a vesicle) without membrane proteins characteristic of endocytic entry into the cell.

The vesicle becomes "invisible" to the cell and will not be the target of lysosomes.

Activated macrophages can actively phagocytose *T. gondii* and eliminate the parasite in phagolysosomes.

Toxoplasma gondii. DIAGNOSIS AND TREATMENT

In immunocompetent individuals, the diagnosis of acute toxoplasmosis is made on the basis of elevated IgM antibody titers.

Immunocompromised patients (AIDS) are unable to produce a significant increase in antibody titers. Occurrence of new neurological symptoms and detection of brain lesions → toxoplasmosis of the nervous system.

AIDS + characteristic medical history + positive brain scanner + serological evidence of previous contact with *T. Gondii* (specific IgG antibodies) → will be treated for cerebral toxoplasmosis: pyrimethamine with sulfadiazine / clindamycin.

Toxoplasma gondii. Congenital infection

T. Gondii can be transmitted to the fetus if the mother becomes infected during pregnancy.

Since the greatest damage to the fetus infection can produce *in utero*, treatment of the infection after birth is too late.

Women are routinely tested for *T. Gondii* in early pregnancy.

Women who have been detected antibodies to *T. Gondii* (indicating an earlier infection) are not at risk for congenital fetal infection.

Seronegative women receive preventive advice, while women with detected seroconversion undergo therapy.

Possibilities are either **abortion, in early pregnancy**, or therapy with experimental drugs, such as **spiramycin**.

Toxoplasma gondii. Congenital infection

Chorioretinitis, which many children develop early after birth, is often the only manifestation of a congenital infection.

Unfortunately, various developmental disorders can also occur in early "asymptomatic" children.

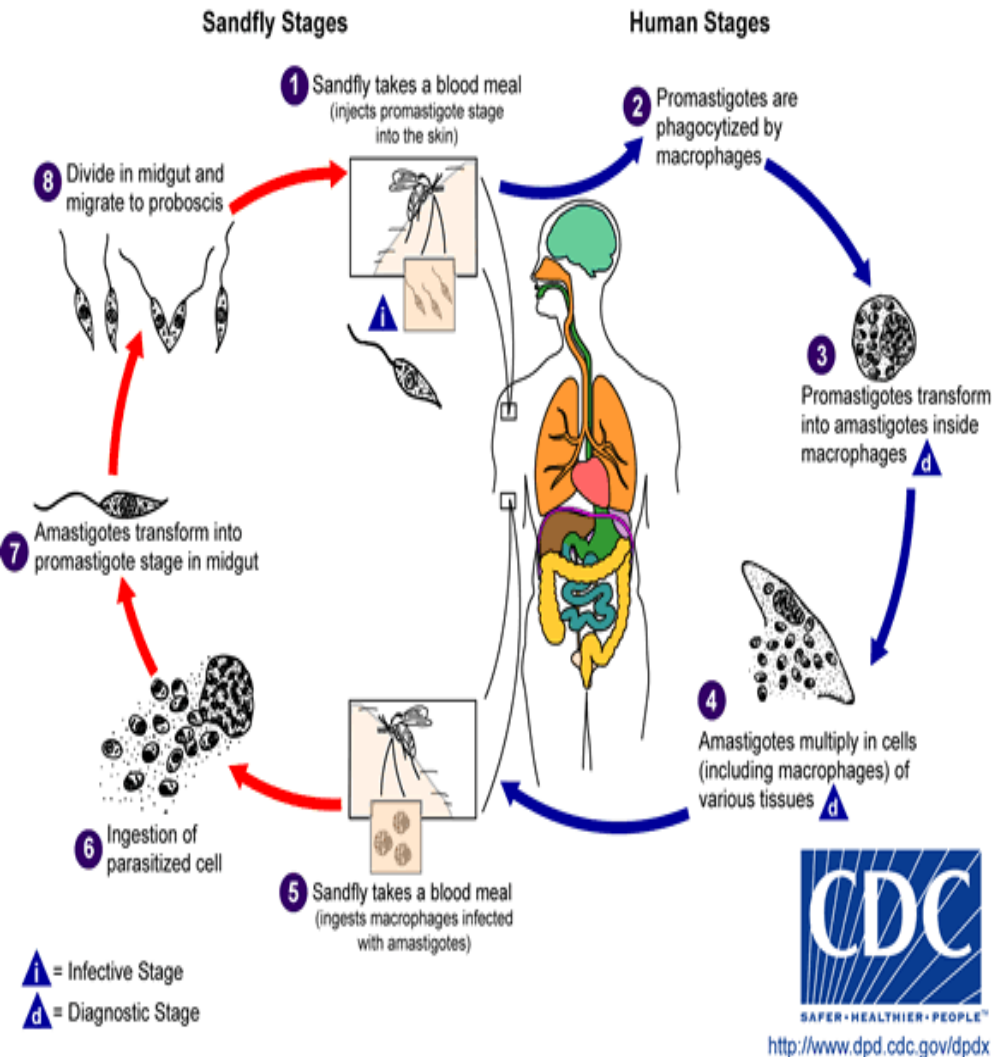


Leishmania species

- From superficial ulcers to severe damage of the liver, spleen and bone marrow.
- Fever, weight loss or anemia.
- Superficial lesions - species that grow better on 25-30°C.
- Those that invade the internal organs grow better on 37°C.
- Flagellates. Flagella attached to kinetoplast.
- *Leishmania* is transmitted by the bite of the sand fly (nevid), a short-lived insect that feeds on the blood of many mammals.
- Tropical and subtropical regions, rare in Europe and North America.
- "Imported disease"
- The reservoir is rodents, dogs, many other animals and infected people.




Leishmania species. PATHOGENESIS



- The **promastigote**, with the flagellum, reaches the man with a bite of the nevid (sand fly).
- Phagocytosis of parasite via complement receptors on macrophages.
- **Superoxide dismutase** protects against oxygen radicals.
- **Amastigote**, flagellar form, resistant to lysosomal enzymes.
- Dissemination:
 - Localized skin ulcers
 - mucocutaneous lesions
 - disseminated cutaneous leishmaniasis
 - disseminated visceral leishmaniasis (kala azar).

Leishmania species. DIAGNOSIS AND TREATMENT

- Immune response against leishmaniasis- Th-1 response.
- Parasites facilitate survival in the host → Th-2.
- AIDS patients → severe infections.
- Diagnosis: histological examination of biopsies, PCR.
- Preparations containing antimony have been used with great success in the treatment of various forms of leishmaniasis.
- Some forms of cutaneous leishmaniasis can be treated with allopurinol or ketoconazole.



CASE • Mr. S., a 58-year-old Brazilian businessman, was admitted to a hospital in Sao Paulo for the evaluation of chronic constipation. Radiologic examination of his gastrointestinal tract revealed a large, dilated colon (megacolon) and a somewhat less-dilated esophagus (megaesophagus). A blood sample revealed antibodies to *Trypanosoma cruzi*. Because no drugs are effective after the onset of complications, Mr. S. was not given antiparasitic treatment. His chronic constipation was treated symptomatically with a high-fiber diet. A few years

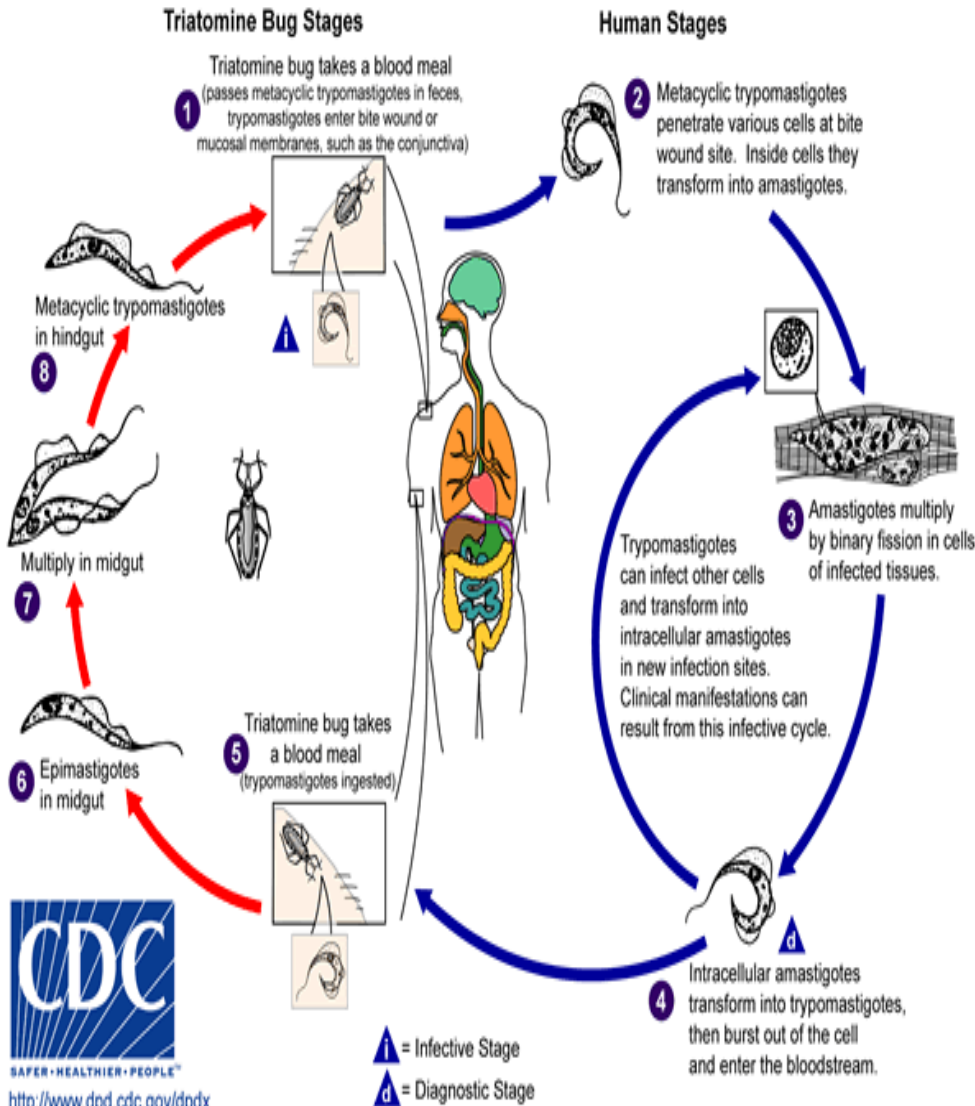
later, Mr. S. was hospitalized for treatment of cardiomyopathy with congestive heart failure. Although that complication was adequately compensated with medical therapy, Mr. S. expired suddenly at home 1 year later.

This case raises two questions:

1. What does the case reveal about Mr. S.'s past?
2. Why were antiparasitic drugs not given?

See Appendix for answers.

Trypanosoma species. Trypanosoma cruzi



- **Chagas disease**, Latin American region.
- Manifest disease is much rarer than infection.
- Most people become infected with *T. Cruzi* by biting an infected bed bug as a child.
- At the site of the bite → chancre or swelling of tissues and lymph nodes.
- Mild illness accompanied by fever and rapid recovery.
- A small number of complications, 10 to 20 years later.



Triatoma megista

Trypanosoma cruzi

- Complications are due to damage:
 - nerves in the GIT ([megaesophagus](#), [megacolon](#))
 - conduction system of the heart ([right branch block](#)) or
 - of the heart muscle itself ([cardiomyopathy](#)).
- Sudden death due to cardiac arrhythmia is common.
- Fibrosis is characteristic of these pathological processes.
- Autoimmune mechanisms play a significant role in these damages.
- Diagnosis:
 - Parasites in the blood of an infected person.
 - Specific antibodies a few weeks after bed bug bites.
 - Chronic infection with complications - finding an elevated antibody titer plus the complications themselves.
- Therapy: in the early stage - benznidazole.

CASE • Mr. B., a 32-year-old student from Senegal living in Canada, had fevers of 38°C and swollen lymph nodes at the back of his neck for 8 months. Two weeks ago, he developed a severe headache, stiff neck, and an aversion to light (photophobia). Trypanosomes were seen on Giemsa-stained specimens of blood and cerebrospinal fluid under the oil immersion objective. Mr. B. was treated with eflornithine for both the hemolymphatic and central nervous system infection. He recovered after 6 weeks of treatment.

This case raises two questions:

1. How did a parasite survive in Mr. B.'s blood for 8 months? Is he immunocompromised?
2. How would Mr. B.'s illness have been different if he had immigrated from South Africa rather than West Africa?

See Appendix for answers.

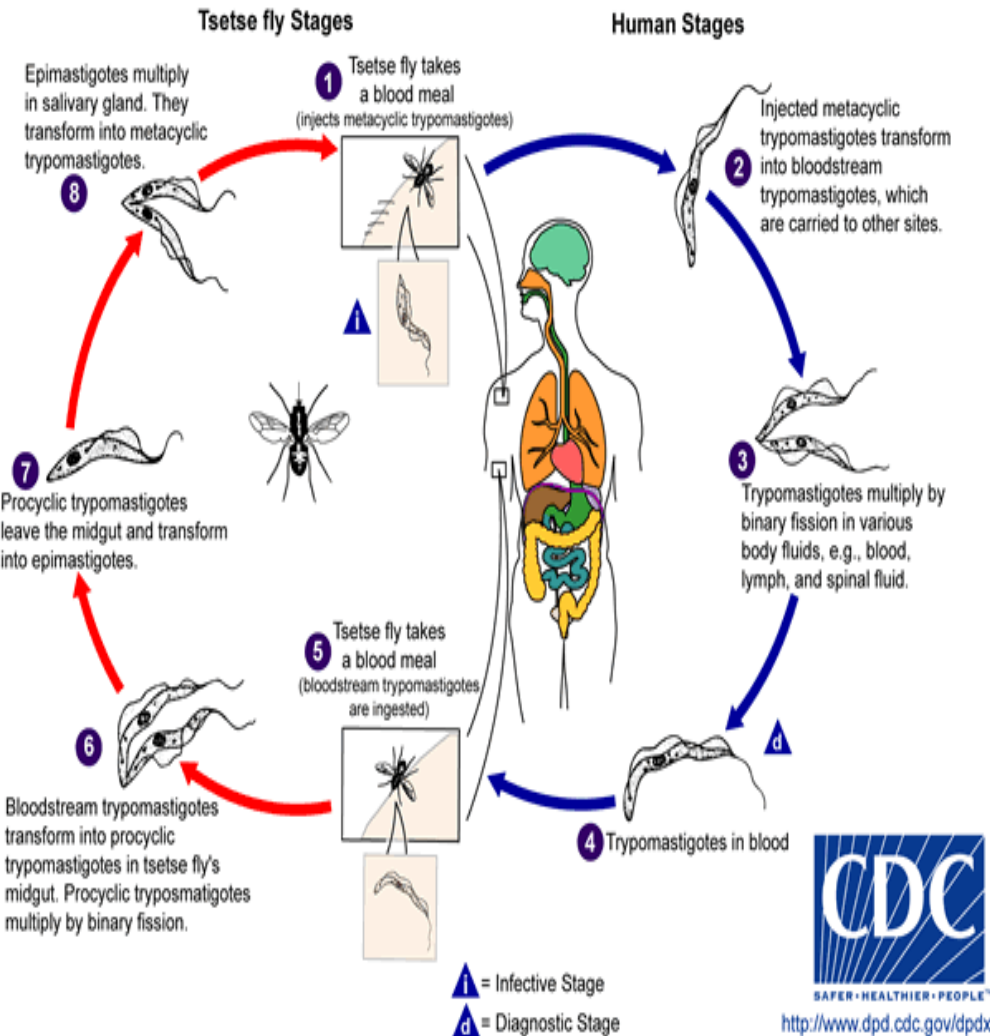
Trypanosoma species. Trypanosoma brucei

- African sleep sickness is caused by *T. Brucei*.
- Endemic in Africa and transmitted by the bite of an infected tse-tse fly (*Glossina palpalis*).



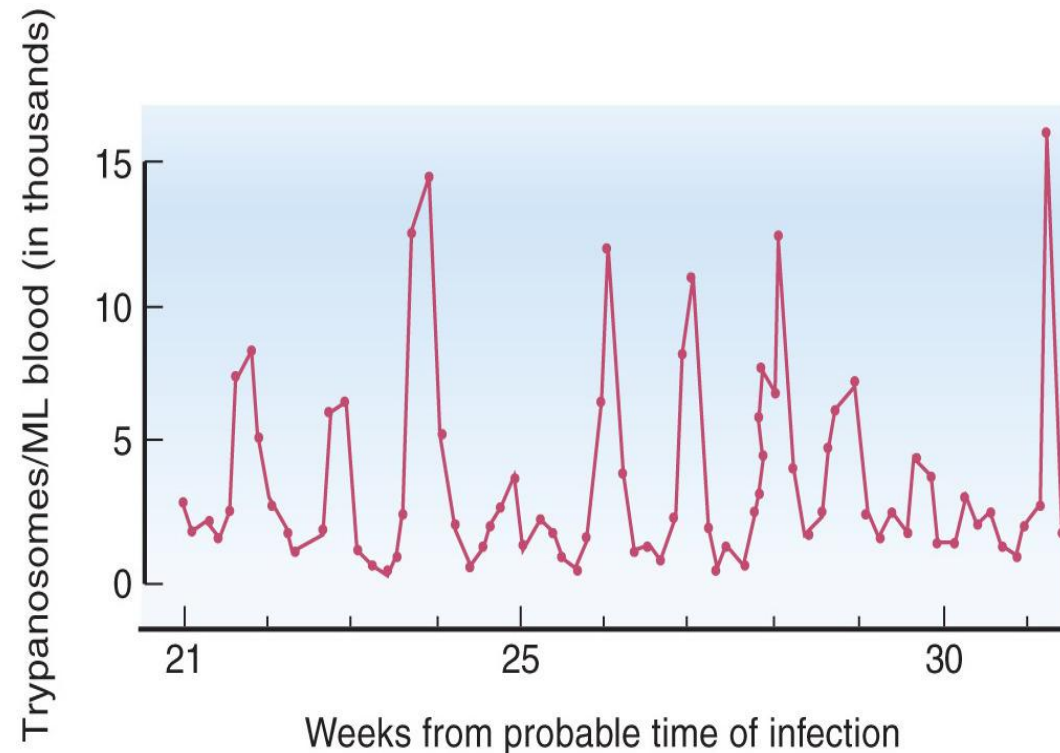
- **Antigenic variations** of immunodominant surface antigens.
- *T. Brucei* vs. *T. Cruzi*:
 - *T. Brucei* lives in the salivary glands of the tse-tse fly and is transmitted directly by the bite.
 - *T. Cruzi* lives in the digestive tract of the bug and is transmitted to humans when the feces of the bug is rubbed (or otherwise come into contact) into a single wound.

Trypanosoma brucei. Pathogenesis



- In East Africa, the reservoir is wildlife (impala), while in West Africa, humans and domestic animals are infected.
- A few weeks / month after the bite, a systemic disease develops with fever and swollen lymph nodes, trypanosomes are present in the bloodstream.
- After a few months (East African type) or a year (West African type), the parasite invades the CNS and infects the brain and cerebrospinal fluid.

Trypanosoma brucei. Pathogenesis



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- During a chronic bloodstream infection, the patient goes through the onset of parasitemia.
- The parasite alters the dominant surface antigen (variable surface glycoprotein) and thus avoids the host immune response.
- The basis of variability is gene rearrangement.

- Each parasite expresses only a glycoprotein gene from one locus, but has a repertoire of alternative genes.

Trypanosoma brucei. Sleeping sickness

- The parasite crosses the blood-brain barrier → Encephalitis → Confusion → Decreased coordination → Sleep disorders → Coma → Death
- **Winterbottom's sign** is seen in the early stages of trypanosomiasis: Swelling of the lymph glands in the neck, posterior cervical chain of lymph nodes - trypanosomes move through the lymph flow and induce inflammation.
- Eflornitine + several drugs (pentamidine or suramin). Therapy is much less successful if the disease affects the CNS.
- <http://www.youtube.com/watch?v=YM7yB1QBDIo&feature=related>

Intestinal protozoa

Organism	Reservoir	Modes of Transmission	Clinical Manifestations
<i>Entamoeba histolytica</i> (amebiasis)	Infected humans	Fecal–oral transmission by the ingestion of feces containing infectious cysts	Bloody diarrhea (dysentery), distant abscesses (especially liver), asymptomatic intestinal infection
<i>Giardia lamblia</i> (giardiasis)	Infected humans and other mammals	Fecal–oral transmission by ingestion of feces containing infectious cysts	Watery diarrhea; may also cause steatorrhea and malabsorption
<i>Cryptosporidium parvum</i> (cryptosporidiosis)	Infected humans and a wide variety of other animal hosts (zoonosis)	Fecal–oral transmission by the ingestion of feces containing infectious cysts	Watery diarrhea; intractable diarrhea in people with AIDS
<i>Cyclospora cayetanensis</i>	Unknown	Foodborne and waterborne; person-to-person spread unlikely	Watery diarrhea
<i>Isospora belli</i>	Infected humans	Foodborne and waterborne	Watery diarrhea; intractable diarrhea in people with AIDS
Microsporidia	Unknown	Unknown	Watery diarrhea, biliary tract infection, etc.

CASE • Two years ago, 26-year-old Mr. A. was discharged from the U.S. Army after 6 years of service. He was stationed abroad for 3 years, on tours of duty in Korea, Panama, and Germany. During the last 2 years, he developed intermittent diarrhea, with blood and mucus visible in the stool (i.e., dysentery). Sigmoidoscopy (endoscopic examination of the colon) and a radiographic study of the intestine following a barium enema revealed pseudopolyps consistent with inflammatory bowel disease. He was diagnosed with ulcerative colitis, an inflammatory bowel disease of unknown cause, and was treated with steroids.

At the time of admission to the hospital, 4 months after beginning steroid therapy, Mr. A. reported a weight loss of about 24 pounds (down to 147 pounds) and a recent increase in bloody stools and abdominal pain. He had no fever (probably because he was medicated with large doses

of steroids). Examination of his stool under the microscope showed many white and red blood cells but no amebas. However, a serological test for *Entamoeba histolytica* antibodies in serum (indirect hemagglutination) revealed a high titer (1:2,000). A computerized tomography scan showed an 8-cm abscess in the right lobe of the liver.

He had a stormy hospital stay with several episodes of bacteremia (secondary to disruption of the intestinal mucosa by the parasite). He finally recovered after the steroids were tapered and he was treated with the antiamebic agent metronidazole.

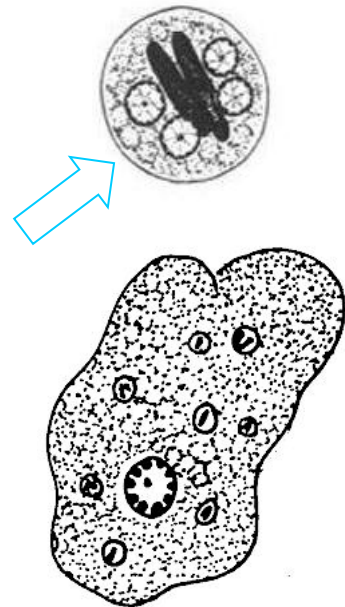
This case raises two questions:

1. Why were no amebas seen in Mr. A.'s stool?
2. What was the role of steroids in this case?

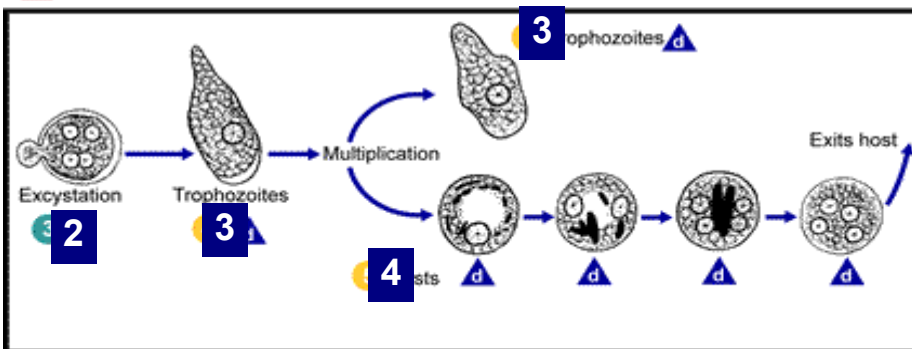
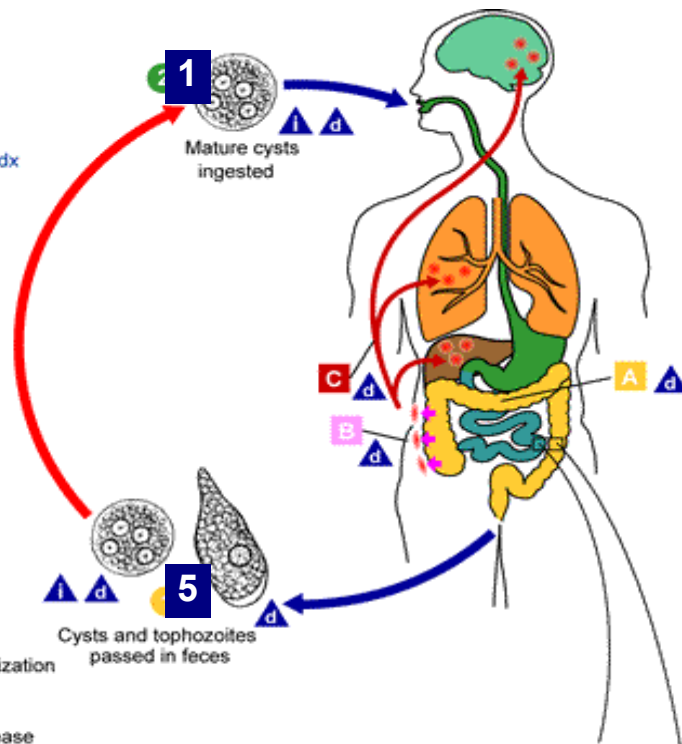
See Appendix for answers.

Entamoeba histolytica

- It causes diseases - amoebiasis, destruction of tissues, especially the colon.
- Amoebae spread from small ulcerations and enter the deeper layers of the colon wall, sometimes the muscular layer.
- It often does not cause symptoms in the GIT.
- Many people have non-pathogenic amoebae.
- It is transmitted by feco-oral route.
- Sexual transmission is also possible.
- **cyst**- inactive form, resistant in the external environment.
- **trophozoite**- active form
- Cysts can survive for a long time in water, on land, food, especially in a humid environment.
- High temperature and freezing kill cysts.



Entamoeba histolytica. ENCOUNTER



1. Feco-oral (cyst, contaminated water)
 2. In the gut, excystation
 3. Multiplication
 4. Incystation in the lower parts of the GIT
 5. Cysts in the stool
- Patients with diarrhea have a low chance of transmitting the disease because they excrete primarily trophozoites
 - Asymptomatic patients excrete the cystic, representing the greatest danger of spreading the infection.

Entamoeba histolytica.

SPREAD, MULTIPLICATION AND DAMAGE

- It is often in the colon of people who do not have symptoms of the disease.
- Amoeba adherence is prevented by glucose, [intestinal mucus](#).
- Cell damage - direct intercellular contact:
 - (1) binding to the target cell via a specific receptor using Gal-galNAc binding lectin
 - (2) killing the target cell probably by inserting proteins that make holes in the membrane of the target cell (amoeba-pores) and
 - (3) ingestion of a killed cell.
- In an [unimmunized host](#), amoebae kill neutrophils and macrophages.
- In an [immunized host](#)- cellular immune response, activated macrophages kill amoebae.
- People on corticosteroid therapy have a disseminated infection despite a high titer of specific antibodies.

Entamoeba histolytica. Amoebic dysentery

- Amoeba sinks into the intestinal wall causing damage to the intestinal wall and intestinal pathology - **diarrhea** (dehydration)

- Epithelial invasion
- Ulcers
- Diarrhea
- Blood and mucus
- Bowel perforation

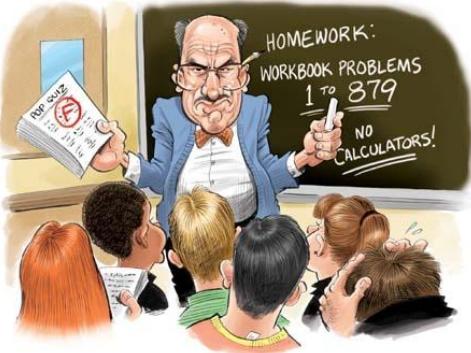


- It can reach the bloodstream (breaking through the intestinal wall) and thus vital organs, usually the liver and sometimes the lungs, brain and spleen. A very common outcome is a **liver abscess** that can be fatal if left untreated.
- <http://www.youtube.com/watch?v=lkNsFmc9DLs>

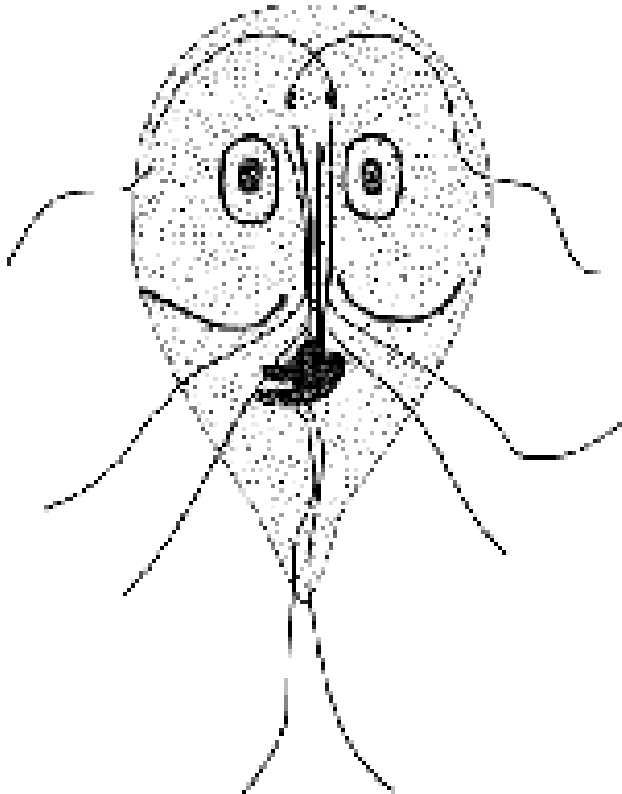
Entamoeba histolytica. Amoebic dysentery

- **Diagnosis:** microscopic identification of trophozoites in stool or from a sample taken from colonic ulcers by endoscopy.
 - *E. Histolytica* may contain ingested erythrocytes.
 - *E. Histolytica* trophozoites without internalized erythrocytes and cysts are no different from nonpathogenic amoebae.
- Immunological identification of *E. histolytica* antigen in stool.
- Serological diagnosis, anti-amoebic antibodies persist for several years after infection.
- **Therapy:** metronidazole, especially effective in invasive infections because it penetrates well into most tissues, including the brain. Because it is less effective in killing amoebae in the lumen of the GIT, another drug is used to eliminate parasites from the intestinal lumen: diloxanide, paromomycin and others.

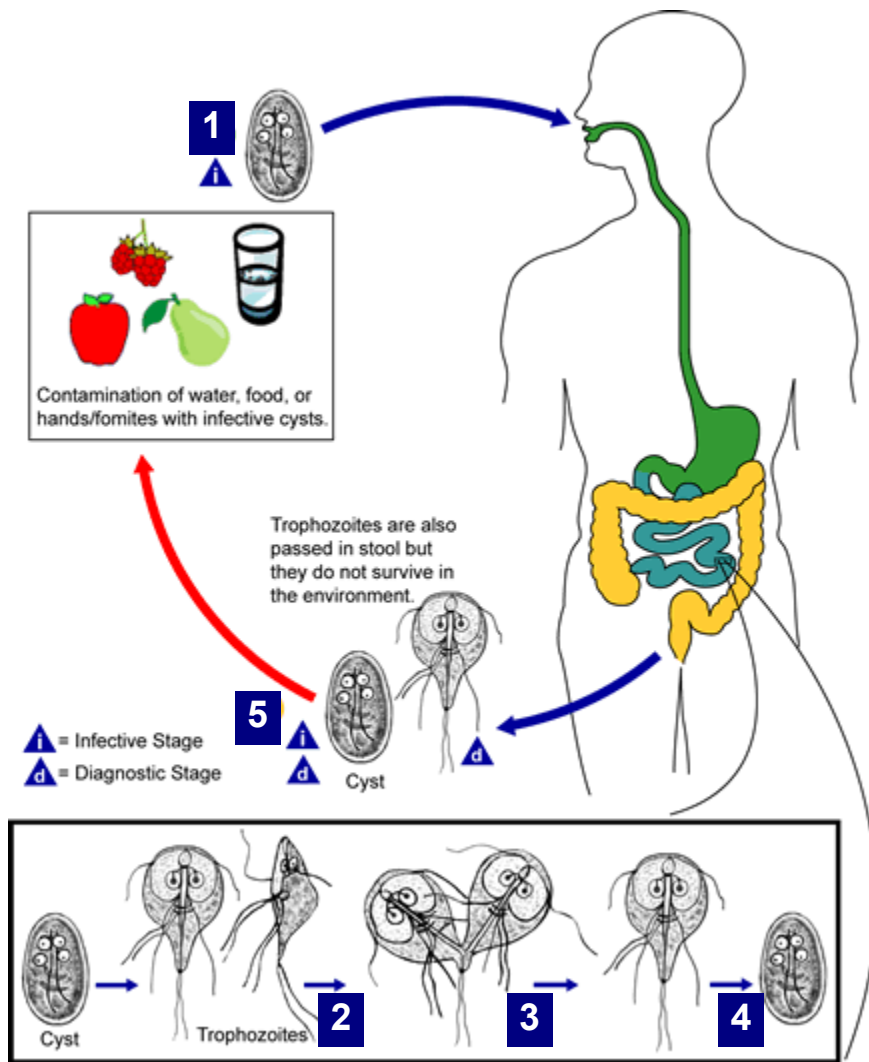
Giardia lamblia



- *Giardia intestinalis*- intestinal protozoa that causes **giardiasis**.
- Widespread around the world.
- Giardiasis is a **zoonosis** caused by ingestion of water contaminated with feces.
- **Cysts** are resistant to chlorination, and waterborne epidemics have occurred around the world in the past.
- The infection is accompanied by a mild but long-lasting **diarrheal syndrome**, with parasites localized in the duodenum and jejunum.

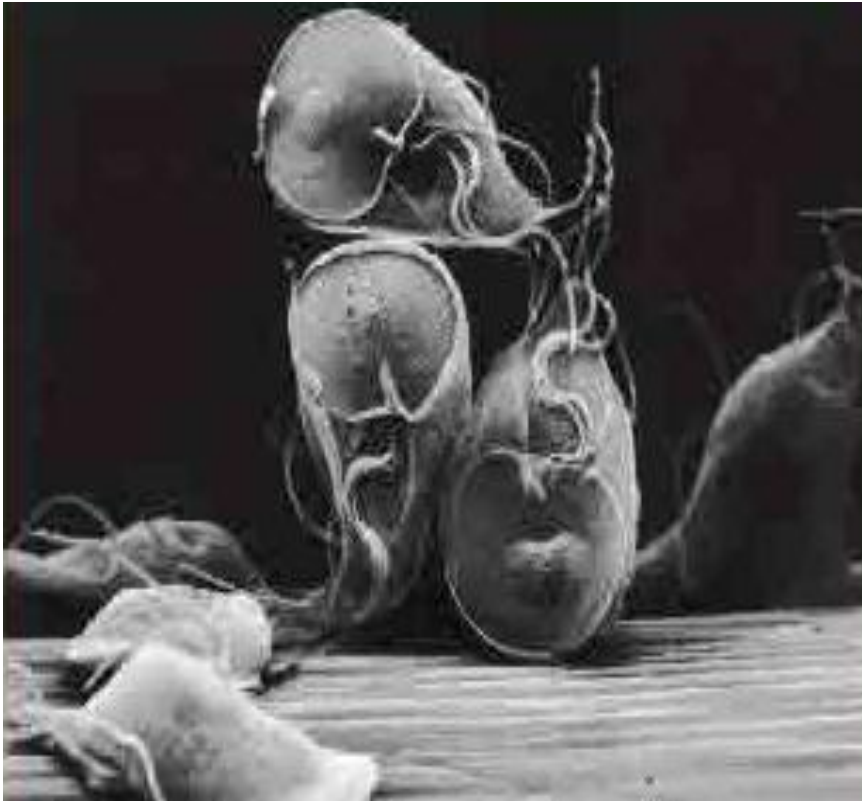


Giardia lamblia. Transmission and multiplication



- Ingestion of cysts, resistant in the external environment.
- Stomach acid- excitation.
- Trophozoites bind to the epithelial cells of the duodenum and jejunum, using a ventral sucker.
- in the lower parts of the GIT
- Cysts in the stool

Giardia lamblia. Damage



- Long infection → malabsorption → **malnutrition**
- Parasites cover the surface of the GIT mucosa.
- Unlike *E. histolytica*, it is not invasive and does not cause bloody diarrhea and metastatic infections.
- Submucosal infiltration of lymphocytes and withdrawal of the villi → the total absorption surface decreases.
- Fat malabsorption → greasy, foul-smelling stools, deficiencies of liposoluble vitamins (A, K, D and E) and weight loss.

▪ <http://www.youtube.com/watch?v=bGMor71WkFc&feature=related>

Giardia lamblia.

- Diagnosis: direct identification of parasites in stool and / or duodenal aspirate.
- Trophozoites are rare in stool, 3-4 stools per examination to identify cysts.
- Antigen identification *G. Lamblia*-e.



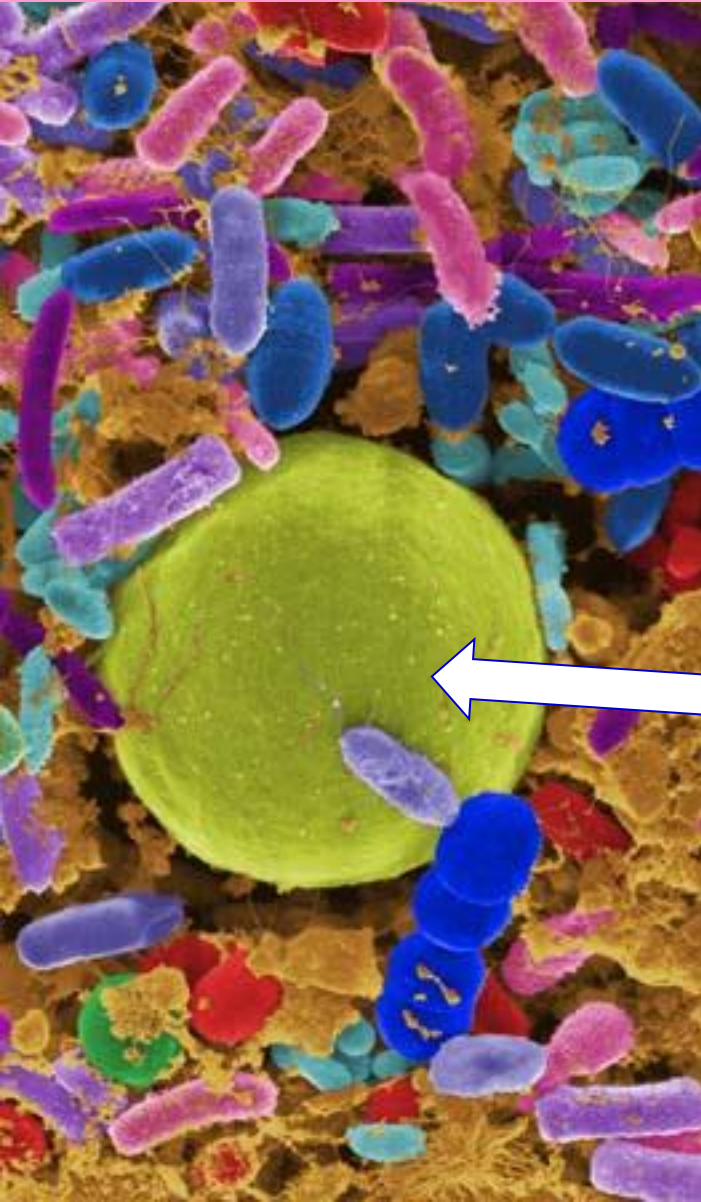
- Therapy: metronidazole.
- Prevention: boiling or filtering drinking water.

Cryptosporidium. Cryptosporidiosis

- **Zoonoses**, accompanied by diarrhea in developed and developing countries.
- **Mode of transmission:** They are more common in rural areas due to more frequent contact with animals. They can also be transmitted interhumanly.
- They are especially severe in AIDS patients.
- **Hydric epidemics** through the public water supply system.
Cryptosporidium oocysts can be found in many surface waters.

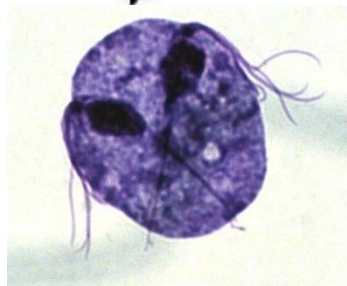
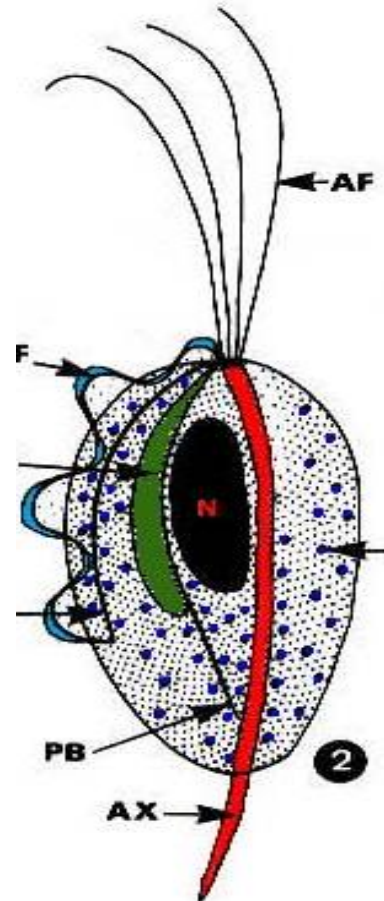


Cryptosporidium. Multiplication



- Infectious oocysts live in the GIT.
 - They do not invade the intestinal wall and do not give systemic infections.
 - In the immunocompetent, the life cycle is repeated 1-2, resulting in one episode of diarrheal syndrome.
 - In the immunocompromised, the life cycle is repeated several times and is accompanied by persistent watery diarrhea.
-
- Diagnosis: identification of cysts in the stool.
 - Nitazoxanide in immunocompetent.
 - Rehydration and antiretroviral therapy is an adjunct to immunodeficiency therapy.

Trychomonas vaginalis



- A common "resident" of the vaginal mucosa (15% of women) occasionally causes vaginitis.
- a normal resident of the final parties of the colon.
- He is actively moving, so improper hygiene, as well as other factors, can lead to infection with this very persistent, unpleasant and recurrent cause.
- It is transmitted through sexual contact.
- Most infections in men are asymptomatic (urethritis, epididymitis or prostatitis).

Groups of vaginal secretions

- **The first group** of vaginal secretions is characterized by the presence of mucus and some leukocytes. This finding is quite rare and occurs before puberty.
- **The second group** of vaginal secretions contains few leukocytes and mucus, some streptococci, staphylococci and rare bacillus colic. Such a finding is considered normal.
- **The third group** of vaginal secretions contains a lot of leukocytes, many pathogenic bacteria, and sometimes some trichomonas vaginalis.
- **The fourth group** of vaginal secretions is characterized by abundant yellowish secretion. The causative agent is gram-negative diplococci-**gonococci**.
- **The fifth group** of vaginal secretions is caused by **Trichomonas vaginalis**.
- **The sixth group** of vaginal secretions is caused by **Candida albicans** infection.

Trychomonas vaginalis. Diagnosis and therapy

- It is usually possible to see motile parasites in the vaginal secretions of infected women.
- One dose of metronidazole or tinidazole is the recommended therapy.
- Male sexual partners of the tapeworm should be treated to avoid "**ping-pong**" **relapses**, common in many sexually transmitted diseases.



Cyclospora, Issospora, Microsporidia

- *Cyclospora cayetanensis* is a protozoa, a cause of diarrhea in developed and developing countries.
- Oocysts become infectious on days of incubation in the external environment.
- Ingestion of contaminated food or water. Interhuman transmission is rare.
- Watery stools with loss of appetite, nausea, vomiting and fever. The disease can last from a few days to a few months.
- *Issospora belli* is a protozoa that causes watery diarrhea in the tropics.
- *Microsporidia-e* are obligatory intracellular parasites, transient diarrhea in immunocompetent and long-term watery diarrhea in people with AIDS.
- Diagnosis: large oocysts in stool.
- Therapy: trimetropin or sulfamethoxazole.