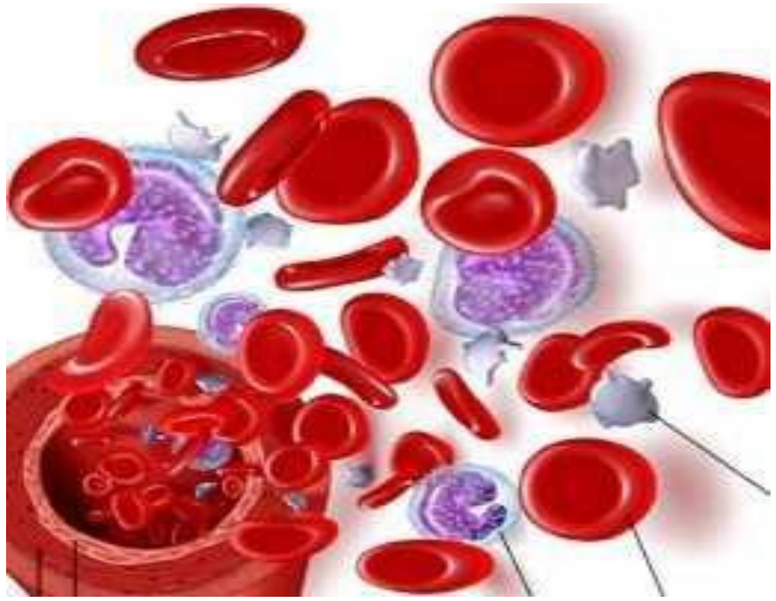
Blood and Lymphatic System Block - HEM-210

Parasitic infections of blood and lymphatic system lect. 1



by

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By the end of the lecture the student will be able to:

1. list the parasitic diseases which involved in blood and lypmhatic System pathology (Leishmania donovani, Toxoplasma gondii, Wuchereria bancrofti and Brugia malayi, Trypanosomes and plasmodium spp).
2. Describe the mode of infection, infective stage, diagnostic stages and life cycle of these parasites.
3. Describe the clinical picture and pathogenesis of each parasite
4. Describe diagnostic methods for each disease.
5. Describe the recommended treatment for each of the previous parasites.
6. Describe the preventive measures for each of the previous parasites.

Parasites of lymphatic and reticulo-endothelial system

A.Parasites of Lymphatic system

B.Helminthes (Tissue Nematoda)

- Filarial worms 1. *Wuchereria bancrofti.* 2. *Brugia malyai.*

B. Parasites of reticulo-endothelial system

- **Protozoa**

1. Toxoplasma gondii

2.Leishmania

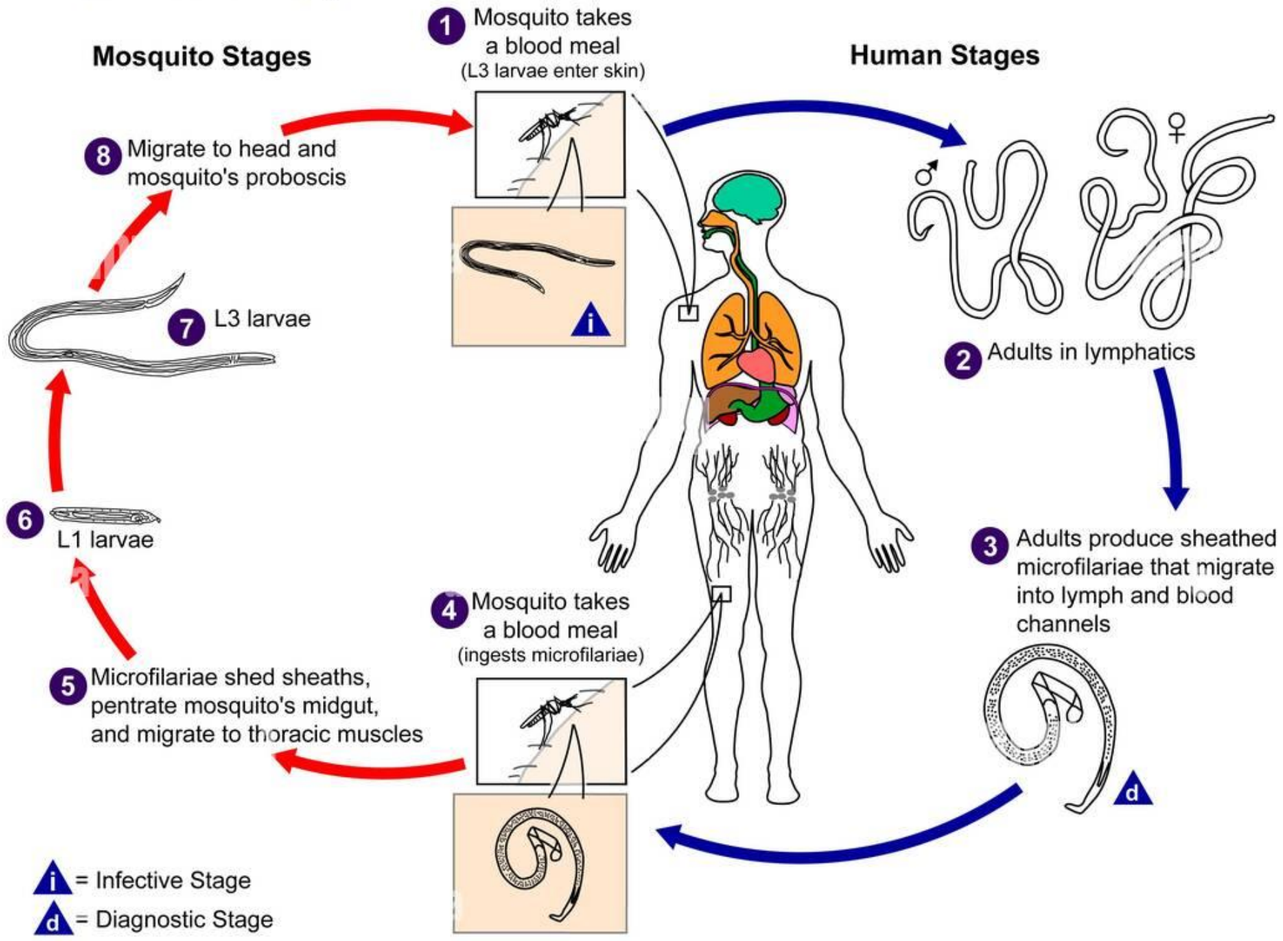
3.Trypanosoma

1. *Wuchereria bancrofti* (elephantiasis)

Disease	Elephantiasis
Geog. distribution:	➢ Tropics and subtropics in Africa, Asia and South America ➢ In Egypt it is present in Qalubiya, Dakahlia, Sharkia, Cairo, Giza and Assuit.
D.H **Vector (I.H.)**	➢ Man ➢ Female Mosquitoes (Culex, Anopheles and Aedes).
Habitat	lymphatics of the lower limbs mainly, sometimes affect genital organs , upper limbs and the breast.
Mode of transmission	by bite of female mosquitoes as *Culex* , *Anopheles*, and *Aedes* spp.
Infective stage	3rd stage larva (filariform larva)
Diagnostic stage	Microfilariae in peripheral blood by night, between 10 pm and 2 am

Filariasis

(Wuchereria bancrofti)



Pathogenesis and clinical pictures:

Incubation period: From the entry of the third stage infective larvae into the skin until the microfilariae appear in the blood. It may last for one year.

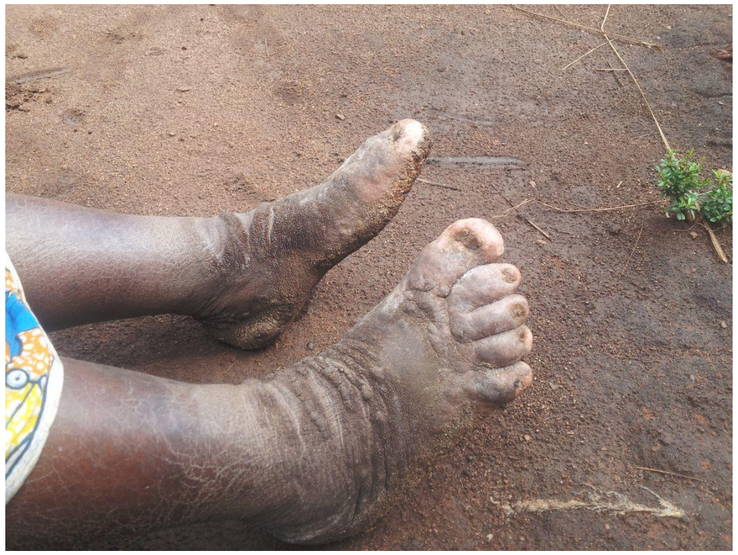
***A* symptomatic stage:** detected only by blood examination especially in endemic areas

Inflammatory (acute) stage:

a- Recurrent attacks of lymphangitis and Lymphadenitis:

- Lymphangitis: The affected lymph vessels of lower limb and genitalia appear raised, red, hot, swollen, and tender streaks.
- Lymphadenitis: Regional lymph nodes are enlarged and tender with temporary oedema of the affected limb. Abscesses may occur due to secondary bacterial infection.

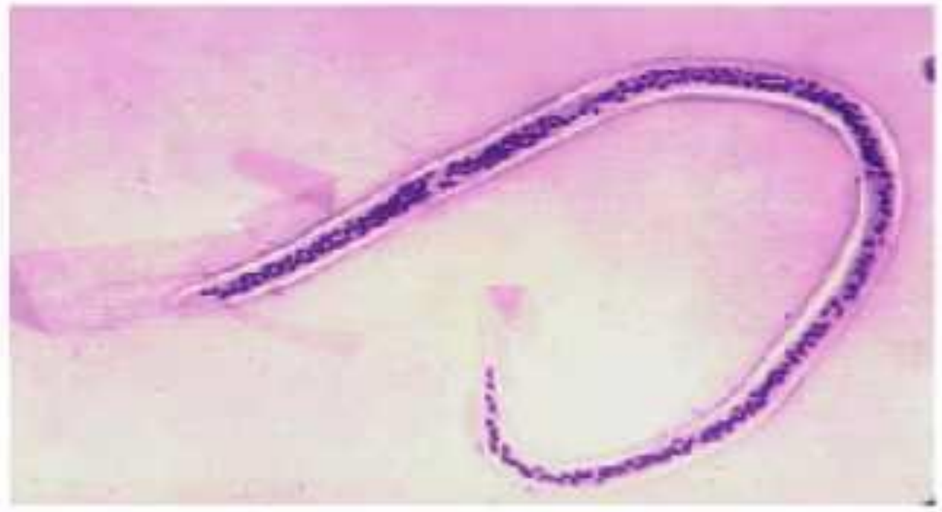
- Repeated inflammatory attacks lead to fibrosis and obstruction of lymphatics, distally lymphedema occurs with hard, brawny edema, thickening and verrucous changes in the skin (**elephantiasis)**
- **Tropical Eosinophilia:** characterized by pulmonary infiltrates, peripheral eosinophilia, cough and asthmatic like attacks (especially at night). These patients have high IgE levels, high antifilarial antibody titers, and no microphilaria in peripheral blood (amicrofilaremic filariasis). It is considered a hyperimmune reaction against lymphatic filariasis. The patients improve dramatically with antifilarial treatment.



Diagnosis:

Direct method:

1. Detection of microfilariae in peripheral blood (taken at night between 10 pm & 2 am while the patient is sleeping.
2. Wet drop: Examination of a drop of fresh blood to detect living moving microfilariae.
3. Thick and thin blood film stained with Giemsa to identify the species according to the morphology.
4. Provocative test: If it is difficult to obtain blood l O mg Diethyl Carbamazine (DEC) orally and examine tl



Indirect methods (immunodiagnosis) :Serological tests :Detection of antibody by ELISA, IFAT and CFT (antigen prepared from the dog filarial worm, Dirofilaria immitis).

Blood examination: High eosinophilia.

Radiological examination :Ultrasonography: For detection of adult. Viable adults may be seen moving in lymphatics (filarial dance sign).

X-ray: Shows calcified worms .

Lymphangiography: May show characteristic lymphatic changes specially dilatation of vessels.

Treatment:

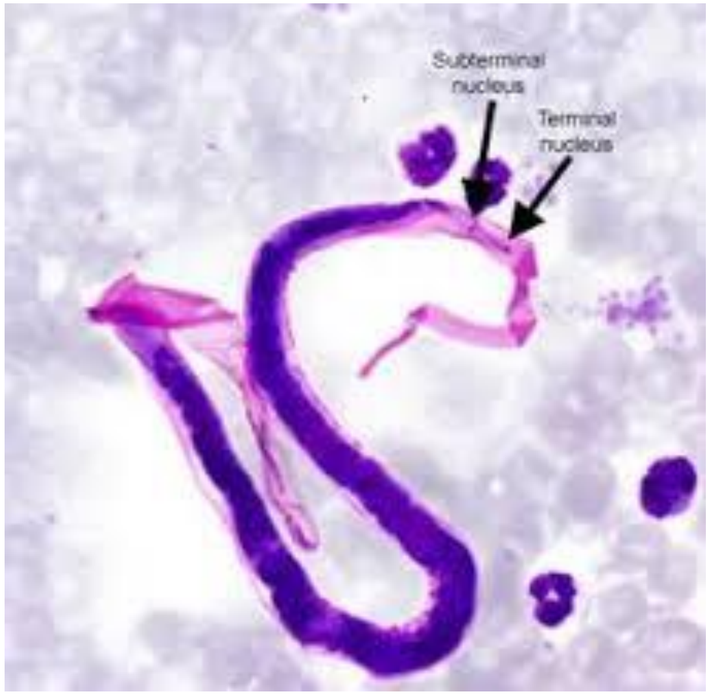
1.Diethylcarbamazine (DEC) in three divided doses of 6 mg/ kg/day for 12 days kills adults and microfilariae.

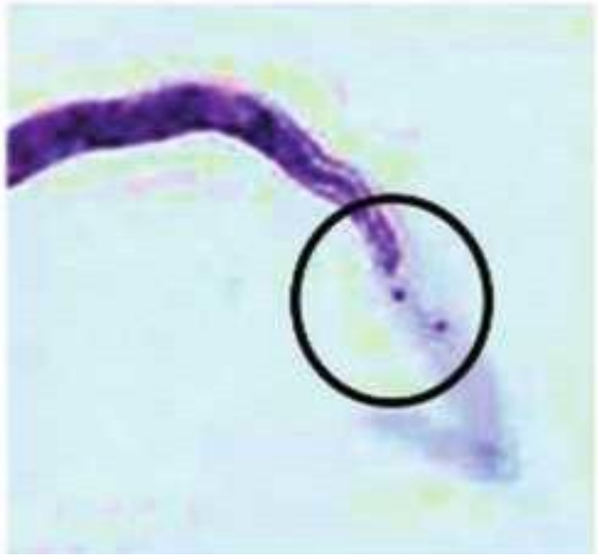
2.Ivermectin is effective only against microfilariae and has an important role in control programmes.

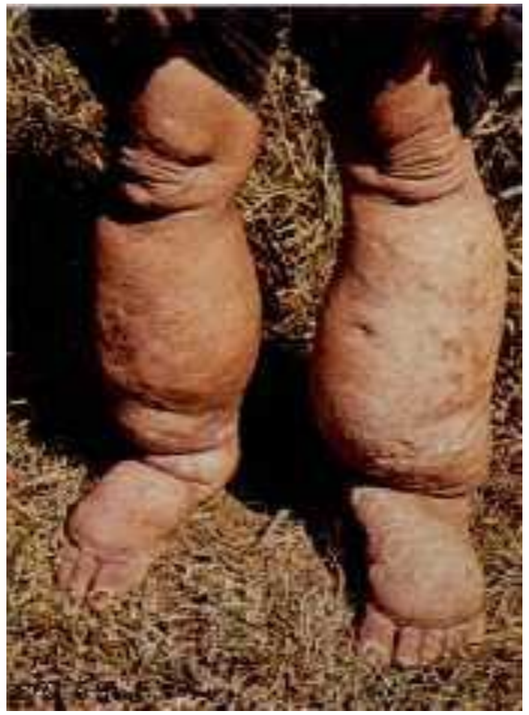
3.Surgery for scrotal elephantiasis.

2. *Brugia malayi*

- The life cycle of *B. malayi* is similar to that of *W. bancrofti*
- There is some morphologic difference, e.g. the miccrofilaria has 2 separate terminal nuclei.
- If elephantiasis occurs, the swelling is restricted to the lower extremities below the knee.

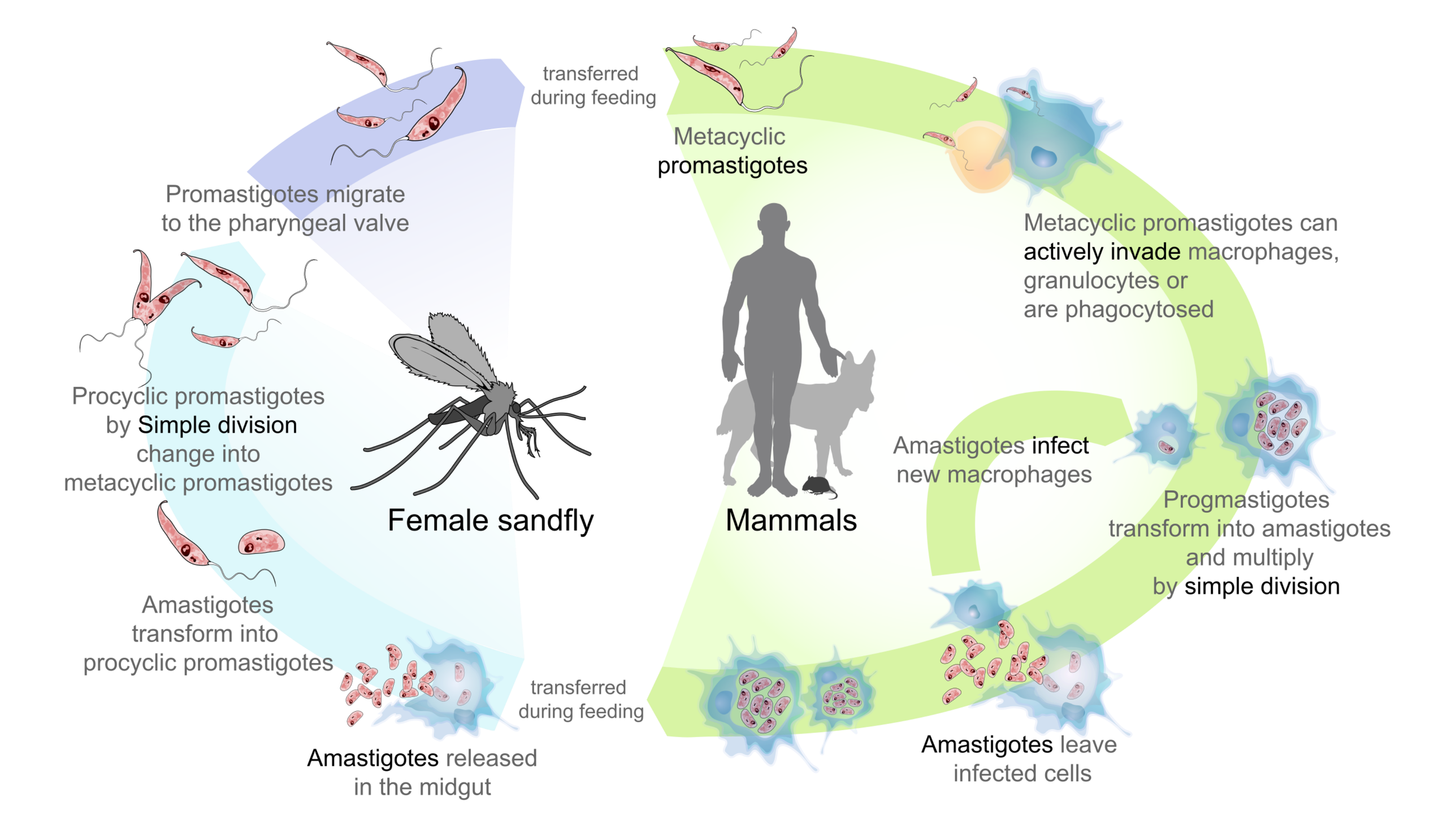






3. Visceral leishmaniasis

Causative protozoa :	***Leishmania donovani***
Definitive host: **vector**	Man and other mammalian hosts ***Phlebotomus papatasii* (sandfly)**
Habitat:	Intracellular found in reticuloendothelial cells of the spleen, bone marrow, leucocytes, liver cells and lymph nodes
Infective stage: **Diagnostic stage:**	➢ promastigotes) ➢ Amastigote forms
Mode of infection:	1. Through the bite of Phlebotomus papatasii. 2. blood transfusion 3. Congenital transmission.


transferred
during feeding
Metacyclic
promastigotes
Promastigotes migrate
to the pharyngeal valve
Metacyclic promastigotes can
actively invade macrophages,
granulocytes or
are phagocytosed
Procyclic promastigotes
by Simple division
change into
metacyclic promastigotes
Female sandfly
Mammals
Amastigotes infect
new macrophages
Progmastigotes
transform into amastigotes
and multiply
by simple division
Amastigotes
transform into
procyclic promastigotes
transferred
during feeding
Amastigotes leave
infected cells
Amastigotes released
in the midgut

Pathogenesis and cclinical picture

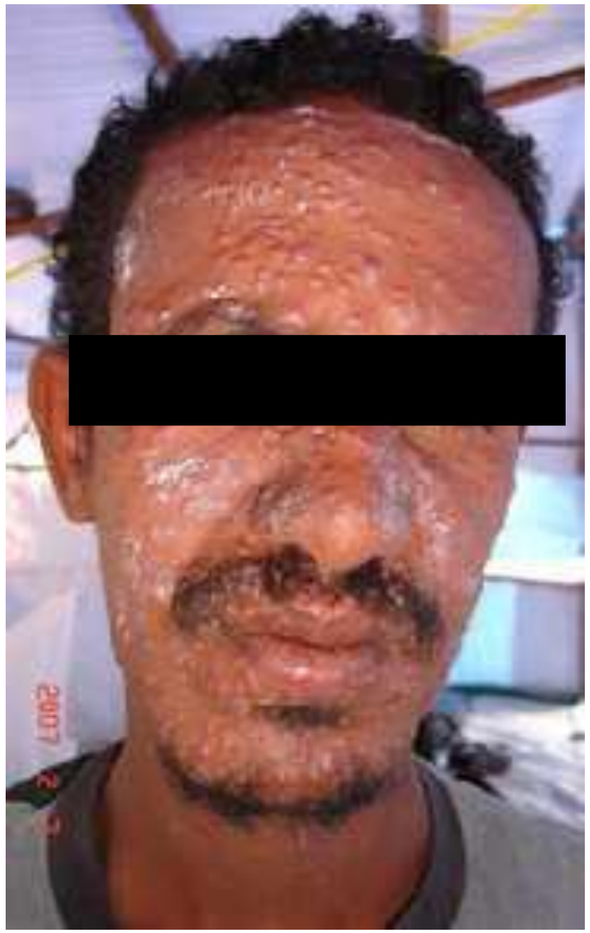
- Incubation period: Long (about 4 months).
- Promastigotes are engulfed by skin macrophages and transformed to amastigotes that start multiplication.
- The phagocytosed parasites are present in small numbers in blood since they are taken by the reticuloendothelial cells of the spleen, liver, lymph nodes, bone marrow, intestinal mucosa and various other organs which will show marked hyperplasia

Clinical picture

1. Visceral leishmaniasis (VL), also known as kala-azar is fatal if left untreated
2. The incubation period usually ranges from 2 to 6 months.
3. It is characterized by irregular bouts of high fever, chills, anorexia, malaise, weight loss, anaemia and diarrhea.
4. Common clinical signs include an enlarged liver, a markedly enlarged spleen, femoral and inguinal lymphadenopathy.
5. Skin changes occur on the face, hands, feet, and abdomen, particularly in India, where patients acquire an earth-gray color; this darkening of the skin gave the name kala azar (black sickness).

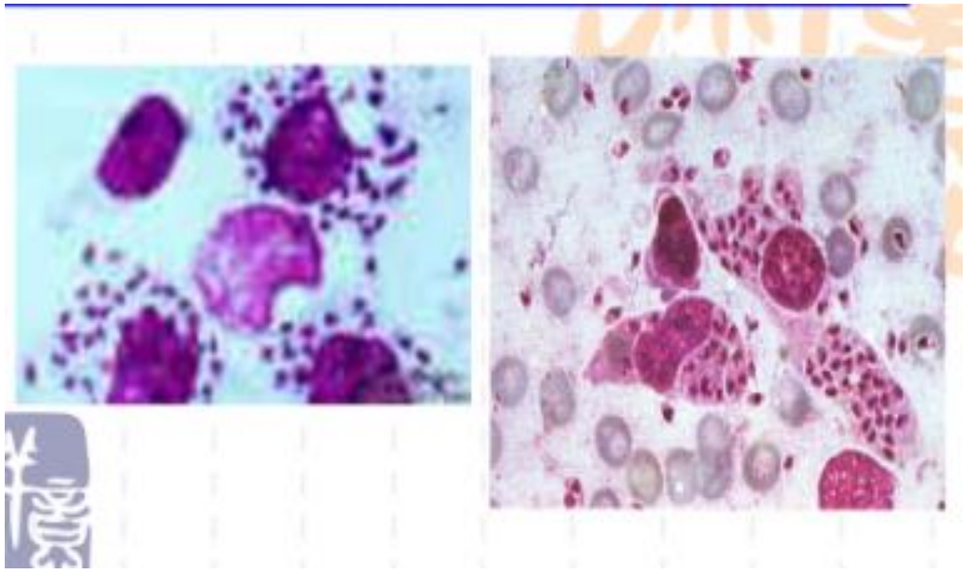
- **Post-Kala Azar Dermal Leishmaniasis.** PKDL usually develops after apparent successful cure from VL and is confined to two distinct zones, namely South Asia and East Africa, mainly Sudan.

Macules and papules usually appear first around the mouth and spread to the face and then to the extensor surface of the arms, the trunk, and the legs. They enlarge, fuse and may resemble leprosy. These patients may serve as reservoirs of infection.



Diagnosis:

1. Clinical picture with presence of anemia (normocytic and normochromic), leukopenia and thrombocytopenia.
2. Demonstration of the amastigotes in tissues or clinical specimens



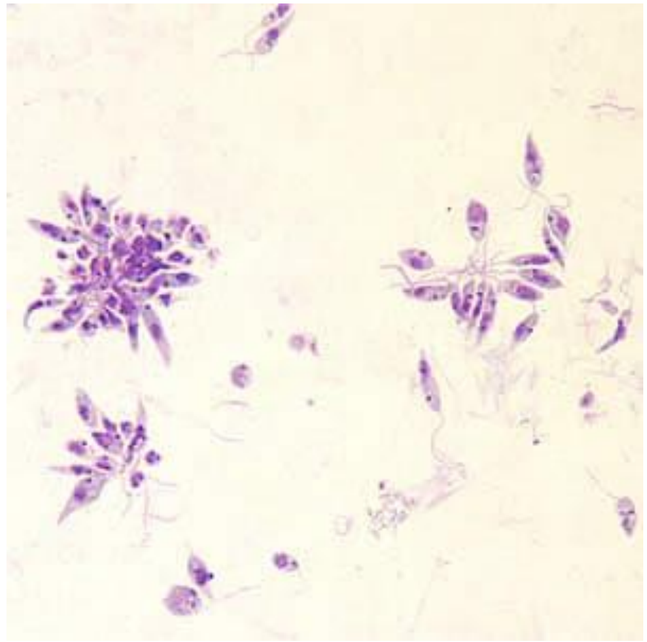
3. Splenic puncture (highest rate of organism detection (98%), but with high degree of risk for the patient) and , liver biopsy,
4. Tissue aspirate: lymph nodes and bone marrow (to differentiate it from lymphomas and leukemia in children).

5. Culture on NNN media. the promastigotes are detected in the culture.

6. Formol-Gel Test (Hypergammaglobulinemia) the patient's serum becomes solid if mixed with formalin,

7. skin test (Montenegro or LST).

8. Detection of parasite genetic material by PCR or antigen detection (ELISA, IHAT, FAT) is sufficient for confirmation.



Treatment

1. Patients should receive supportive care.
2. Pentavalent antimony compounds have been the drugs of choice.
3. Rcent treatment is lipid-associated Amphotericin B.

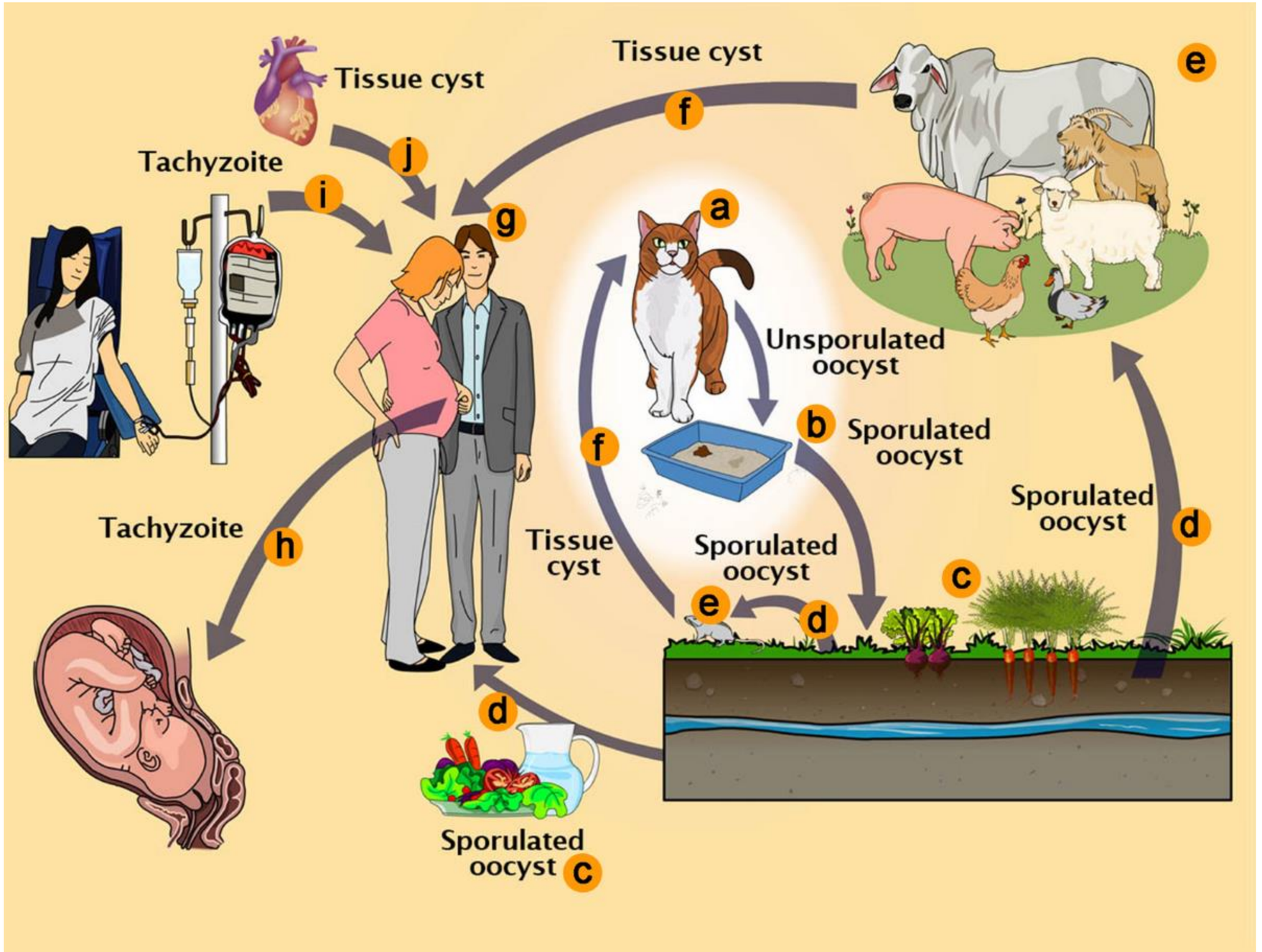
Epidemiology and prevention:

1. Depends on a number of factors including the interaction between sand flies, reservoir hosts, and susceptible humans.
2. **Use of residual insecticides** is the main preventive measure.

4. Toxoplasmosis

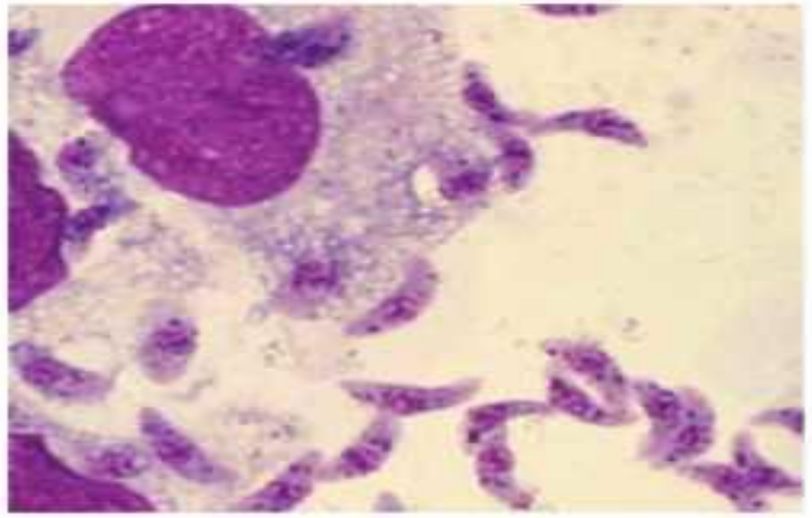
Causative parasite:	**Toxoplasma gondii**
Geog. Dist.	cosmopolitan distribution
Definitive host: **Intermediate host:**	The domestic cat **(predator)** All vertebrate hosts including humans serve as **prey hosts.**
Habitat	obligate intracellular parasites and are found in all nucleated cells
Mode of infection	1. Ingestion of sporulated oocysts in contaminated vegetables or water or during handling of litter trays or by aids of flies 2. Ingestion of tachyzoites or bradyzoites in cysts in undercooked meat or during handling infected raw meat. 3. Blood transfusion and organ transplant. 4. Congenital transmission
Infectious stages	the tachyzoites, the bradyzoites (in tissue cysts), and the sporozoites (in oocysts in cat feces).

The life cycle of *Toxoplasma gondii*

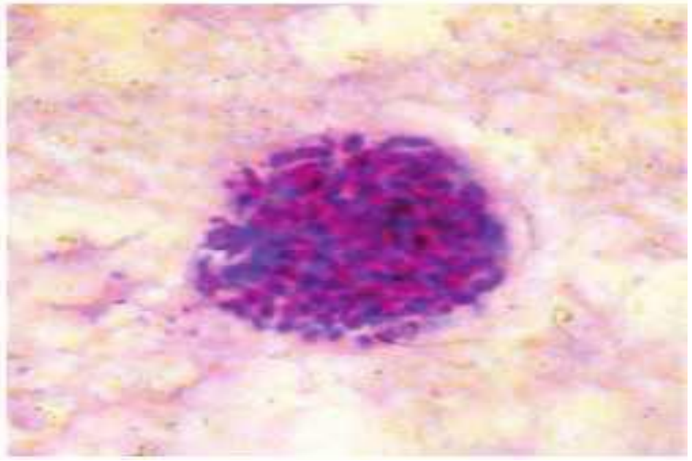


The organisms are obligate intracellular parasites and are found in two forms:

1. The actively proliferating trophozoites or tachyzoites are usually seen in the early, more acute phases of the infection, they invade any tissue, proliferating in the macrophages
2. The resting forms or cysts are found primarily in muscle and brain, probably as a result of the host immune response



Toxoplasma tachyzoites



Toxoplasma tissue cyst

Pathogenesis and clinical picture:

A. **Congenital infection from mother to fetus** results from primary acquired maternal infection during prgnancy.

1. Fetal abnormalities could occur depending on the stage of pregnancy. The infection is more severe in the first trimester of pregnancy causing abortion or stillbirth.
2. Neurological affection includes hydrocephalus, microcephaly, intracranial calcifications with epilepsy, psychomotor or mental retardation.
3. Chorioretinitis, strabismus, or even blindness.
4. Hepatic enlargement, ascites, cardiomegaly, thrombocytopenia, and anemia.
5. Low birth weight and preterm labor

B. Acquired toxoplasmosis

1. Usually asymptomatic or mononucleosis-like syndrome (fever, rash, lymphadenopathy, hepatosplenomegly and pneumonia) in immune- competent patient.
2. Infection remains latent for life unless reactivation due to immunosuppression.

C. Immunocompromised (most commonly AIDS)

1. Encephalitis with focal CNS lesions seen as single or multiple ring- enhancing masses on CT (and focal neurological signs)
2. Lymph node, liver, and spleen enlargement and pneumonitis, may proceed to heart failure and death.
3. Chorioretinitis.

Diagnosis:

1. History and clinical picture
2. Serological tests: ELISA and Indirect immunofluorescence tests can be used for the detection of IgM (acute infection) and IgG antibodies (chronic infection).
3. PCR technique.
4. Biopsy from liver or lymph node aspirates stained with Giemsa to detect the parasite.
5. Ultrasonography for detection of congenital infection and intracranial calcification.

Treatment and Prevention:

1. There is no completely satisfactory treatment. The damage caused by transplacental infection is irreversible.
2. Spiramycin could be used to prevent transplacental transmission pyrimethamine + sulfadiazine (add folinic acid).
3. Prvention is perfoemed through proper hand hygiene and cooking meat thoroughly to the proper temperature.

Hemoflagellates

. Trypanosomes

***Genus Trypanosoma*:**

1. African trypanosomes; *Trypanosoma gambiense* and *Trypanosoma rhodesiense*. They cause sleeping sickness. Vector is Tse tse fly (*Glossina*)
2. American trypanosome; *Trypanosoma cruzi*. It causes Chagas disease. Vectors are reduviid bugs

Trypanosomes occur in blood and tissue fluids extracellularly; *T. cruzi* proliferates as intracellular amastigotes in muscles especially the heart

Trypanosoma

Causes

Trypanosomiasis

West African Trypanosomiasis	East African Trypanosomiasis	American Trypanosomiasis
T.brucei gambiense	*T.brucei rhodesiense*	*T.cruzi*
Sleeping sickness		Chagas' disease
Transmitted by *Glossina* (tsetse fly)		Transmitted by *Triatoma* (winged bug)

Human African trypanosomiasis (Sleeping sickness)

Causative parasite:	✓ *Trypanosoma brucei gambiense* (West African trypanosomiasis) ✓ *Trypanosoma brucei rhodesiense* (East African trypanosomiasis)
Habitat:	Blood, lymph channel throughout the body, CSF, connective tissue, intracellular space, brain
Infective stage:	Metacyclic trypomastigotes
Diagnostic stage:	Trypomastigotes form in blood film
Mode of infection:	1. By the vector which is tsetse fly. 2. Transplacental (Mother-to-child). 3. Blood transfusion 4. contaminated needle

Pathogenesis:

- **During early "Haemolymphatic " stage** of infection the parasites multiply and spread throughout the bloodstream, lymphatic system, and lymph nodes.
- **Late "Encephalitic " stage** of the disease, the trypanosomes traverse the (blood brain barrier) BBB to the CNS where it shows picture of meningoencephalitis.

Clinical picture:

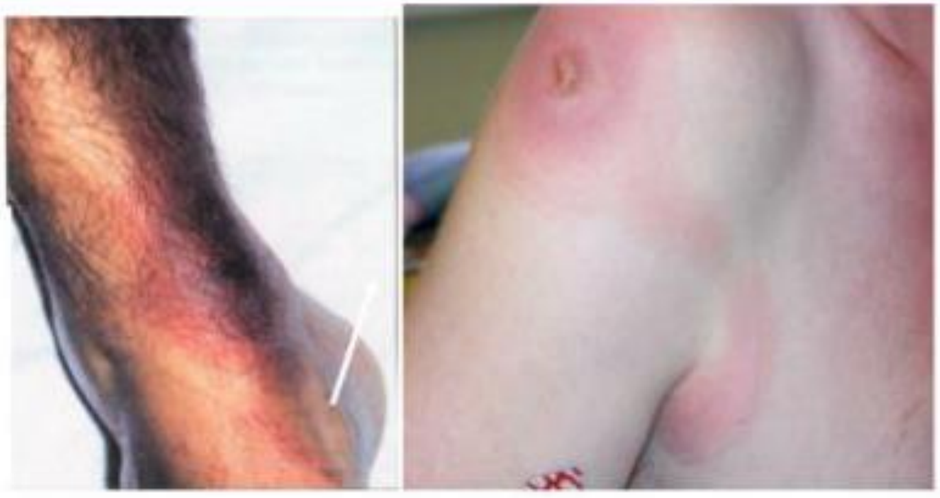
Stage 1:

- Chancre occurs especially 3-7 days after infection.
- followed by fever and parasitemia for few days.
- followed by enlargement of lymph nodes. A characteristic sign is enlarged posterior cervical nodes (Winterbottom's sign).
- followed by remittent fever, anemia, leukocytopenia, high IgM.
- Heart involvement, jaundice, pneumonia are frequent in T.b. rhodesiense which may be fatal.

Stage 2:

1. Involvement of the CNS within 3-4 weeks (rapid) in ***T. b. rhodesiense***, whereas it takes many months or years (slow) in ***T. b. gambiense.***
2. Associated with changes of behavior, confusion, sensory disturbances, and poor coordination.
3. Characteristic disruption of the normal sleep-wake cycle gives the disease its name, with the presence of nocturnal insomnia and daytime somnolence
4. ends in deep coma and death.

Pathogenesis and Clinical Picture



Trypanosoma chancre

Winterbottom sign

Emaciation

Coma before death

Diagnosis

1. Clinical picture
2. Laboratory diagnosis:

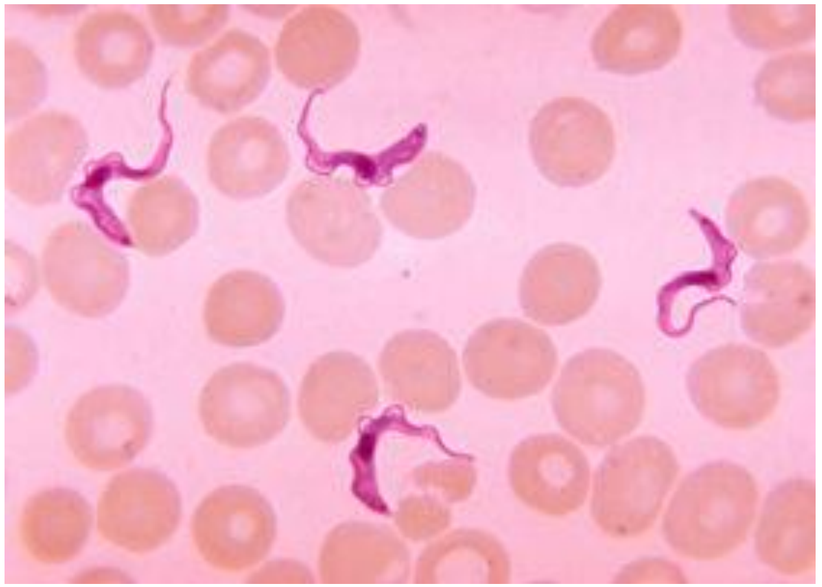
A. Direct by demonstration of trypomastigotes. Stained thin blood smears showed polymorphic flagellates.

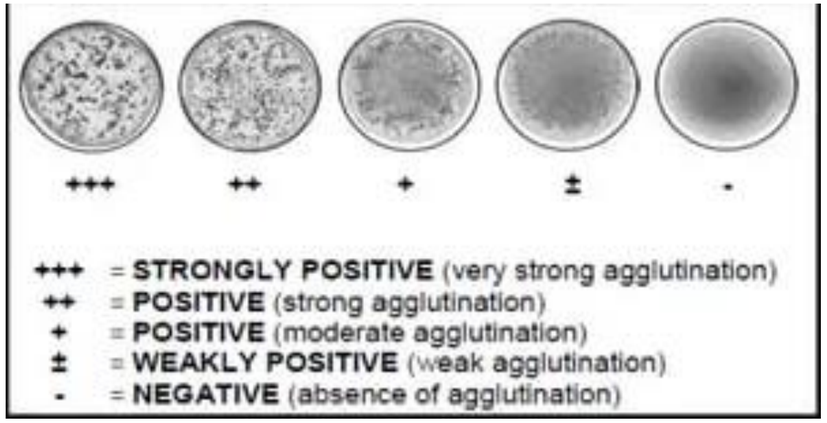
B. Indirect diagnosis

I. Serology: antigen or antibody detection: The Card Agglutination Test for Trypanosomiasis (CATT) has been used extensively for disease screening.

II. PCR for detection of the parasite DNA.

III. Culture on NNN media in case of low parasitemia for better demonstrate of the parasite.





Treatment:

During blood and lymphatic stages:

1. Pentamidine isothionate.
2. Suramin sodium.

In late stage with C.N.S. invasion:

1. Melarsoprol.
2. Tryparsamid.

Control:

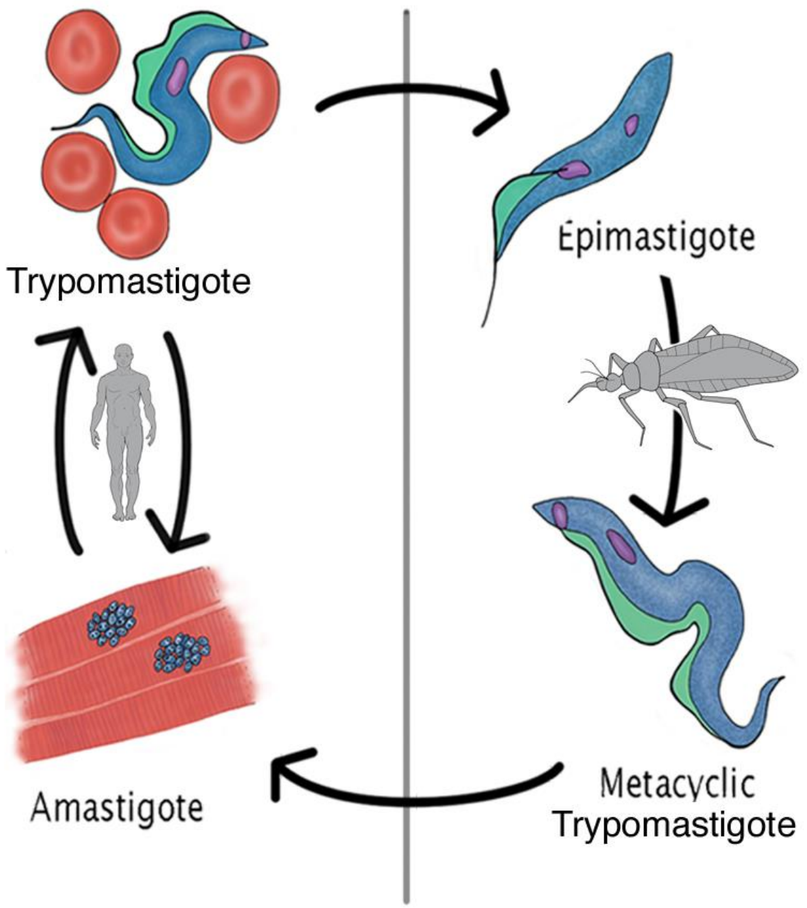
1. Treatment of carriers.
2. Prophylactic treatment with pentamidine isothionate.
3. Destruction of insect vector.

1. *Trypanosoma cruzi*
"Chagas disease"

- Disease: American trypanosomiasis "Chagas disease"
- Geographical distribution: Central and South America.
- Host: Man, especially infants and young children.
- Reservoir host: The most important reservoir hosts are armadillos.
- Vector: *Triatoma megista* (kissing or cone-nosed or winged-bug).
- Habitat: Cells of the reticulo-endothelial system (liver, spleen, bone marrow, and lymph nodes), myocardium, smooth muscles, and nervous system.
- Infective stage: metacyclic trypomastigotes.

Mode of infection:

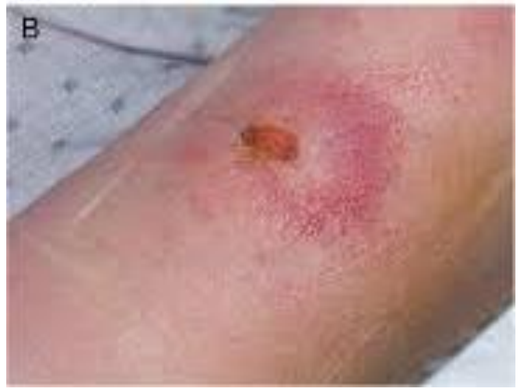
1. Biological transmission by Triatomine bugs (posterior station transmission).
2. Blood transfusion.
3. Congenital transmission (via the placenta from the mother to the fetus).
4. Organ transplants by using organs from infected donors.



Clinical picture:
Chagas disease (acute and chronic)

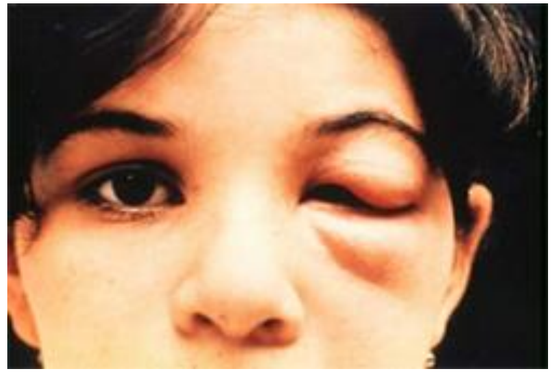
Acute form: common in infants and young children.

1. **Chagoma:** primary cutaneous indurated lesion develops at the site of vectors bite due parasite multiplication inside macrophages.



2. **Romana's sign:** It is a unilateral swelling of the patient's eyelids associated with inflammation of the lacrimal gland and conjunctivitis. **It is a marker of acute Chagas disease.**

3. Invasion of the reticulo-endothelial cells causes generalized lymphadenopathy, splenomegaly and hepatomegaly.



4. Presence of anemia, continuous fever and severe headache.

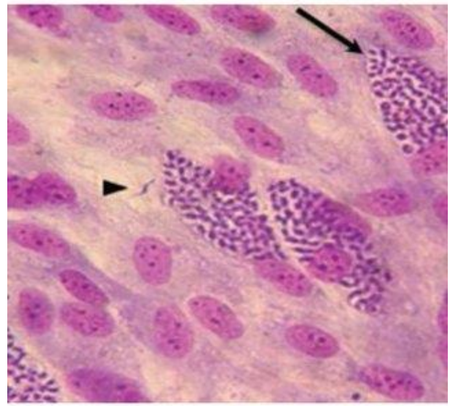
5. In rare cases, infected individuals may develop acute myocarditis or acute meningoencephalitis which is life-threatening

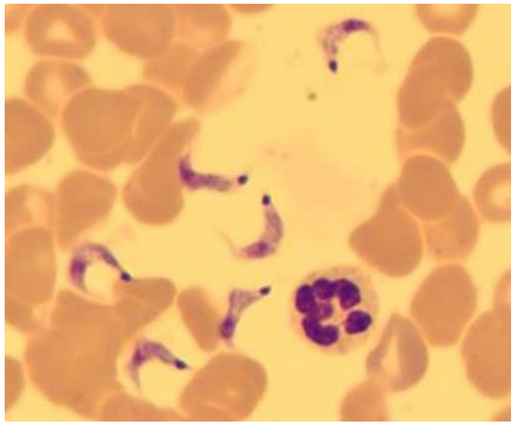
Chronic form: common in adults

- The parasites are hidden in organs (the heart, digestive smooth muscles and nervous system), no parasites found in blood.

- Destruction of autonomic nerve ganglion in muscles of the heart and hollow organs resulting in mega organ disease
  - **Cardiomegaly.**
  - **Megaesophagus:** dilatation of the esophagus leading to dysphagia and chronic achalasia.
  - **Megacolon:** dilatation of the colon leading to constipation and patients with advanced disease can go for weeks between bowel movements

Diagnosis:



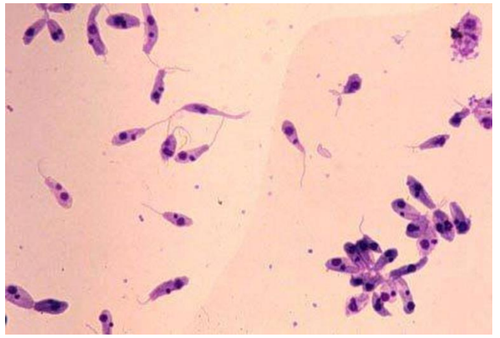


I. Clinical picture.

II. Laboratory diagnosis:

1. In acute cases:

- Monomorphic trypomastigotes can be found by microscopic examination of thin blood smears and aspirates from chagoma, lymph node, bone marrow, and CSF



- Tissue sections from lymph nodes or heart for definitive diagnosis of acute stage Chagas disease (Amastigote form).
- Cultivation of the suspected blood on N.N.N. medium (Novy-MacNeal-Nicolle Medium) and examined after (1-4 weeks) to show epimastigotes and trypomastigotes

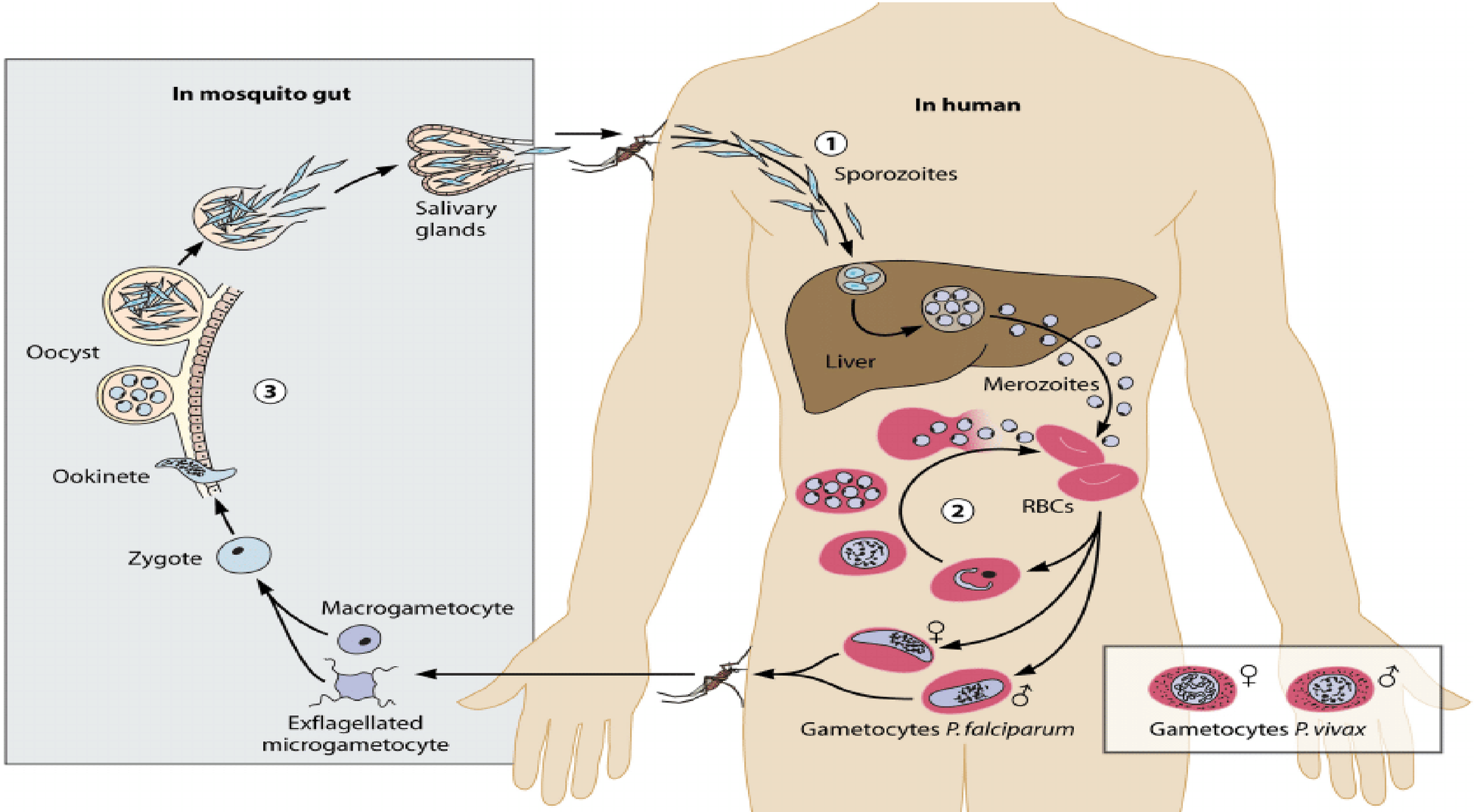
Plasmodium species affecting man:

1. *Plasmodium vivax* (most common): (benign tertian malaria) is the most common cause of malaria and is found in subtropical and temperate areas of the world.
2. *P. falciparum (malignant subtertian malaria)* is found in tropical regions and causes the most severe and fatal disease.
3. *P. malariae (quartan malaria) is* limited to subtropical areas.
4. *P. ovale (ovale tertian malaria) is* the least common malarial species and is endemic in Africa

Malaria

Causative protozoa :	*Plasmodium vivax, Plasmodium ovale,* *Plasmodium malariae, Plasmodium falciparum*
Definitive host: **Intermediated host**	Mosquitoes man
Habitat:	Liver cells and R.B.Cs
Infective stage: **Diagnostic stage:**	➢Sporozoites ➢blood stages.
Mode of infection:	1. Through the bite of female Anopheles mosquitoes. 2. blood transfusion 3. Congenital transmission .

- All four species of *Plasmodium* have complex sexual cycles in their insect vectors (anopheline mosquitoes) and asexual cycle in the human host.



Clinical Presentation

1. **Flu-like prodrome (till establishment of cycles)**
2. **Malaria Paroxysms includes 3 stages:**
    i. Cold stage: The patient complain of sudden chill, extreme cold
    ii. Hot stage: there is headache, high fever.
    iii. Sweating stage: there is profuse sweating, temperature falls the patient is weak and exhausted

- *P. vivax* and *P. ovale*: chills and fever x48 h but can be variable (benign tertian malaria)
- *P. malariae*: chills and fever x72 h but can be variable (Quartan malaria)
- *P. falciparum*: less predictable fever interval, can be highly variable (malignant tertian, subtertian)

3. **Anaemia due to destruction of RBCs**
4. **Hepatosplenomegaly.**

Complications:

1. **Plasmodium malariae** can cause nephrotic syndrome.
2. ***Plasmodium falciparum* (most lethal and called malignant malaria):**

- **Cerebral malaria** - with progressive headache followed by coma, uncontrollable rise in temperature and convulsions.
- **Algid malaria**, which is a rapid development of shock, with circulatory failure. The skin is cold, and the peripheral veins are constricted.
- **Black water fever**: It is an acute, massive lysis of RBCs, which lead to high levels of free hemoglobin and breakdown products of hemoglobin in the blood and urine. The urine is quite dark, hence the name of the condition. There is also jaundice, fever and vomiting.
- **Sever hemolytic anemia**: due to the massive lysis of RBCs occurs as a result of destruction of both parasitized and non-parasitized erythrocytes due to autoimmune mechanism.

Diagnosis

A. Clinical picture:

B. Laboratory:

- **Direct by detection of the parasite in blood smear:**

- Thin blood film (Giemsa stain) to detect the erythocystic stages
- Sternal puncture in case of malignant malaria when the parasite does not appear in blood films.

- **Indirect**

- Serological tests: Fluorescent antibody test and ELISA.

Treatment and Prevention

1. **Prophylaxis:** proguanil
2. **Clinical cure:** chloroquine.
3. **Radical cure:** Primaquine.
4. **If drug resistance occurred:** a combination of pyrimethamine and sulphadoxin.

Prevention and control:

1. Treatment of patients.
2. Destruction of breeding places by draining ponds or by filling them with earth or by using larvicidal oil.
3. The use of small fish (*Gambusia*) which eat mosquito larvae.
4. The use of insecticides on the inner walls of houses to destroy adult mosquitoes.
5. Screening of houses and the use of bed nets.
6. Application of skin repellents over exposed areas of skin.
7. prevention with antimalarial prophylaxis,


QUIZ!

1. The definitive host of *Toxolasma gondii* is:

a) Human b) Cat.,

c) Cattle d) Sheep.

2. T. gondii in human occurs as either …… or ……..

3. **What is the infective stage in filariasis:**

a)Micsrofilaria, b) Third stage larva

c) Second stage larva, d) Embryonated egg

4. Scrotal swelling and inguinal lymph node enlargement is characteristic of infection with:

a) Wucerieria bancrofti b) *Loa loa*,

c) Leishmania donovani. d) Toxplasma gondii

5. Kala azar caused by which of the following parasite?

a) Wucerieria bancrofti b) *Loa loa*,

c) Leishmania donovani. d) Toxplasma gondii


thank
you