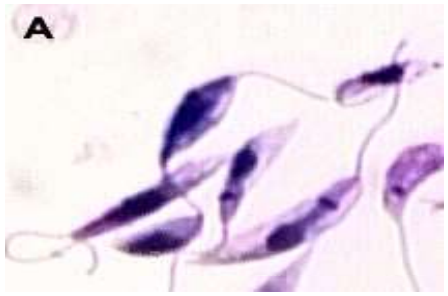
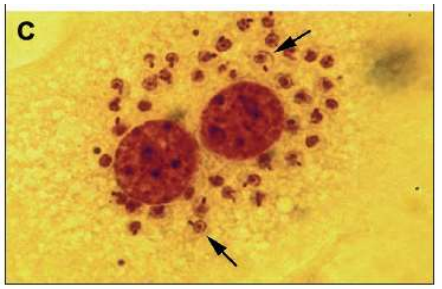
PARASITIC PROTOZOA





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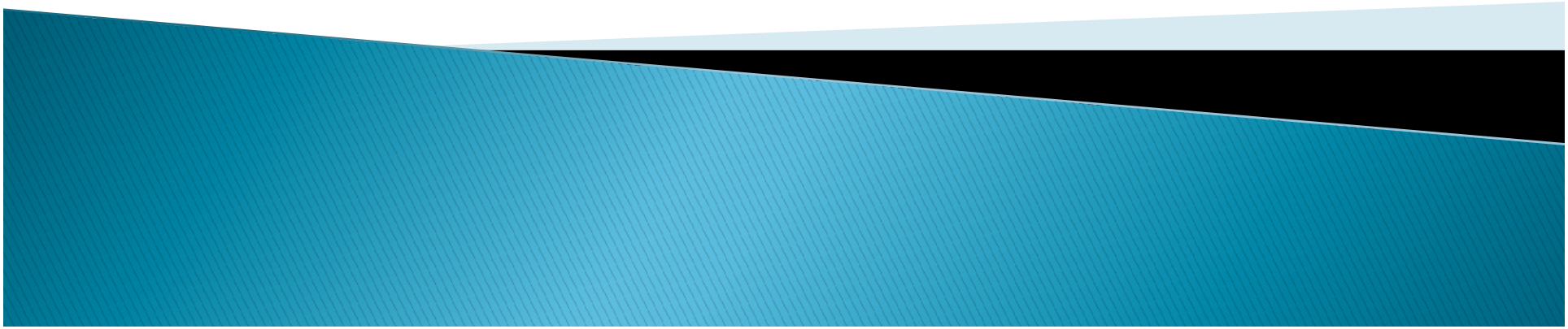
Parasite & Parasitism

Parasites are living organisms, which depend on a living host for their nourishment and survival. They multiply or undergo development in the host.

Parasitism is a relationship in which one of the participants, the parasite, either harms its host or in some sense lives at the expense of the host.



Types of Parasites

Ectoparasite

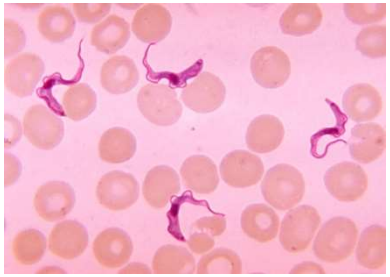
Lives outside on the surface of the body of the host.

Example Lice, ticks, mites, fleas

Endoparasite

Lives inside the body of the host; in the blood, tissues, body cavities,digestive tract or other organs.

Example: Protists and helminths



Types of Parasites

Temporary Parasite

Visits its host for a short period. Example mosquitoes and bed bugs

Permanent Parasites

Leads a parasitic life throughout the whole period of its life. Example Intestinal helminth

Facultative Parasite

Lives a parasitic life when oppurtunity arises. Example Free living Amoeba

Obligatory Parasites

Cannot exist without a parasitic life. Example *Trypanosoma. Wuchereria*

Types of Parasites

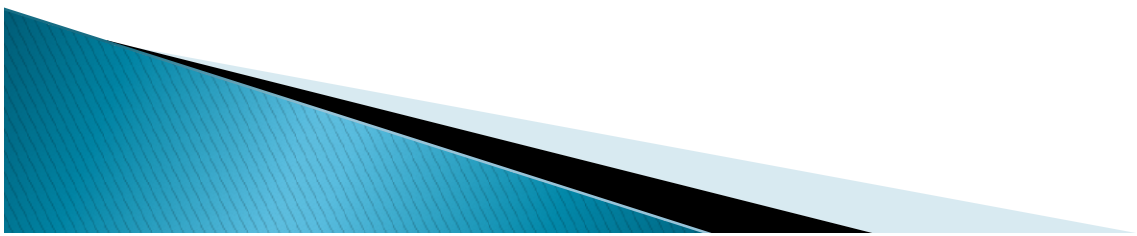
Occasional or Accidental Parasite

Attacks an unusual host.

Example *Echinococcus granulosus infects man accidentally*

Aberrant or Wandering parasites:

Infects a host where they cannot develop further are known as aberrant or wandering parasites, e.g. *Toxocara canis* (dog roundworm) infecting humans



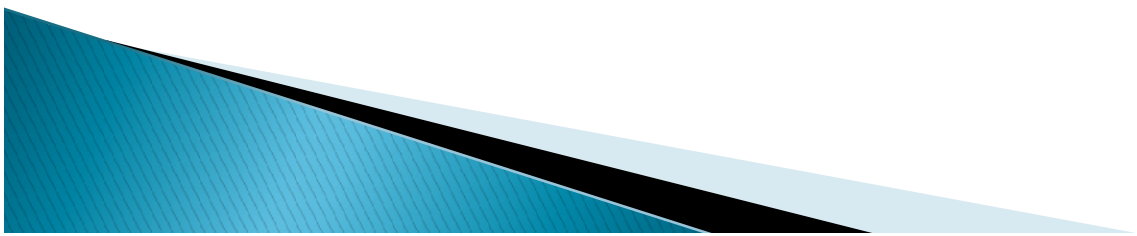
Types of Host

Definitive host:

The host, in which the adult parasite lives and undergoes sexual reproduction is called the definitive host, e.g. mosquito acts as definitive host in malaria, man as definitive host e.g. filaria, roundworm, hookworm.

Intermediate host:

The host, in which the larval stage of the parasite lives or asexual multiplication takes place is called the intermediate host. In some parasites, 2 different intermediate hosts may be required to complete different larval stages. These are known as first and second intermediate hosts, respectively.



Types of Host

Paratenic host (A Carrier or Transport Host)

A host, in which larval stage of the parasite remains viable without further development is referred as a paratenic host. Such host transmits the infection to another host.

Reservoir host:

In an endemic area, a parasitic infection is continuously kept up by the presence of a host, which harbors the parasite and acts as an important source of infection to other susceptible hosts, e.g. dog is the reservoir host of hydatid disease.

Accidental host:

The host, in which the parasite is not usually found, e.g. man is an accidental host for cystic echinococcosis.

Zoonosis

The word zoonosis was introduced by Rudolf Virchow in 1880 to include the diseases shared in nature by man and animals. Later, in 1959, the World Health Organization (WHO) defined zoonosis as "*those diseases and infections, which are naturally transmitted between vertebrate animals and man".*

It is of following types:

Protozoal zoonoses, e.g. toxoplasmosis, leishmaniasis, balantidiasis, and cryptosporodiasis

Helminthic zoonoses, e.g. hydatid disease, taeniasis

Anthropozoonoses: Infections transmitted to man from lower vertebrate animals, e.g. cystic Echinococcosis

Zooanthroponoses: Infections transmitted from man to lower vertebrate animals, e.g. human tuberculosis to cattle.

Vectors

Insect vectors: A vector is an agent, usually an arthropod that transmits an infection from man to man or from other animals to man, e.g. female *Anopheles is* the vector of malarial parasite.

Biological vectors: The term biological vector refers to a vector, which not only assists in the transfer of parasites but the parasites undergo development or multiplication in their body as well. They are also called as true vectors. Example of true vectors are:
Mosquito—Malaria, filariasis , Sandflies—Kala-azar, Tsetse flies—Sleeping sickness, Reduviid bugs—Chagas' disease, Ticks—Babesiosis.

Mechanical vectors: The term mechanical vector refers to a vector, which assists in the transfer of parasitic form between hosts but is not essential in the life cycle of the parasite. Example of Mechanical vectors is: . Housefly—amoebiasis.

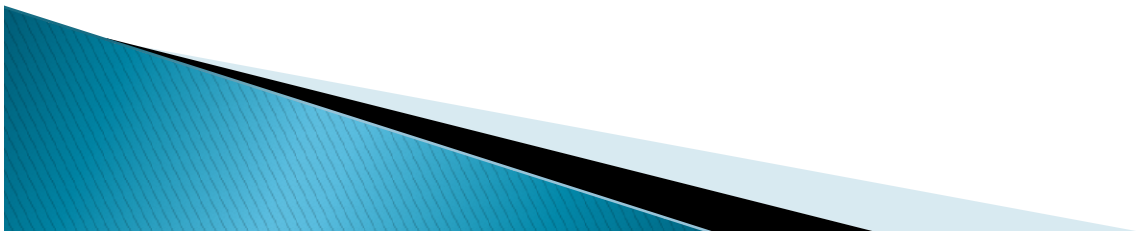
Immune Evasion

Parasite escape mechanisms	Example
Intracellular habitat	Malarial *parasite*, *Leishmania*
Encystment	*Toxoplasma* *Trypanosoma cruzi*
Resistance to microbial phagocytosis	*Leishmania*
Masking of antigens	Schistosomes
Variation of antigen	Trypanosomes *Plasmodium* spp.
Suppression of immune response Malarial parasite	*Trichinella spiralis* *Schistosoma mansoni*
Interference by polyclonal activation	Trypanosomes
Sharing of antigens between parasite and host-molecular mimicry	Schistosomes
Continuous turnover and release of surface antigens of parasite	Schistosomes

Protozoa

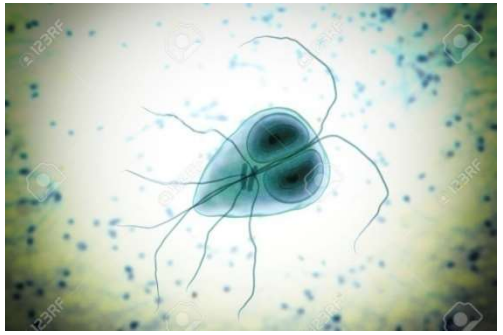
General Features

- Single-celled eukaryotic microorganisms belonging to kingdom protista are classified as Protozoa (Greek *Protos: first; zoon: animal).*
- Unicellular (consist of one cell) this cell performs all phsiological function (activities) of life such as locomation , reproduction , respiration , ingestion , digestion and excretion .
- They vary in size and shape some are visible while others require high magnification (by microscope).
- The majority of protozoa are free living but some are parasitic .
- Both sexual and asexual reproduction occur in protozoa (the majority of protozoa reproduce by asexual reproduction).
- Locomotory organs psedopodia, flagella, cilia.



Giardia intestinalis

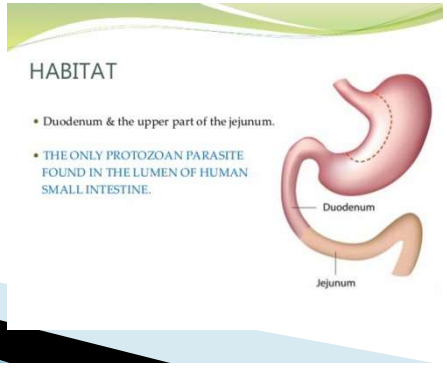
Giardia, a microscopic parasite, is responsible for disease giardiasis. There are many species of *Giardia*. *Giardia* intestinalis (synonymous *Giardia lamblia*) can infect human beings.

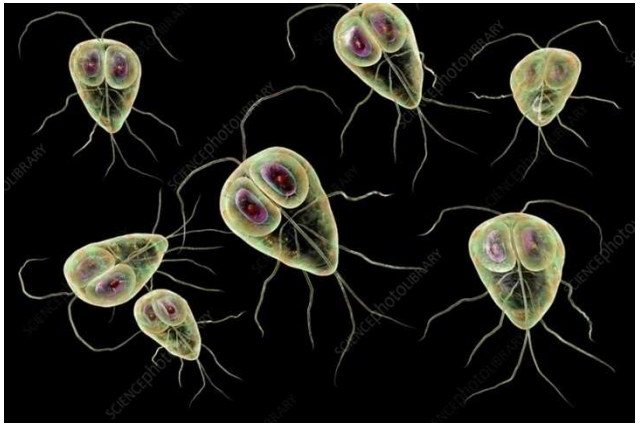


Phylum: Sarcomastigorphora

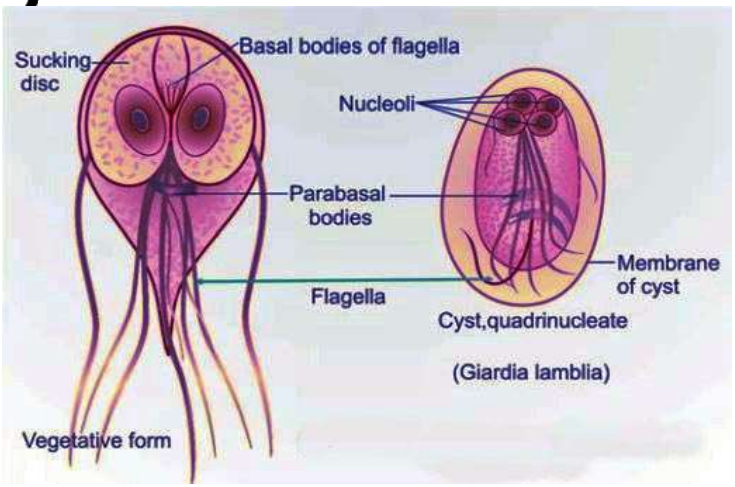
Habitat

Duodenum and upper jejunum. It is the only protozoan parasite found in the lumen of the human small intestine.





Morphology



It exists in 2 forms:
Trophozoite (or vegetative form)
Cyst (or cystic form).

Trophozoite

- The trophozoite is motile.
- The trophozoite is in the shape of a tennis racket (heartshaped or pyriform shaped) and is rounded anteriorly and pointed posteriorly.
- Dorsally, it is convex and ventrally, it has a concave sucking disc, which helps in its attachment to the intestinal mucosa.
- It is bilaterally symmetrical and possesses.
- 1 pair of nuclei
- 4 pairs of flagella
- Blepharoplast, from which the fl agella arise (4 pairs)
- 1 pair of axostyles, running along the midline
- Two sausageshaped parabasal or median bodies, lying transversely posterior to the sucking disc.

Morphology

Cyst

- It is the infective form of the parasite.
- The cyst is small and oval, is surrounded by a hyaline cyst wall.
- Its internal structure includes 2 pairs of nuclei grouped at one end.
- A young cyst contains 1 pair of nuclei.
- The axostyle lies diagnonally, forming a dividing line within cyst wall.
- Remnants of the flagella and the sucking disc may be seen in the young cyst.

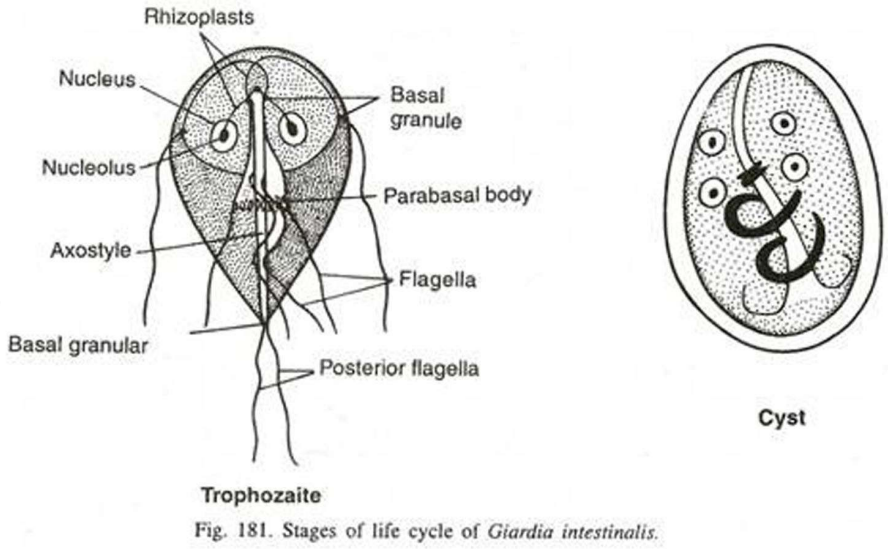
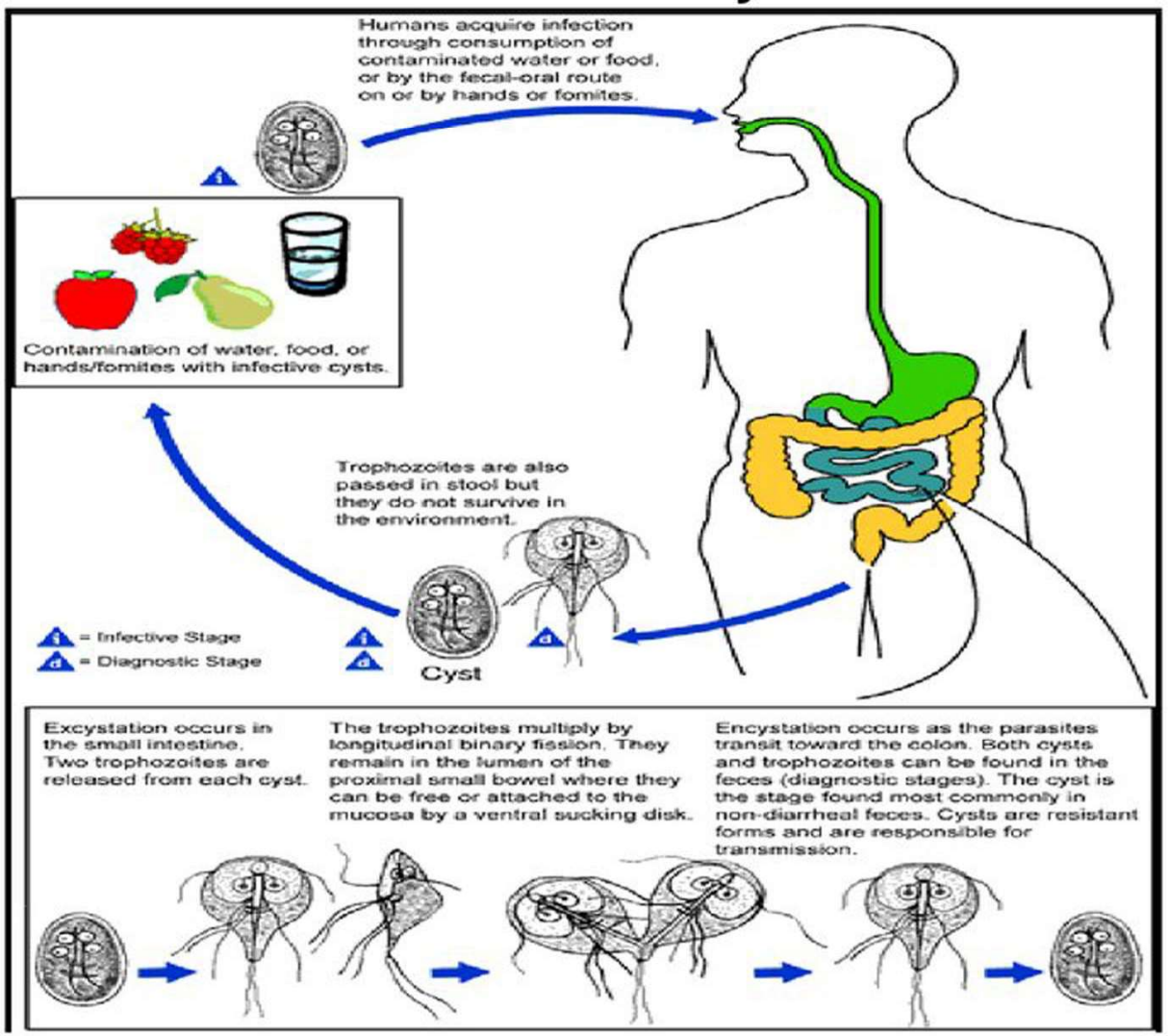


Fig. 181. Stages of life cycle of *Giardia intestinalis*.

Life Cycle of *Giardia*



Life Cycle of *Giardia*

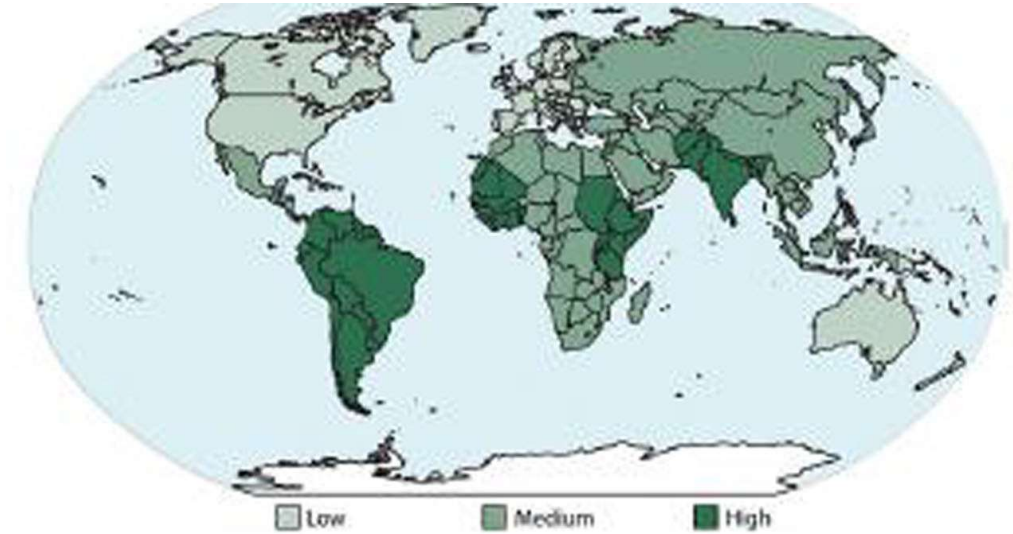
Giardia passes its life cycle in 1 host.

Infective form: Mature cyst.

Mode of transmission:

- Man acquires infection by ingestion of cysts in contaminated water and food. Other frequent mode of infection is from person-to-person in day-care centers or workplace. Potential zoonotic risks can berendered by infected dogs and cats which evidently serve as a source for contamination of the environment with the organism.
- Within half an hour of ingestion, the cyst hatches out into two trophozoites, which multiply successively by binary fission and colonize in the duodenum
- The trophozoites live in the duodenum and upper part of jejunum, feeding by pinocytosis.
- During unfavorable conditions, encystment occurs usually in colony.
- Cysts are passed in stool and remain viable in soil and water for several weeks.
- There may be 200,000 cysts passed per gram of feces.
- *Infective dose is 10-100 cysts.*

Distribution



Risk of disease caused by *Giarda species with different degrees*

Giardiasis is caused by *Giardia* isolated worldwide and is ranked among the top 10 parasites of man (Farthing and Kelly, 2005). Its occurrence is worldwide and prevalence very high in areas with poor sanitation and in institutions.

Human infections usually originate from other humans but may result from contact with dogs, cats, rodents, beavers, or nonhuman primates.

The prevalence of the disease varies from 2% to 5% in developed to 20% to 30% in developing countries.

The variation in prevalence might be attributed to factors such as the geographical area, the urban or rural setting of the society, the age group composition and the socio-economical conditions of the study subject.

Epidemiology

A substantial amount of data has revealed that *Giardia intestinalis should be considered as a species complex as it comprises at least eight distinct genetic groups which are referred to as assemblage A to H.*

Assemblage A has a broad host range which includes human beings, primates, livestock, pets and wildlife.

Assemblage B is the predominant isolate type together with assemblage A and has even broader range which includes human beings, livestock, dog, beaver, horse, rat and muskrat .

Assemblage C and D can reside in dog, cat and wild carnivores and other canid includes foxes, wild dogs, coyotes and wolves.

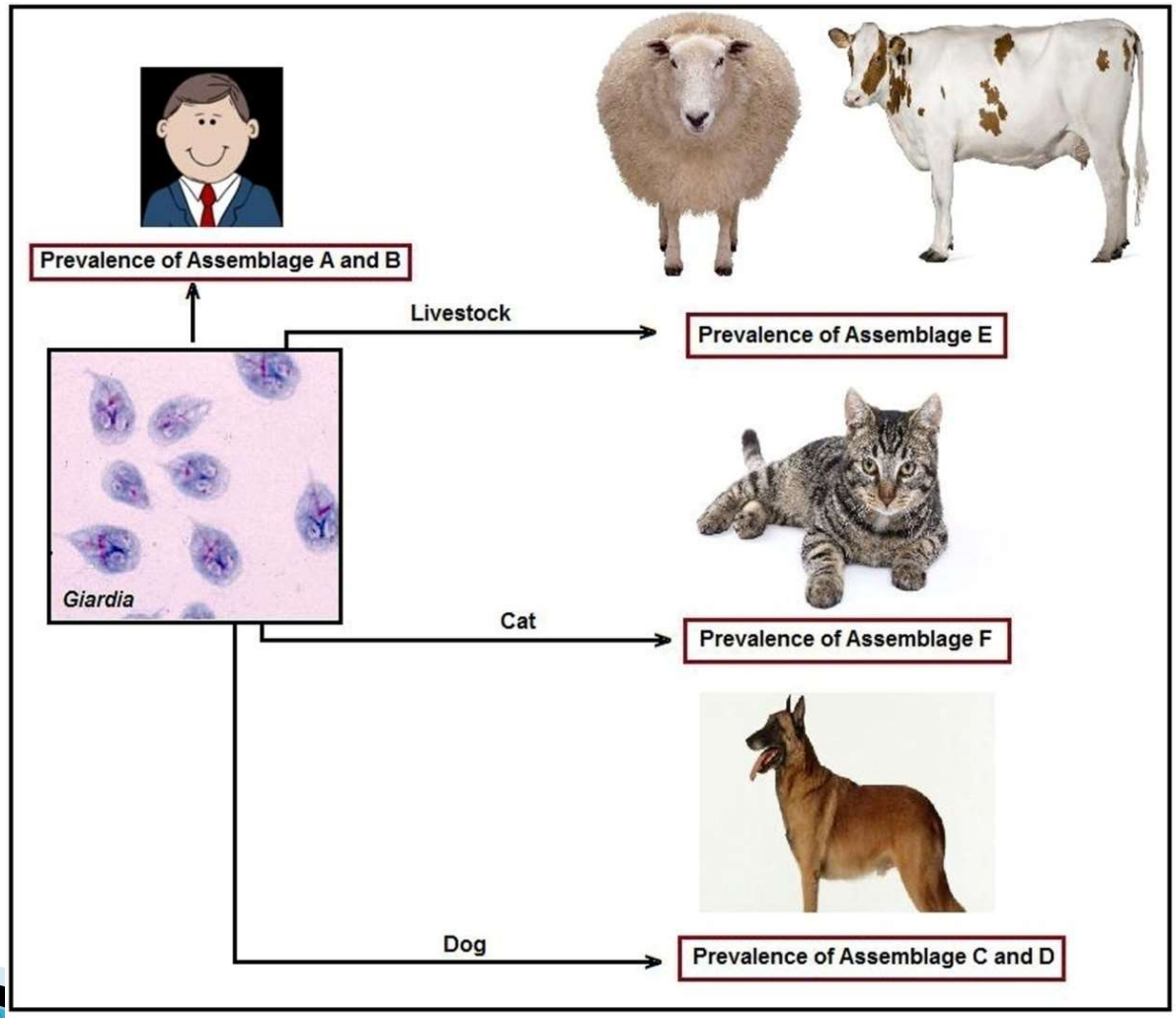
Assemblage E is typically predominant type in livestock.

Assemblage F has been found mainly in cats and appears to be adapted to this species.

Assemblage G is seen largely in rodents including rats.

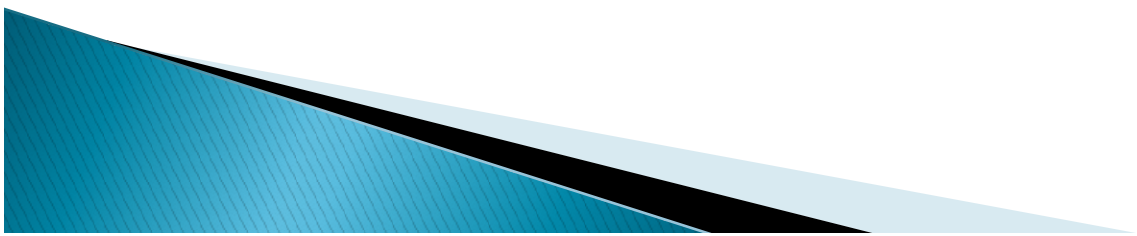
Assemblage H has been reported from seals and gulls.

Epidemiology

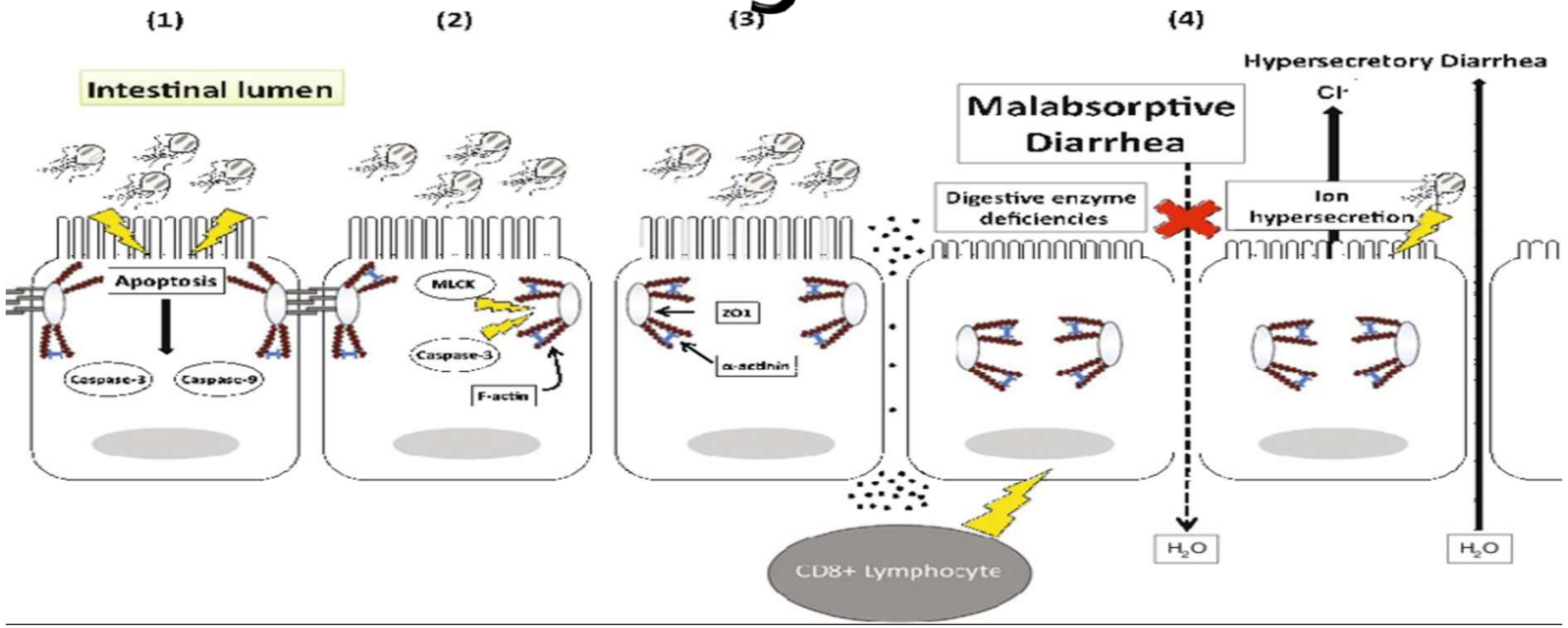


Pathogenesis

- *Giardia is typically seen within the crypts of duodenal* and jejunal mucosa. It does not invade the tissue, but remains tightly adhered to intestinal epithelium by means of the sucking disc.
- They may cause abnormalities of villous architecture by cell apoptosis and increased lymphatic infiltration of lamina propria.
- Variant specifi c surface proteins (VSSP) of giardia play an important role in virulence and infectivity of the parasite.
- Often they are asymptomatic, but in some cases, *Giardia may lead to mucus diarrhea, fat malabsorption* (steatorrhea), dull epigastric pain, and flatulence. The stool contains excess mucus and fat but no blood.
- Children may develop chronic diarrhea, malabsorption of fat, vitamin A, protein, sugars like xylose disaccharides, weight loss, and spruelike syndrome.
- Occassionally, *Giardia may colonize the gall bladder,* causing biliary colic and jaundice.
- Incubation period is variable, but is usually about 2 weeks.



Pathogenesis



1 The pathophysiology of Giardia duodenalis–mediated diarrheal disease is multifactorial. (1) After exycstation, Giardia trophozoites colonize the lumen of the small intestine and induce heightened rates of enterocyte apoptosis via the activation of caspase-3 and caspase-9. (2) Following the induction of apoptosis, zonula occludens 1 (ZO-1), F-actin, and α-actinin are relocated from apical junctional complexes to the cell interior via activated caspase-3 and myosin light chain kinase (MLCK). (3) The G. lamblia–mediated breakdown of apical junctional complexes causes an increase in intestinal permeability that facilitates the translocation of various luminal antigens, including microbial factors and food antigens, into the sub-epithelial compartment that promotes the recruitment of host lymphocytes. (4) CD8+ lymphocyte populations induce the diffuse shortening of brush border microvilli resulting in brush border enzyme defi ciencies, and small intestinal malabsorption. Trophozoites also induce the secretion of chloride ions. Together, the accumulation of undigested carbohydrates and secretion of ions generates an osmotic gradient within the small intestinal lumen that results in the loss of water, intestinal distension, and rapid peristalsis that ultimately causes malabsorptive and hypersecretory diarrheal disease. Small intestinal malabsorption is believed to be the major cause of diarrhea during Giardia infection , while chloride hypersecretion further contributes to symptoms of diarrheal disease

Source publication

Symptoms

Symptoms include: diarrhea, flatulence, floating slimy stool, abdominal cramps, upset stomach, Nausea and dehydration.

Stage	Symptoms
Acute (often lasts 3–4 days, subsiding spontaneously)	✓ Explosive, watery, foul-smelling diarrhea ✓ Low-grade fever ✓ Chills ✓ Abdominal bloating and cramping ✓ Vomiting ✓ Distention, associated with flatulence ✓ Blood and mucus in stools (rare)
Chronic	✓ Intermittent diarrhea ✓ Abdominal bloating and cramping ✓ Weight loss ✓ Malnutrition ✓ Growth retardation

Laboratory Diagnosis

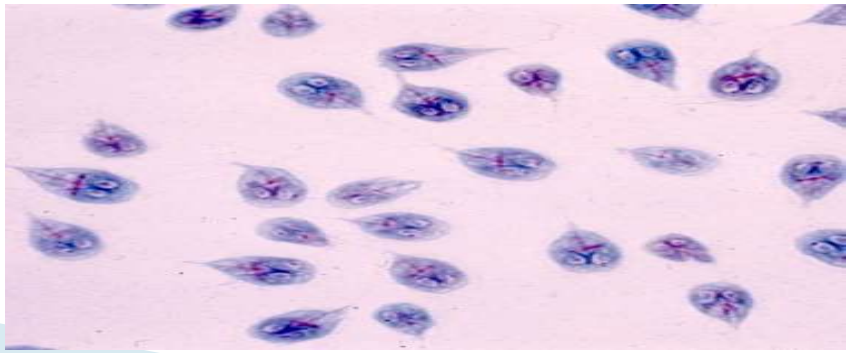
Laboratory Diagnosis of *Giardia*

Stool examination
- Macroscopic examination
- Miroscopic examination of stained prepration

Enterotest (string test)

Serological test
- **Antigen detection**
  - ELISA
  - IIF test
- **Antibody detection**
  - ELISA
  - IIF test

Molecular diagnosis
- DNA probe
- PCR



Treatment & Prophylaxis

Treatment

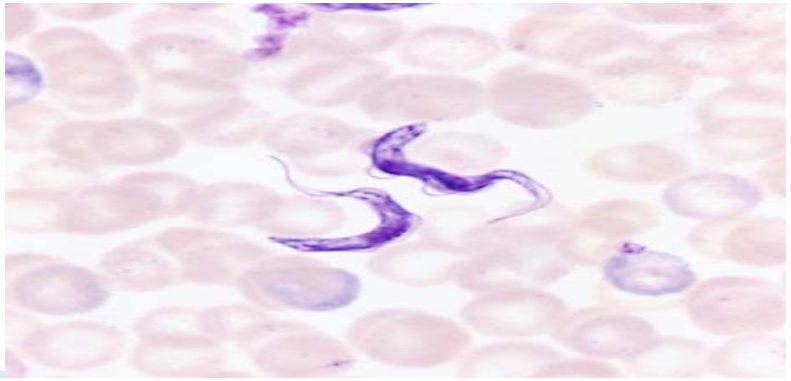
- Metronidazole (250 mg, thrice daily for 5–7 days) and tinidazole (2 g single dose)
- are the drugs of choice. Cure rates with metronidazole are more than 90%.
- Tinidazole is more effective than metronidazole.
- Furuzolidone and nitazoxamide are preferred in children, as they have fewer adverse effects.
- Parmomycin, an oral aminoglycoside can be given to symptomatic pregnant females.

Prevention or Prophylaxis

- Giardiasis can be prevented by following measures:
- Proper disposal of waste water and feces.
- Practice of personal hygiene like hand-washing before eating and proper disposal of diapers.
- Prevention of food and water contamination. Community chlorination of water is ineffective for inactivating cysts.
- Boiling of water and filtration by membrane filters are required

Trypanosoma gambiense

- African Sleeping Sickness is caused by *Trypanosoma* gambiense or *Trypanosoma rhodesiense* and is transmitted to humans by the bite of tsetse flies.
- There are two types of African trypanosomiasis (also called sleeping sickness); each is named for the region of Africa in which they were found historically. West African trypanosomiasis is caused by the parasite *Trypanosoma brucei gambiense.* East African trypanosomiasis is caused by the parasite *Trypanosoma brucei rhodesiense*. Both types of African trypanosomiasis are transmitted by the tsetse fly which is found only in rural Africa.
- *T. b. gambiense*, causing chronic African trypanosomiasis ("West African sleeping sickness") and *T. b. rhodesiense*, causing acute African trypanosomiasis ("East African sleeping sickness").
- Phylum Sarcomastigophora
- Class Zoomastigophra
- Oder Kinetoplastida
- Insect Vector *Glossina*

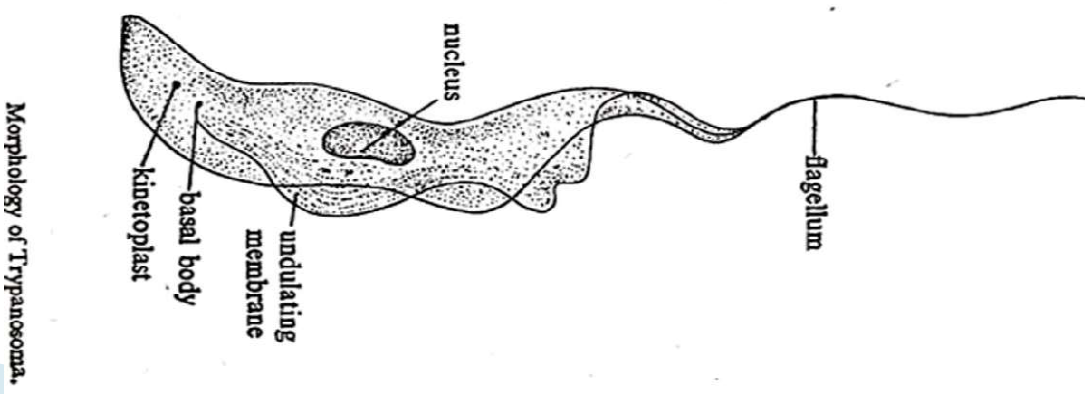


Morphology

In the blood plasma of man is found the Trypanosome form which looks like a thin, flattened and leaf-like body tapering at both ends. The pointed end is considered as anterior end and the blunt end is considered as posterior end. The length of the body is 15-32 micra and the breadth in the middle is about 2·5 micra.

The body is covered by a thin, elastic and firm pellicle. The pellicular part to which the flagellum is attached draws out as undulating membrane during flagellar movement (Fig. 50C). A whip-like long flagellum arise from a basal body (also called blepharoplast or centriole) located at the posterior end.

The flagellum skirts the whole body and projects out of the anterior end. Just posterior to the basal body there lies a small, spherical or disc-shaped Kinetoplast. The nucleus lies almost in the centre of the cell body as a large, oval, vesicular body. The nucleolus is large. Some vacuoles and volutine granules are present in the cytoplasm.



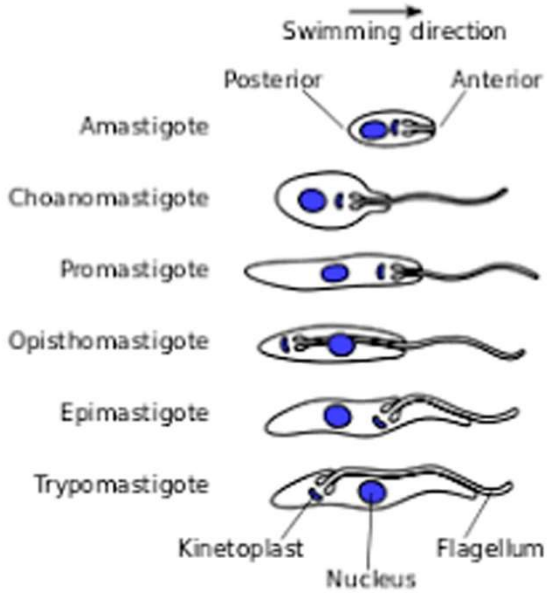
Morphology of Trypanosoma.

Morphology

Trypanosomatids show several different classes of cellular organisation of which two are adopted by *Trypanosoma brucei* at different stages of the life cycle:[10]

Epimastigote, which is found in tsetse fly. Its kinetoplast and basal body lie anterior to the nucleus, with a long flagellum attached along the cell body. The flagellum starts from the centre of the body.

Trypomastigote, which is found in mammalian hosts. The kinetoplast and basal body are posterior of nucleus. The flagellum arises from the posterior end of the body.



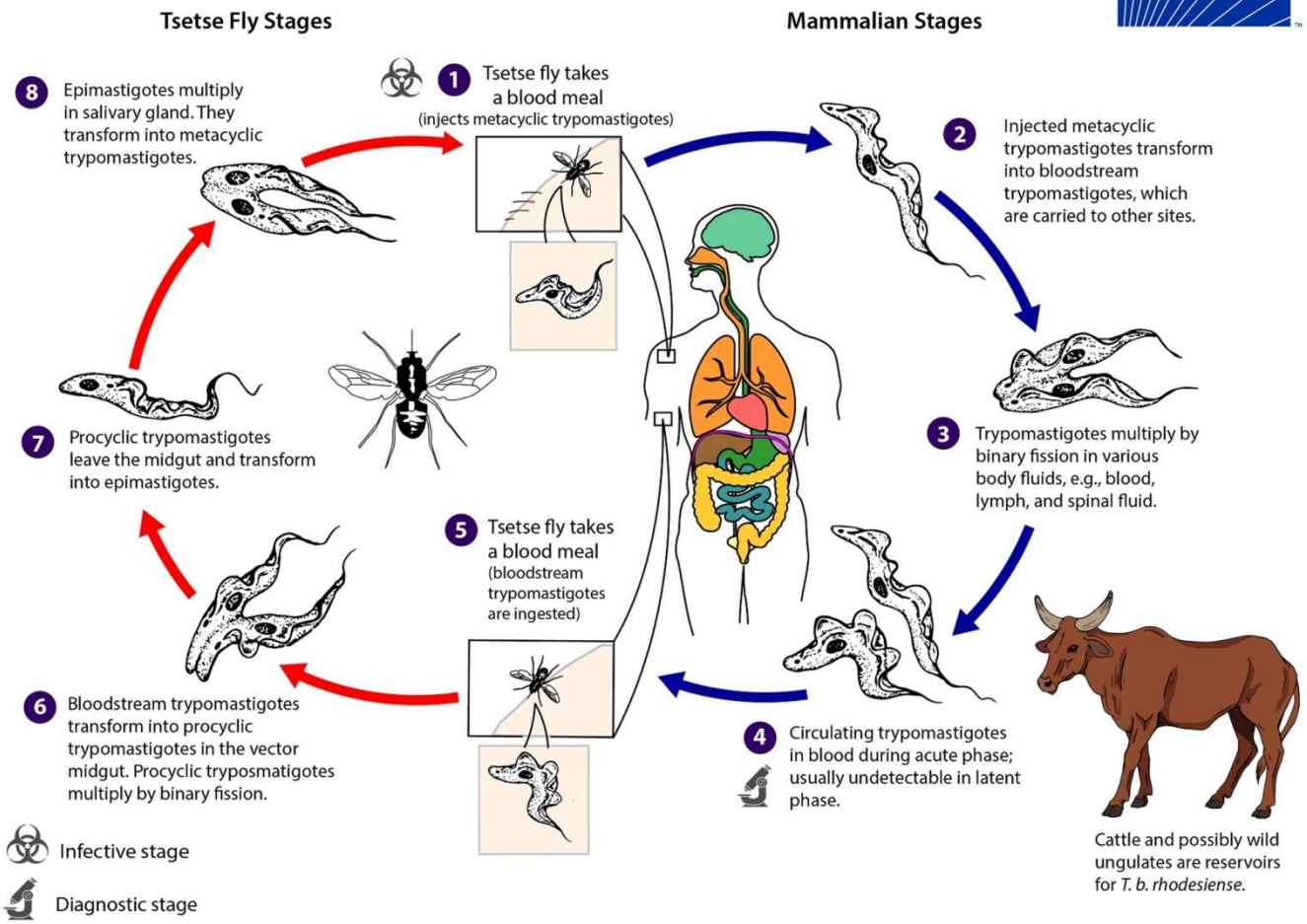
Life Cycle

DPDx

African Trypanosomiasis

Trypanosoma brucei gambiense & Trypanosoma brucei rhodesiense

CDC

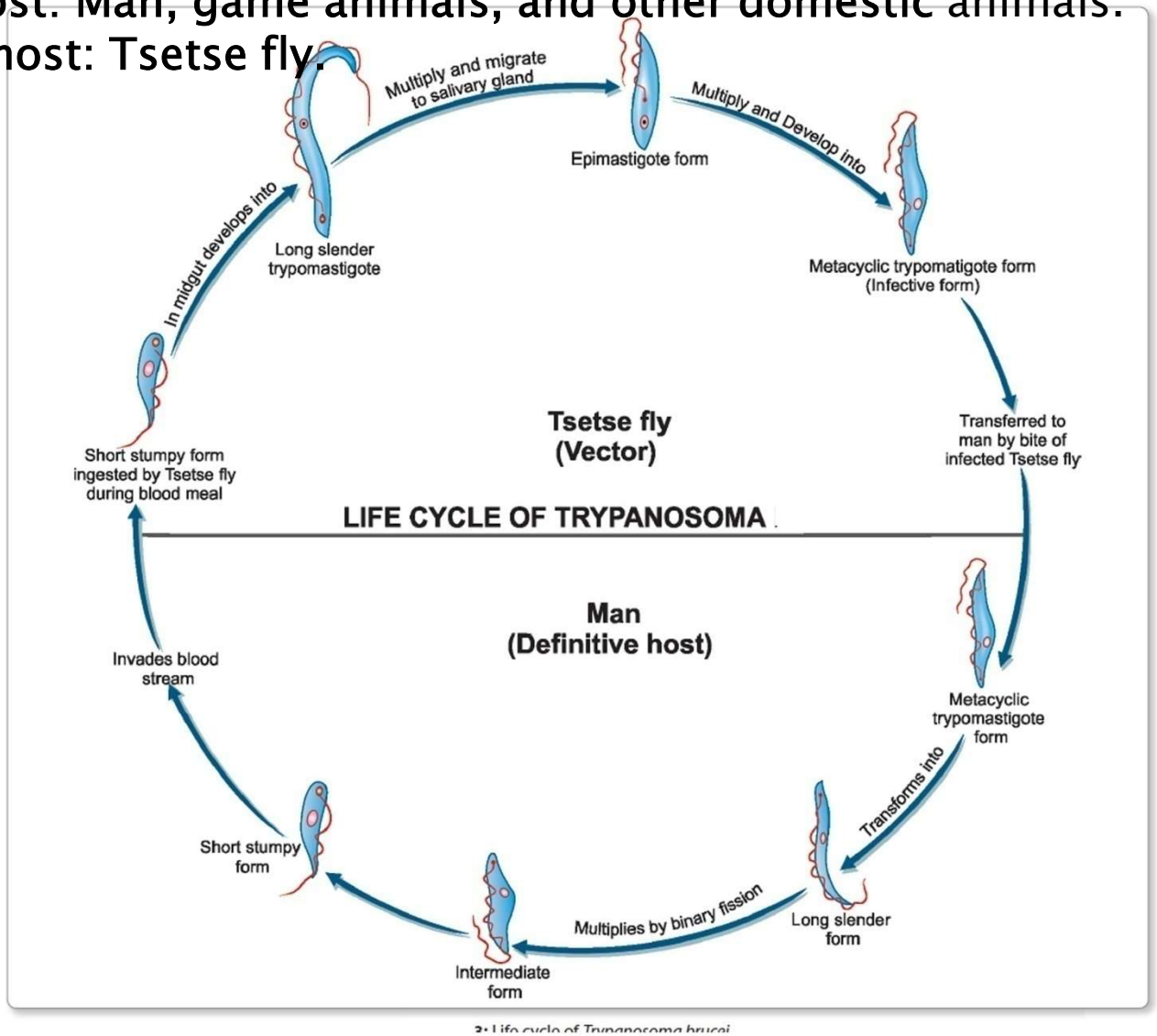


Life Cycle

T. gambiense passes its life cycle in 2 hosts.

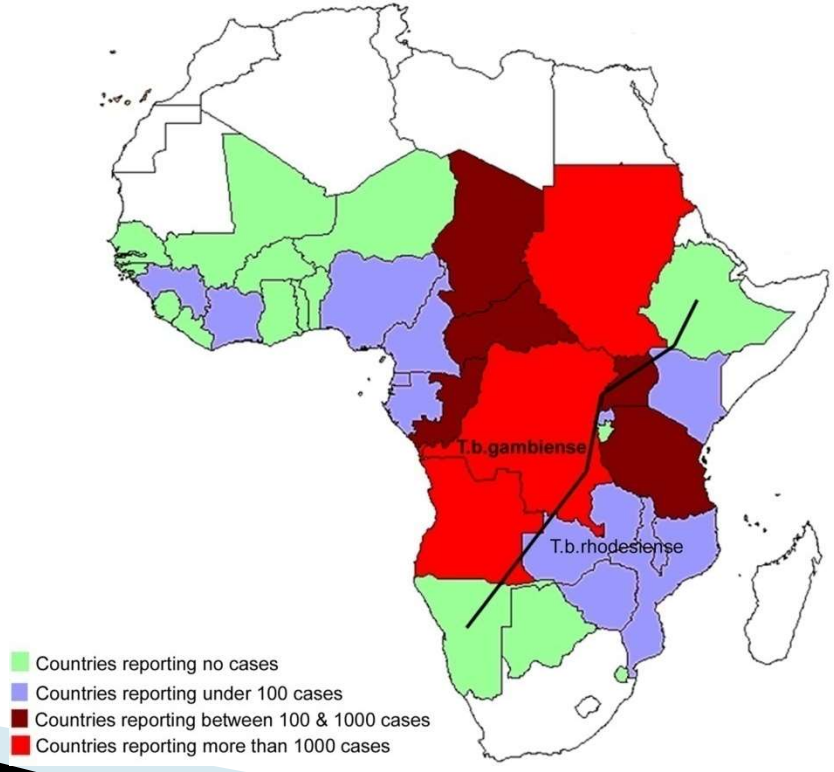
Vertebrate host: Man, game animals, and other domestic animals.

Invertebrate host: Tsetse fly.



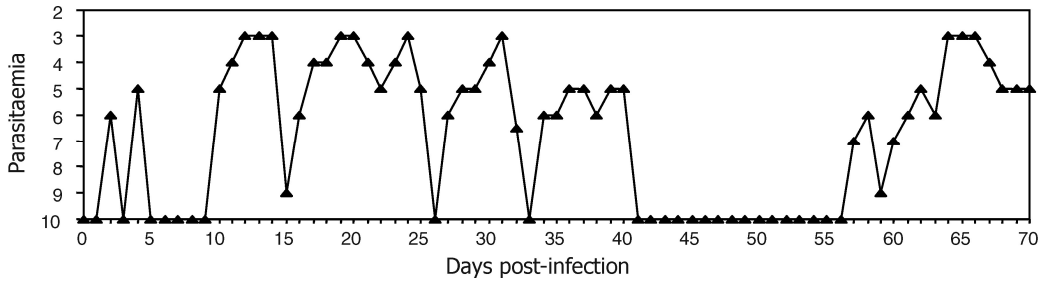
Epidemiology

Trypanosoma brucei gambiense is found in 24 countries in west and central Africa. This form currently accounts for 98% of reported cases of sleeping sickness and causes a chronic infection. A person can be infected for months or even years without major signs or symptoms of the disease. When more evident symptoms emerge, the patient is often already in an advanced disease stage where the central nervous system is affected.

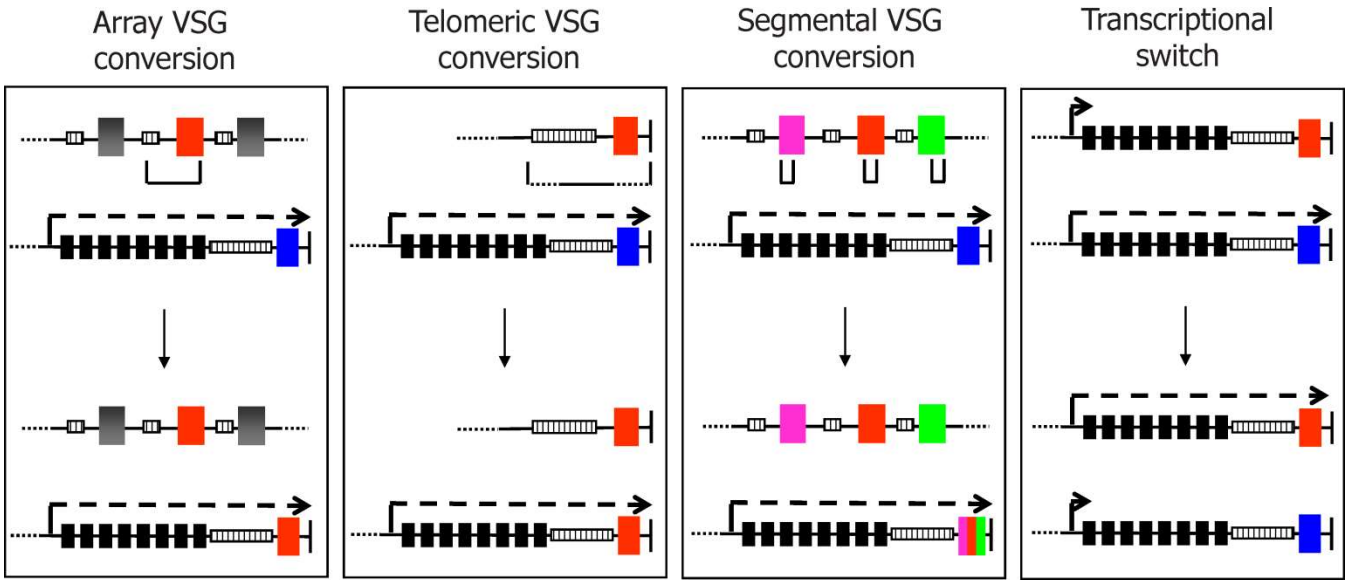


Antigenic Variation

- Trypanosomes exhibit unique antigenic variation of their
- glycoproteins. There is a cyclical fluctuation in the trypanosomes in the blood of infected vertebrates after every 7-10 days.
- Each successive wave represents a variant antigenic type (VAT) of trypomastigote posssesing variant surface specific antigens (VSSA) or variant surface glycoprotein (VSG) coat antigen.
- It is estimated that a single trypanosome may have as many as 1,000 or more VSG genes, that help to evade immune response. Besides this, trypanosomes have other mechanisms also that help them to evade host immune responses.



Antigenic Variation



Mechanisms of *VSG* Switching during Antigenic Variation in T. brucei
The *VSG* gene expressed prior to a switch (indicated by a blue box) is transcribed from an expression site (ES) that is found at the telomere (vertical black line) of a chromosome (horizontal black line); active transcription of the ES is indicated by a dotted arrow, *ESAG*s are depicted by black boxes, and 70-bp repeat sequence is shown as a hatched box. Gene conversion to generate a *VSG* switch can occur by copying a silent *VSG* (red box) from a subtelomeric array into the ES, replacing the resident *VSG*; the amount of sequence copied during gene conversion is illustrated, and normally encompasses the *VSG* ORF and extends upstream to the 70-bp repeats. The silent *VSG* donor can also be telomeric (either in a mini chromosome or in an inactive ES); here, the downstream limit of conversion can extend to the telomere repeats, while the upstream limit can either be in the 70-bp repeats or the *ESAG*s (if the donor is in an ES). Segmental *VSG* conversion involves the copying of sequence from multiple, normally nonfunctional *VSG*s (pink, red, or green boxes) to generate a novel mosaic *VSG* in the ES. In transcriptional *VSG* switching, recombination appears not to be involved; instead, limited transcription at a silent *VSG* ES (indicated by a small arrow) becomes activated to generate fully active transcription, while the previously active ES is silenced.

https://doi.org/10.1371/journal.pbio.0060185.g002

Pathogenesis

The illness is chronic and can persist for many years.

There is an initial period of parasitemia, following which parasite is localized predominatly in the lymph nodes.

A painless chancre (trypanosomal chancre) appears on skin at the site of bite by tsetse fly, followed by intermittent fever, chills, rash, anemia, weight loss, and headache.

Systemic trypanosomiasis without central nervous system involvement is referred to as stage I disease. In this stage, there is hepatosplenomegaly and

lymphadenopathy, particularly in the posterior cervical region (Winterbottom's sign).

Hematological manifestations seen in stage I include anemia, moderate leucocytosis, and thrombocytopenia. High levels of immunoglobulins mainly immunoglobulin (Ig)M are a constant feature.

Stage II disease involves invasion of central nervous system. With the invasion of central nervous system, which occurs after several months, the 'sleeping sickness' starts. This is marked by increasing headache, mental dullness, apathy, and day time sleepiness. The patient falls into profound coma followed by death from asthenia.

Laboratory Diagnosis

Laboratory Diagnosis of Trypanosomiasis

Microscopy
Detection of Trypanosomes in-
- Wet mount preparation of lymphnode aspirate
- Giemsa stained thick peripheral blood smear or concentrated blood smear
- Wet mount, stained smear of CSF

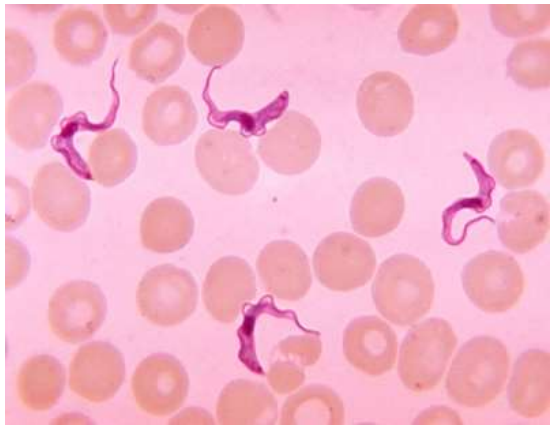
Culture
In Weinman's or Tobie's medium

Imaging
- **CT scan**
Shows cerebral edema
- **MRI**
Shows white matter enhancement

Serodiagnosis
- **Antibody detection**
  - IHA
  - IIF
  - ELISA
  - CATT
  - CFT
- **Antigen detection**
  - ELISA

Molecular diagnosis
- PCR

Others
- Animal inoculation
- Blood examination reveals anemia, monocytosis, raised ESRand reversed albumin: globulin ratio



Treatment

In the initial stages, when central nervous system is not involved i.e. stage I, pentamidine is the drug of choice for gambiense HAT (human African trypanosomiasis)

In patients with central nervous system involvement, melarsoprol (MelB) is the drug of choice, as it can cross the blood brain barrier. Dose: 2–3 mg/kg/per day (max. 40 mg) for 3–4 days

Treatment of Human African Trypanosomiasis

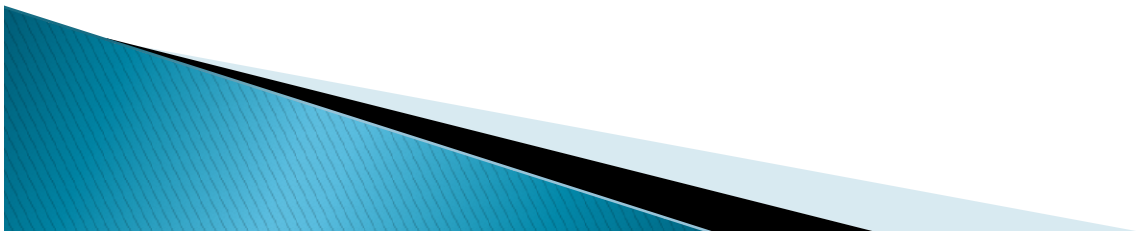
Causative organism	Clinical stage	
	I (Normal CSF)	II (Abnormal CSF)
T. brucei gambiense (West African)	Pentamidine	Eflornithine

Prophylaxis

Control is based on early diagnosis and treatment of cases to reduce the reservoir of infection.

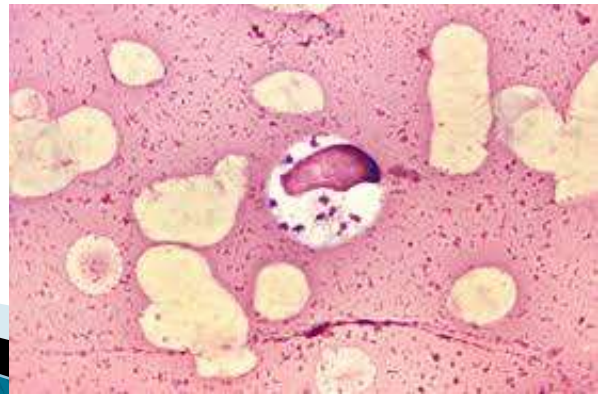
Control of tsetse fly population (most important preventive measure) by wide spraying of insecticides, traps, and baits impregnated with insecticides.

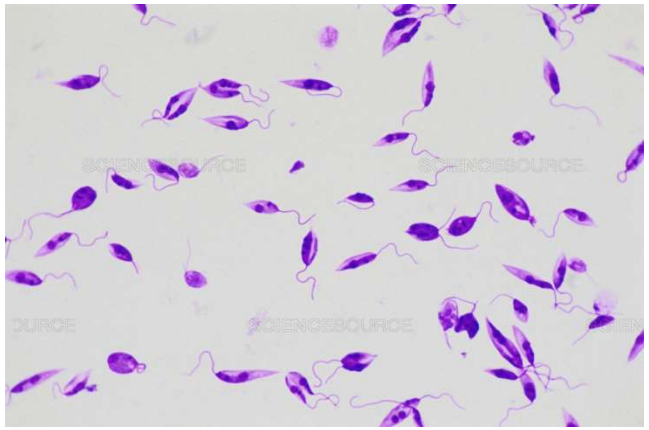
No vaccine is available.



Leishmania donovani

- *Leishmania donovani* is a species of intracellular parasites belonging to the genus *Leishmania*, a group of haemoflagellate kinetoplastids that cause the disease **leishmaniasis.** It is a human blood parasite responsible for visceral **leishmaniasis** or kala-azar, the most severe form of **leishmaniasis.**
- *L. donovani* complex with 2 species (*L. donovani*, *L. infantum* [also known as *L. chagasi* in the New World])
- **Phylum Sarcomastigophora**
- **Class Zoomastigophra**
- **Oder Kinetoplastida**
- Insect Vector Sand Fly *Phlebotomus*
- **Reservoir Dog**
- **Habitat**
- **Reticuloendothelial tissue**





Leishmania donovani

- The genus *Leishmania is named after Sir William Leishman,* who discovered the fl agellate protozoa causing Kalaazar, the Indian visceral leishmaniasis.

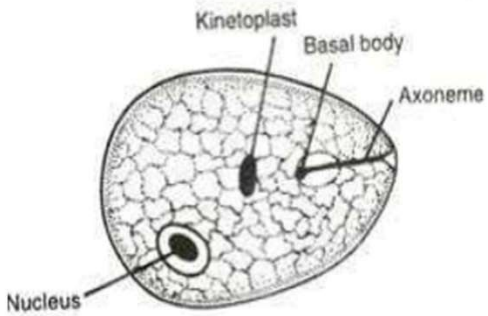
Table 5.5: *Leishmania* species Involved in Human Disease

Species	Disease	Geographical distribution	Vector	Reservoir	Transmission
Leishmania donovani	Visceral leishmaniasis (Kala-azar or dumdum fever)	Middle East, Africa, and Indian Subcontinent	*Phlebotomus argentipes, Phlebotomus orientalis*	Humans	Anthroponotic, occasionally zoonotic
Leishmania infantum	Visceral leishmaniasis, cutaneous leishmaniasis	Mediterranean Coast, Middle East, and China.	*Phlebotomus perniciousus, Phlebotomus ariasi, Phlebotomus papatasi*	Dog, fox, jackal, and wolf	Zoonotic
Leishmania chagasi	Visceral leishmaniasis	Tropical South America	*Lutzomyra longipalpis*	Fox and wild canines	Zoonotic
Leishmania tropica	Cutaneous Leishmaniasis (oriental sore, Baghdad boil)	Middle East and Central Asia	*Phlebotomus sergenti*	Humans	Anthroponotic
Leishmania major	Cutaneous leishmaniasis	Africa, Indian Subcontinent, and Central Asia	*Phlebotomus papatasi, Phlebotomus duboscqi*	Gerbil	Zoonotic
Leishmania aethiopica	Cutaneous and diffuse cutaneous leishmaniasis	Ethiopia and Kenya	*Phlebotomus longipes Phlebotomus pedifer*	Hydraxes	Zoonotic
Leishmania braziliensis complex	Mucocutaneous leishmaniasis (Espundia)	Tropical South America	*Lutzomyra umbratilis*	Forest rodents and peridomestic animals	Zoonotic
Leishmania mexicana complex	Mucocutaneous leishmaniasis (Chiclero's ulcer)	Central America and Amazon basin	*Lutzomyra olmeca, Lutzomyra flairscutellata*	Forest rodents and marsupials	Zoonotic

Morphology

- The parasite exists in two forms . ▪ a. Amastigote form ; In humans and other mammals. ▪ b. Promastigote form ; In sandfly and artificial culture.

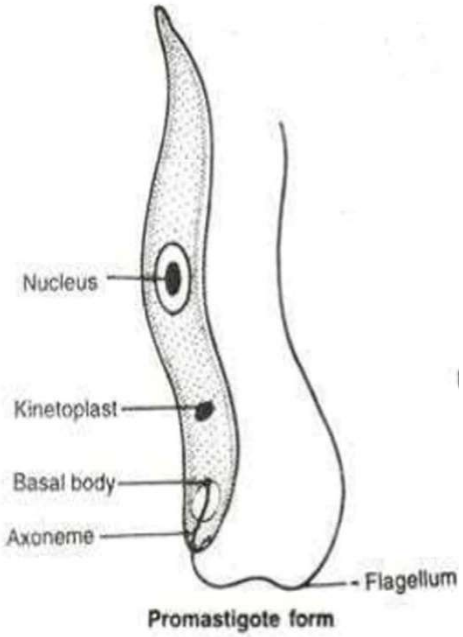
- The amastigote form (LD body) is an ovoid or rounded cell,
- about 2–4 µm in size (Fig. 5.9A).
- It is typically intracellular, being found inside macrophages,
- monocytes, neutrophils, or endothelial cells.
- They are also known as LD bodies.
- The large oval nucleus is present. Lying at the right a nucleus, Kinetoplast is present.
- Flagellum is absent



Amastigote form

Morphology

- It is a flagellar stage and is present in insect vector, sandfl y and in cultures.
- The promastigotes, which are intitially short, oval or Pearshaped forms, subsequently become long spindleshaped cells, 15–25 µm in length and 1.5–3.5 µm in breadth
- A single nucleus is situated at the center. The kinetoplast lies transversely near the anterior end.
- The fl agellum is single, delicate, and measures 15–28 µm. Promastigote forms, which develop in artifi cial cultures,
- They have the same morphology as in the sandfly.



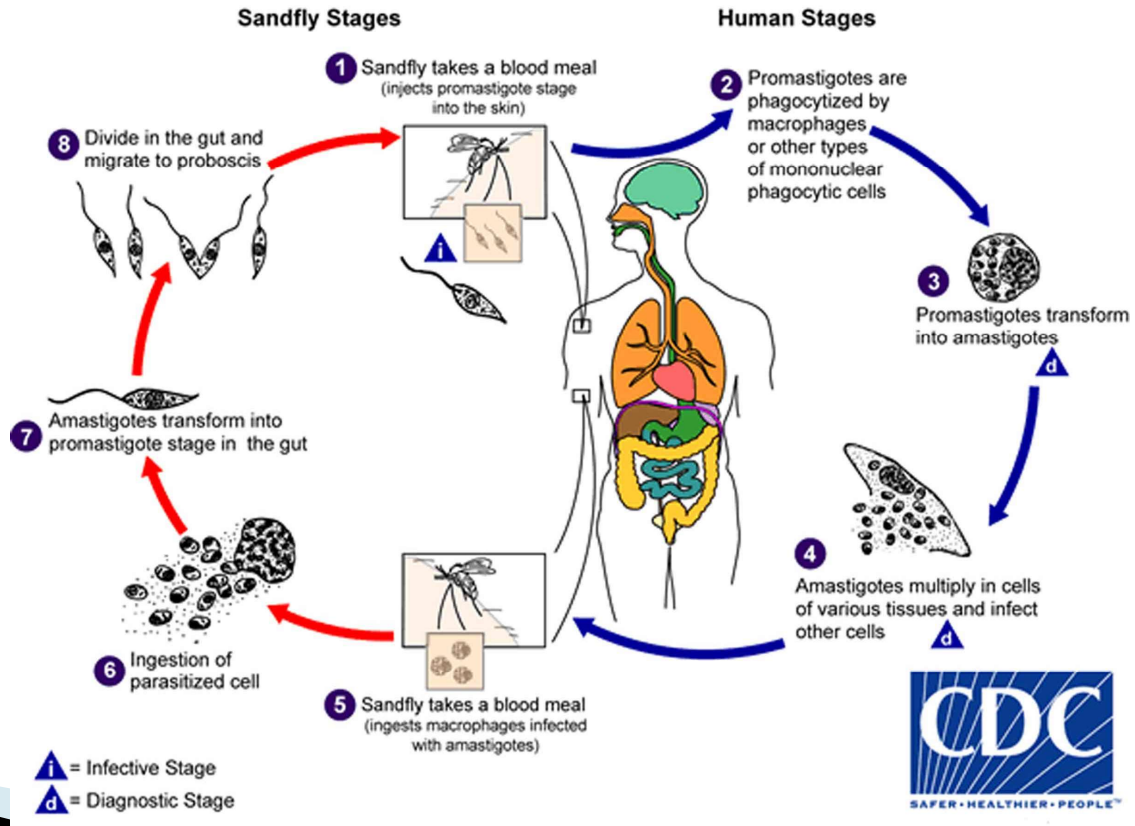
Life Cycle

L. donovani completes its life cycle in 2 hosts (Fig. 5.10).

Defi nitive host: Man, dog, and other mammals.

Vector: Female sandfl y (*Phlebotomus species).*

Infective form: Promastigote form present in midgut of female sandfl y.

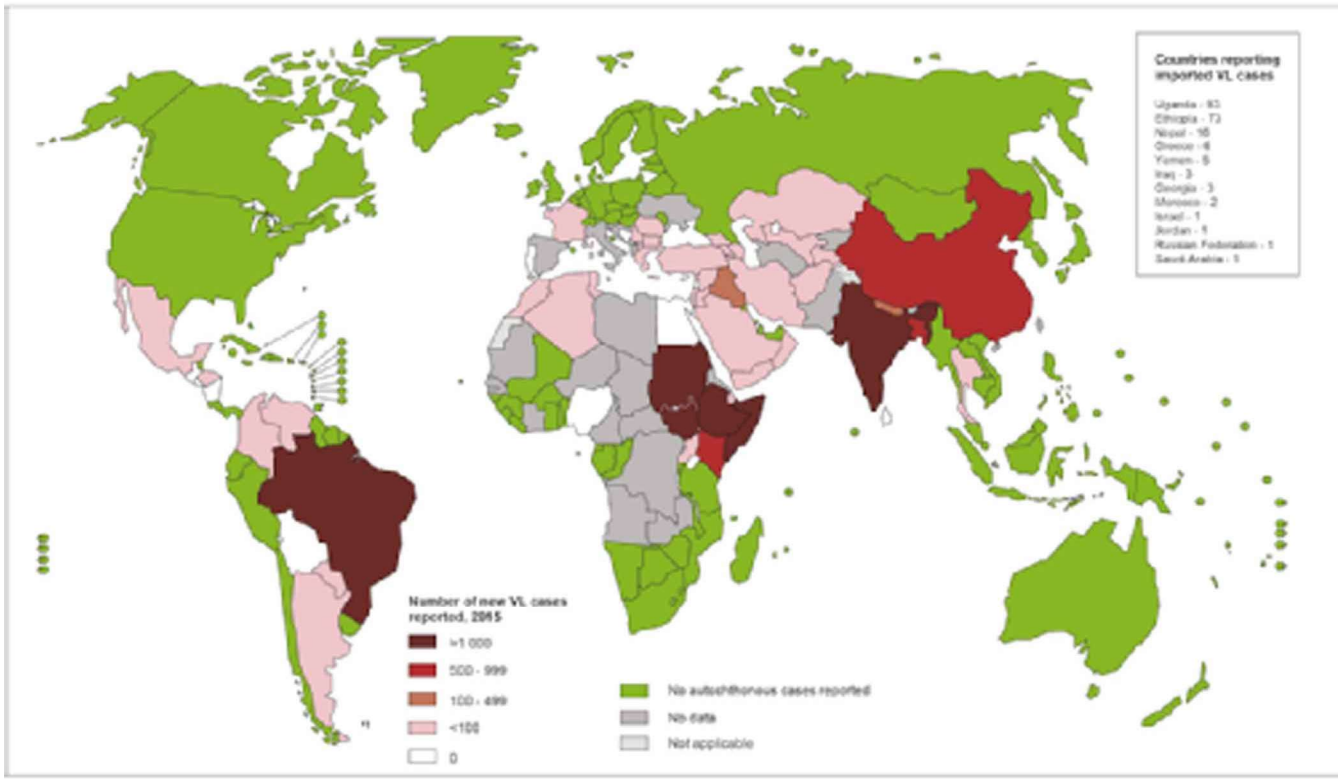


Epidemiology

- It is estimated that visceral leishmaniasis (VL) affects more than 100 million people worldwide, with 500,000 new cases and more than 50,000 deaths each year.[Although *L. donovani* is only the second-most prevalent *Leishmania* causing VL, it is the most dangerous form and directly fatal to humans. Over 90% of reported cases are from India, Bangladesh, Nepal, Sudan and Brazil.[In India it is prevalent in the eastern region including Bihar, West Bengal, eastern Uttar Pradesh, Assam and foothills of Sikkim.[It is responsible for tens of thousands of mortality among Africans in eastern and southern parts of Sudan. During the epidemic of 1984–1994 death toll was as high as 70% in he Sudanese population.[

Epidemiology

Status of endemicity of visceral leishmaniasis worldwide, 2015



The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement. © WHO 2017. All rights reserved

Data Source: World Health Organization
Map Production: Control of Neglected Tropical Diseases (NTD)
World Health Organization

World Health Organization

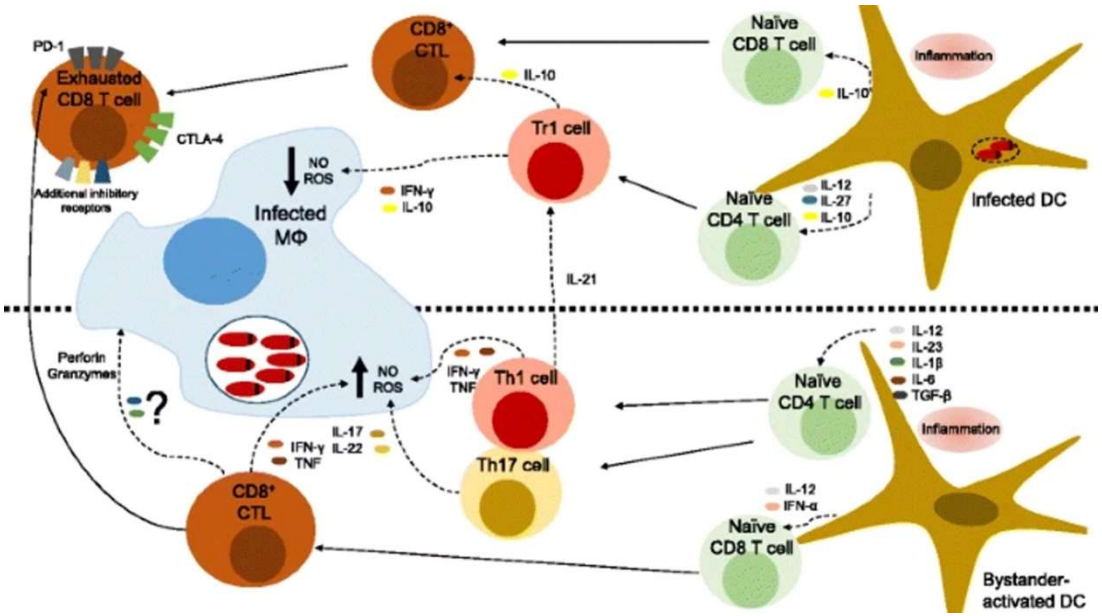
Pathogenesis

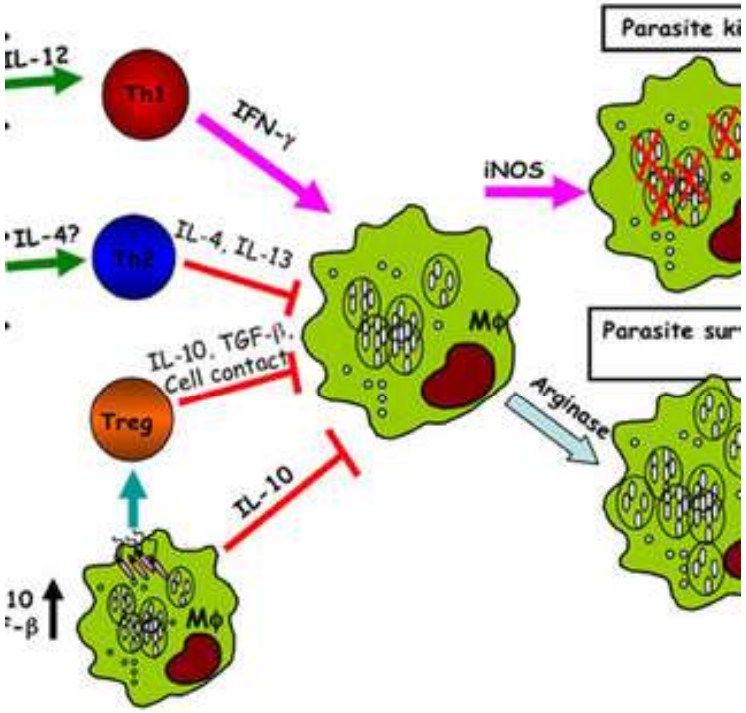
- *L. donovani causes visceral leishmaniasis or kala-azar.*
- Kala-azar is a reticuloendotheliosis resulting from the
- invasion of reticuloendothelial system by *L. donovani.*
- The parasitized macrophages disseminate the infection to all parts of the body.
- In the spleen, liver, and bone marrow particularly, the amastigotes multiply enormously in the fixed macrophages to produce a 'blockade' of the reticuloendothelial system. This leads to a marked proliferation and destruction of reticuloendothelial tissue in these organs.

Pathogenesis

- Amastigotes of *L. donovani* enter macrophages via a Rac1- and Arf6-dependent process, and are found in phagocytic vacuoles that interact with endosomes and lysosomes and acquire lysosomal features.[During phagocytosis by macrophages, the promastigotes inhibit the formation of the phagolysosome, a cellular product by which invading pathogens are removed. The promastigote can do this using its glycolipid lipophosphoglycan (LPG) on its cell membrane. LPG causes disorganisation of F-actin and disruption of phagosomal lipid microdomains.[They are capable of evading the microbicidal actions of macrophages, which can kill ordinary pathogens using reactive nitrogen and oxygen intermediates. They effectively subvert the production of reactive oxygen species. In this way the amastigotes are able to survive and replicate inside these primary immune systems. The parasites manipulate the cell signalling pathway of the macrophages, such as down-regulating of Jak/stat signalling, NO and TNF-α production, and also by blocking the NF-κB-dependent pathway.[There are two major mechanisms of immune evasion such as induction of immune suppressive IL-10 responses and the generation of poor and functionally impaired CD8(+) T-cell responses.[

Pathogenesis

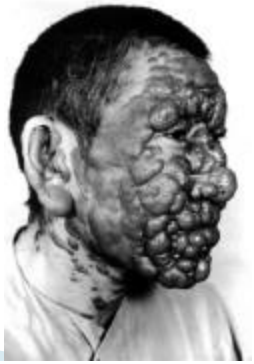




Symptoms

- Splenomegaly starts early and is progressive and massive .
- Hepatomegaly and lymphadenopathy also occur but are not so prominent.
- Skin becomes dry, rough, and darkly pigmented (hence, the name Kala-azar).
- The hair become thin and brittle.
- Cachexia with marked anemia, emaciation, and loss of weight is seen.
- Epistaxis and bleeding from gums are common.

- Post Kala-azar Dermal Leishmaniasis
- About 3-10% cases of patients of visceral leishmaniasis in endemic area develop PKDL, about an year or 2 after recovery from the systemic illnes
- PKDL is seen mainly in India and East Africa and not seen elsewhere.
- PKDL is a nonulcerative lesion of skin.



Laboratory Diagnosis

Laboratory diagnosis of *Kala-azar*

Direct evidence

Demonstration of LD bodies
In stained smears of thick blood film, splenic, bone marrow, and lymphnode aspirate

Culture
In NNN medium or Schneider's liquid medium to demonstrate promastigote form

Animal inoculation
In hamster or mice

Indirect evidence

Serodiagnosis

Detection of antigen
- ELISA

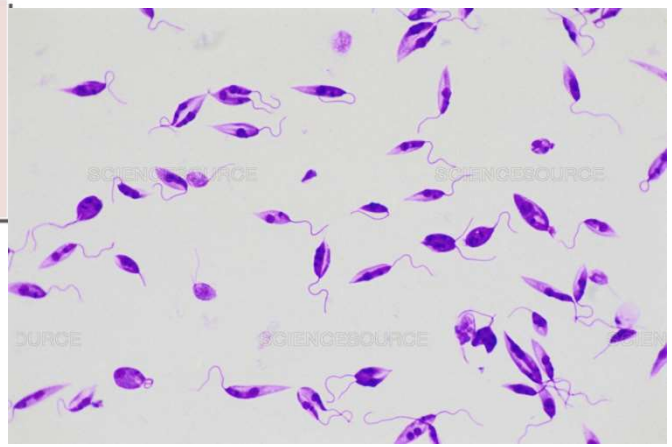
Detection of antibody
- CFT using WKK antigen
- DAT
- IFAT
- CIEP
- DOT–ELISA
- ICT using rK39 antigen

Molecular diagnosis
- DNA probe
- PCR

Non-specific serum test
- Aldehyde test
- Chopra's antimony test. The tests are positive in hypergammaglo-bulinemia

Skin test
Leishmanin or Montenegro test

Blood picture
- Anemia
- Progressive leucopenia
- Reverse albumin: globulin ratio

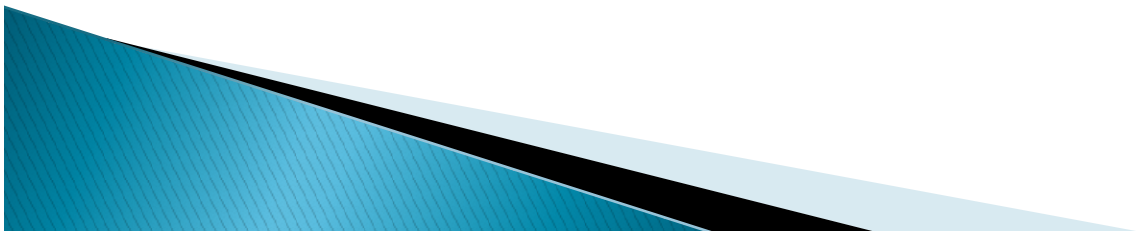


Treatment

- Kala-azar responds to treatment better than other forms of visceral leishmaniasis. The standard treatment consists pentavalent antimonial compound, which is the drug of choice in most of the endemic regions of the world, but there is resistance to a ntimony in Bihar in India, where amphotericin-B-deoxycholate or miltefosine is preferred.
- *Pentavalent Antimonial Compound*
- Two pentavalent antimonial (Sbv) preparations are available:
- Sodium stibogluconate (100 mg of Sbv/mL)
- Meglumine antimonate (85 mg of Sbv/mL).
- *Amphotericin B*
- Amphotericin B is currently used as a first-line drug in Bihar. In other parts of the world, it is used when initial antimonial treatment fails. Liposomal amphotericin B: It has been developed and used extensively to treat visceral leishmaniasis in all parts of the world. It is the only drug approved by the US Food a nd Drug Administration (FDA) for the treatment of visceral leishmaniasis;
- *Paromomycin*
- Paromomycin is an intramuscular aminoglycoside antibiotic with antileishmanial activity.
- *Miltefosine*
- Miltefosine is the first oral drug, approved for the treatment of leishmaniasis.
- Treatment of PKDL is same as that for visceral leishmaniasis.

Prophylaxis

- Early detection and treatment of all cases.
- Integrated insecticidal spraying to reduce sandfly
- population.
- Destruction of animal reservoir host in cases of zoontic
- Kala-azar.
- Personal prophylaxis by using anti-sandfly measures
- like, using thick clothes, bed nets, window mesh, or insect repellants and keeping the environment clean.
- No vaccine is available against Kala-azar.



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