

Trypanosoma

1. American trypanosomiasis (Chagas' disease)

Trypanosoma cruzi

African trypanosomiasis (sleeping sickness)

Trypanosoma gambiense

Trypanosoma rhodesiense

Trypanosoma cruzi

Disease

T. cruzi is the cause of Chagas' disease (American trypanosomiasis).

Important Properties

The life cycle involves the reduviid bug (Triatoma, cone-nose or kissing bug) as the vector & both humans & animals as reservoir hosts.

The animal reservoirs:

Domestic cats & dogs

Wild species such as the armadillo, raccoon,& rat.

Important Properties

The cycle in the reduviid bug begins with the ingestion of trypomastigotes in the blood of the reservoir host.

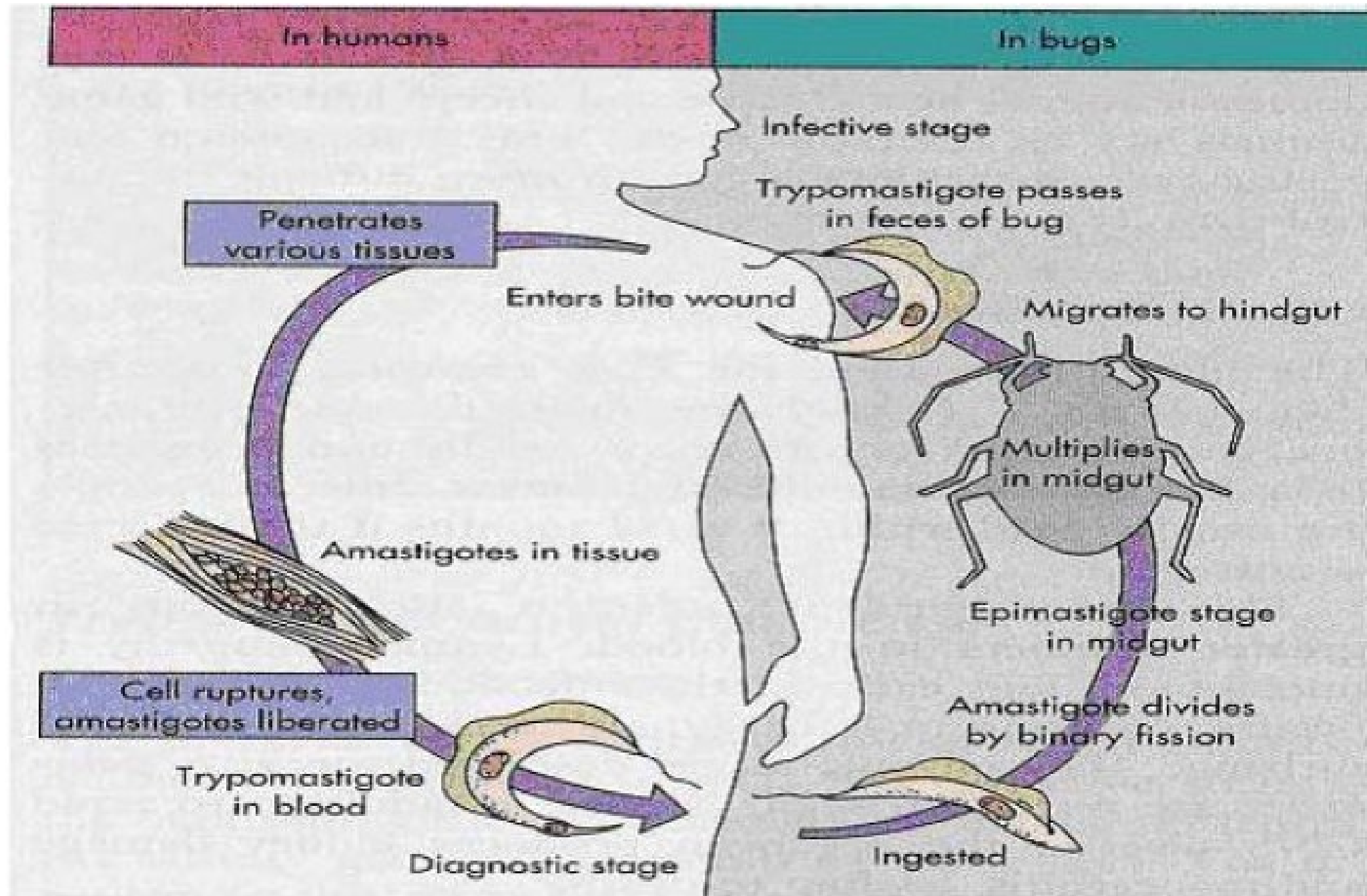
In the insect gut, they multiply & differentiate first into epimastigotes & then into trypomastigotes.

When the bug bites again, the site is contaminated with feces containing trypomastigotes, which enter the person's blood (or another reservoir) & form non flagellated amastigotes within host cells.

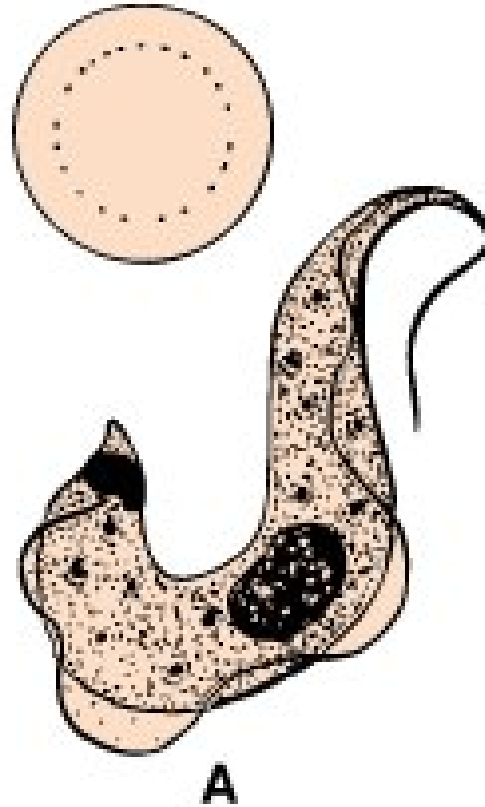
Many cells can be affected, but myocardial, glial, & reticuloendothelial cells are the most frequent sites.

To complete the cycle, amastigotes differentiate into trypomastigotes, which enter the blood & are taken up by the reduviid bug.

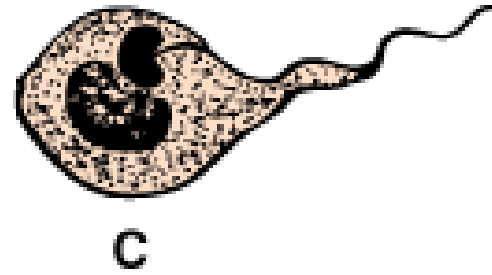
Life
cycle
of
Trypanosom
a cruzi



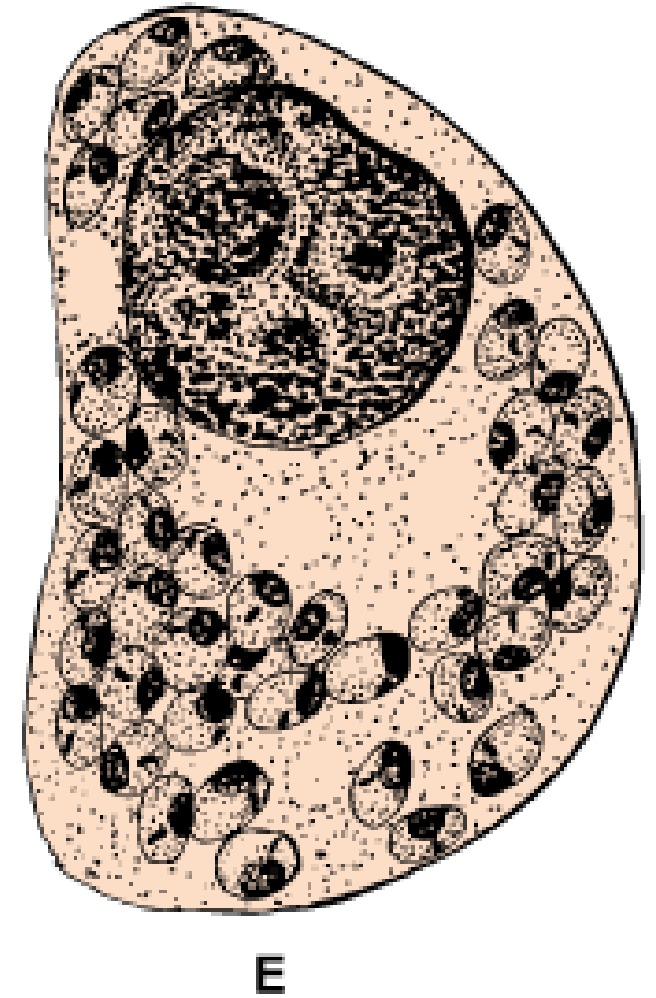
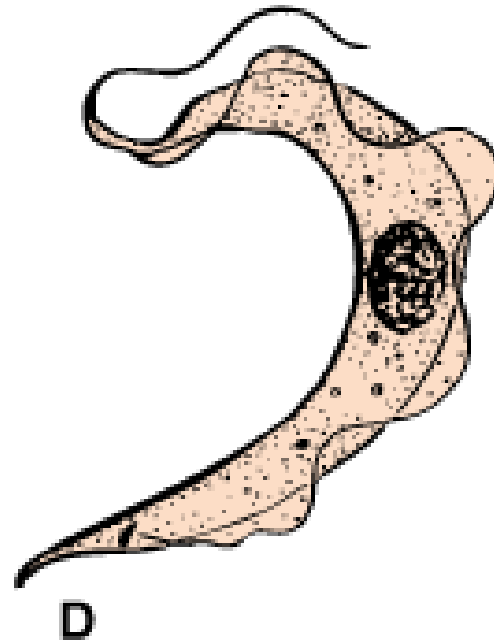
A: *Trypanosoma cruzi* trypomastigote found in human blood.



B: *T. cruzi* amastigotes found in cardiac muscle



c: *T. cruzi* epimastigote
found in reduviid bug.



E: *Leishmania donovani*
amastigotes within splenic
macrophages.



Trypanosoma cruzi –Amastigotes.
Arrow points to an amastigote (nonflagellated form) in
cytoplasm.

Pathogenesis

The amastigotes can kill cells & cause inflammation, consisting mainly of mononuclear cells.

Cardiac muscle is the most frequently & severely affected tissue.

In addition, neuronal damage leads to cardiac arrhythmias & loss of tone in the colon (megacolon) & esophagus (megaesophagus).

During the acute phase, there are both trypomastigotes in the blood & amastigotes intracellularly in the tissues.

In the chronic phase, the organism persists in the amastigote form.

Epidemiology

Chagas' disease occurs primarily in rural Central & South America.

Acute Chagas' disease rarely occurs in the United States.

Chronic form is seen with increasing frequency in immigrants from Latin America.

The disease is seen primarily in rural areas because the reduviid bug lives in the walls of rural huts & feeds at night. It bites preferentially around the mouth or eyes, hence the name "kissing bug."

Chagas' disease has occurred in the United States in recipients of either blood transfusions or organ transplants from infected donors.

The organism can also be transmitted congenitally from an infected mother to the fetus across the placenta.

Clinical Findings

The acute phase of Chagas' disease consists of facial edema & a nodule (chagoma) near the bite, coupled with fever, lymphadenopathy, & hepatosplenomegaly.

A bite around the eye can result in unilateral palpebral swelling called Romaña's sign.

The acute phase resolves in about 2 months.

Most individuals then remain asymptomatic, but some progress to the chronic form with myocarditis & megacolon.

Death from chronic Chagas' disease is usually due to cardiac arrhythmias & failure.

Chagoma



Trypanosoma
cruzi
(acute
Chagas,
Romana sign)



Laboratory Diagnosis

Acute disease is diagnosed by demonstrating the presence of trypomastigotes in thick or thin films of the patient's blood.

Both stained & wet preparations should be examined for motile organisms.

Laboratory Diagnosis

Because the trypomastigotes are not numerous in the blood, other diagnostic methods may be required, namely,

- (1) a stained preparation of bone marrow aspirate or muscle biopsy specimen (which may reveal amastigotes)
- (2) culture of the organism on a special medium
- (3) xenodiagnosis consists of allowing an uninfected, laboratory-raised reduviid bug to feed on the patient & after several weeks, examining the intestinal contents of the bug for the organism.

Laboratory Diagnosis

Serologic tests can be helpful also.

The indirect fluorescent antibody test is the earliest to become positive.

Indirect hemagglutination & complement fixation tests are also available.

Diagnosis of chronic disease is difficult because there are few trypomastigotes in the blood.

Xenodiagnoses & serologic tests are used.

Treatment

The drug of choice for the acute phase is nifurtimox, which kills trypomastigotes in the blood but is much less effective against amastigotes in tissue.

Benznidazole is an alternative drug.

There is no effective drug against the chronic form.

Prevention

Prevention involves protection from the reduviid bite, improved housing, and insect control.

No prophylactic drug or vaccine is available.

Blood for transfusion is tested for the presence of antibodies to *T. cruzi*.

Blood containing antibodies should not be used.



Trypanosoma gambiense
Trypanosoma rhodesiense

They are also known as:
Trypanosoma brucei gambiense
Trypanosoma brucei rhodesiense .

Trypanosoma gambiense & Trypanosoma rhodesiense

Disease

These organisms cause sleeping sickness (African trypanosomiasis).

Important Properties

The morphology & life cycle of the two species are similar.

The vector for both is the tsetse fly, *Glossina*, but different fly species are involved for each.

Humans are the reservoir for *T. gambiense*, whereas *T. rhodesiense* has reservoirs in both domestic animals (especially cattle) & wild animals (e.g., antelopes).

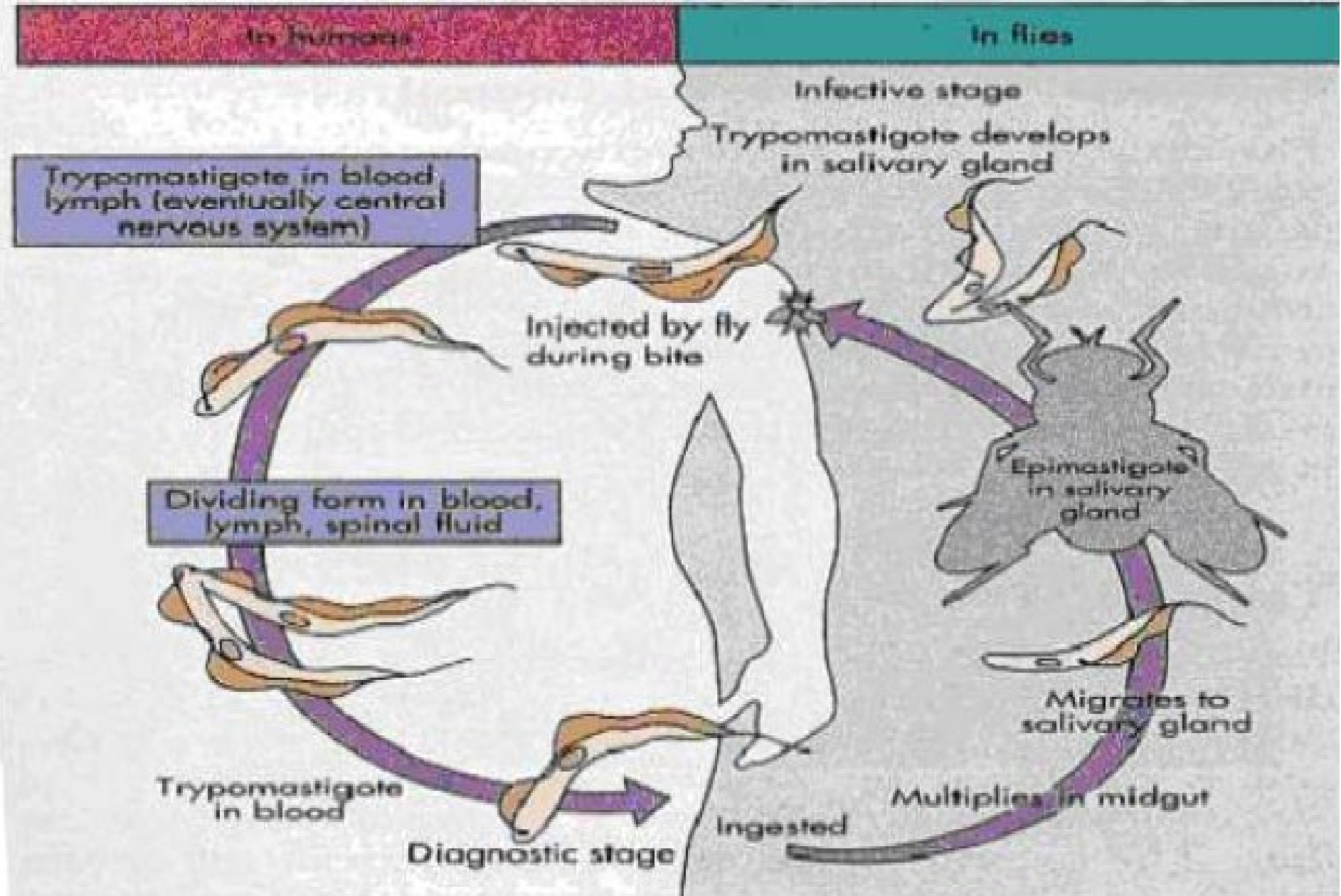
The 3-week life cycle in the tsetse fly begins with ingesting trypomastigotes in a blood meal from the reservoir host.

Important Properties

They multiply in the insect gut & then migrate to the salivary glands, where they transform into epimastigotes, multiply further, & then form metacyclic trypomastigotes, which are transmitted by the tsetse fly bite.

The organisms in the saliva are injected into the skin, where they enter the bloodstream, differentiate into blood-form trypomastigotes, & multiply, thereby completing the cycle

Note that these species are rarely found as amastigotes in tissue, in contrast to *T. cruzi* & *Leishmania* species, in which amastigotes are commonly found.



Life cycle of *Trypanosoma brucei*



Trypanosoma brucei –Trypomastigotes.
Arrow points to a trypomastigote (the flagellated form) in the
blood

Epidemiology

The trypomastigotes spread from the skin through the blood to the lymph nodes & the brain.

The typical somnolence (sleeping sickness) progresses to a coma as a result of demyelinating encephalitis.

In the acute form, a cyclical fever spike (approximately every 2 weeks) occurs related to antigenic variation. As antibody-mediated agglutination & lysis of the trypomastigotes occur, the fever subsides.

However, a few antigenic variants survive, multiply, & cause a new fever spike. This cycle repeats itself over a long period. The lytic antibody is directed against the surface glycoprotein.

Epidemiology

The disease is endemic in sub-Saharan Africa, the natural habitat of the tsetse fly.

Both sexes of fly take blood meals & can transmit the disease.

The fly is infectious throughout its 2- to 3-month lifetime.

T. gambiense is the species that causes the disease along water courses in west Africa, whereas

T. rhodesiense is found in the arid regions of east Africa.

Both species are found in central Africa.

Clinical Findings

Although both species cause sleeping sickness, the progress of the disease differs.

T. gambiense–induced disease runs a low-grade chronic course over a few years, whereas

T. rhodesiense causes a more acute, rapidly progressive disease that, if untreated, is usually fatal within several months.

Clinical Findings

The initial lesion is an indurated skin ulcer ("trypanosomal chancre") at the fly bite site.

After the organisms enter the blood, intermittent weekly fever & lymphadenopathy develop.

Enlargement of the posterior cervical lymph nodes (Winterbottom's sign) is commonly seen.

The encephalitis is characterized initially by headache, insomnia, & mood changes, followed by muscle tremors, slurred speech, & apathy that progress to somnolence & coma.

Untreated disease is usually fatal as a result of pneumonia.



Tsetse fly
(A)



(B) a trypanosomal chancre in a patient
with East African trypanosomiasis

Trypanosoma brucei
(Winterbottom's
sign)



Laboratory Diagnosis

During the early stages, microscopic blood examination (either wet films or thick or thin smears) reveals trypomastigotes.

An aspirate of the chancre or enlarged lymph node can also demonstrate the parasites.

The presence of trypanosomes in the spinal fluid, coupled with an elevated protein level & pleocytosis, indicates that the patient has entered the late encephalitic stage.

Serologic tests, especially the ELISA for IgM antibodies, can be helpful.

Treatment

Treatment must be initiated before the development of encephalitis, because suramin, the most effective drug, does not pass the blood-brain barrier well.

Suramin will effect a cure if given early.

Pentamidine is an alternative drug.

If CNS symptoms are present, suramin (to clear the parasitemia) followed by melarsoprol should be given.

Prevention

The most important preventive measure is protection against the fly bite, using netting & protective clothing.

Clearing the forest around villages & using insecticides are helpful measures.

No vaccine is available.



Leishmania

Leishmania

The genus *Leishmania* includes four major pathogens:

- 1. *Leishmania donovani*,
- 2. *Leishmania tropica*,
- 3. *Leishmania mexicana*,
- 4. *Leishmania braziliensis*.

Leishmania donovani

Disease

L. donovani is the cause of kala-azar (visceral leishmaniasis).

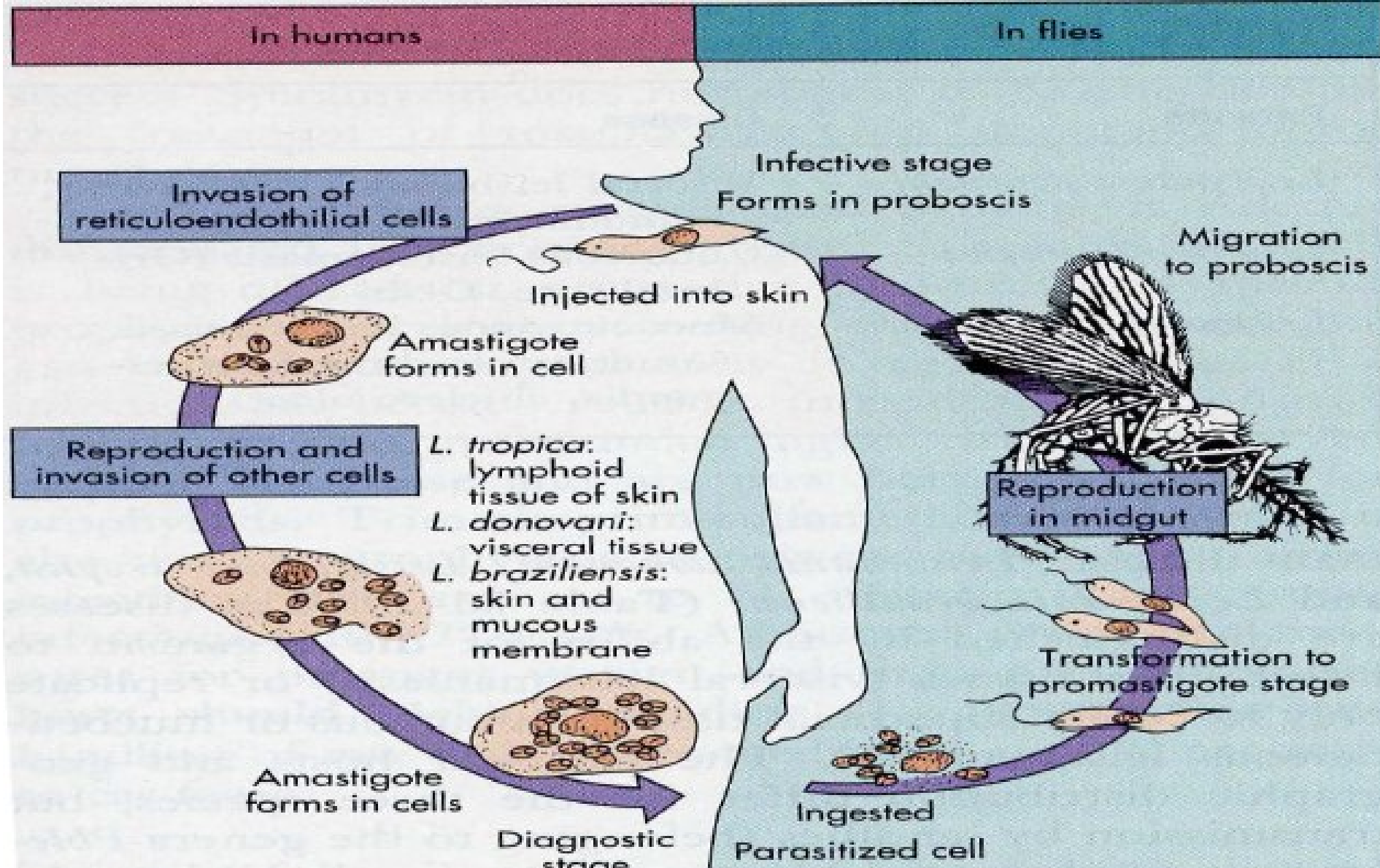
Important Properties

The life cycle involves the sandfly as the vector

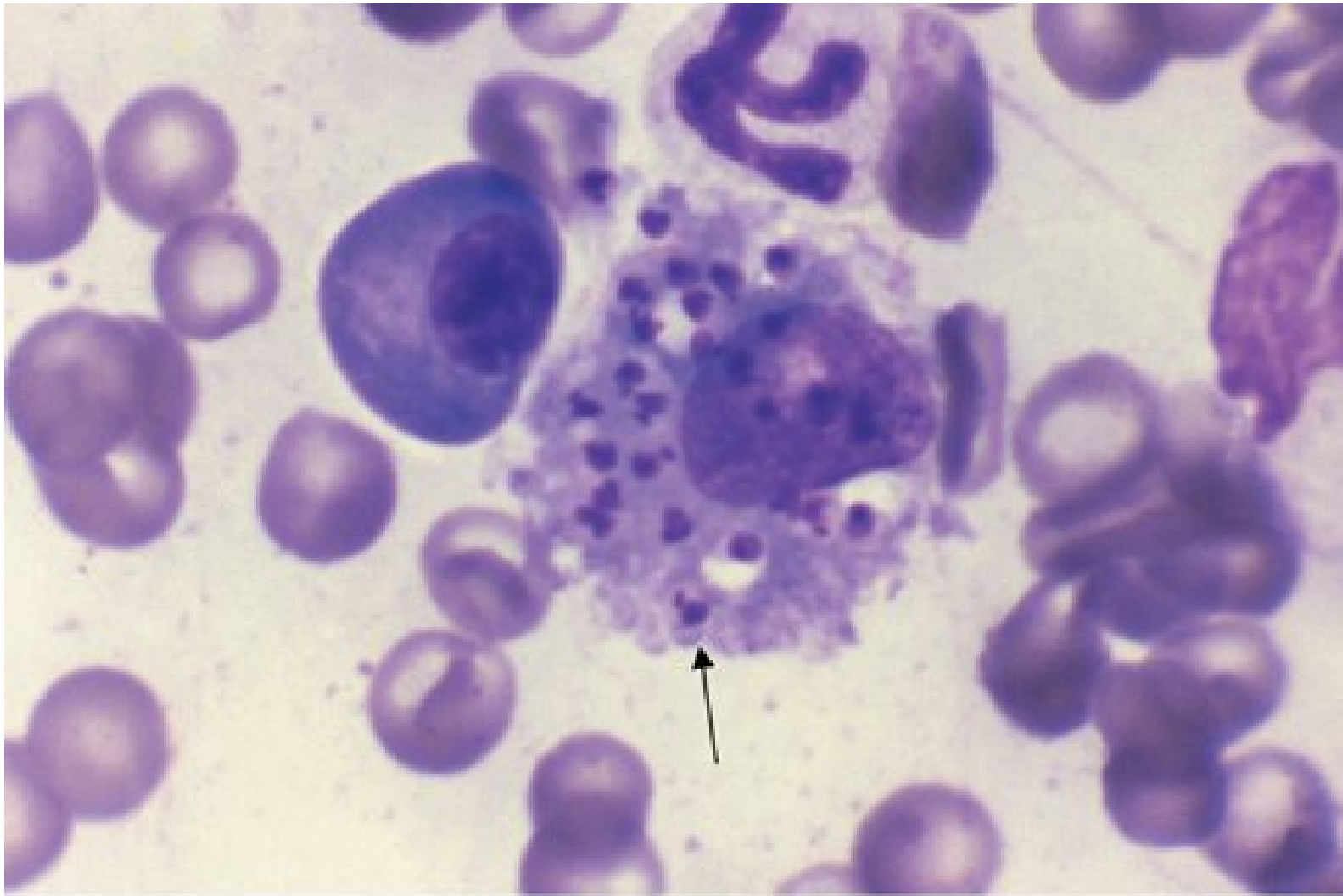
Only female flies are vectors because only they take blood meals (a requirement for egg maturation).

A variety of mammals such as dogs, foxes, & rodents as reservoirs.

When the sandfly sucks blood from an infected host, it ingests macrophages-containing amastigotes



Life cycle of *Leishmania* species



Leishmania donovani—Amastigotes.
Arrow points to an amastigote (nonflagellated form) in
cytoplasm of bone marrow cell.

Important Properties

After the dissolution of the macrophages, the freed amastigotes differentiate into promastigotes in the gut.

They multiply & then migrate to the pharynx, where they can be transmitted during the next bite.

The cycle in the sandfly takes approximately 10 days.

Shortly after an infected sandfly bites a human, the promastigotes are engulfed by macrophages, where they transform into amastigotes

Amastigotes can remain in the cytoplasm of macrophages because they can prevent the fusion of the vacuole with lysosomes.

The infected cells die & release progeny amastigotes that infect other macrophages & reticuloendothelial cells.

The cycle is completed when the fly ingests macrophages containing the amastigotes.

Pathogenesis

In visceral leishmaniasis, the organs of the reticuloendothelial system (liver, spleen, & bone marrow) are the most severely affected.

Reduced bone marrow activity, coupled with cellular destruction in the spleen, results in anemia, leukopenia, & thrombocytopenia.

This leads to secondary infections & a tendency to bleed.

The striking enlargement of the spleen is due to a combination of proliferating macrophages & sequestered blood cells.

The marked increase in IgG is neither specific nor protective.

Epidemiology

Kala-azar occurs in three distinct epidemiologic patterns.

1. In one area, which includes the Mediterranean basin, the Middle East, southern Russia, & parts of China, the reservoir hosts are primarily dogs & foxes.
In sub-Saharan Africa, rats & small carnivores, e.g., civets, are the main reservoirs.
3. A third pattern is seen in India & neighboring countries (& Kenya), in which humans appear to be the only reservoir.

Clinical Findings

IP can differ from several months to over a year in most cases.

Symptoms begin with
intermittent fever
weakness
weight loss.

Massive enlargement of the spleen is characteristic.

Hyperpigmentation of the skin is seen in light-skinned patients (kala-azar means black sickness).

Clinical Findings

The course of the disease runs for months to years. Initially, patients feel reasonably well despite the persistent fever.

As anemia, leukopenia, & thrombocytopenia become more profound, weakness, infection, & gastrointestinal bleeding occur.

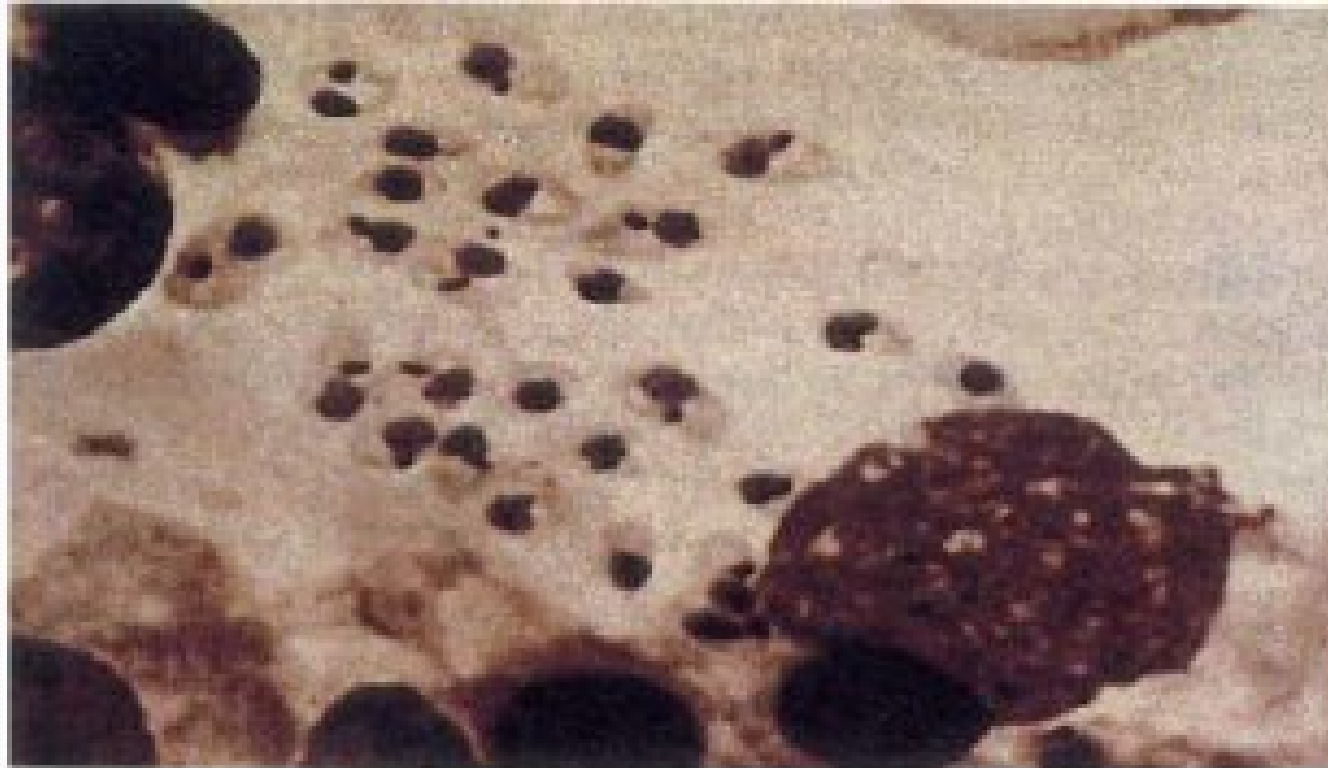
Untreated severe disease is nearly always fatal due to secondary infection.

Visceral
leishmaniasis
Kala Azar



Laboratory Diagnosis

Diagnosis is usually made by detecting amastigotes in a bone marrow, spleen, or lymph node biopsy or "touch" preparation.



Giemsa-stained amastigotes
(Leishmania Donovan bodies)

Laboratory Diagnosis

The organisms can also be cultured.

Serologic (indirect immunofluorescence) tests are positive in most patients. Although not diagnostic, a very high IgG concentration indicates infection.

A skin test using a crude homogenate of promastigotes (leishmania) as the antigen is available.

The skin test is negative during active disease but positive in recovered patients .

Treatment

The treatment is sodium stibogluconate, a pentavalent antimony compound.

Amphotericin B is also effective.

With proper therapy reduces the mortality rate to near 5%.

Recovery results in permanent immunity.

Prevention

Prevention involves protection from sandfly bites (use of netting, protective clothing, & insect repellents) & insecticide spraying.

Leishmania tropica, Leishmania mexicana, & Leishmania braziliensis

Disease

L. tropica & *L. mexicana* both cause cutaneous leishmaniasis; the former organism is found in the Old World, whereas the latter is found only in the Americas.

L. braziliensis causes mucocutaneous leishmaniasis, which occurs only in Central & South America.

Important Properties

Sandflies are the vectors for these three organisms, as they are for *L. donovani*.
Forest rodents are their main reservoirs.

The life cycle of these parasites is essentially the same as that of *L. donovani*.

Pathogenesis

The lesions are confined to:

The skin in cutaneous leishmaniasis

The mucous membranes, cartilage, & skin in mucocutaneous leishmaniasis.

A granulomatous response occurs, & necrotic ulcer forms at the bite site.

The lesions tend to become superinfected with bacteria.

Epidemiology

Old World cutaneous leishmaniasis (Oriental sore, Delhi boil), caused by *L. tropica*, is endemic in the Middle East, Africa, & India.

New World cutaneous leishmaniasis (chicle ulcer, bay sore), caused by *L. mexicana*, is found in Central & South America.

Mucocutaneous leishmaniasis (espundia), caused by *L. braziliensis*, occurs mostly in Brazil & Central America, primarily in forestry & construction workers.

Clinical Findings

Cutaneous leishmaniasis

The initial lesion of cutaneous leishmaniasis is a red papule at the bite site, usually on an exposed extremity.

This enlarges slowly to form multiple satellite nodules that coalesce & ulcerate.

There is usually a single lesion that heals spontaneously in patients with a competent immune system.

However, if CMI does not develop in certain individuals, the lesions can spread to involve large areas of skin & contain enormous numbers of organisms.



Clinical Findings

Mucocutaneous leishmaniasis begins with a papule at the bite site, but then metastatic lesions form, usually at the mucocutaneous junction of the nose & mouth.

Disfiguring granulomatous, ulcerating lesions destroy nasal cartilage but not adjacent bone.

These lesions heal slowly, if at all.

Death can occur from secondary infection.



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Laboratory Diagnosis

Microscopically by demonstrating the presence of amastigotes in a smear taken from the skin lesion.

The leishmanin skin test becomes positive when the skin ulcer appears & can be used to diagnose cases outside the area of endemic infection.

Treatment

The drug of choice is sodium stibogluconate, but the results are frequently unsatisfactory.

Prevention

Prevention involves protection from sandfly bites by using netting, window screens, protective clothing, and insect repellents.