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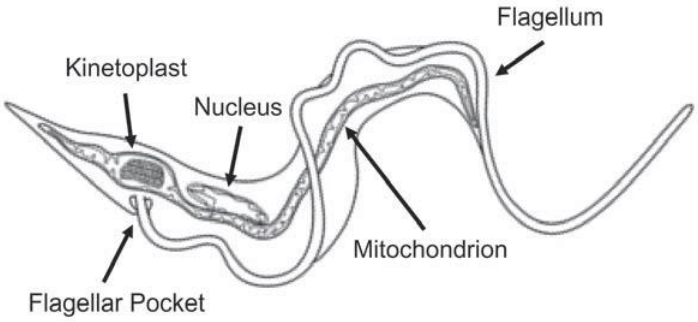
Trypanosome spp.

There are three type of trypanosome species which are pathogenic for human include:

- Trypanosome cruzi: cause American trypanosomiasis
- Trypanosome rhodesiense : cause African trypanosomiasis
- Trypanosome gambiense : also cause African trypanosomiasis

❖ *Trypanosome cruzi:* (chagas disease)

*Trypanosomacruzi*is a protozoan parasite, possessing the organelles ofall eukaryotes including a membrane bound nucleus and mitochondrion. A single membrane-bound flagellum emerges from the trypanosome's flagellarpocket and runs the length of the cell, attached to the cell body membranevia a desmosome-like adhesive junction. At its origin, the flagellum is physicallyconnected to the mitochondrial DNA, which resides in a specializedregion of the mitochondrion termed the kinetoplast.

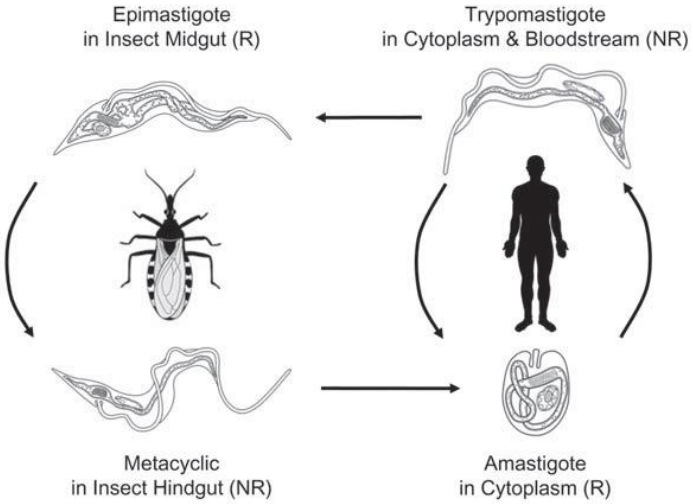


American trypanosomiasis is a vector-borne infection caused by the protozoanparasite *Trypanosomacruzi*. Also called Chagas disease, it is found only on the American continent. The parasite alternately infects triatomine insects(reduviid, assassin or "kissing" bugs) and a wide range of vertebrate hosts in acomplex lifecycle.

***T. cruzi*Life Cycle and Transmission**:

*T. cruzi*has four distinct life cycle stages:

- Within the midgut of the reduviid bug, parasites replicate as flagellated **epimastigotes (**epi).
- As (epis) replicate and increase in number they migrate to the hindgut of the bugwhere they differentiate into infective metacyclic**trypomastigotes (meta).**
- **(Metas**) are discharged in the feces of the bug as they take a blood meal. Infection results from the contamination of the insect bite or open wounds, mucous membranes or conjunctiva with parasite laden bug feces.
- Once in the vertebrate host, the (meta), which is unable to replicate, must invade host cell within which it can differentiate into the replicating **amastigote (ama).**
- During invasion the meta is initially present within a membrane bound vacuole, but it escapes this vacuole and differentiates into the aflagellated (ama), which divides in the cytoplasm.
- After a number of rounds of replication, the (amas) fill the cytoplasm and differentiate into motile trypomastigotes**(tryp**), which lyse the infected cell and escape to infect adjacent cells or disseminate throughout the body via the bloodstream and lymphatics.
- (Tryps), like (metas), cannot replicate and must invade host cells and differentiate into (amas) to survive. Alternatively, they may be taken up by a triatomine insect during a blood meal and differentiate into **(epis)** in the insect midgut, thereby completing the life cycle.
- Within the vertebrate host, parasites can infect any nucleated cell, but have a predilection for muscle, particularly of the heart and gastrointestinal tract.



Life cycle of T.cruzi (R: replicating, NR: nonreplicating)

Pathogenesis of Chagas Disease

1. Acute *T. cruzi* infection results from the contamination of wounds or mucous membranes with insect feces containing expelled infective parasites.
2. Locally deposited parasites bind to and invade host tissue and transform into and replicate as intracellular amastigotes.
3. Infection leads to the formation of parasite "pseudocysts," so named because the amastigote nests are intracellular.
4. This stimulates a localized inflammatory response mediated predominantly by lymphocytes and macrophages.
5. Lymphatic drainage of the infected area into regional lymph nodes results in activation and proliferation of cells, resulting in regional lymphadenopathy.
6. As the process continues, the amastigote transform into trypomastigotes, escape host cells and disseminate throughout the body.
7. Infection and lysis of liver cells results in transient increases in serum liver enzyme levels.
8. In chronic infection, tissue parasites are difficult to detect but significant interstitial fibrosis occurs, damaging the affected tissue

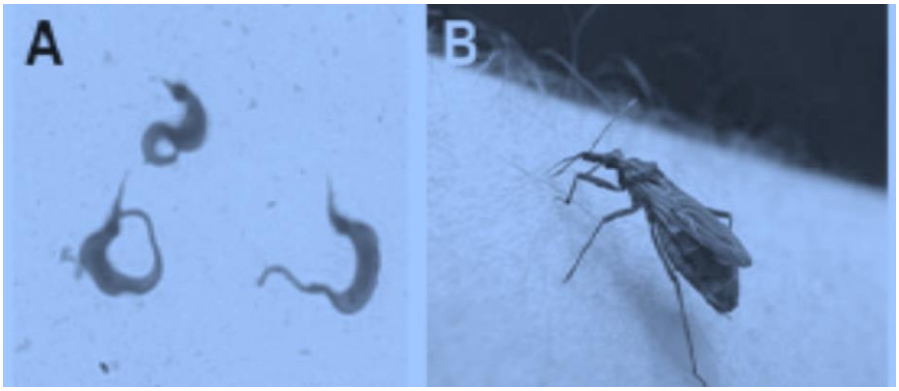
Clinical Syndromes of Chagas Disease

- Acute infection by *T. cruzi* is marked by the development of localized swelling and erythema at the site of the insect bite, which is termed a **chagoma**. This is a result of the local replication of parasites and the influx of fluid and inflamatory cells into the infected area.
- Infection through the conjunctiva can result in periorbital swelling, termed **Romana's sign** .
- As parasites disseminate patients experience nonspecific symptoms such as fever, malaise and anorexia.

- Parasite infestation of peripheral tissues can give rise to hepatosplenomegaly and,in some cases, meningeal signs.
- Initial infection of heart tissue can lead to acute myocarditis and cardiac sudden death due to parasitization of the cardiac conduction system.
- The signs and symptoms of acute *T. cruzi*infection can last from days to weeks but are often unrecognized due to their nonspecific nature.
- The disease then proceeds to a quiescent phase lasting months to years and often decades,prior to the onset of chronic disease.
- The two disorders that occur in chronically infected patients are cardiomyopathy and megaorgansyndromes.
- Heart involvement lead to fibrosis of heart muscles and heart failure
- In the gastrointestinal tract, chronic infection lead to massivedilatation of the esophagus and/or colon
- Clinical disease in this setting is often fulminant with moreextensive involvement of the central nervous system.

Diagnosis of disease

- The presence of, or recent historyof a chagoma or Romana's sign are indicators of recent infection.
- The mainstay of diagnosis is detection of trypomastigotes in the blood or the presence of *T.cruzi*-specific antibodies in serum to indicate acute or chronic infection, respectively. The shape of *T.cruzi* appear as U or C shape in blood film.
- Heavyparasite burdens in the tissues of such patients can permit diagnosis via direct examination of tissue (lymph nodes, or bone marrow) or fluids (cerebrospinal orpericardial fluid)
- these specimens can be cultured in vitro in liquidmedium or by growth within uninfected insect vectors (xenodiagnoses)
- in chronic infection parasites are frequently not detectable in the blood, and the presence of *T. cruzi*IgG, using commercial immunoassays, ELISA, complementfixation, or hemagglutination based tests, establishes the diagnosis.
- Direct detection of parasites using PCR.



A: C or U shape of parasite, B: reduviid bug(kissing bug)

Treatment

Benznidazole, an imidazole and Nifurtimox, a nitrofuran are the two agents approved for treatment of Chagas disease

Prevention of *T. cruzi*Infection

- Limiting exposure to *T. cruzi* infected insects and blood is the mainstay of the prevention of Chagas disease.
- Persons living in or traveling to areas endemicfor *T. cruzi* should avoid residing in substandard housing frequented by reduvii bugs. The use of bed nets and insect repellent are also recommended for this purpose.
- Barrier protection for those working with *T. cruzi* in the laboratory setting, such as protective clothing, gloves and eyewear is a must.
- Since the incidence of transfusion- and transplantation-associated *T. cruzi* infection is increasing in theAmericas, serologic screening of donated blood seems advisable

African Trypanosomiasis

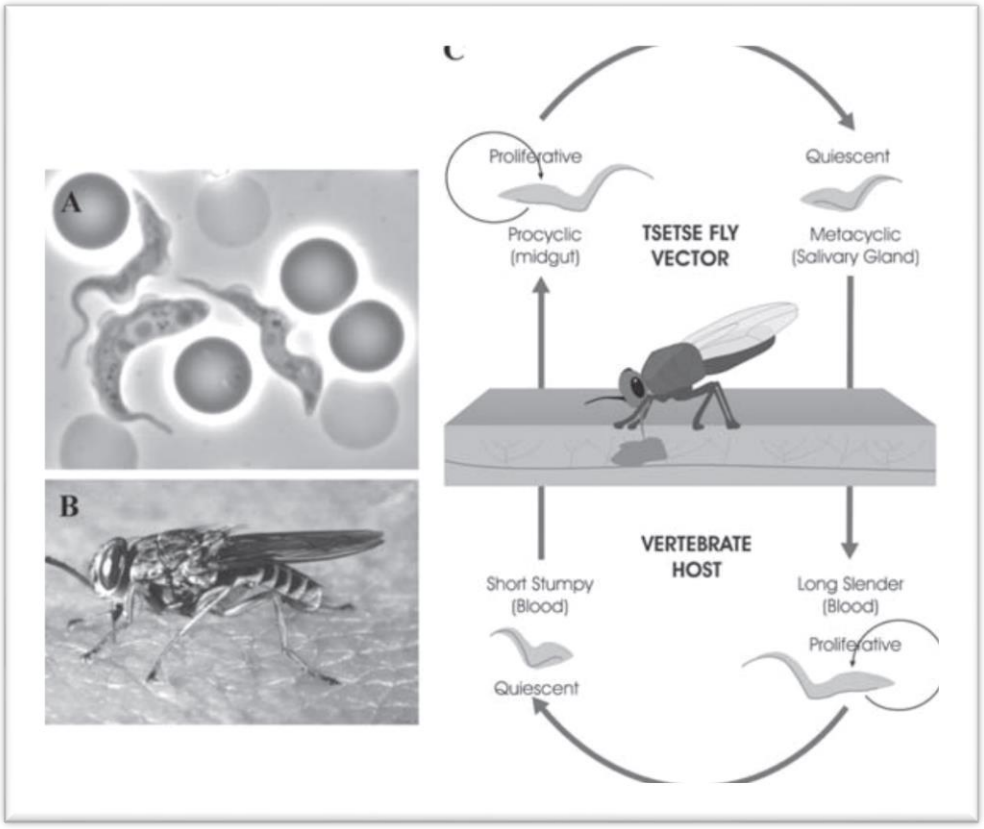
African trypanosomes are extracellular protozoan parasites that cause lethal infections in humans and livestock in large parts of sub-Saharan Africa. The responsible flagellated parasite (*Trypanosoma sp*.) and relies on tsetse flies for its transmission. Two species of this parasite are ***Trypanosomabruceirhodesiense*and *Trypanosomabruceigambiense*.**

Although both subspecies are pathogenic to human, they differ significantly in virulence and geographical occurrence. *T. b. gambiense* causes chronic infections in **West and Central Africa which can persist up to 10 years** while *T. b. rhodesiense* is more prevalent **in Eastern Africa and mostly results in acute human infections that can be lethal within a few months**. The diseases caused by both subspecies are

categorized under human African trypanosomiasis, better known as sleeping sickness and are responsible for an estimated 50,000 deaths a year

Life cycle

- The arthropods are obligate bloodsucking insects (genus *Glossina*), that get infected through feeding on a parasitized host and accommodate the trypanosome during their entire lifespan.
- trypanosomes colonize the midgut, proliferate and undergo differentiation while directionally migrating towards the insect salivary glands.
- The vertebrate-infective metacyclic form of the parasite resides in the salivary glands or mouthparts of the fly, using the blood feeding behaviour for its transmission to a new host.
- Upon transmission to the vertebrate host, trypanosomes will transform into actively proliferating (long slender) forms to allow a systemic colonization of the host.
- trypanosomes in the bloodstream become quiescent (short stumpy) and pre-adapt to uptake and subsequent survival in the tsetse fly



Pathology

- African trypanosomiasis is lethal unless the parasite is completely eliminated from the body of the infected individual by drug treatment.

- In human infections, mortality results from neurological complications after penetration of the parasite into the central nervous system.
- Human African trypanosomiasis (HAT) is characterized by two disease stages:
- During the first (haemolymphatic) stage of the infection, parasites will proliferate in the blood and the lymphatic circulation. Symptoms at this stage are nonspecific and include fever, lymphadenopathies, splenomegaly and endrocrine disorders.
- Systemic inflammation finally leads to increased blood-brain barrier(BBB) permeability allowing parasites to penetrate the central nervous system and cerebrospinal fluid, ushering in the second (encephalitic) stage of HAT.
- Thesymptoms of this stage include sensory, motoric and psychic disturbances, neuroendocrineabnormalities and disturbed circardian rhythms, eventually resulting in coma and death.
- The disturbed day-night cycles in the late stage of infection are characteristic for sleeping sickness

Diagnosis

- diagnosis of *African Trypanosomiasis* first stage HAT mainly relies on microscopic detection of trypanosomes in blood smears and lymph node aspirates.
- Second stage HAT diagnosis is based on parasite detection or lymphocyte counting in the cerebrospinal fluid (CSF) taken by lumbar puncture.
- Card agglutination test for trypanosomiasis (**CATT)** is the preferred first-line serological detection method for *T. b. gambiense*, but must be followed by parasitological confirmation and stage determination.
- T. b. gambiense specific polymerase chain reaction (PCR) was developed,based on the presence of a T. b. gambiense-specific gene

Treatment

Suramineis a polysulphonated symmetrical naphthalene derivative first used to treat HAT in 1922. The drug is administered through slow intravenous injection,