- ***Trypanosoma SPP*.**

Taxonomic Classification of *Trypanasoma* spp.

- **Kingdom:** Protozoa
- **Phylum:** Sarcomastigophora
- **Subphylum** : Mastigophora
- **Class:** Zoomastigophora
- **Order:** Kinetplastida
- **Family:** Trypanosomatidae
- **Genus:** *Trypanosoma*

- **Disease :** typansomiasis

1- **West African Trypanosomiasis:** " West African Sleeping Sickness" caused by *T. brucei gambiense*.

2- **East African Trypanosomiasis:** " East African Sleeping Sickness" caused by *T. brucei rhodesiense*.

Chronic form: caused by *T. brucei gambiense.* While **Acute Form** is caused by *T. brucei rhodesiense.*

- African Sleeping Sickness *is* the 3rd important parasitic disease globally after Malaria & Schistosomiasis,West African Sleeping Sickness is in regions along riverside while East African Sleeping Sickness is in Forest regions (Savannas).

3- American trypanosomiasis (Chagas' disease) is caused by *Trypanosoma cruzi*

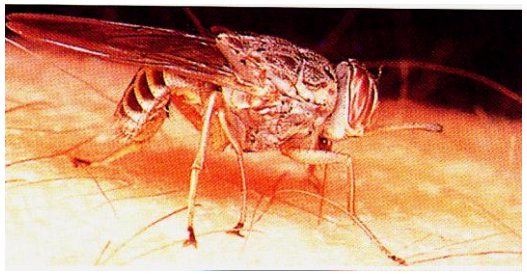
Causes

Trypanosomiasis

- **West African Trypanosomiasis**
- **East African Trypanosomiasis**
- **American Trypanosomiasis**

T.brucei gambiense *T.brucei rhodesiense* → **Sleeping sickness**

Transmitted by
Glossina (tsetse fly)



T.cruzi → **Chagas' disease**

Transmitted by
Triatoma (winged bug)

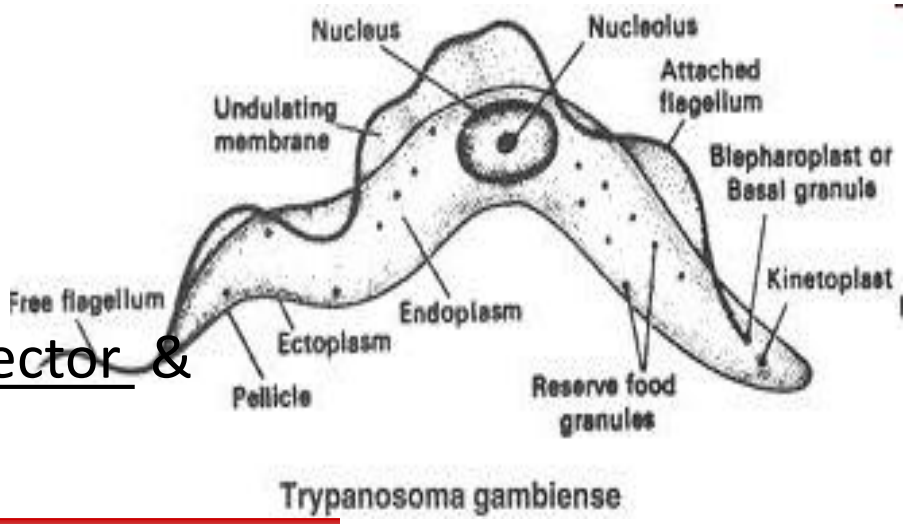
T. brucei complex

Morphology

Exist into 2 inter forms:

Trypomastigote in Blood/ Lymph / tissue space of various organs & C.N.S is terminal & fatal

Epimastigote in salivary gland of vector & Culture media.



Trypanosoma gambiense

Trypomastigote (Polymorphic Trypanosomes

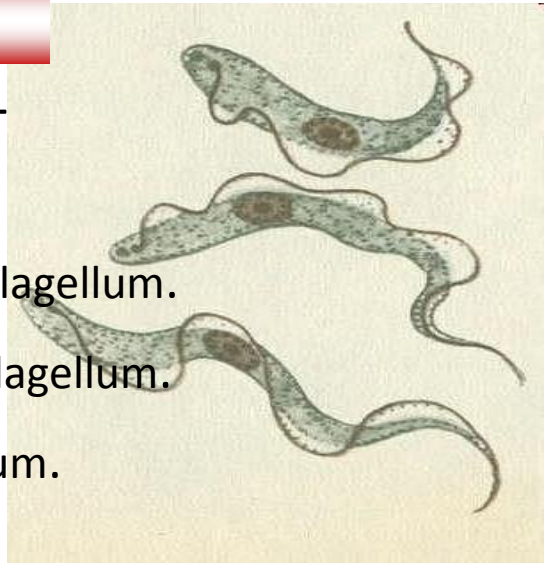
Spindle shaped – Central nucleus – free flagellum – undulating membrane.

3 forms

1- long Slender Form (30µ): active motile with free flagellum.

2- Short stumpy Form (15µ): sluggish without free flagellum.

3- Intermediate Form (20µ): with a short free flagellum.



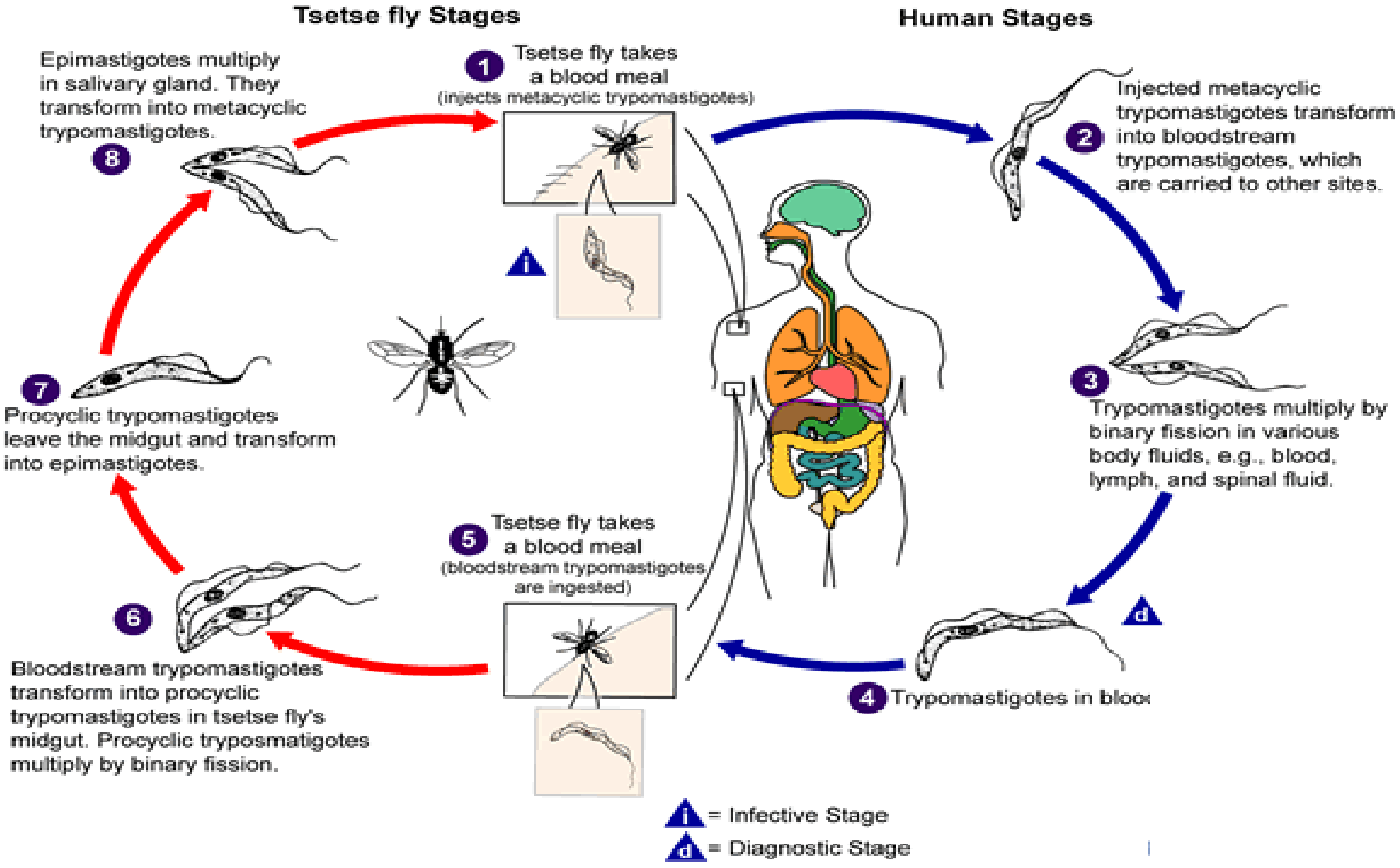
G.palpalis

In West Africa

G.morsitans

In East Africa

African Trypanosomiasis life cycle



Life cycle of *Trypanosoma brucei gambiense & T. b. rhodesiense*

Life cycle

During a blood meal on the mammalian host, an infected tsetse fly (genus Glossina) injects metacyclic trypomastigotes into skin tissue. The parasites enter the lymphatic system and pass into the bloodstream The number 1. Inside the host, they transform into bloodstream trypomastigotes The number 2, are carried to other sites throughout the body, reach other blood fluids (e.g., lymph, spinal fluid), and continue the replication by binary fission The number 3. The entire life cycle of African Trypanosomes is represented by extracellular stages. The tsetse fly becomes infected with bloodstream trypomastigotes when taking a blood meal on an infected mammalian host (The number 4, The number 5). In the fly's midgut, the parasites transform into procyclic trypomastigotes, multiply by binary fission The number 6, leave the midgut, and transform into epimastigotes The number 7. The epimastigotes reach the fly's salivary glands and continue multiplication by binary fission The number 8. The cycle in the fly takes approximately 3 weeks. Humans are the main reservoir for *Trypanosoma brucei gambiense*, but this species can also be found in animals. Wild game animals are the main reservoir of *T. b. rhodesiense*.

Transmission

Via vector – bite from the tse tse fly, Mother to child infection (perinatal death), Blood transfusion, Sexual contact

Pathogenesis and Clinical Picture

Incubation period (2 weeks)

Trypanosoma chancre (at the site of bite)

Via lymphatics: enlarged lymph nodes

especially posterior cervical region. (Winterbottom's sign)

Via blood stream: headache, fever(fluctuating),

muscle & joint pain, irregular erythematous rash.

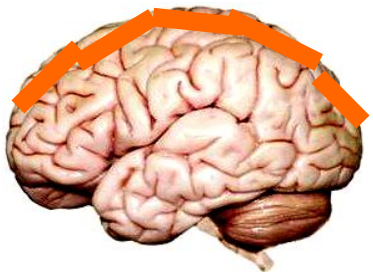
Invasion of bone marrow (hypoplastic anaemia)

Enlarged liver & spleen, generalized weakness.

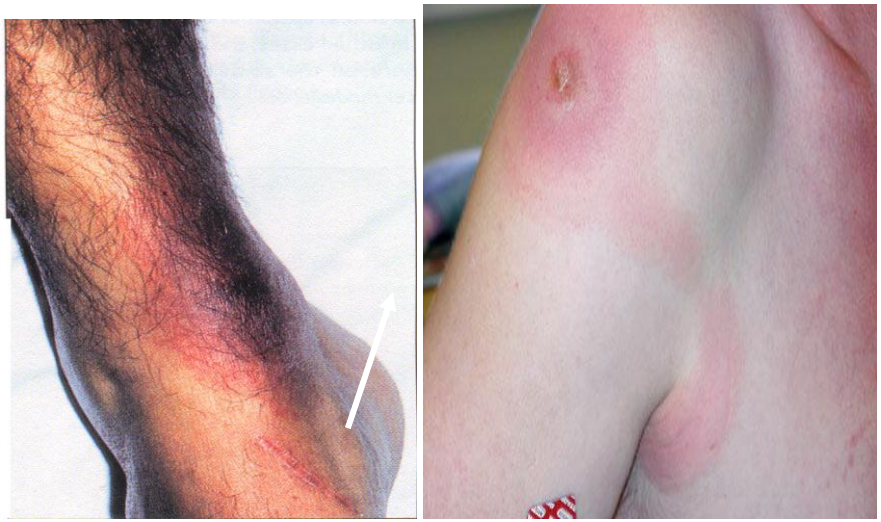
Invasion of CNS: Chronic cases severe headache, mental apathy, slow speech , deep sleep, coma & death

In East African Trypanosomiasis:

Disease runs more rapid & fatal course



Pathogenesis and Clinical Picture



Trypanosoma chancre (ulcer)

Winterbottom sign

Emaciation

Coma before death

Progressive disease may lead to the following C.N.S manifestations:-

1- Insomnia wakefulness

2- Mood changes (dullness / apathy)

3- Motor & Sensory Disorders: (Hyperesthesia / slurred speech / abnormal gait

4- Convulsions

5- Epilepsy

Terminal stage:

1- Permanent Sleep.
2- 2ry Bacterial infection.
3- Coma & Death.

Clinical features of Gambian and Rhodesian disease are similar, but they vary in **severity** and **duration**:

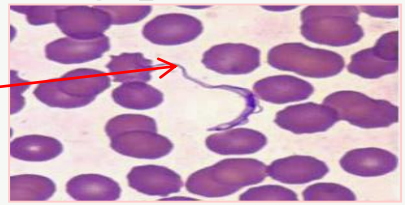
Gambian Sleeping sickness

[*T. gambiense*]

Parasite: Less virulent

Disease Progresses slowly; Chronic

Parasite in blood: Scanty [Low parasitaemia.



Typical sleeping sickness symptoms.

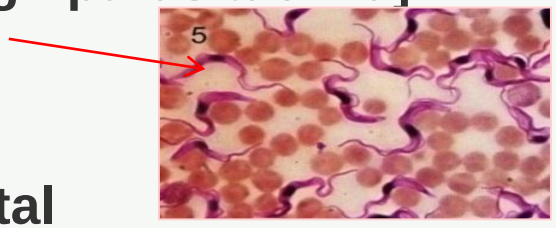
Rhodesian Sleeping Sickness

[*T. rhodesiense*]

Extreme virulence

Progresses rapidly. Acute

Plenty [High parasitaemia].



Usually fatal before sleeping sickness symptoms appear.

Differences between *T.b. gambiense* and *T. b. rhodesiense*.

	T.b. gambiense	*T. b. rhodesiense*
Geographical distribution	**West and central Africa**	**East and central Africa**
Main tsetse vector	***G. palpalis***	***G. morsitans***
Reservoir hosts	**Mainly human**	**Mainly animals**
Virulence	**Less**	**More**
Number of trypomastigote in blood	**Less**	**More**
Course of the disease	**Chronic in nature ,lasting up to 4 years**	**More acute, rarely lasting 9 months before death occurs**
Febrile paroxysms	**Less frequent**	**More frequent**
Lymph node enlargement	**More pronounced**	**Less pronounced**
Marked nervous symptoms	**Present**	**Lacking or not so evident**
Resistance to treatment in advanced stage of the disease	**Less**	**More**

Diagnosis

- Diagnosis of African Sleeping Sickness is a multi-step procedure:

I- Clinical diagnosis (History & examination) by Clinical assessment of fever, neurological signs and/or mental dullness accompanied by enlarged and sensitive cervical lymph nodes - **Winterbottom' sign**

2- Laboratory Diagnosis :

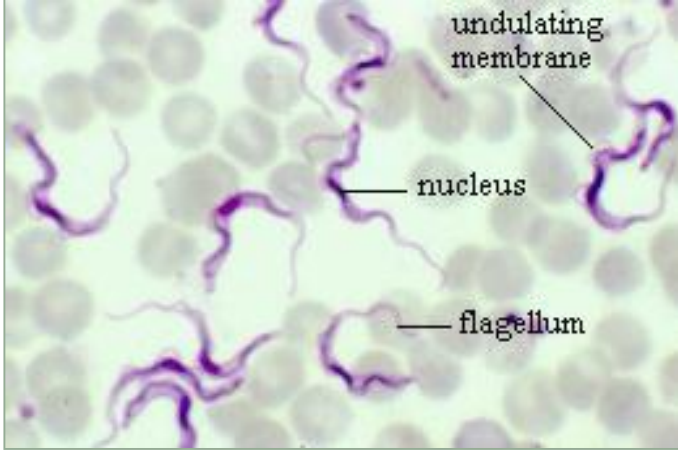
- **Direct.**
- **Indirect.**

Direct Laboratory Diagnosis

To demonstrate the parasite

Early: in chancre aspirate, blood, lymph node, bone marrow &

Late: in CSF **BY :-**



a) **Microscopic** examination of fresh unstained or Giemsa stained films: **>>> polymorphic trypomastigote.**

b) **Culture** (NNN or Weinmann's media: **>>> epimastigote.**

c) **Animal inoculation**

d) **CSF examination: Trypomastigotes**, and Morula cells; vaculoted plasma cell.

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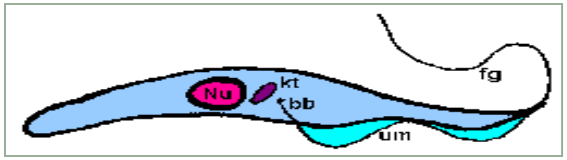
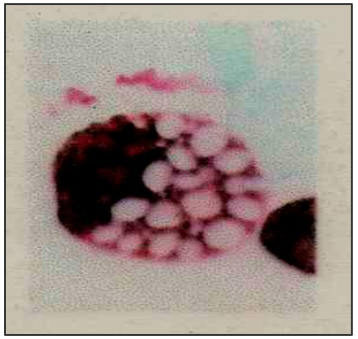
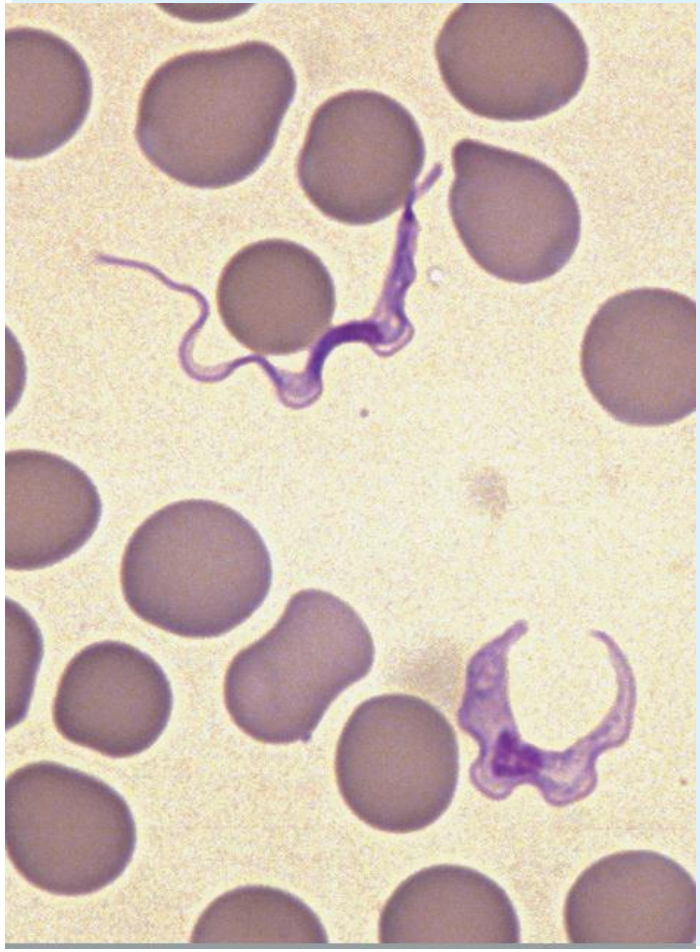
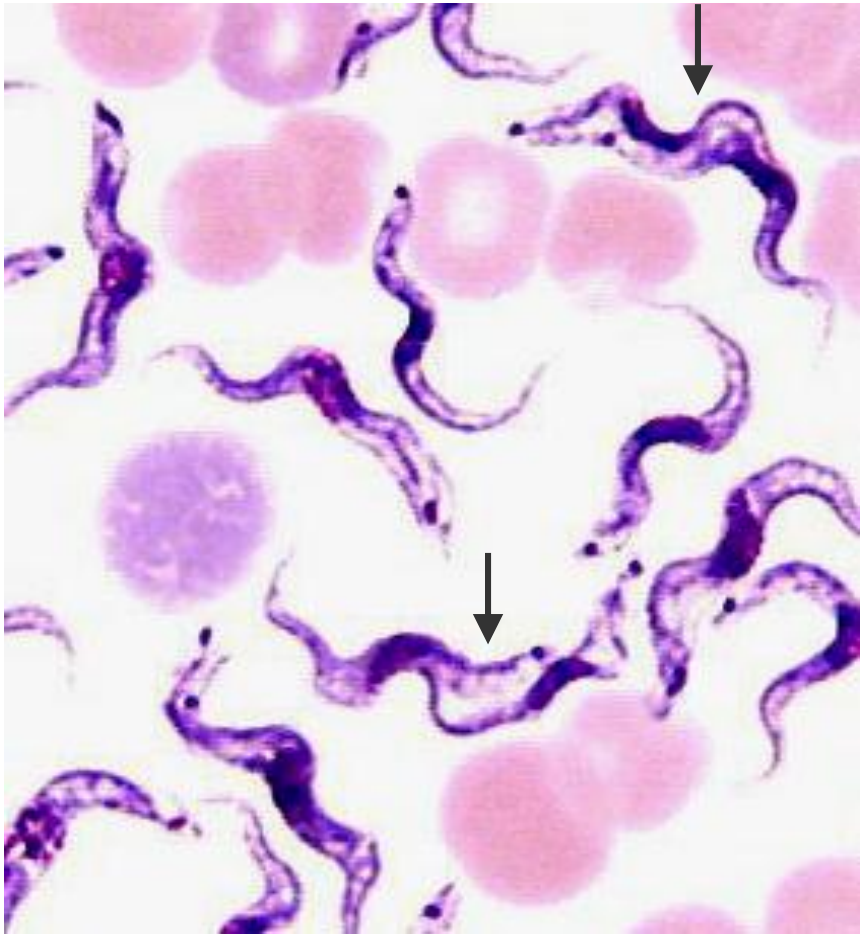




Morula cell of Mott

Polymorphic Trypanosomes in blood film





Diagnosis

Aspiration of swollen gland

Lumber puncture for CSF

Other methods

direct Laboratory diagnosis

By Detection of specific **antigens** in the blood :-

- **Card Agglutination Trypanosomiasis Test** [**CATT**]: It is a simple & rapid test for detection of **circulating antigens** in the blood of the patient. It is useful in surveys specially for *T. b. gambiense.*

- Molecular techniques (e.g. PCR)

- **Indirect Laboratory diagnosis**
- by Detecting **anti-*Trypanosoma* Abs** by serological methods (ELISA, IFA, IHA etc..), But can't distinguish between current and previous infections.
- Increased total IgM level in serum due to **antigenic variation** of the surface coat of the parasite.
- Trypanosome posses genes that code for about 1000 variant forms of their surface glycoproteins (SVG). Switch to a different variant produces a new generation not susceptible to attack by immune factors specific to the previous generation.

Treatment

1- Early stage :

- Suramin **sodium**
- Pentamidine

2- Late stage : Drugs that pass CNS barrier

-Tryparsamide

- Melarsoprol

3- Early & late stages

- Eflornithine

Prevention & control

- 1- Reduction of contact with *Glossina* (vector) through control measures instituted against them
  - traps
  - spraying w/ insecticide
  - skin repellents.
- 2- Reduction of human infection by early diagnosis and prompt treatment
- 3- Chemoprophylaxis in endemic areas

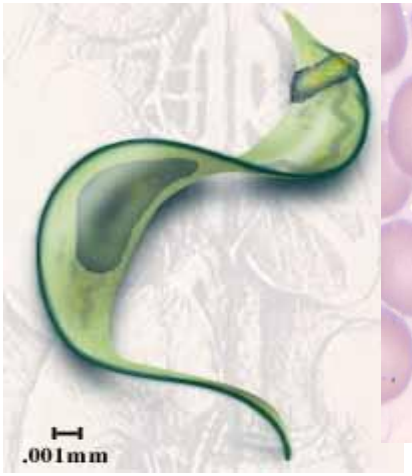
  [**Pentamidine at 4-6 months intervals**].
- **No vaccine**

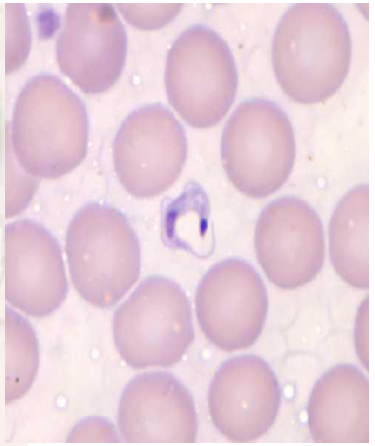
Trypanosoma cruzi causing Chagas' disease

Morphology

Trypomastigote (Monomorphic)

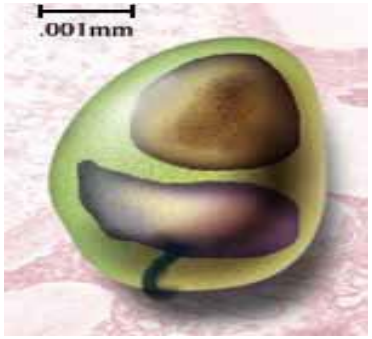
Slender shaped (20µ) – Central nucleus – C or U-shaped –Free flagellum 1/3 body- Large bulging peripheral kinetoplast

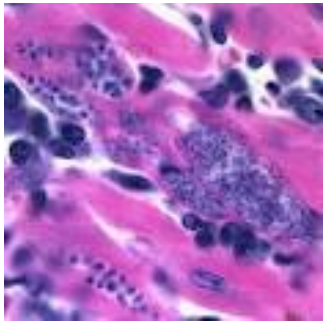




Amastigote

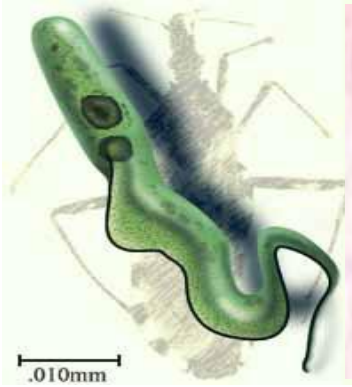
Obligatory intracellular – mainly in cardiac & Skeletal muscles – Brain meninges – Nerve ganglia – cells of GIT …. etc





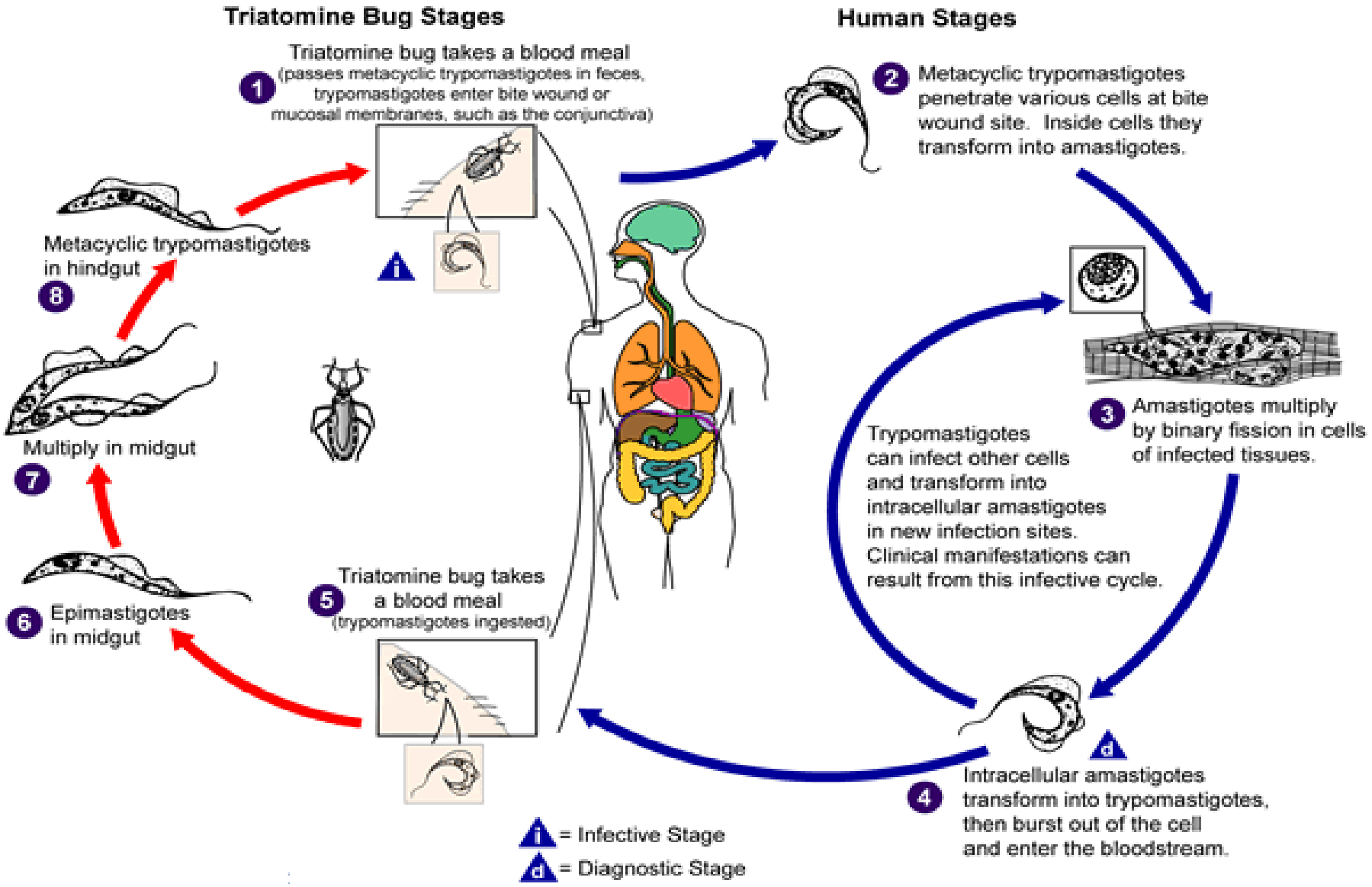
Epimastigote (Vector only)

Spindle shape– Kinetoplast anterior to central nucleus– Undulating membrane is short – terminal free flagellum



Geographical Distribution of Americam Trypanosomiasis

Life cycle of *Trypanosoma cruzi*

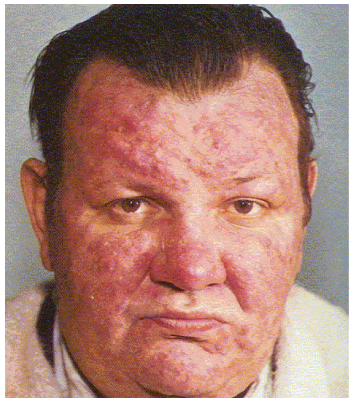


Life cycle

An infected triatomine insect vector (or "kissing" bug) takes a blood meal and releases trypomastigotes in its feces near the site of the bite wound. Trypomastigotes enter the host through the wound or through intact mucosal membranes, such as the conjunctiva The number 1. Common triatomine vector species for trypanosomiasis belong to the genera Triatoma, Rhodnius, and Panstrongylus. Inside the host, the trypomastigotes invade cells near the site of inoculation, where they differentiate into intracellular amastigotes The number 2. The amastigotes multiply by binary fission The number 3 and differentiate into trypomastigotes, and then are released into the circulation as bloodstream trypomastigotes The number 4. Trypomastigotes infect cells from a variety of tissues and transform into intracellular amastigotes in new infection sites. Clinical manifestations can result from this infective cycle. The bloodstream trypomastigotes do not replicate (different from the African trypanosomes). Replication resumes only when the parasites enter another cell or are ingested by another vector. The “kissing” bug becomes infected by feeding on human or animal blood that contains circulating parasites The number 5. The ingested trypomastigotes transform into epimastigotes in the vector’s midgut The number 6. The parasites multiply and differentiate in the midgut The number 7 and differentiate into infective metacyclic trypomastigotes in the hindgut The number 8 .

Trypanosoma cruzi can also be transmitted through blood transfusions, organ transplantation, transplacentally, and in laboratory accidents.

Pathogenesis and Clinical Picture



I- Acute Form

Chagoma occurs at the site of bite.

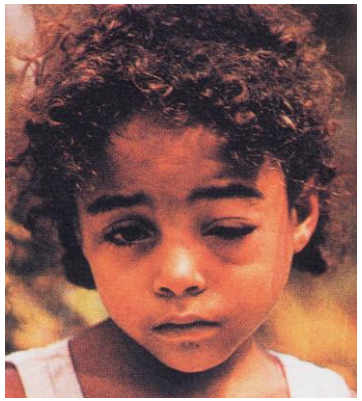
Parasite reaches regional lymph nodes

To ↓

Blood

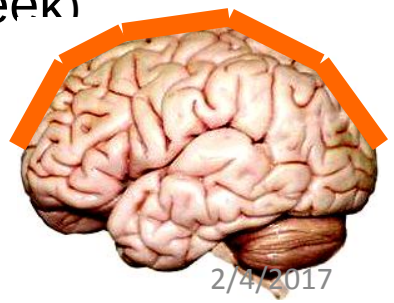
To ↓

Organs and tissues



Fever, enlarged lymph nodes, skin rash, enlarged liver & spleen.

Romana's sign (Unilateral conjunctivitis appear suddenly together with oedema of upper & lower eye lids & cheek)



Meningoencephalitis, heart failure

Death or pass to **C**hronic form

Pathogenesis and Clinical Picture

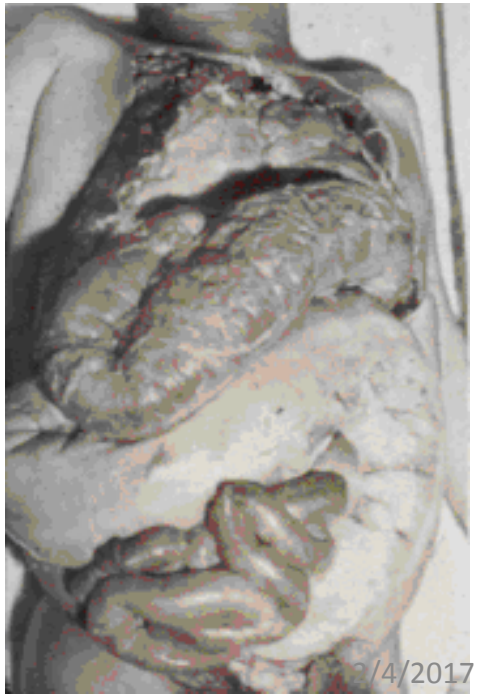
II- Chronic form

Parasite produces antigens similar to patient's self antigens:

The body produces auto-antibodies that cause damage to:

- Heart muscle fibres:
  congestive heart failure.
- Oesophageal muscle fibres:
  megaoesophagus and dysphagia.
  Destruction of Auerbach's plexus
- Colon muscle fibres:
  megacolon and constipation.
- CNS or thyroid gland
  Exacerbation of infection in immunosuppressed patients.

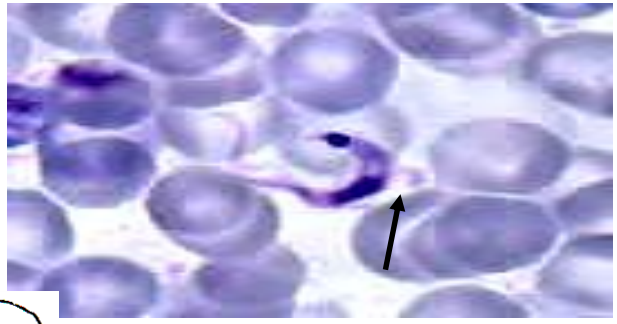
Amastigote form of *T.cruzi*



Diagnosis

Clinical diagnosis : by Clinical assessment of a chagoma swelling , Romana's sign or other features of chagas disease

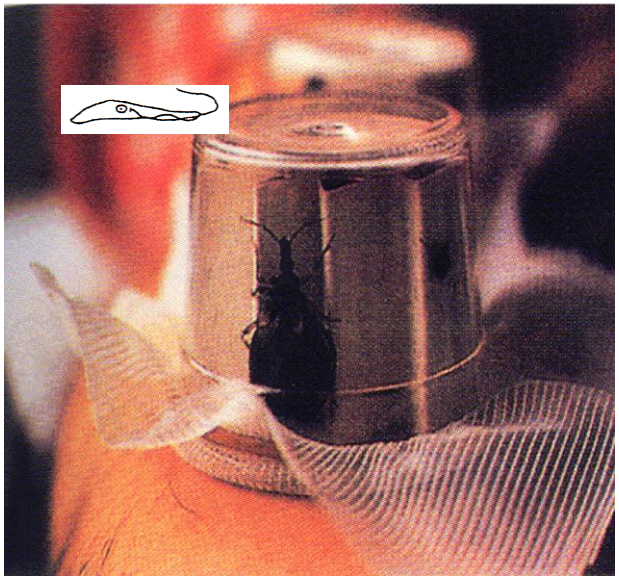
Finding the parasite in:



Blood film (C-shaped *T.cruzi*)

Biopsy from lymph node, liver or spleen (amastigotes)

Culture (Epimastigotes)



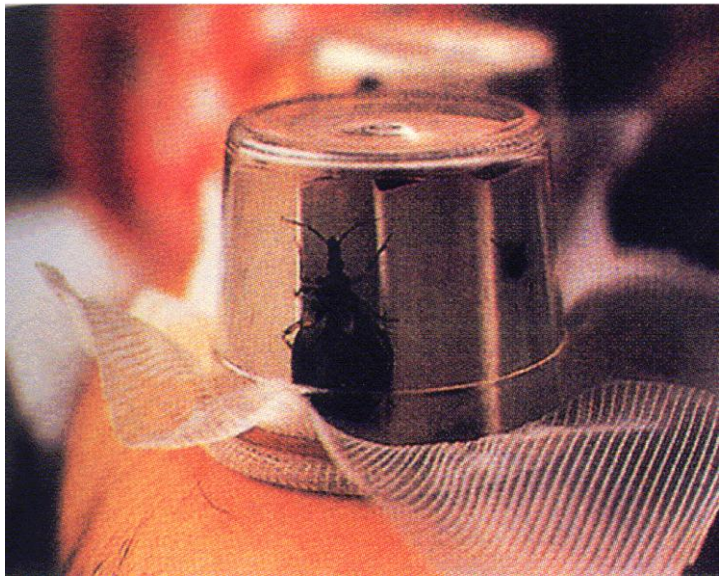
Xenodiagnosis

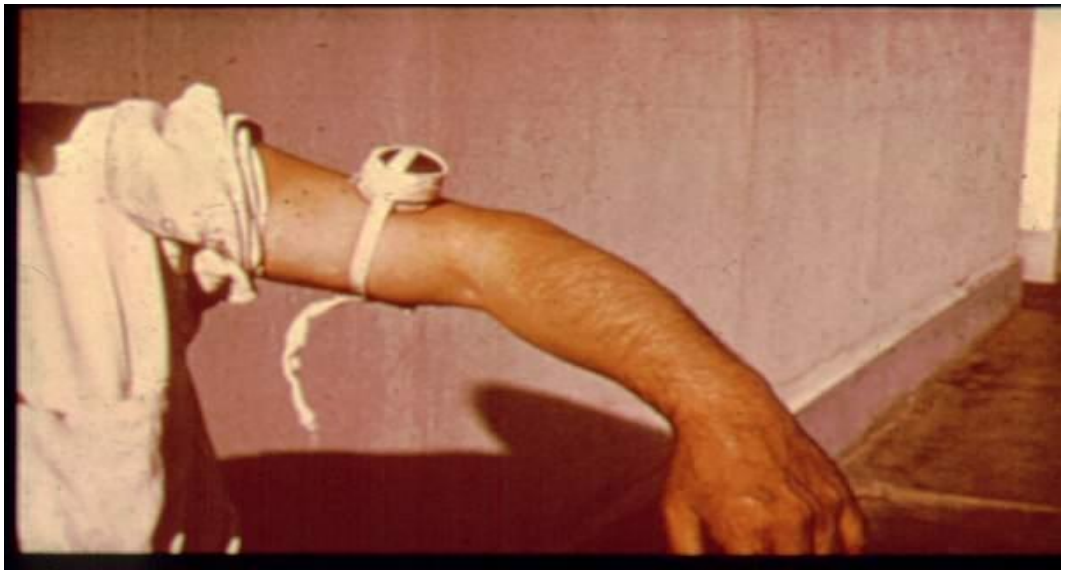
Serological tests :-

- detection of antibodies include complement fixation test, indirect haemagglutination, immunofluorescence and ELISA.
- demonstration of the parasite antigen in blood and urine.

Molecular techniques

Diagnosis (Xenodiagnosis)





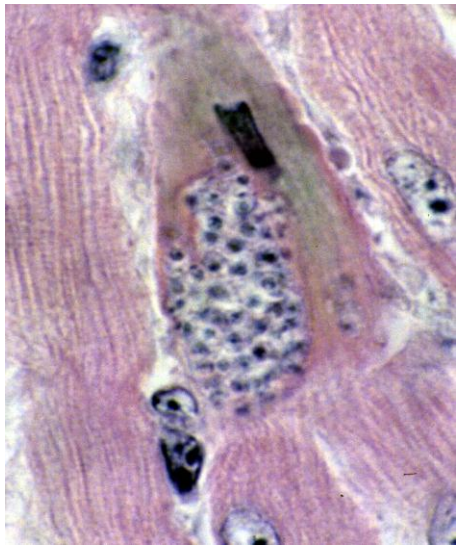
Highly efficient – demonstrate low level of parasite in blood

Method:

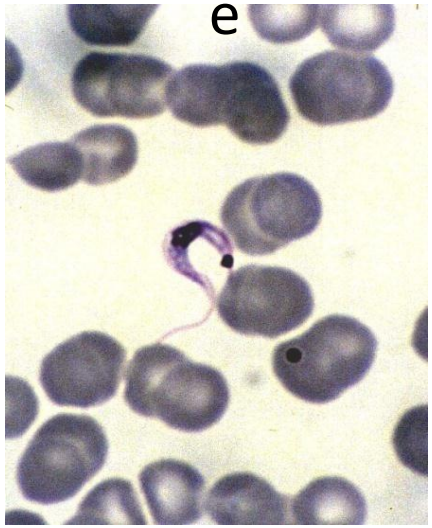
A Laboratory bred winged bug is starved for 2 weeks then fed on suspected patient's blood – 30 days later, it faeces & gut examined for trypanosomes.

Diagnosis

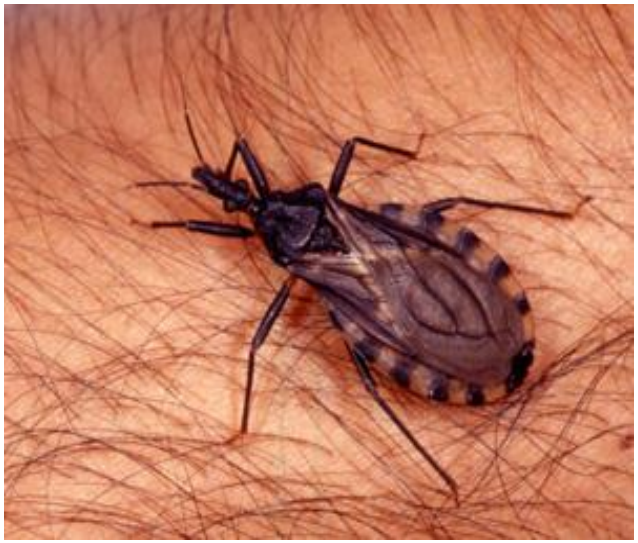
Amastigote

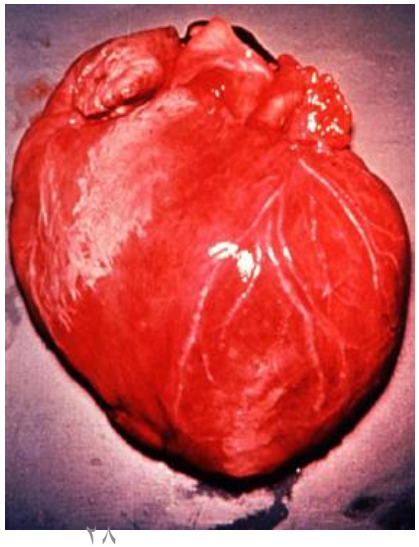


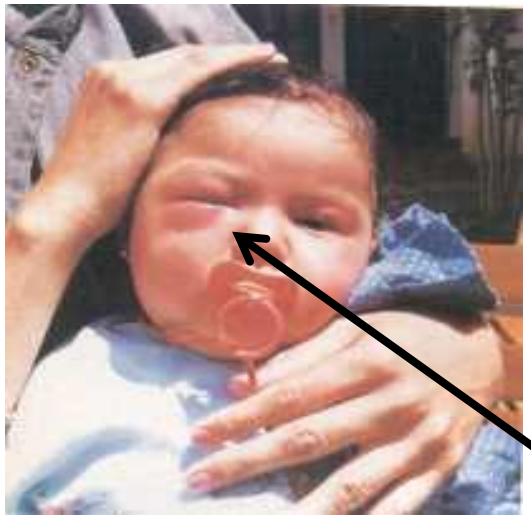
Trypomastigote

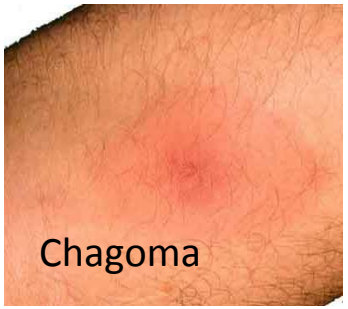


Winged Bug



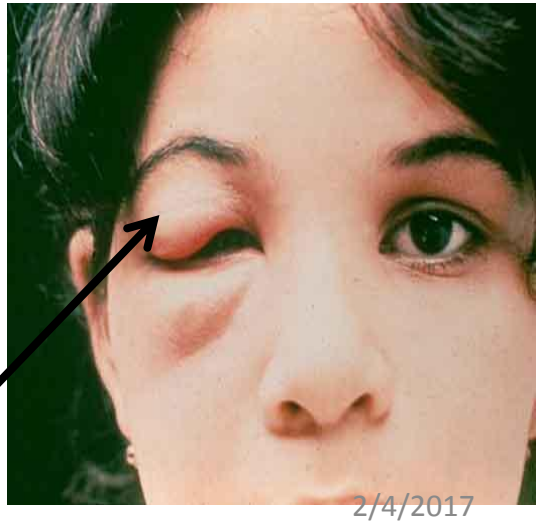






Chagoma

Romana's sign



Treatment

- No effective specific treatment is available.
- Nifurtimox is a drug of choice which Inhibits intracellular development of T. cruzi
- Premaquine and benznidazole have been used with some success in the acute cases.
- Allopurinol and ketoconazole have also been found useful.

Prevention & control

- Control and elimination of domestic and peridomestic vector bugs would help prevent the transmission of disease in endemic areas.
- Triatomine bugs are highly susceptible to chlorinated hydrocarbon insecticides, which form the major weapon for their control.
- Health education
- Sterilization of transfusion blood