INTERNATIONAL SCHOOL OF MEDICINE

Department of Infectious Diseases

The topic of the lecture:

Trypanosomiasis

Professor Kutmanova A.Z.

History

- its species was discovered by a scientist Valentine” in 1841.
- But these are found in mammals after 50 – 80 years later.
- Then further studied about their diseases.

Introduction

- The name is derived from Greek word,
  - trypano means (borer)
  - soma means (body)
- They are unicellular flagellate protozoa.
- Have spiral like motion.
- Need more than one host to complete its life cycle.
- Oftenly transmitted by a vector.
- Generally found in intestine, but some time found in blood stream or in heart.

Trypanosoma

Trypanosomiasis

- West African Trypanosomiasis
  - *T.brucei gambiense*
- East African Trypanosomiasis
  - *T.brucei rhodesiense*

→ Sleeping sickness

Transmitted by *Glossina* (tsetse fly)

- American Trypanosomiasis
  - *T.cruzi*

→ Chagas' disease

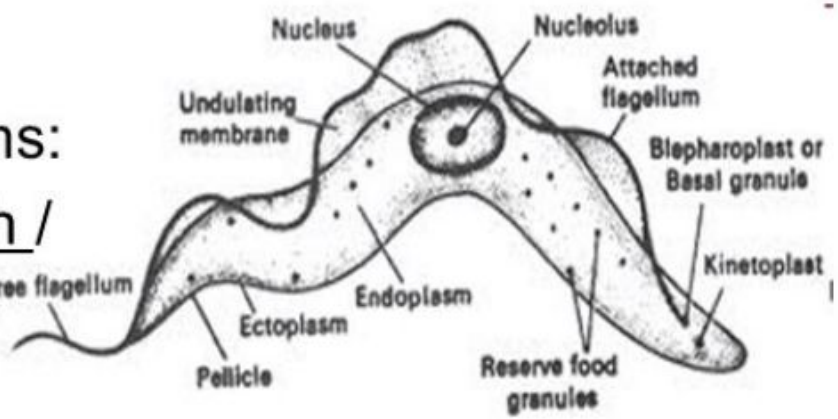
Transmitted by *Triatoma* (winged bug)

Morphology of trypanosome

Morphology

Exist into 2 interchangeable forms:

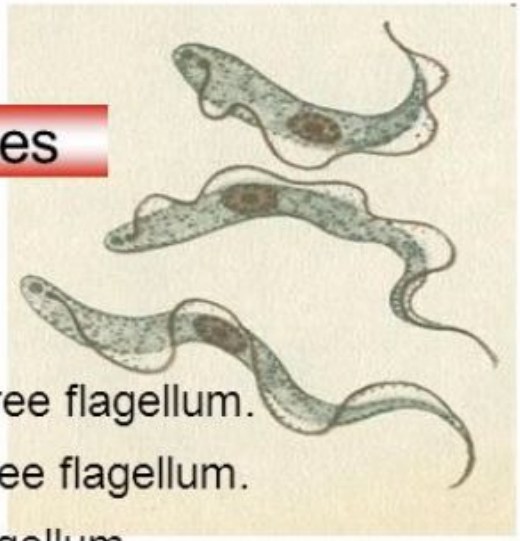
Trypomastigote in Blood/ Lymph / tissue space of various organs & C.N.S is terminal & fatal



Trypanosoma gambiense

Epimastigote in salivary gland of vector & Culture media.

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.

African Trypanosomiasis (Sleeping Sickness)

The parasites

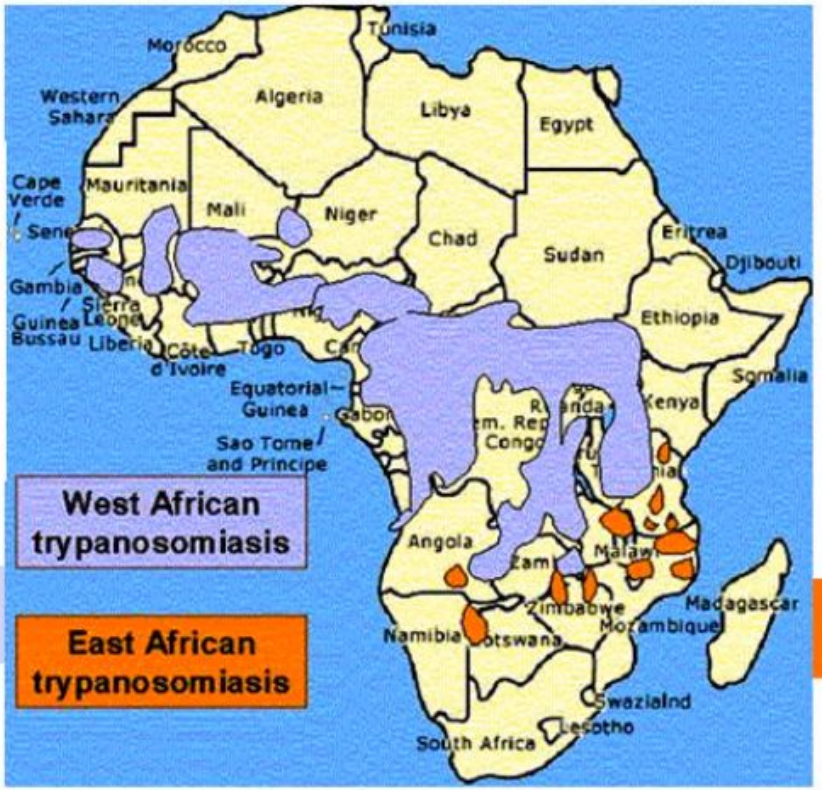
- Belong to a group of closely related trypanosomes in the Trypanosoma brucei species complex. Three morphologically indistinguishable species are recognized:
- T. brucei infects game animals/livestock (causes nagana)
- T. rhodesiense causes E. African trypanosomiasis
- T. gambiense causes W. and Central African sleeping sickness

  (Some authors consider these as subspecies: T. brucei brucei, T. b. rhodesiense, T. b. gambiense.)

Distribution

G.palpalis

In West Africa



G.morsitans

In East Africa

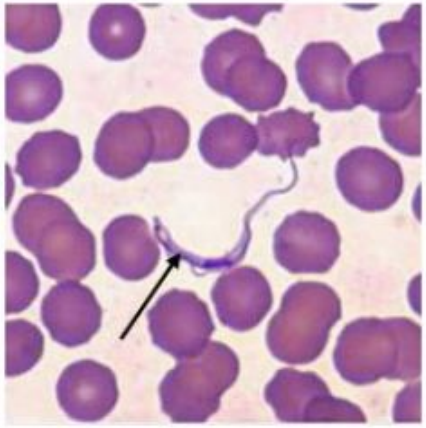
T. rhodesiense causes E. African trypanosomiasis

T. gambiense causes W. and Central African sleeping sickness

Trypanosoma brucei species

West Africa

T.brucei gambiense



Less plentiful

Cannot live in lab animals

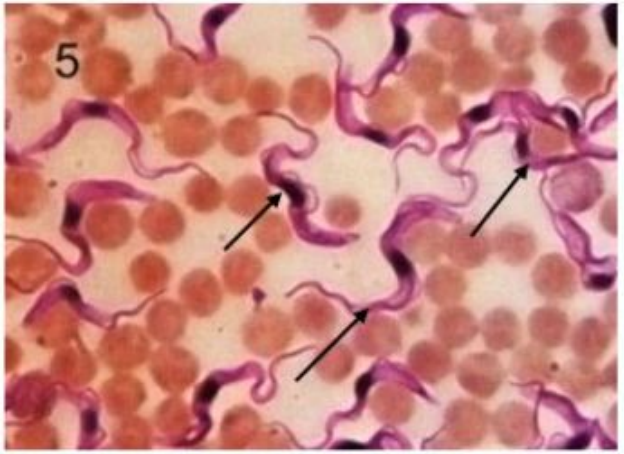
Reservoir host:

goats, cattle & pigs

Transmitted by: *G.palpalis*

East Africa

T.brucei rhodesiense



More plentiful

Can live in lab animals

Nucleus is shifted posteriorly

Reservoir host:

wild game animals

Transmitted by: *G.morsitans*

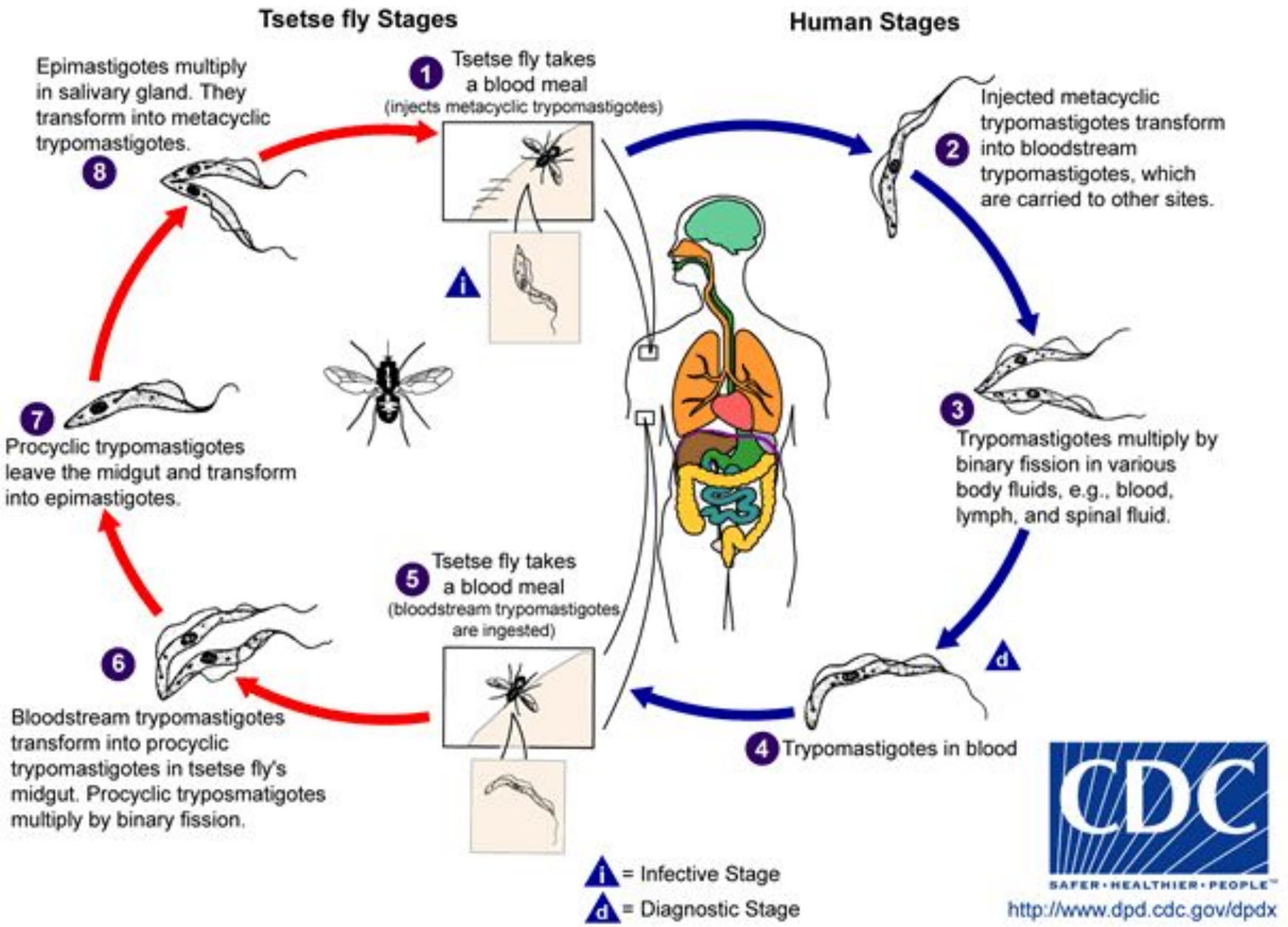
Major Differences Between African Trypanosome Species

Attribute	***T. rhodesiense***	***T. gambiense***
tsetse vector	*G. morsitans* group	*G. palpalis* group
ecology	dry bush, woodland	rainforest, riverine, lakes
transmission cycle	ungulate-fly-human	human-fly-human
non-human reservoir	wild animals	domestic animals
epidemiology	sporadic, safaris	endemic, some epidemics
disease progression	rapid, often fatal	slow (~1 yr) acute ⇒ chronic
parasitemia	high	low
asymptomatic carriers	rare	common

Transmission

- A bite from an infected tsetse fly causes African trypanosomiasis.
- Blood transfusions are a rare cause of parasitic transmission.
- In rare cases, accidental transmission in the laboratory has been implicated.

Life cycle


Tsetse fly Stages
Human Stages
1 Tsetse fly takes a blood meal
(injects metacyclic trypomastigotes)
2 Injected metacyclic trypomastigotes transform into bloodstream trypomastigotes, which are carried to other sites.
3 Trypomastigotes multiply by binary fission in various body fluids, e.g., blood, lymph, and spinal fluid.
4 Trypomastigotes in blood
5 Tsetse fly takes a blood meal
(bloodstream trypomastigotes are ingested)
6 Bloodstream trypomastigotes transform into procyclic trypomastigotes in tsetse fly's midgut. Procyclic tryposmatigotes multiply by binary fission.
7 Procyclic trypomastigotes leave the midgut and transform into epimastigotes.
8 Epimastigotes multiply in salivary gland. They transform into metacyclic trypomastigotes.
i = Infective Stage
d = Diagnostic Stage
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http://www.dpd.cdc.gov/dpdx

Pathogenesis

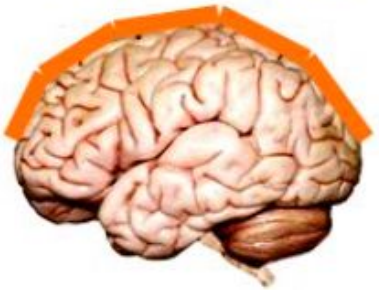
Incubation period (2 weeks)
Trypanosoma chancre (at the site of bite)

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.

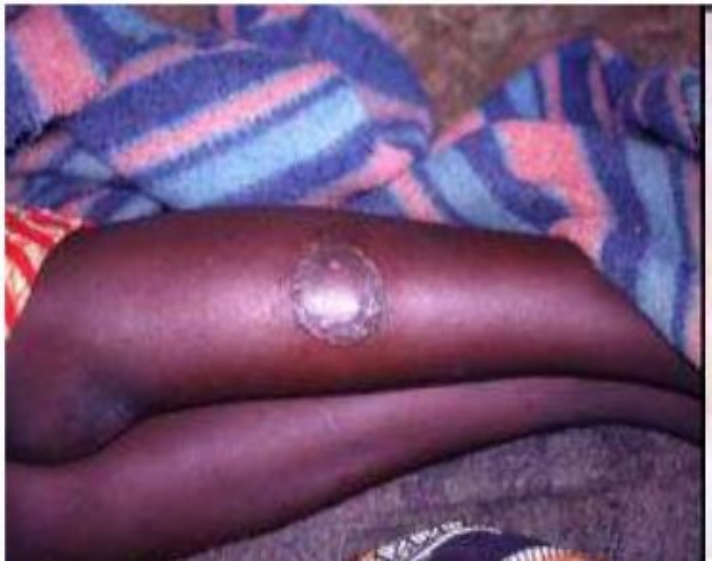
Invasion of CNS: severe headache, mental apathy, slow speech, deep sleep, coma & death



In East African Trypanosomiasis:
Disease runs more rapid & fatal course

Clinical presentation

- Incubation period may be from few days to weeks.
- The first clinical manifestation of African trypanosomiasis chancre occurs at the site of inoculation .



Progression of African Trypanosomiasis

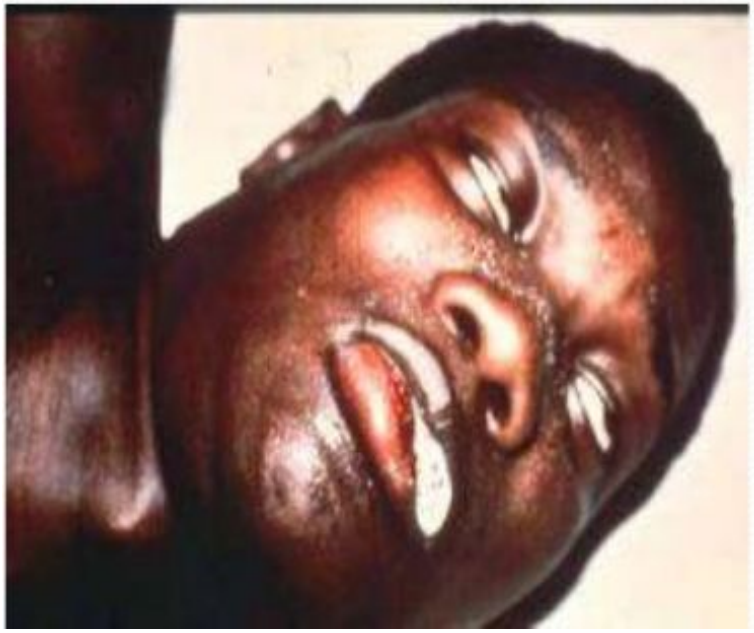
Blood → Lymphatics → CNS → DEATH

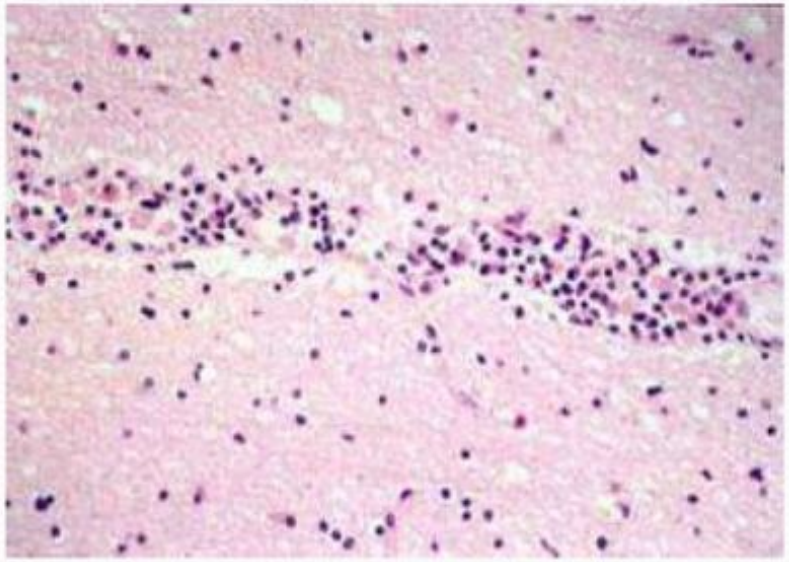
- ± chancre
- • intermittent fever
  • headache
- • continued febrile episodes
  • lymphadenopathy
  • deteriorating health
- • anorexia
  • minor neurological symptoms
  • apathy, lassitude
- • severe sleep disturbances
  • severe neurological symptoms
- • convulsions
  • coma
  • concurrent infections

months to years → *Tg*

weeks to months → *Tr*

Clinical presentation





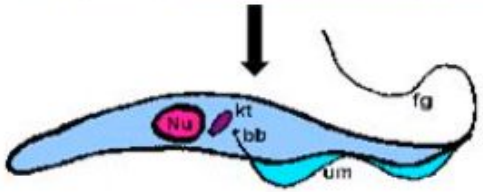
Diagnosis

1- Clinical picture

2- Demonstration of trypanosomes:

- Microscopic examination of unstained or stained blood films

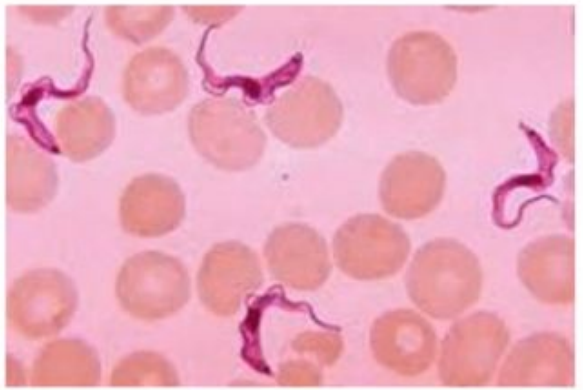
- Culture on suitable medium (N.N.N OR Weinmann's media to detect **Epimastigote**)



- Animal inoculation

N.B. in case of *T.brucei rhodesiense* injected in lab Animal produce a new form "Posterior Nucleus Shift"

Polymorphic Trypanosomes



Diagnosis

- **General**
- Anemia, hypergammaglobulinemia, low complement levels, elevated ESR, thrombocytopenia, hypoalbuminemia, but not eosinophilia or abnormal liver function.
- The total IgM level is higher in blood and CSF.
- A definitive diagnosis of infection requires actual detection of trypanosomes in blood, lymph nodes, CSF, skin chancre aspirates, or bone marrow.
- However, symptomatic improvement after empiric treatment is the usual confirmatory test in areas where diagnostic studies are not readily available.

Imaging Studies

- CT scanning and MRI of the head: Both head CT scanning and MRI reveal cerebral edema and white matter enhancement, respectively, in patients with late-stage African trypanosomiasis.
- EEG in neurologic involvement usually shows slow wave oscillations (delta waves), a nonspecific finding

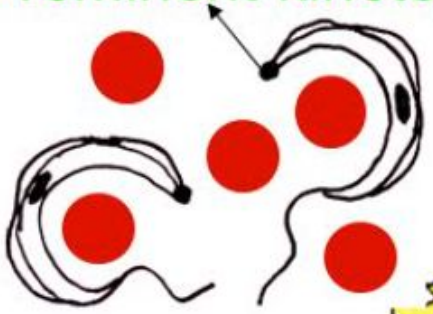
Treatment

Drug	Use	Drawbacks
Pentamidine	Effective against early-stage *gambiense* disease	• Adverse side effects • Non-oral route
Suramin	Effective against early-stage *gambiense* and *rhodesiense* disease	• Adverse side effects • Non-oral route
Melarsoprol	First line drug for late-stage *gambiense* and *rhodesiense* disease involving CNS	• Adverse side effects, especially encephalopathy • Fatal in 1-5% of cases • Parasite resistance • Non-oral route
Eflornithine	Effective against late-stage *gambiense* disease involving CNS	• High cost • Not effective against *T. rhodesiense* • Non-oral route - has to be given intravenously (needs hospitalization for 14 days)

American Trypanosomiasis (Chagas Disease)

Distribution

Prominent kinetoplast



Trypanosoma cruzi

C-shaped

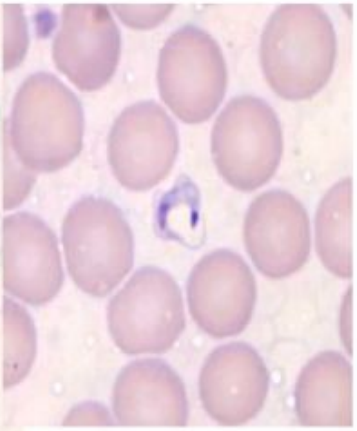
Winged bug
Kissing bug
Triatoma or Rhodnius

Morphology

Morphology

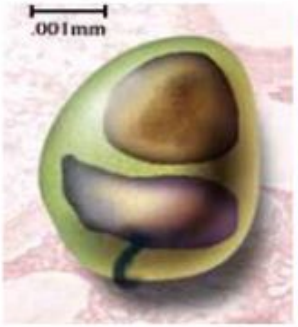
Trypomastigote (Monomorphic)

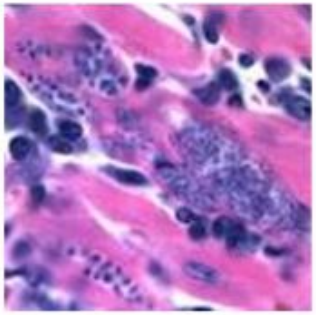
Slender shaped (20µ) – Central nucleus – C or U-shaped –Free flagellum 1/3 body- Large bulging peripheral kinetoplast



Amastigote

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

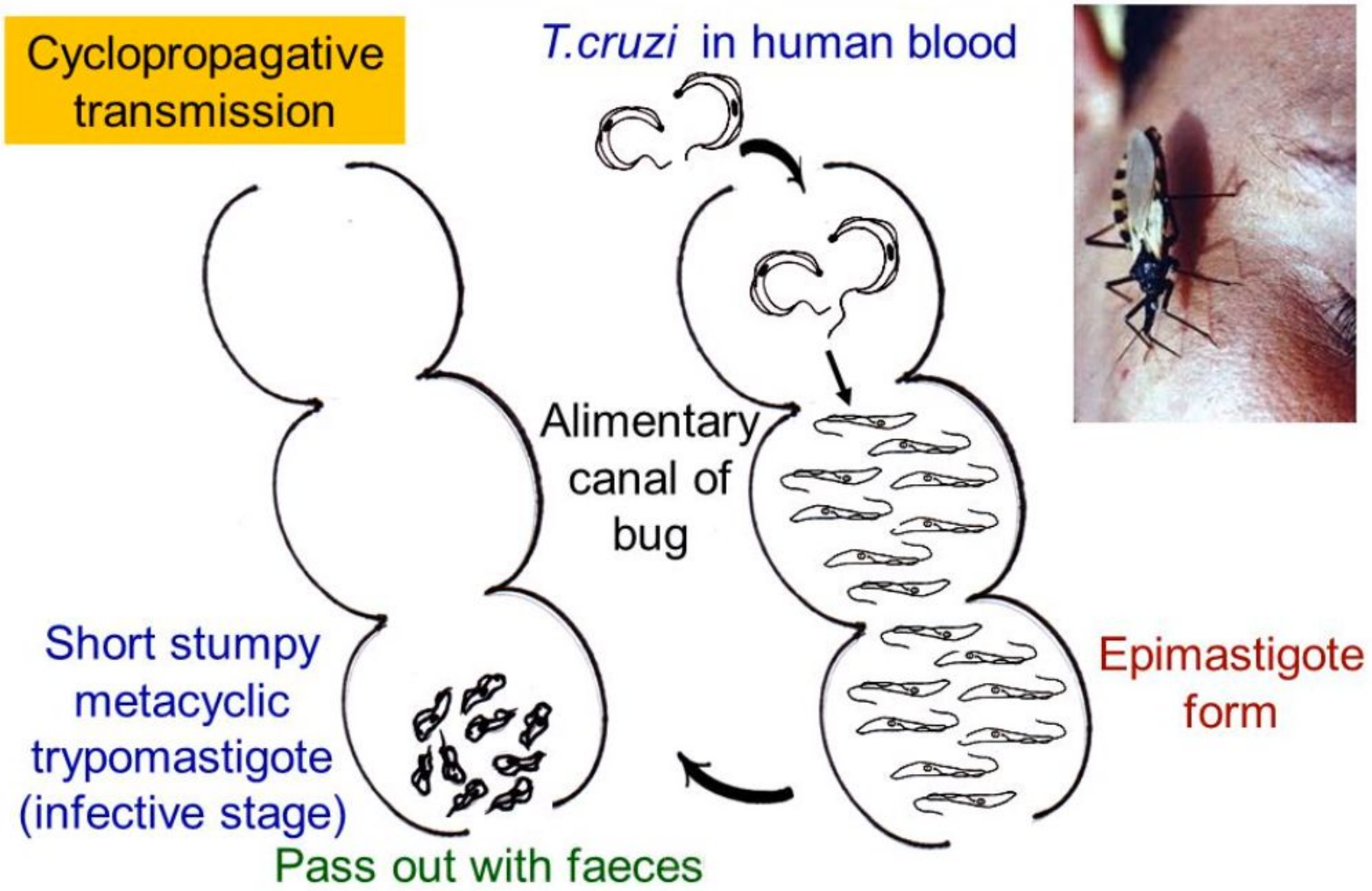




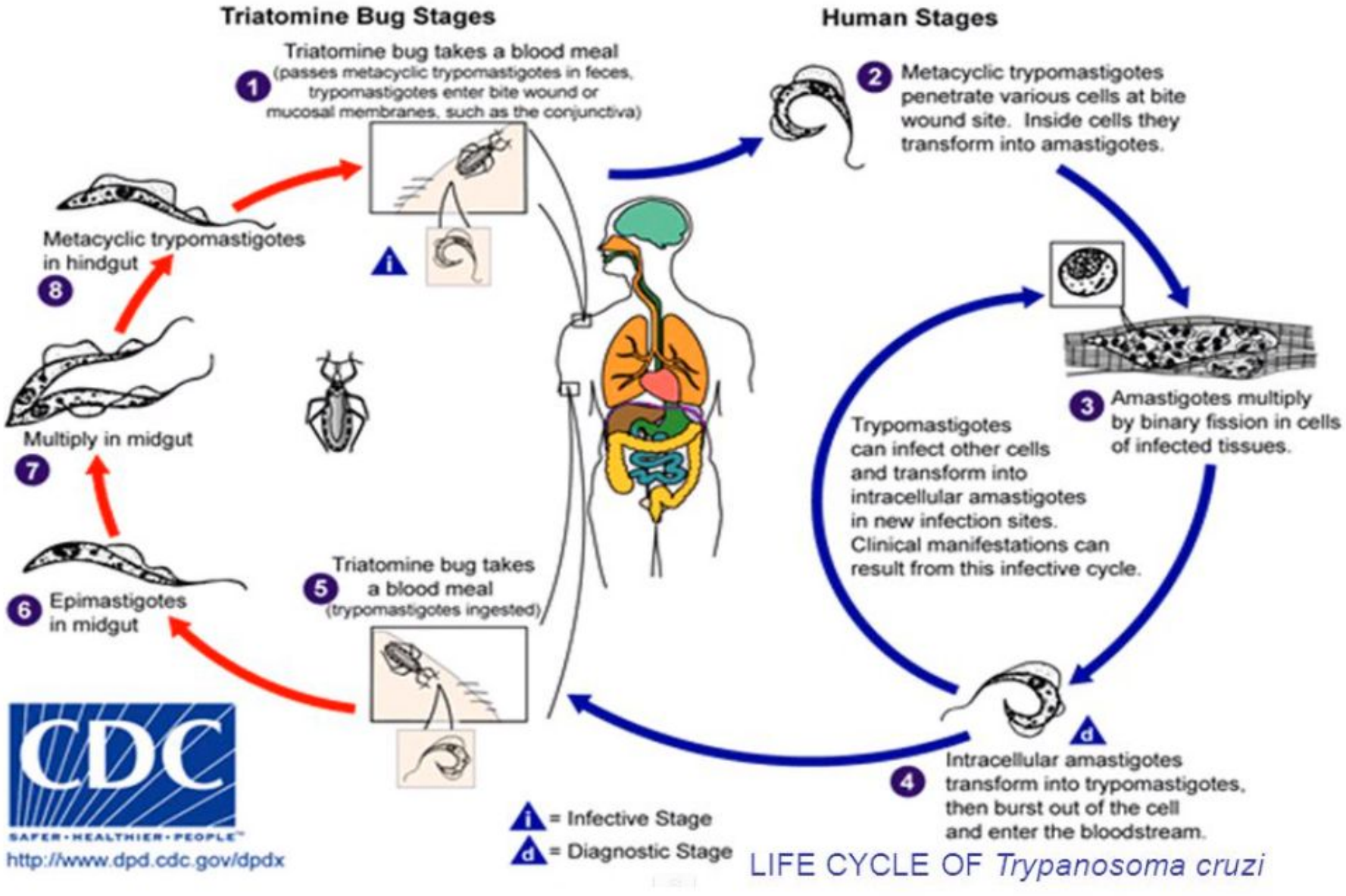
Epimastigote (Vector only)

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

Transmission



Life cycle


Triatomine Bug Stages
Human Stages
Triatomine bug takes a blood meal
(passes metacyclic trypomastigotes in feces, trypomastigotes enter bite wound or mucosal membranes, such as the conjunctiva)
1
2
Metacyclic trypomastigotes penetrate various cells at bite wound site. Inside cells they transform into amastigotes.
Metacyclic trypomastigotes in hindgut
8
Multiply in midgut
7
3
Amastigotes multiply by binary fission in cells of infected tissues.
Trypomastigotes can infect other cells and transform into intracellular amastigotes in new infection sites. Clinical manifestations can result from this infective cycle.
Triatomine bug takes a blood meal
(trypomastigotes ingested)
5
6
Epimastigotes in midgut
4
Intracellular amastigotes transform into trypomastigotes, then burst out of the cell and enter the bloodstream.
CDC
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http://www.dpd.cdc.gov/dpdx
= Infective Stage
= Diagnostic Stage
LIFE CYCLE OF Trypanosoma cruzi

Transmission

Mainly by

Contamination of
skin abrasion by winged bug
faeces

Cone nose Bug – kissing Bug –Assassin bug

Rarely by

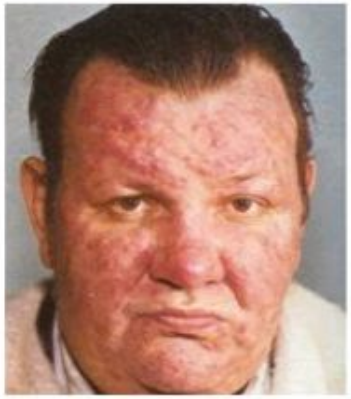
Through infected blood transfusion

Through infected mother's milk

Through the placenta

Pathogenesis

I- Acute Form



Chagoma occurs at the site of bite.

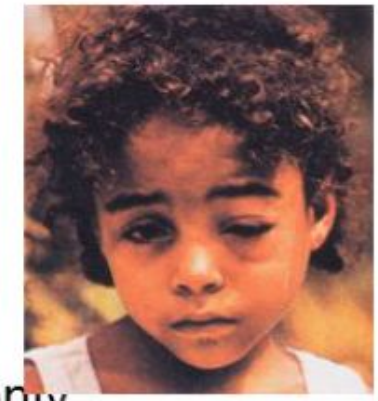
Parasite reaches regional lymph nodes

To ↓

Blood

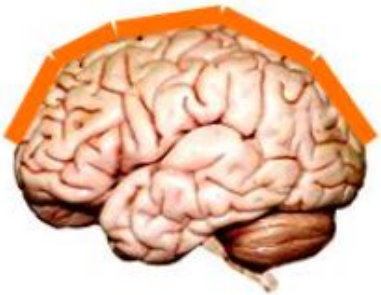
To ↓

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)



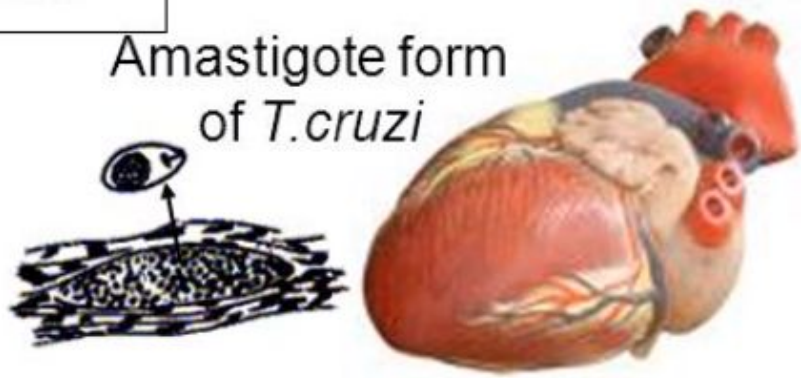
Meningoencephalitis, heart failure

Death or pass to Chronic form

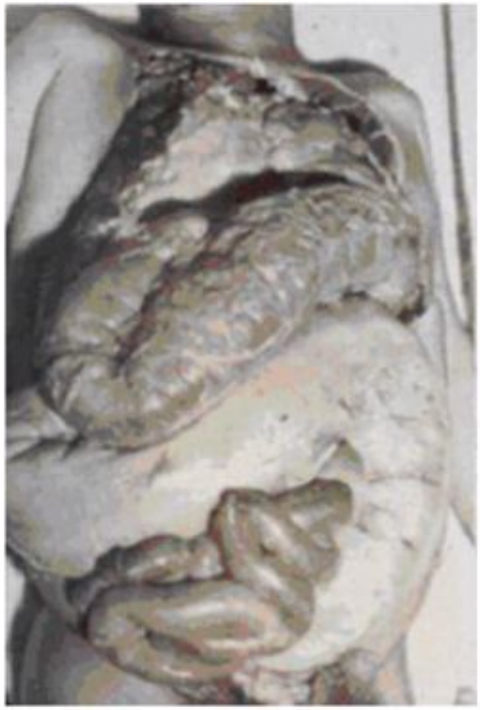
Pathogenesis

II- Chronic form

Parasite produces antigens similar to patient's self antigens:
The body produces auto-antibodies that cause damage to:



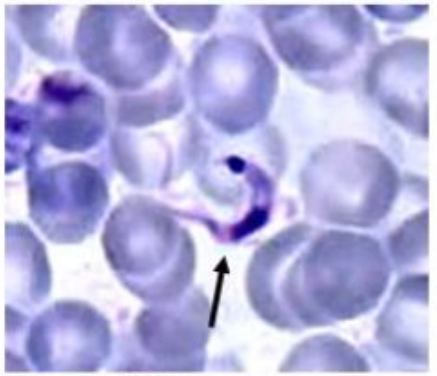
- Heart muscle fibres:
  congestive heart failure.
- Oesophageal muscle fibres:
  megaoesophagus and dysphagia.
  Destruction of Auerbach's plexus
- Colon muscle fibres:
  megacolon and constipation.
- CNS or thyroid gland
  Exacerbation of infection in immunosuppressed patients.



Diagnosis

Finding the parasite in:

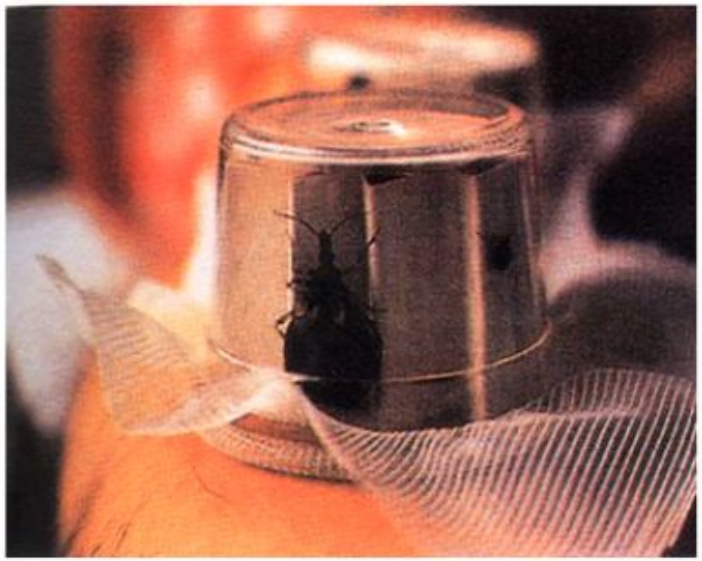
Blood film (C-shaped *T.cruzi*)

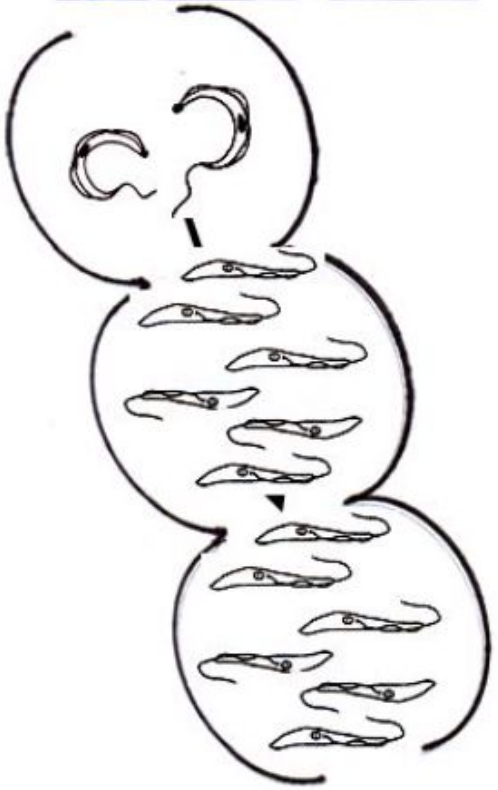


Biopsy from lymph node, liver or spleen (amastigotes)

Culture (Epimastigotes)

Xenodiagnosis



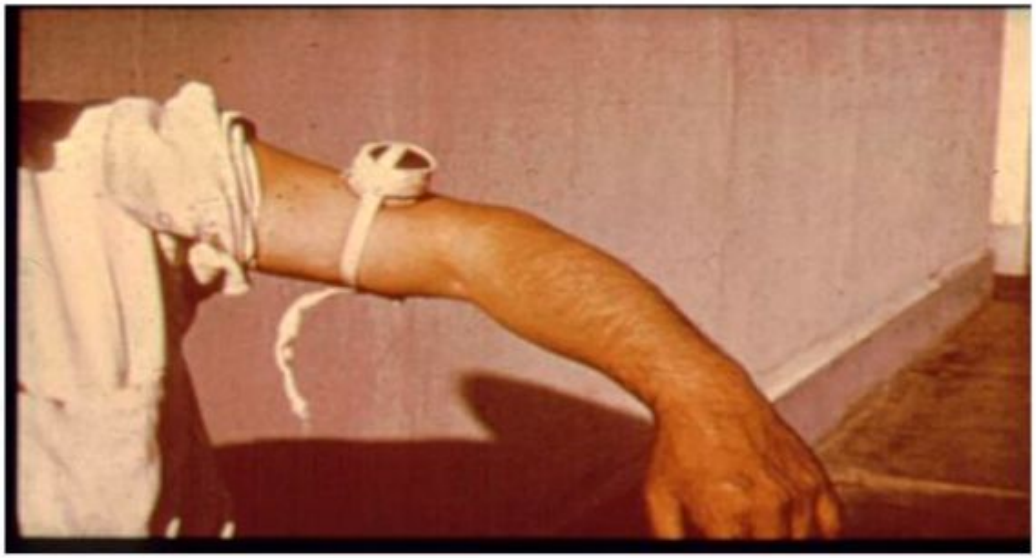


Serological tests

Cruzin test (I.D.)

Molecular techniques

Diagnosis (Xenodiagnosis)



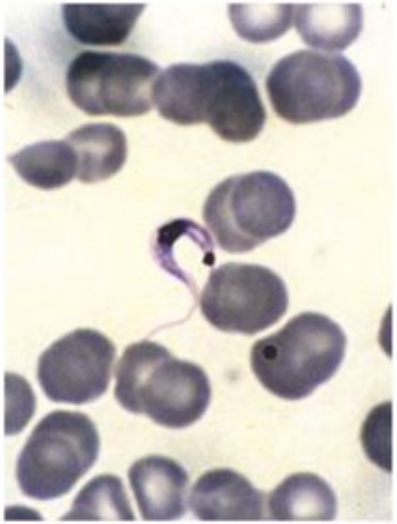
Highly efficient – demonstrate low level of parasite in blood

Method:

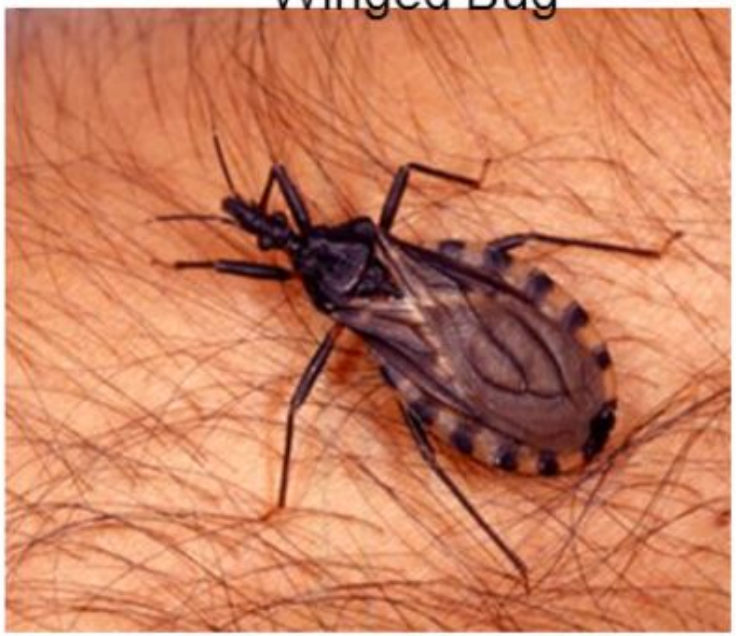
A Laboratory bred winged bug is starved for 2 weeks then fed on suspected patient's blood – 30 days later, it faeces & gut examined for trypanosomes.

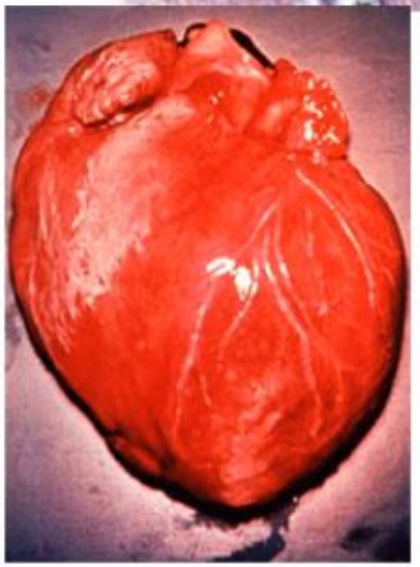
Diagnosis

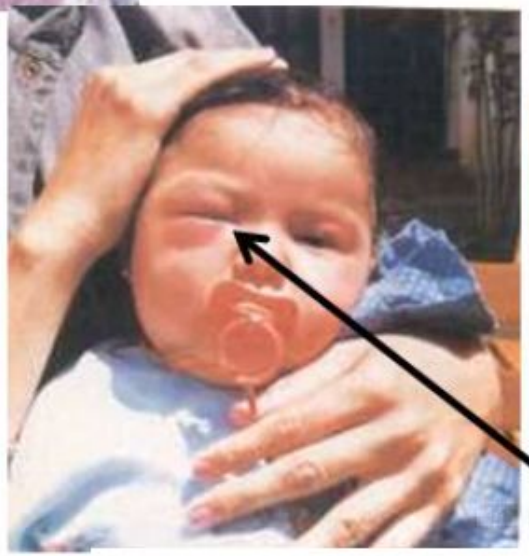
Trypomastigote

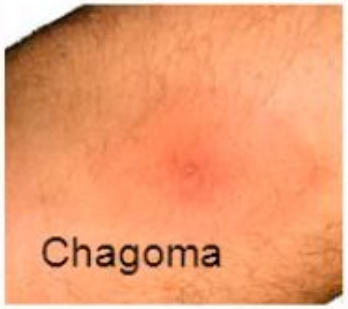


Winged Bug

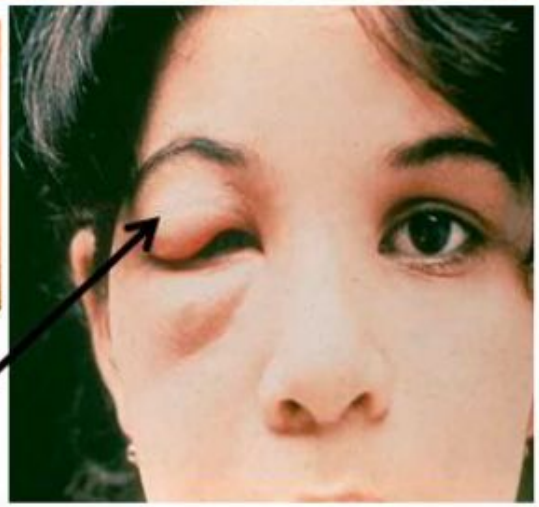






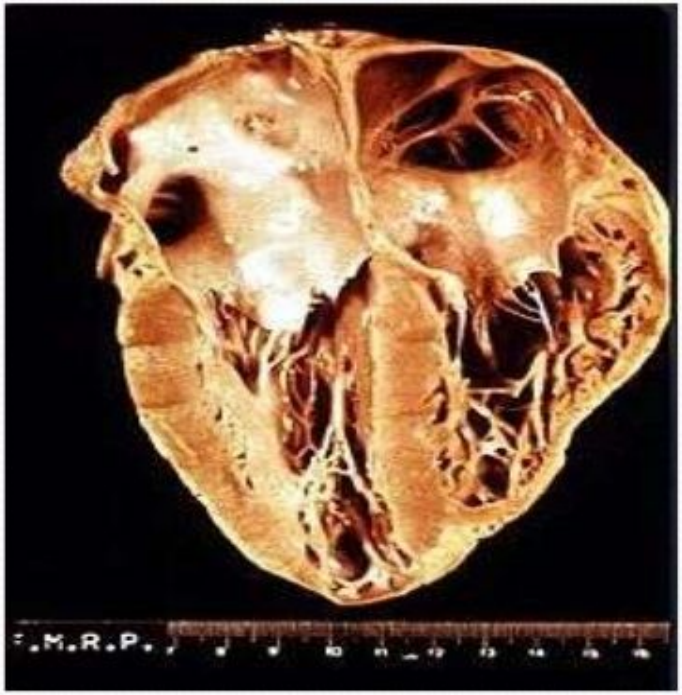


Romana's sign



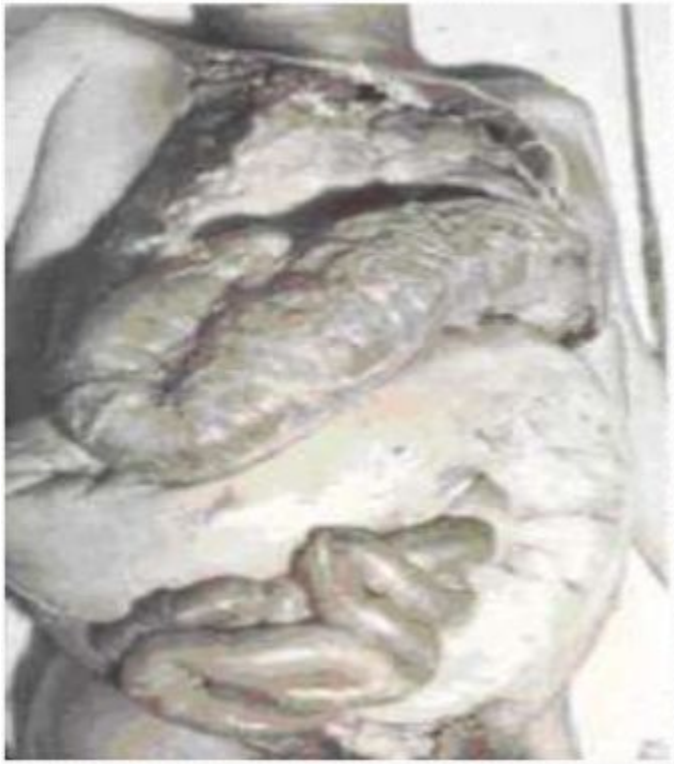
Clinical presentation

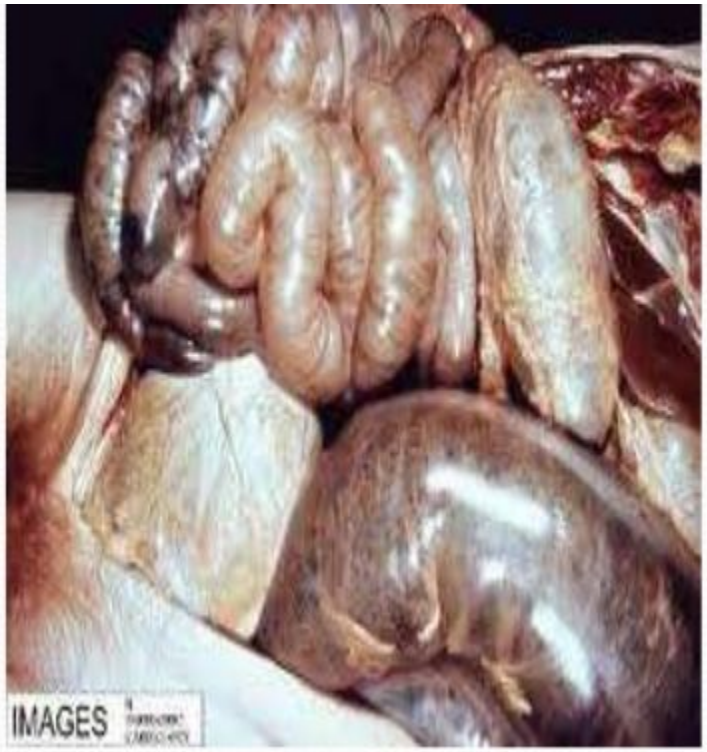
- Chronic stage.
  - In chronic stage these parasites reside in heart and midgut, and some time in hind gut causing giantism of the midgut.



Clinical presentation

- Gigantism of midgut





Treatment

Sleeping Sickness

In early stage of the disease:

Pentamidine OR Suramin

In late stages of the disease:

Tryparsamide

For both early and late stages of the disease:

Eflornithine (DFMO)
Ornidyl

Chagas Disease

Nifurtimox

- inhibits **intracellular** development .
- Drug of choice in acute and early chronic

OR

Primaquine

destroys **Trypanosoma** in blood

Control

Sleeping Sickness	Chagas' disease
Treatment of patients	Treatment of patients
Control of vectors (*Glossina*)	Control of vectors (*Triatoma*)
Pentamidine as prophylactic drug	Elimination of reservoir hosts