

# Trypanosoma Cruzi

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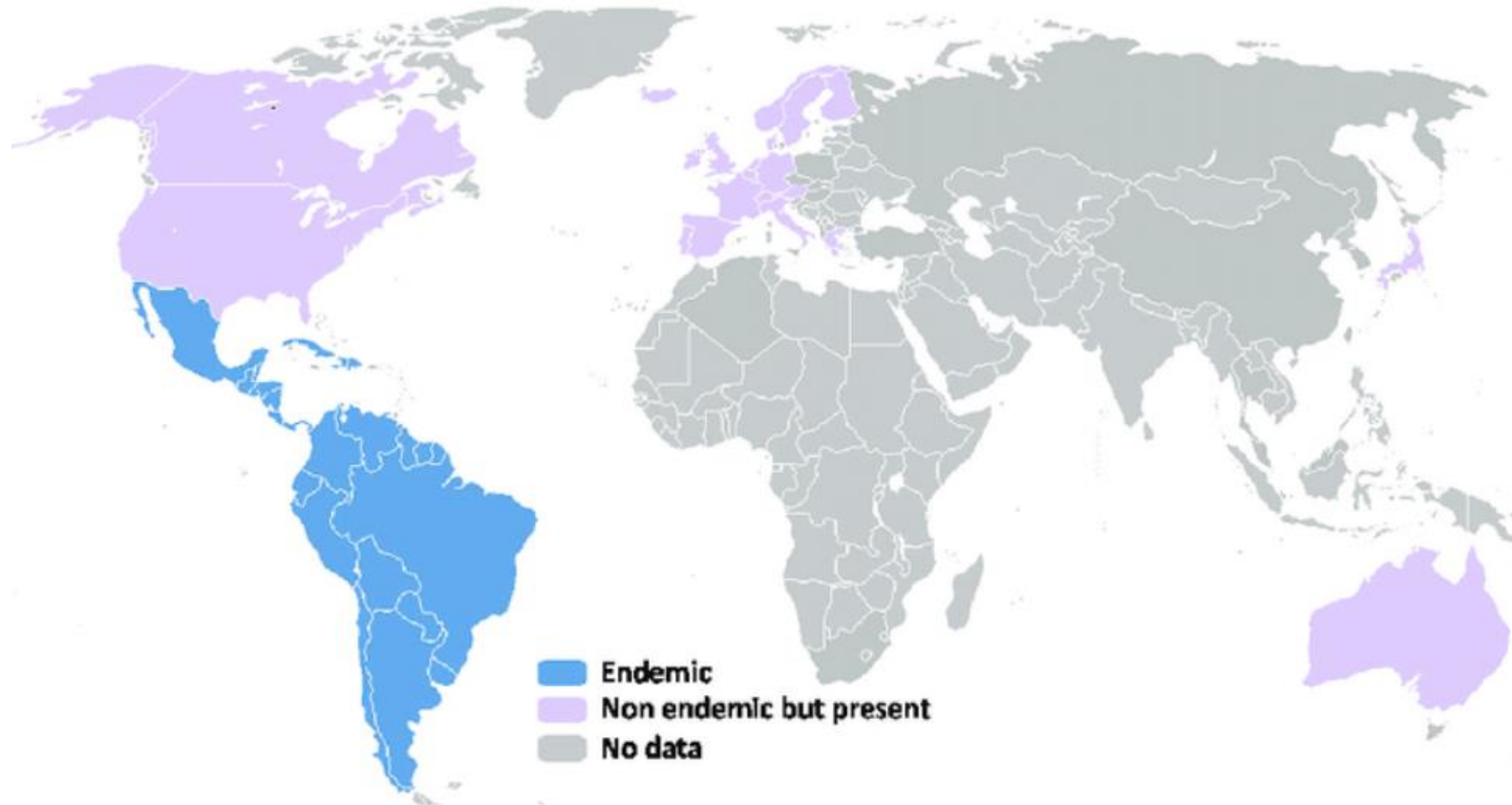
- Causative agent for a vector borne disease called Chagas's or South American trypanosomiasis.
- It is a zoonotic disease

## Epidemiology

- Chagas disease is found mainly in endemic areas of 21 countries in South & central America.
- An estimated 6 to 7 million people worldwide are infected with *T. cruzi*(WHO).
- About 75 million are at risk of infection(WHO)

# Global distribution showing the countries endemic for Chagas disease

**Geographic distribution of Chagas disease**

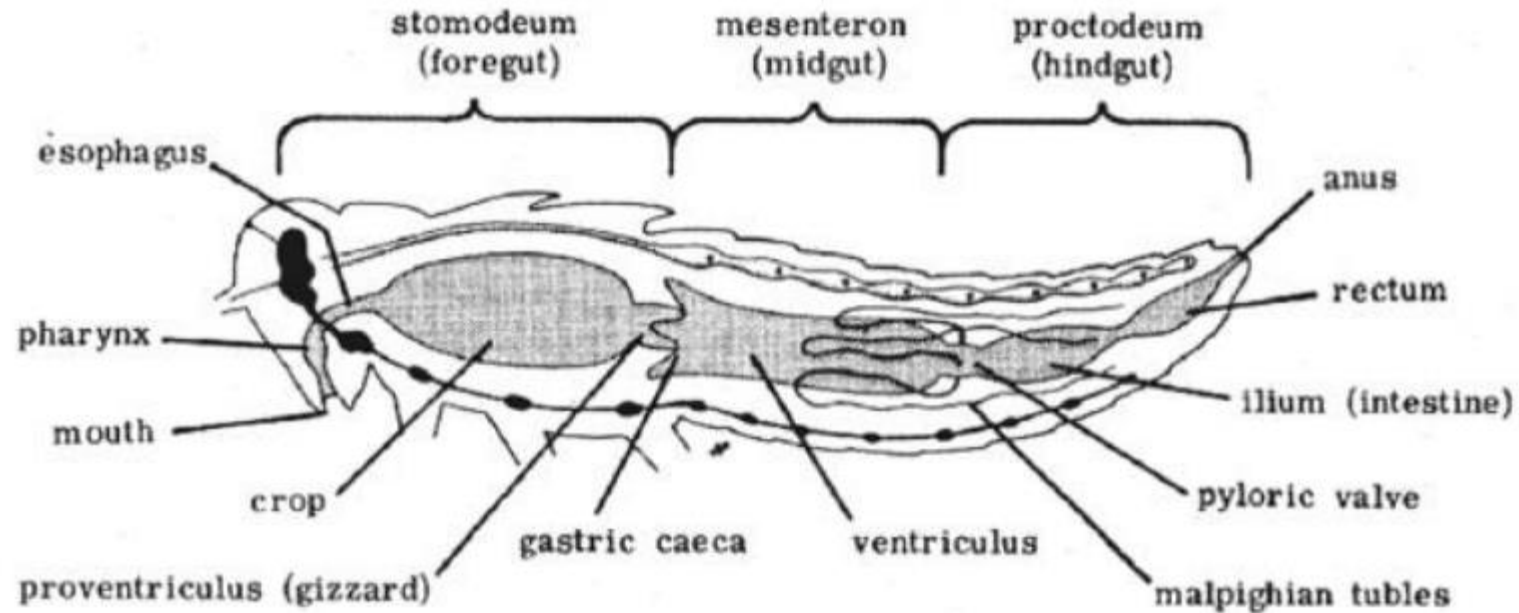


- The epidemiological pattern has however changed mainly due to population mobility, urbanization & emigration.
- As a result, increased number of cases have been detected in Canada, USA, Europe & Western Pacific countries.

# Habitat

- Two forms are found in humans.
  - Amastigote
  - Trypomastigote.
- These parasite forms are found in different tissues-peripheral blood ,muscle tissue, nervous tissue & RES.
- Amastigotes are intracellular parasites while trypomastigotes are found in the peripheral blood.

- In the insect vector-reduviid bugs, amastigotes are found in midgut & metacyclic trypomastigotes are found in hindgut & feces.

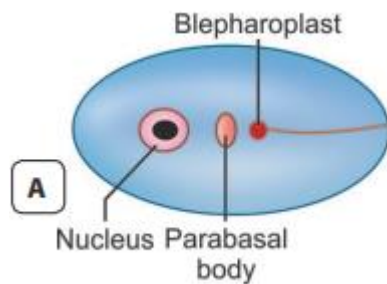


The "generalized" digestive system of insects.

# Morphology

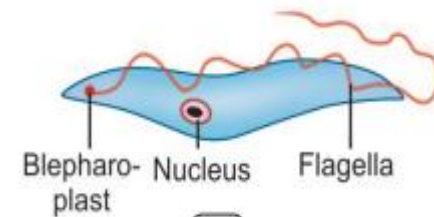
## □ Amastigote

- Amastigotes are oval (2–4  $\mu\text{m}$  in diameter) with a nucleus, kinetoplast & absent flagellum.
- It is the multiplication stage of the parasite.
- Found in muscles, nerve cells & reticulo-endothelial system.



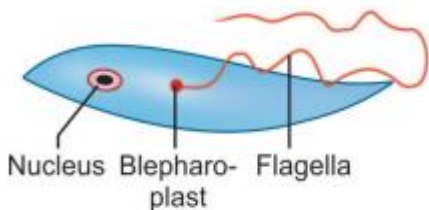
## □ Trypomastigote

- Do not multiply & found in the peripheral blood of man/mammalian hosts.
- May appear as long slender flagellates (20  $\mu\text{m}$  long) or short stumpy form (15  $\mu\text{m}$  long) in blood.
- They assume different shapes in stained smears- e.g. letters U,S or C.
- This is the form taken up by the insect vector.



## □ Epimastigote

- Are found in the insect vector- the reduviid bug and also in culture.
- Epimastigotes divide by binary fission in hindgut of the vector
- It has a kinetoplast adjacent to the nucleus & an undulating membrane situated along its anterior half.



# Life Cycle

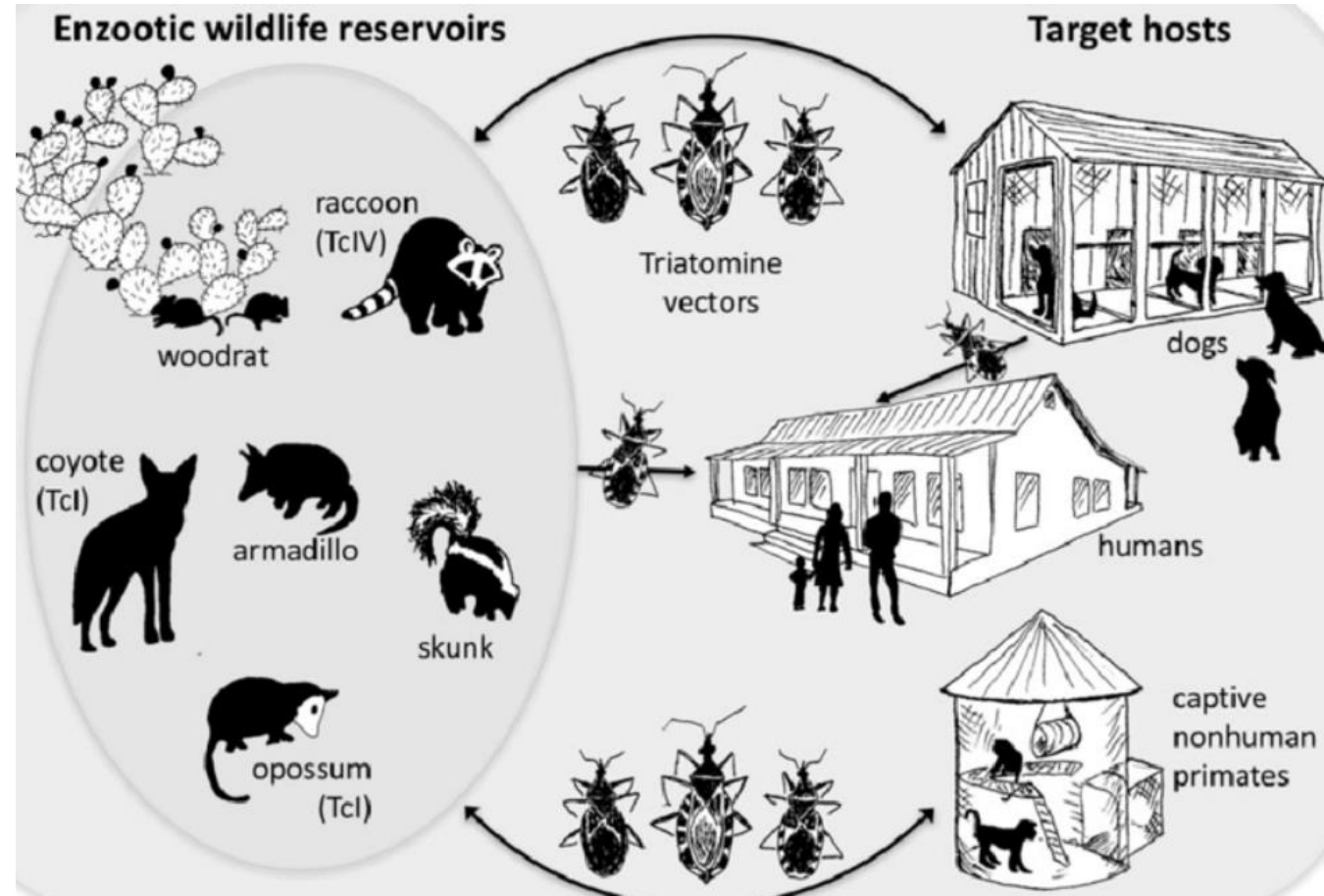
- T. cruzi passes its life cycle in 2 hosts.
- **Definitive host:** Man
- **Intermediate host (vector):** Reduviid bug or triatomine bug.
- **Reservoir host:** Armadillo & domestic animals- cat, dog & pigs.
- **Infective form:** The infective forms are metacyclic trypomastigotes found in feces of reduviid bugs.

# Different reservoir hosts for T.Cruzi



- The parasite occurs in 3 different but overlapping infection cycles.
- Sylvatic zoonosis in wild animals e.g. armadillos, peri-domestic cycle in domestic animals e.g. cat/dogs & a domestic cycle in humans.
- Different vector species are active in these infection cycles.
- The reduviid bugs-Triatoma infestans, Rhodnius prolixus & Panstrongylus megistus are important vectors in human infection.
- These are adapted to living in human habitations-cracked walls & roofs.
- These are night-biting bugs which typically defecate while feeding.
- The feces of infected bugs contain the metacyclic trypomastigote.

# Sylvatic zoonosis, peri-domestic & a domestic cycle in humans.



## □ Mode of transmission

- Infection in man & other reservoir hosts occur when mucus membranes or a sore on skin is contaminated by feces of the bug with metacyclic trypomastigotes.
- Other modes of transmission are:-blood transfusion
  - organ transplantation
  - vertical transmission
  - rarely ingestion of contaminated food or drink.

## □ Development in Man

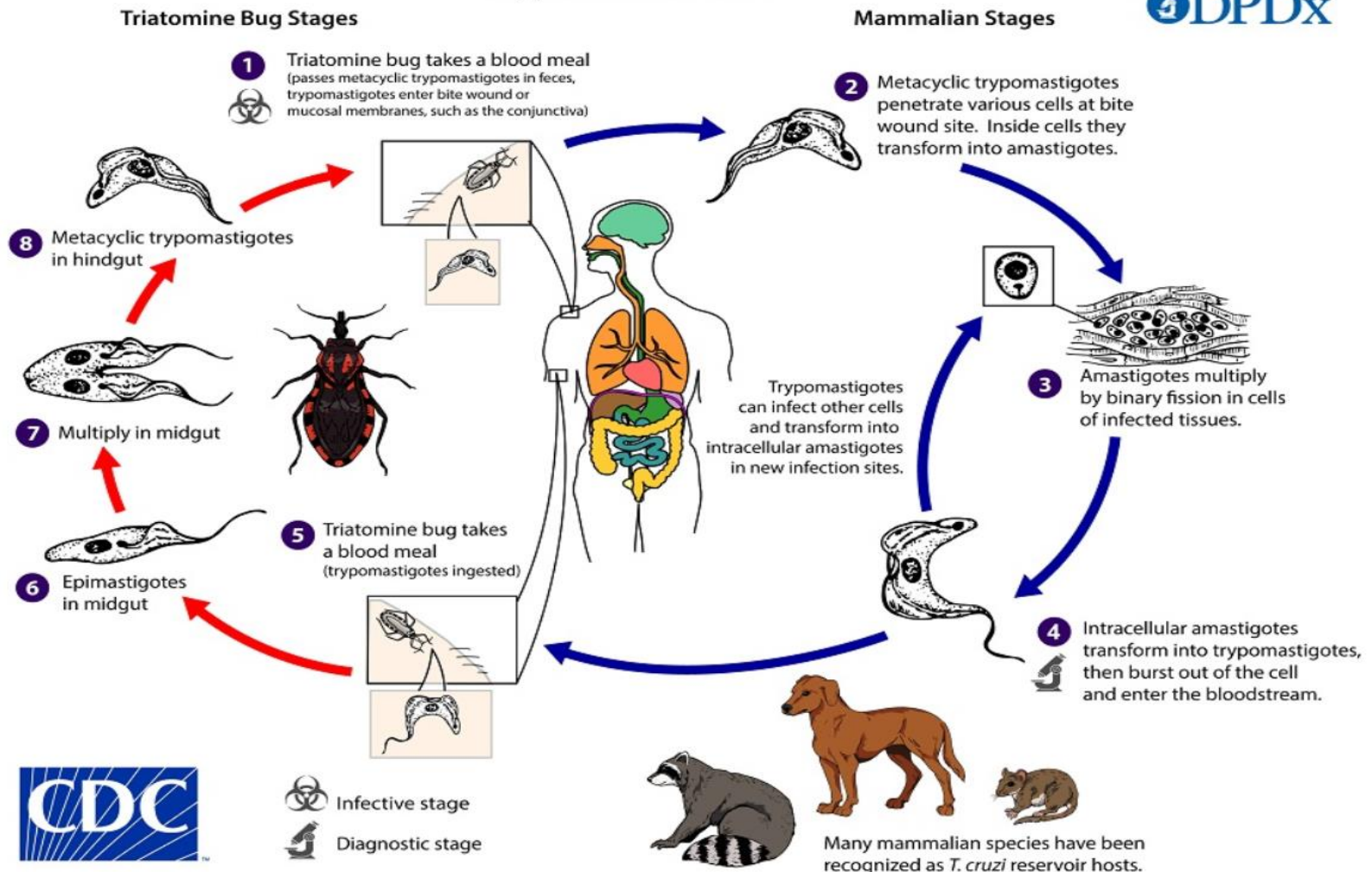
- The metacyclic trypomastigotes introduced by bite of bug invade the RES & spread to other tissues.
- After passing through promastigote & epimastigote forms, they again become trypomastigotes which are the infective stage for reduviid bug.
- No multiplication occurs in this stage except intracellularly in the amastigote form.

## □ Development in Reduviid Bugs

- Acquire infection by feeding on an infected host.
- Most triatomine bugs are nocturnal i.e. active at night.
- The ingested trypomastigotes transform into epimastigotes in the midgut then migrate to the hindgut and multiply.
- These, in turn become metacyclic trypomastigotes (infective form) which are excreted in feces (stercorarian transmission).
- Incubation period in the vector takes 8–10 days (extrinsic incubation period).

# Life cycle

## Trypanosoma cruzi



# Pathogenesis & Clinical Features

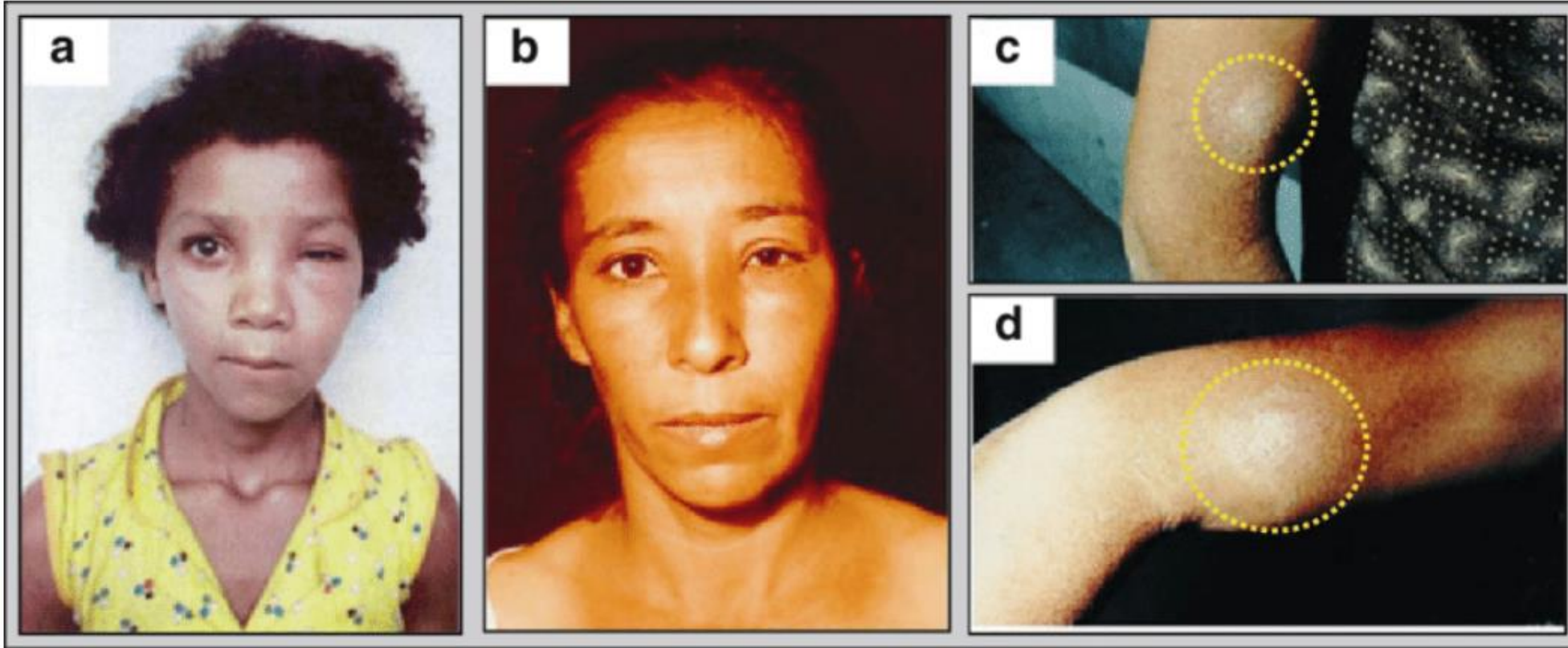
- The disease manifests in an acute and chronic form.
- Average incubation period in man is 1–2 weeks.
- Acute Chagas' Disease
  - Often occur in children under 2 years of age & occurs soon after infection.
  - May last 1–4 months with the first sign appearing within a week post infection.
  - Chagoma is the typical subcutaneous lesion occurring at the site of infection.

# Chagoma at infection site



**Fig. 1** - Inoculation chagoma on the dorsal surface of the left hand at the base of the thumb, 21 days after accidental inoculation with blood trypomastigote forms of *Trypanosoma cruzi* in a 42-year-old female patient.

Inoculation of the parasite in conjunctiva causes unilateral, painless edema of periocular tissues in the eye called as Romana's sign.



Signals of portal of entry (a) and (b): Romana's sign; (c) and (d): chagoma in the arm (circle)

This is the classical finding of the acute Chagas' disease.

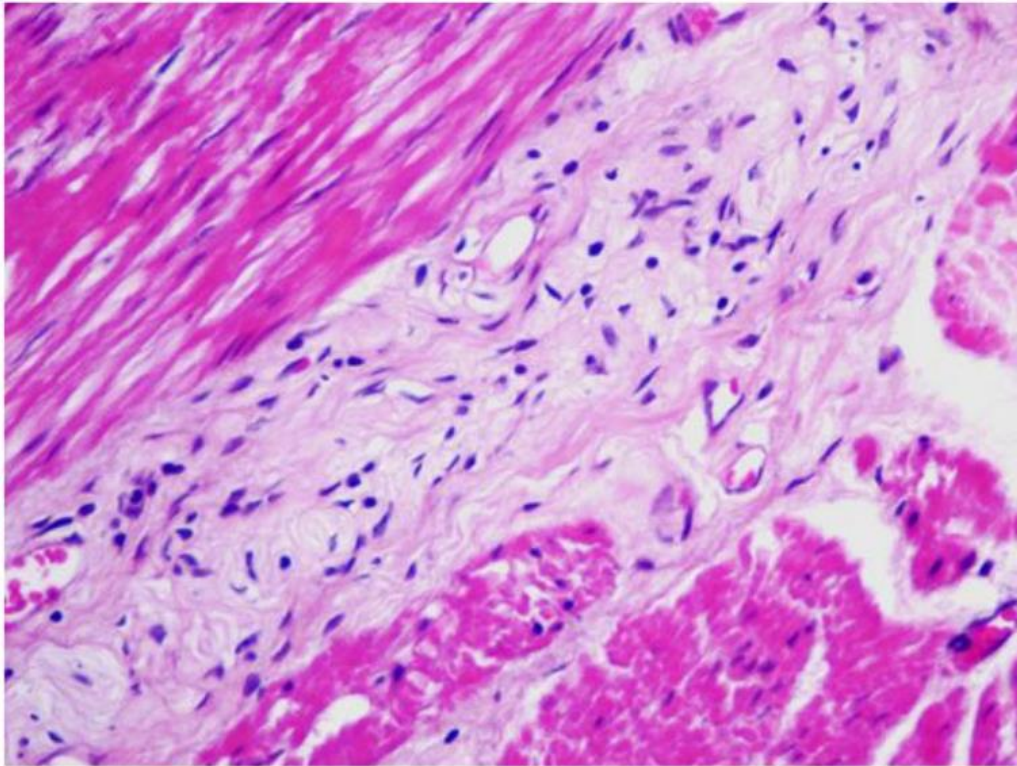
- In some cases, patients may have generalized infection with fever, lymphadenopathy & hepatosplenomegaly.
- The patient may die of acute myocarditis and meningoencephalitis.
- Acute signs and symptoms usually resolve spontaneously within 4–8 weeks.
- Thereafter patients ,enter the asymptomatic or indeterminate phase of chronic *T. cruzi* infection.

## ❑ Chronic Chagas' Disease

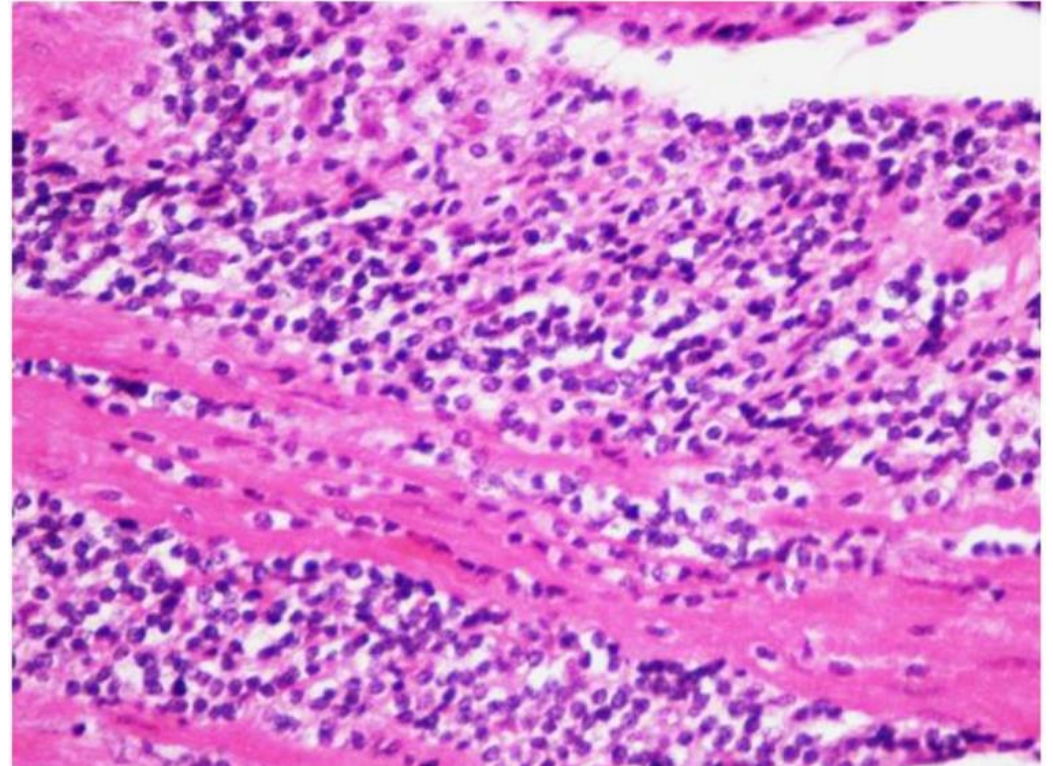
- Usually seen years or even decades after the initial infection.
- The chronic form is found in adults and older children.
- In chronic phase, *T. cruzi* produces an inflammatory response, cell destruction, fibrosis of muscles and nerves that control muscle tone of hollow organs like heart, esophagus, colon etc.
- Thus, it can lead to cardiac myopathy and mega-esophagus & megacolon (dilation of esophagus and colon).

# Inflammatory response in chronic phase

Aganglionosis & fibrosis in myenteric plexus in case of megaesophagus

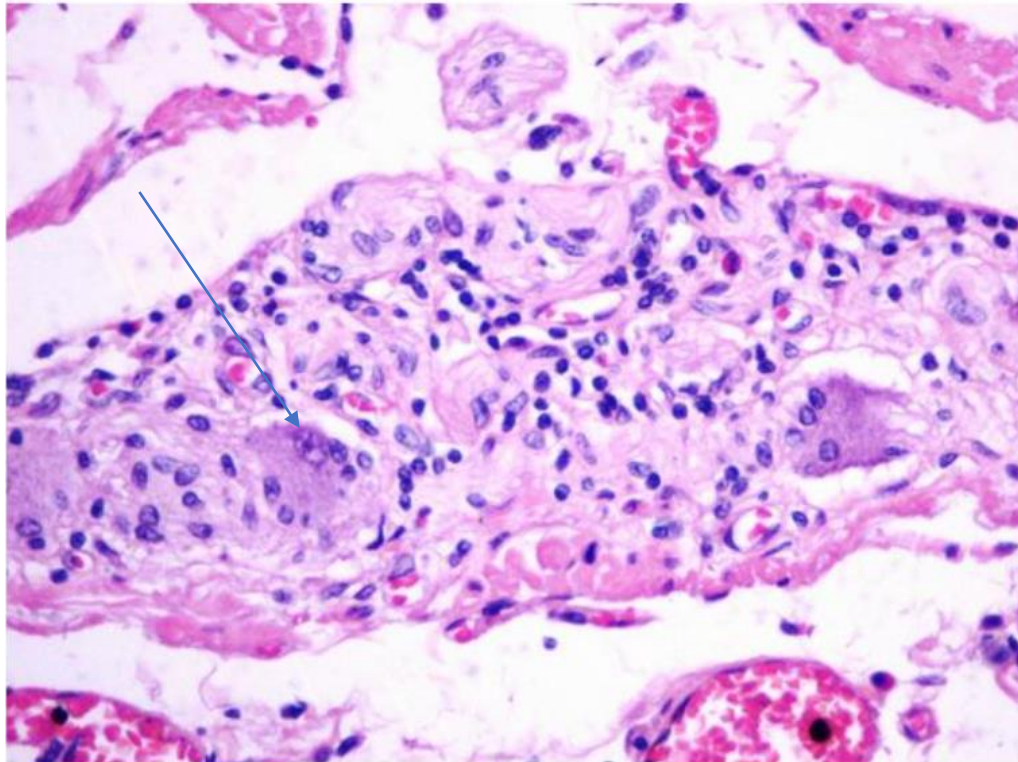


Severe chronic myositis in a case of megaesophagus

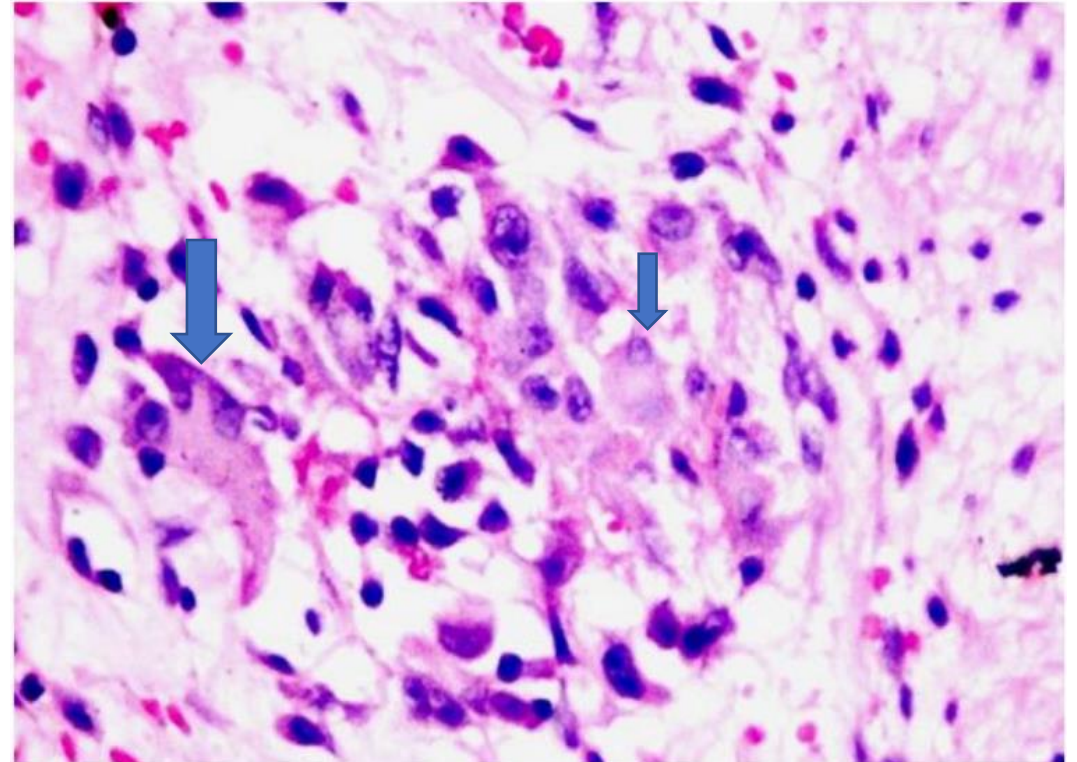


# Inflammatory response in chronic phase

**Mild chronic ganglionitis in esophagus without mega-arrow at ganglion cell**

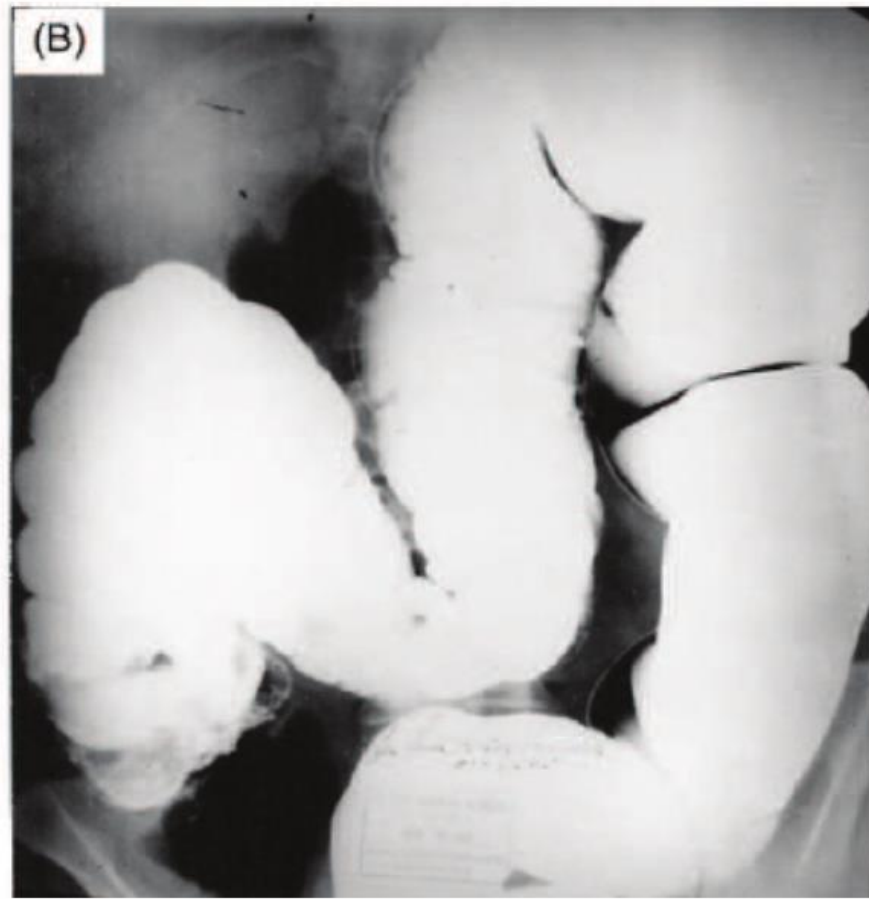
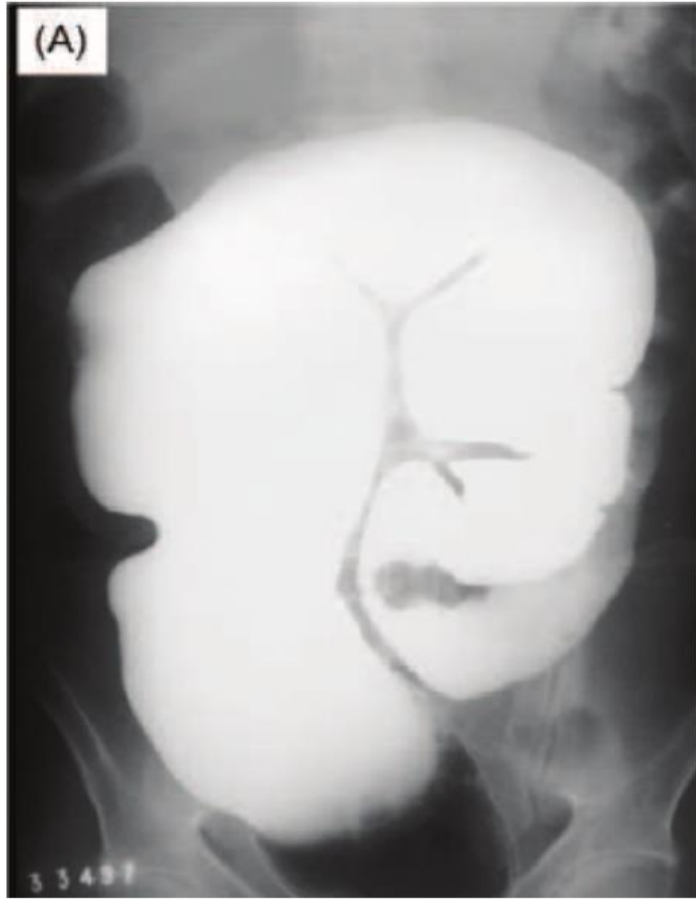


**Myositis with granuloma in a case of megacolon-see giant cell & histiocyte**



Chest X-ray showing increased cardiac area of a patient with Chagas cardiomyopathy





13 Chagasic megacolon. (A) Dilatation is mainly at the rectum and sigmoid. (B) Total megacolon (rare).

## ❑ Congenital Infection

- Congenital transmission is possible in both acute & chronic phase of the disease causing myocardial and neurological damage in the fetus.

# Laboratory Diagnosis

- Diagnosis is done by demonstration of *T. cruzi* in blood or tissues or by serology.
- Microscopy
  - The diagnosis of acute Chagas' disease requires detection of parasites.
  - Microscopic examination of fresh anticoagulated blood or the buffy coat is the simplest way to see motile organisms.
  - In wet mount, trypomastigotes are faintly visible but their snake-like motion against RBC's makes their presence apparent.
  - Trypomastigotes can also be seen in thick and thin peripheral blood smear, stained with Giemsa stain.

## □ Culture

- Novy, Neal, and Nicolle (NNN) medium or its modifications are used for growing *T. cruzi*.
- Epimastigotes and trypomastigotes are found in the culture.
- Culture is more sensitive than smear microscopy

## ❑ Animal Inoculation

- Done in Guinea pig or mice where blood, CSF or lymph node aspirate are inoculated.
- Trypomastigotes are looked for in the blood smears in a few days after successful inoculation.

## ❑ Histopathology

- Biopsy examination of lymph nodes and skeletal muscles and aspirate from Chagoma may reveal amastigotes of *T. cruzi*.

## ❑ Serology

- Antigens can be detected in urine and sera in patients with chronic Chagas' disease.
- ELISA has been developed for detection of antigens.
- Antibody detection done by the following the following tests – IHA ,CFT ,ELISA,IIF,Direct agglutination test (DAT).
- Antibody tests are recommended for field use.
- Cross reaction occur syphilis & leishmaniasis hence false positives. Major drawback for antibody based tests.

## ❑ Intradermal Test

- The antigen 'cruzin' is prepared from *T. cruzi* culture is used for the test.
- A delayed hypersensitivity reaction is seen.

## ❑ Molecular Diagnosis

- PCR can be done but not commercially available.

## ❑ Other Tests

- Electrocardiography (ECG) and chest X-ray are useful for diagnosis and prognosis of cardiomyopathy seen in chronic Chagas' disease.
- The combination of right bundle branch block (RBBB) and left anterior fascicular block is a typical feature of Chagas' heart disease.
- Endoscopy helps in visualization of megaesophagus in Chagas' disease.

# Treatment

- No effective specific treatment is available for treating Chagas' disease.
- Nifutrimox and benznidazole have been used with some success in both acute and chronic Chagas disease.
- These drugs kill only the extracellular forms but not the intracellular forms.
- Dose: Nifutrimox: 8–10 mg/kg for adults and 15 mg/kg for children.
- The drug should be given orally in 4 divided doses each day for 90–120 days.
- Benznidazole: 5–10 mg/day orally for 60 days.

- Anti-failure medication is used for cases of cardiac myopathy.
- Surgical intervention is indicated where required.

# Prevention

- Use of insecticide to control the vector bug.
- Personal protection using insect repellent and mosquito net.
- Improvement in rural housing & environment to eliminate breeding places of bugs.

End!!!

Thank you