Reduviid Bugs

1. Many species defecate during feeding, host rubs feces into wound.
   a. Trypanosomes also seem to be transmitted among bugs – horizontal transfer.
1. Cannibalism occurs.
2. Possible transmission during mating.

Trypanosoma cruzi - Chagas' Disease

b. Discovered them in bugs first before it was recognized as a disease.

Habitat of T. infestans
Chagas was sent by the Director of a new Medical Institute in Rio de Janeiro in Brazil, Oswaldo Cruz, to carry out an antimalaria campaign in support of the construction of a rail line in the State of Minas Gerais.

Though Chagas was convinced he had found the vector of a human disease he did not know what that disease was. In 1909, two or three weeks after finding triatomines and a cat infected with T. cruzi he was called to treat a seriously ill 2 year old child named Berenice. She was feverish, had an enlarged spleen, liver and swollen lymph nodes and her blood teemed with trypanosomes similar in morphology to those found in the marmoset. He wrote: "Examination between cover glass and slide revealed the existence of flagellates in good number and fixing and staining of blood films made it possible to characterize the parasite's morphology and to identify it with Schizotrypanum cruzi".

After he had been there for one year, a railroad engineer, named Cantarino Mota, told him about blood sucking bugs in the local huts, which were called "barbeiros" or "kissing bugs" due to their behavior of biting sleeping people on the face. Chagas then became interested in seeing if this bug could be transmitting some disease to humans or animals. He examined the hindgut contents of a bloodsucking triatomine bug (Panstrongylus megistus), and found numerous flagellates which resembled stages of a trypanosome he has described previously from a marmoset. Chagas sent infected triatomine bugs to the Institute in Rio where they were allowed to bite monkeys and after 30 days large numbers of trypanosomes were found in the peripheral blood. Subsequently, it was found that other animals i.e. rabbits, pigs, dogs and other monkeys, could also be infected.

In 1911 Chagas described the dividing forms in heart muscle. The connection between human disease and the bloodsucking bug had been made. In 1912 Chagas found that the armadillo was a reservoir host.

The species name was given to honor the scientist, Oswaldo Cruz, who was the mentor of Carlos Chagas and the Director of the Oswaldo Cruz Institute where Chagas worked. The disease is named after Chagas. At 29 years of age, Carlos Chagas had described the agent, the vectors, clinical symptoms in humans and animals, and the existence of a new disease.

Unfortunately he made some enemies, including Charles Donovan and a German microbiologist named Krause. Krause denounced Chagas’ findings and for 20 years his work was forgotten.

Trypanosoma cruzi

a. Chagas thought they underwent schizogony in lungs.

b. A form of division that results in multiple trypanosomes.
**T. cruzi Infections**

b. Repeated binary fission causes cells to lyse – infect other cells.
   1. Often with intermediate forms interstitially - promastigotes and epimastigotes.

![Trypanosoma cruzi image](image)

*Figure 5.9*
*Trypanosoma cruzi amastigotes in cardiac muscle (> 700)*

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**Trypanosoma cruzi**

b. Chagas named them *Schizotrypanum cruzi*.

1. This is probably the appropriate name by priority.
2. They have an amastigote stage in tissues.
   a. This is part of their unusual pathology

**T. cruzi Transmission**

1. Infected bugs feed and introduce metacyclic trypanosomes in feces.
2. Reproduction of trypanosomes occurs in subcutaneous cells.
   a. often causes a local swelling or *chagoma*
   b. local lymph gland swelling.

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**T. cruzi Transmission**

*Romaña’s Sign*

2. Can also occur through eye as well.
   a. Distinctive conjunctivitis is called *Romana’s sign.*

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**Romaña’s Sign**

*Hepatosplenomegaly*
T. cruzi Life Cycle

1. Trypomastigotes enter blood, are picked up by feeding bug
   a. In bug gut, become short epimastigotes.
   b. Replicate to become slender epimastigotes.

2. Later (8-10 days) become metacyclic trypomastigotes.

3. Become infective from other bites.

T. cruzi Infections

1. Trypanosomes are initially abundant in blood but then are rapidly cleared by immune system.
   a. Cryptic infections diagnosed by allowing cleared bugs to feed and examining them.
   b. When seen in blood, tryps have an "S" or "U" shape.
The ACUTE phase of *Trypanosoma cruzi* infection

1. Romaña’s Sign  
2. Fever  
3. Hepatosplenomegaly  
4. Trypomastigotes in Blood  
5. Lasts 2–8 weeks  
6. 10% Mortality

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*T. cruzi* Infections

2. Contrary to Chagas, do not replicate until they enter cells of spleen or smooth/cardiac muscle.  
a. Then form amastigote forms - pseudocysts full of amastigotes

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The INDETERMINATE phase

1. No parasite evident in blood  
2. Amastigote nests in muscle tissue  
3. Anti-*T. cruzi* IgG present

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CHRONIC phase of Chagas Disease

1. Nerve Degeneration  
2. Cardiomyopathy (80%)  
   Heart arrhythmia and blocks  
   Heart enlargement (cardiomegaly)  
   Apical aneurism  
3. Megaesophagus (25%)  
4. Megacolon (30%)
**T. cruzi: The Disease Process**

1. Is more severe in younger people.
   a. Tissue destruction due to *pseudocysts*
      1. Especially esophagus, colon stretched out – *megacolon*.

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**Megacolon**

- Constipation
- Abdomen

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**T. cruzi: The Disease Process**


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**Cardiomegaly**

**Apical Aneurysm**

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**Hepatosplenomegaly**

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**Figure 5.10**

Pseudocyst of *Trypanosoma cruzi* in brain tissue.

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**Figure 5.11**

Diaphanised tricuspid valves with zinc-orange impregnation of nerve fibers (dark lines). (a) Normal heart; (b) Chagas’ cardiopathy with marked reduction of nerve fibers.

**T. cruzi Distribution**

1. New world, where there are biting bugs a. Has been reported in Verde Valley b. Travel has caused spread to other areas of world.

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**Fecal transmission of T. cruzi**

There are several genera of Reduviidae that can transmit the protozoan. Triatoma infestans, as its name suggests, frequently invades homes (mud and stick huts) and is responsible for what is termed the domestic transmission cycle. Other reduviids, such as Rhodnius prolixus, reside in rural settings or forests; they are associated with the sylvatic cycle of transmission, which includes many wild animals as vertebrate hosts. As mentioned above, the common reduvid vectors R. prolixus and Panstrongylus megistus defecate during the blood meal, allowing efficient infection by the parasite.

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**T. cruzi Treatment**

1. Not much available (!) although ketoconazole seems to work fairly well experimentally.

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**Development of a Vaccine against T. cruzi**

Vaccines consisting of attenuated parasites, crude parasite lysates, partially purified proteins, and synthetic peptides have been tested with varying success. Some gave partial protection. Crude flagellar extracts were found to induce more than 90% protective immunity in mice and to reduce tissue lesions after a challenge infection. A series of studies from the Manning laboratory since 1995 have defined several protein components of the flagellar apparatus which appear to provide this protection.

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**Infection of Charles Darwin**

1. Correspondence indicates that he was bitten by a wheel bug while in Tierra del Fuego. 2. He reported crushing the insect in disgust after a painful bite.
The Voyage of the Beagle

In his own words:

“We slept in the village, which is a small place, surrounded by gardens, and forms the most southern part, that is cultivated, of the province of Mendoza; it is five leagues south of the capital. At night I experienced an attack (for it deserves no less a name) of the Benchuca (a species of Reduvius) the great black bug of the Pampas. It is most disgusting to feel soft, wingless insects, about an inch long, crawling over one’s body. Before sucking, they are quite thin, but afterwards become round and bloated with blood, and in this state are easily crushed. They are also found in the northern parts of Chile and in Peru.”

This insect was the triatomid, Triatoma infestans, of which today more than 70% of the insects in that region are infected with T. cruzi. Also 12% of the population in Mendoza today has antibodies against T. cruzi. Darwin returned to his ship and even brought back some of these insects and fed them on the sailors. Darwin was at that time one of the most active members of the Beagle’s crew. He often took long overland expeditions and was a mountain climber. He returned to England in 1836 and in 1838 his health suddenly became poor. His health became progressively worse and he suffered from periodic vomiting, fatigue and flatulence. After social dinners he had violent shivering and vomiting attacks, and mainly for these reasons he gave up all social interactions. His diaries are full of descriptions of his mysterious illness. He wrote to the Botanist, Joseph Hooker, in 1845:

“I believe that I have not had a whole day, or rather night, during these last three years, without my stomach being greatly disordered, and most days great prostration of strength.” In 1849 he was too ill to attend his father’s funeral. He wrote: “I was quite broken down, head swimmy, hands trembling and never a week without violent vomiting.”

Infection of Charles Darwin

2. Later years of his life were marked by weakness, heart palpitations, malaise and flatulence.
   a. These are all symptoms of Chagas disease.

Other Stercoraria

1. *T. rangeli* - South American, similar to *T. cruzi*.
   a. Often mixed infections occur.

Other Stercoraria

2. *T. lewisi* - common in rodents, especially rats.
   a. Vectored by fleas.

Other Flagellates

1. Many of species discussed for next few lectures are intestinal or mucous membrane parasites or commensals
The Vertebrate Gut
a. pH 1.5-8.5
b. Enzymes and acids
c. Variable O2 levels
d. Peristaltic action
e. Flushing
d. Lots of other commensals!

How Parasites May Cope
1. Attachment.
2. Changing the environment - part of their pathology.
3. Cloaking themselves to prevent detection (minor here).
4. Escape: into intestinal mucosa.

Phylum Retortamonada
a. Intestinal parasites, lacking mitochondria.
b. Three anterior flagella, one recurrent flagellum

Chilomastix mesnili
1. Pyriform gut parasite of humans (other characters in lab and book).
   a. Actively feeding form is trophozoite.

Chilomastix mesnili
b. Usually diagnosed by cysts that form in lower intestine.
c. Considered nonpathogenic, causes mild diarrhea.

C. mesnili Life Cycle
1. Transmitted by cysts in stools, thus indicate contaminated water.
2. Cysts hatch in intestine, trophs live in lower gut.
   a. Distinctive with lemon shape, large nucleus, fibrils.