Chagas Disease

FACTORS
Impact: 18-25 million cases
Risk: 100 million in 21 countries
Agent: *Trypanosoma cruzi*
Vector: *Triatomes*
Distribution: North, Central and South America

4th leading cause of mortality in Latin America
45,000 deaths per year directly attributed to Chagas

Leading cause of cardiac disease in S. and Central America

Discovered by Carlos Chagas- named organism after mentor, Oswaldo Cruz
determined life cycle described salient features of disease
Chagas Disease Transmission

Transmission Routes by Significance:

- Vector-borne transmission  >80%
- Blood transfusion  16%
- Congenital  2%
- Other routes  <1%
  (i.e. oral, organ transplant, laboratory accident)
In the US: Trypanosomiasis is rare in the United States, but it has been reported in Texas, Oklahoma, and California. As many as 5% of immigrants in Washington, DC, were found to have *T. cruzi*, and as many as 50,000-100,000 immigrants in the United States are thought to be infected. Transfusion-related cases, although rare, are increasingly recognized.
Chagas disease is a protozooan infection widespread among small wild mammals (enzootic sylvatic cycle).

Human disease constitutes a more recent situation in which bio-ecological and socioeconomic factors have placed the rural population in contact with the sylvatic cycle.

Because of the new opportunities certain vector species have adapted to humans and their households.

Cost not easily measured: significant loss of hours at work, and medical treatment estimated at >500 million US
Triatominne Bug Stages

1. Triatominne bug takes a blood meal (passes metacyclic trypomastigotes in feces, trypomastigotes enter bite wound or mucosal membranes, such as the conjunctiva)

2. Metacyclic trypomastigotes penetrate various cells at bite wound site. Inside cells they transform into amastigotes.

3. Amastigotes multiply by binary fission in cells of infected tissues.

4. Intracellular amastigotes transform into trypomastigotes, then burst out of the cell and enter the bloodstream.

5. Triatominne bug takes a blood meal (trypomastigotes ingested)

6. Epimastigote stage in midgut

7. Trypomastigotes can infect other cells and transform into intracellular amastigotes in new infection sites. Clinical manifestations can result from this infective cycle.

8. Metacyclic trypomastigotes in hindgut

i = Infective Stage

= Diagnostic Stage
Four forms

1) Trypomastigote is the infective form in the mammalian blood (blood trypomastigote) and in rectum of the vector (metacyclic trypomastigote) Trypomastigotes do not divide. Motility is due to the free flagellum.

2) Epimastigote is the replicative stage in the insect and in tissue culture. It is elongated and very mobile

3) Amastigote is the intracellular replicative stage in the vertebrate. It is spherical, has no flagellum, and is not motile.

4) Spheromastigote is found in the stomach of the vector.
Cell organization dominated by presence /absence of flagella and its point of emergence from the cell, whether kinetoplast is anterior or posterior to nucleus in relation to locomotion.
Triatomine Vectors

- >100 species can transmit
- 3 primary vectors
  - *T. dimidiata* (Central Am.)
  - *R. prolixus* (Colombia and Venezuela)
  - *T. infestans* (‘southern cone’ countries)
Triatomine Species Diversity

Domiciliary, Peridomiciliary, Feral
# Types of Vector Transmission

<table>
<thead>
<tr>
<th>Salivarian</th>
<th>Stercorarian</th>
</tr>
</thead>
<tbody>
<tr>
<td>• transmission via mouth parts</td>
<td>• hind gut station</td>
</tr>
<tr>
<td>• very efficient</td>
<td>• acquired from feces or eating vector</td>
</tr>
<tr>
<td>• infection rate in vector is low</td>
<td>• inefficient</td>
</tr>
<tr>
<td></td>
<td>• infection rate in vector is high</td>
</tr>
</tbody>
</table>
As opposed to mosquitoes and flies, all stages bloodfeed!
There are three stages of the human disease:

The **acute stage** which appears shortly after the infection.

The **indeterminate stage** in which the person is infected, but apparently asymptomatic.

The **chronic stage** which appears after a silent period that may last several years. The lesions of the chronic phase irreversibly affect internal organs namely the heart, oesophagus and colon and the peripheral nervous system.

After several years of an asymptomatic period, ~30% of those infected develop cardiac symptoms which may lead to sudden death, 6% develop digestive damage mainly megaviscera, and 3% will present peripheral nervous involvement.
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
The INDETERMINATE phase

1. No parasite evident in blood

2. Amastigote nests in muscle tissue

3. Anti-\textit{T. cruzi} IgG present

Normal Heart

Chagasic Heart
**Chronic Stage**: For whatever reason the parasites invade most organs of the body, often causing heart, intestinal and oesophageal damage and progressive weakness.

In ~30% of those infected, fatal damage to the heart and digestive tract occurs during this chronic phase.

**Pathophysiology**

Acute phase: cells destroyed directly.  
Initial reaction is swelling, area infiltrated with macrophages, lymphocytes, eosinophils  
Spread by lymph to other areas of body  
Parasites inside cells (some ingested by blood cells, others in penetrated cells) become trypomastigotes, enter bloodstream and can infect cells/tissues, and can form pseudocysts containing hundreds of amastigotes).
Ten to 20 years after infection, people may develop the most serious symptoms of Chagas disease.

The ganglia can be destroyed- both in intestine and heart. Early in infection heart may be normal size- enlargement later. Heart becomes dilated, thin muscular wall, cannot function. In GI tract damage to ganglia can stop procesing- megacolon.

Cardiac problems, including an enlarged heart, altered heart rate or rhythm, heart failure, or cardiac arrest are symptoms of chronic disease.

In persons who are immune compromised, including persons with HIV/AIDS, Chagas disease can be severe. Not everyone will develop the chronic symptoms of Chagas disease.
Megaviscerae

- colon and esophagus most frequently affected
- megaesophagus
  - painful swallowing
  - regurgitation
- megacolon
  - severe constipation
Thin section of heart muscle (haemotoxylin & eosin stain) showing amastigote stage of Trypanosoma cruzi. Amastigotes multiply, destroying adjoining tissue, and form pseudocysts. Darkly stained, rod-like kinetoplasts are visible.
Chronic Chagas Disease

- 20% will develop symptoms:
  - Cardiomiopathy
  - Megasindrome: tubular organ disease
DIAGNOSIS

- parasite detection
  - direct examination
  - stained blood smears
  - inoculation into mice
  - in vitro culture
  - xenodiagnosis
  - PCR
- serological tests
  - hemagglutination
  - immunofluorescence
  - ELISA
  - complement fixation
The disease

Sudden Death in 10% of minors < 5yrs

No symptom (seropositive)

Acute phase

Indeterminate phase

Chronic phase

35%

5-20 yrs

Treatment and diagnosis

(benznidazole, Nifurtimox)

Cure (95%)

Pediatric cases

Questionable cure

(65%)
TREATMENT

• acute stage
  – nifurtimox (8-16 mg/kg/day, 60-90 days)
  – benzidazole (5-7 mg/kg/day, 30-120 days)
  – allopurinol (experimental)
  – azole antifungal agents (experimental)

• chronic stage
  – treat symptoms
Chagas Control

- improvement of human dwellings
- separation of animal stalls from house (??)
- health education
- insecticides
  - synthetic pyrethroids
  - eg., Southern Cone Initiative
    - major ↓ in Chagas (T. infestans)
    - little effect with R. prolixus
- gentian violet in blood for transfusions
Chagas Disease Vector Control - Key Components

- Effective implementation
- Domiciliary insecticide application
  - residual pyrethroid formulations
- Broad geographic coverage
- Community-based surveillance
- Improved housing conditions
Chagas disease is a socioeconomic disease:

The risk of infection with Chagas disease is directly related to poverty: the blood-sucking triatomine bug which transmits the parasite finds a favourable habitat in crevices in the walls and roofs of poor houses in rural areas and in the peripheral urban slums. The rural/urban migration movements that occurred in Latin America in the 1970's and 1980's changed the traditional epidemiological pattern of Chagas disease and transformed it into an urban infection that can be transmitted by blood transfusion.

The figures of infection of blood in blood banks in some selected cities of the continent vary between 3.0 and 53.0 % thus showing that the prevalence of T. cruzi-infected blood is higher than that of HIV infection and Hepatitis B and C.
Housing Characteristics

- TECHOS DE ZINC
- PAREDES DE BAHAREQUE
- SITUADAS CERCA A BOSQUES
- PISOS DE TIERRA
Parasite-Vector reservoirs

Human alteration of Ecosystems
Transmission of *T. cruzi* in Venezuela

*Rhodnius prolixus*
Reservoirs

Cows, horses, tapirs and other large mammals generally are not susceptible.

Pigs, sheep, goats are infected but parasitemias is very low and transient.

Birds not susceptible but serve as blood source for vectors.

Small domestic mammals: guinea pigs, cats, dogs

Infected synanthropic mammals like opossums, armadillo, rats etc. are often highly infected and frequently invade the domestic and peridomestic areas.
Chagas Disease Transmission

Transmission Routes by Significance:
- Vector-borne transmission >80%
- Blood transfusion 16%
- Congenital 2%
- Other routes <1%
  (i.e. oral, organ transplant, laboratory accident)

HOW ELSE COULD TRANSMISSION TAKE PLACE?
2006: Outbreak in Amazon region of Brazil: in fruit juice
Açaí is the fruit of a palm of the family *Aracaceae*: Collected fruit, ground it up for fruit juice, it contained infected insects, whole family infected

2005 and 2009: Contaminated sugar cane juice is thought to be the source of a Brazilian outbreak of Chagas disease: Santa Catarina-recorded 45 cases of patients developing symptoms of Chagas disease after drinking the juice. At least five of the patients died.

Ingestion is “new” mode of transmission—very efficient for the parasites to enter via the mouth, cross mucosa

Probably the most common transmission mode in sylvatic cycle
Probably the most common transmission mode in remote villages

Insects crushed with sugar cane/fruit juice; few parasites needed to initiate the infection
Evidence that trypanosomiasis existed in the Americas is to be found in 2000 year-old mummies from Chile that show enlarged hollow viscera and cardiac fibrosis.
Indigenous *Trypanosoma cruzi* (& Chagas Disease) in the United States

### Indigenous Chagas Disease in the United States

1. **TEXAS**—Corpus Christi (1955)  
   2-year old child
2. **TEXAS**—(1955)  
   child
3. **CALIFORNIA**—Lake Don Pedro (1982)  
   56-year old adult
4. **TEXAS**—(1983)  
   7-month old child
Parasite Development in Vectors

Development of Parasites in Tsetse fly and *Rhodnius prolixus*

Parasites ingested with bloodmeal

Parasites remain for a period in midgut

Parasites do not enter the hemolymph

Parasites move anteriorly in tsetse fly, enter salivary glands

Parasites move posteriorly in reduviidae, enter rectum

Parasites transmitted during next bloodfeeding:
  - via saliva
  - via fecal contamination of feeding site

*Why stay in the GI tract? Why not move to salivary glands?*
The Case of Charles Darwin

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.
1. a) Are you feeling well today? ..................................................................................................................................................
b) Do you have a cold, flu, sore throat, fever, infection or allergy problem today?.................................................................

2. a) In the last 3 days have you taken any medicine or drugs (pills including Aspirin or shots), other than birth control pills and vitamins? ..........................................................................................................................................................
b) In the last 3 days have you had dental work? ........................................................................................................................................

3. In the last week, have you had a fever with headache? ............................................................................................................

4. a) In the last 3 months have you had a vaccination? .........................................................................................................................
b) In the last 3 months have you taken Accutane for skin problems? ..........................................................................................

5. a) In the last 6 months have you been under a doctor’s care, had surgery, taken Cyclomen (Danazol)? .........................................................................................................................
b) If female, in the last 6 months have you been pregnant? ...........................................................................................................
c) In the last 6 months have you taken Proscar, Avodart (Dutasteride), Propecia or Methotrexate? ............................................

6. a) In the last 12 months have you had a tattoo, ear piercing, skin piercing, acupuncture, electrolysis, graft, injury from a needle, or come in contact with someone else’s blood? ..........................................................................................................
b) In the last 12 months have you had a rabies shot? ....................................................................................................................
c) In the last 12 months have you had close contact with a person who has had hepatitis or yellow jaundice? .....................

7. a) Have you ever taken Tegison or Soriatane for skin problems? ..........................................................................................
b) Have you ever taken human pituitary growth hormone, human pituitary gonadotrophin hormone (sometimes used for treatment of infertility or to promote weight loss)? ...........................................................................................................
c) Have you ever received a dura mater (brain covering) graft? .................................................................................................

8. Have you ever had:
   a) yellow jaundice (other than at birth), hepatitis or liver problems? ..........................................................................................
b) epilepsy, coma, stroke, convulsions or fainting? ..........................................................................................................................
c) heart or blood pressure problems or heart surgery? ....................................................................................................................
d) cancer, diabetes, ulcerative colitis or Crohn’s disease? ...........................................................................................................
e) kidney, lung or blood problems? ............................................................................................................................................
f) Chagas’ disease, babesiosis or leishmaniasis? ..........................................................................................................................

9. a) Have you ever had malaria? ..................................................................................................................................................

10. a) Have you spent a total of 3 months or more in the United Kingdom (England, Northern Ireland, Scotland, Wales, the Isle of Man, or the Channel Islands) since January 1, 1980? .........................................................................................................................
b) If you have been in the United Kingdom since 1980, did you receive a blood transfusion or any medical treatment with a product made from blood? ..........................................................................................................................
c) Have you spent a total of 3 months or more in France since January 1, 1980? ........................................................................
d) Have you spent a total of 5 years or more in Europe since January 1, 1980? ..........................................................................

11. Are you aware of a diagnosis of Creutzfeldt-Jakob Disease among any of your blood relatives (parent, child, sibling)? .....

12. Have you ever had an AIDS (HIV) test other than for donating blood? ...........................................................................................

13. In the past 12 months, have you been in jail or prison? .............................................................................................................

RECORD OF DONATION