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Objectives

- Cite the population at risk for Chagas disease in the United States
- Describe the manifestations of Chagas disease in pregnant women and in infants
- Employ the best practice procedures for diagnosis and treatment of Chagas disease
“In the Los Angeles clinic of Sheba Meymandi, MD, about 20% of Latin American patients with heart failure can trace their illness to a cause many US physicians would never suspect: Chagas disease.”

“Chagas disease is joining an increasing list of infectious diseases such as dengue and chikungunya that are a concern in the United States.”

“It’s not an exotic disease any more”.

_JAMA_ March 24/31, 2015; 313:1195.
What is Chagas Disease?

- Chagas disease is a vector-borne zoonosis with many animal reservoirs that is caused by the protozoan parasite, *Trypanosoma cruzi*

- Most people who have Chagas disease live in Mexico, Central America or South America.

- The parasite is only found in the Americas. An estimated 8-10 million people in Latin America have Chagas disease.

- An estimated ~10,000 die each year from Chagas disease, usually from chronic heart disease.
The triatomine bug, often known as the “kissing bug” is the vector for Chagas disease. The bug becomes infected after biting an animal or a person who is already infected with *T. cruzi*. They are also called “benchuca”, “vinchuca” or “chinche”.

Triatomines defecate during or after taking a blood meal. A person bitten is inoculated by rubbing insect feces into the bite or on mucous membrane.
Trypanosomiasis, American (Chagas disease)
(Trypanosoma cruzi)

**Triatomin Bug Stages**
1. Triatomin 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. Triatomin bug takes a blood meal (trypomastigotes ingested).
6. Epimastigotes in midgut
7. Multiply in midgut
8. Metacyclic trypomastigotes in hindgut

**Human Stages**

- Infective Stage
- Diagnostic Stage
Blood smear with *T. cruzi* trypomastigote, the extracellular form of the parasite

CDC Public Health Image Library
Trypanosomiasis, American (Chagas disease)
(Trypanosoma cruzi)

Triatomine Bug Stages
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Human Stages

- Infective Stage
- Diagnostic Stage

Trypomastigotes can infect other cells and transform into intracellular amastigotes in new infection sites. Clinical manifestations can result from this infective cycle.
The amastigote form of *T. cruzi* multiplies in infected tissues.
*T. cruzi* amastigotes in infected heart muscle tissue

CDC Public Health Image Library
Trypanosomiasis, American (Chagas disease)
(Trypanosoma cruzi)

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**Human Stages**
1. Infective Stage
2. Diagnostic Stage
States with Triatomine Vectors and Mammalian Reservoir Species

> 18 infected reservoir species identified

Those exposed to infected vectors/reservoirs in the US are at risk

* States with human vector-associated cases (total = 28)
  - Both vectors and reservoir species
  - Vector species

> 18 infected reservoir species identified
Distribution of Vectors and Disease

- Endemic for human Chagas disease
- Infected vectors, nonhuman mammals*

*Including opossums, raccoons, foxes, armadillos, skunks, squirrels, dogs.
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Who in the United States has Chagas Disease?

- Approximately 300,000 persons living in the United States have Chagas disease.
- The country of origin for at least 85% of these is Mexico, El Salvador, Guatemala or Honduras.
- Southern states from California to Tennessee, have established enzootic cycles of *T. cruzi* and rare autochthonous transmission of infection is well-documented.

Cantey PT et al. *Transfusion* 2010; 52:1922.
18 Million People in the US were Born in Mexico, Central or South America

Chagas Disease Blood Donor Screening

- December, 2006: FDA approved the first blood donation screening assay for *T. cruzi* antibody by EIA
- Early 2007: Most blood centers began screening
- April, 2010: A second screening test was approved
- Dec, 2010: FDA issued guidance:
  - Deferral of donors based on positive screening test
  - Initial screen for all donors; if negative, no need to test future donations
  - Look-back of previous donations by positive donors
- As of January, 2016: >95% of the blood supply is screened

AABB Chagas Biovigilance Program as of August 15, 2016.

AABB Chagas Biovigilance Program, as of August 15, 2016.
Modes of Transmission

- **Vector-borne:** Contact with an infected triatomine bug is the most common mode of transmission

- **Bloodborne:** Contaminated blood products, organs or tissue

- **Food or waterborne:** In endemic regions, drinking water contaminated with triatomine bug feces or eating contaminated foods

- **Laboratory accidents:** Rare mode of transmission

- **Congenital:** Mothers with acute or, more often, chronic infection transmit infection to their infants

*Trypanosoma cruzi* parasite in a thin blood smear. CDC photo.
Chagoma or Romaña sign is thought to be from parasite penetration of the conjunctiva. The swelling is firm and lasts weeks.
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Acute phase of Chagas disease ~4-8 weeks

T. cruzi infection

Chronic phase

Indeterminate form
No signs or symptoms of Chagas disease

Life-long infection if untreated

60 - 80% remain indeterminate throughout life

20 - 40% progress over years - decades

Determinate forms
- Chagas cardiomyopathy &/or
- Gastrointestinal disease

Can reactivate if immunosuppressed
Mother-to Child Transmission of *T. cruzi*

- Transmission occurs transplacentally in the 2\textsuperscript{nd} or 3\textsuperscript{rd} trimester of gestation. There is little evidence to suggest intrapartum or postpartum transmission.
- Mothers usually asymptomatic.
- Mother-to-infant transmission rates are 1\% to 10\%.
- Transmission rates are higher (5\%) in countries where *T. cruzi* is endemic than in those where it is not (3\%)\(^*\).
- One study found a 13.8\% transmission rate among 59 women from Bolivia (97\%) or Paraguay (3\%) living in Spain\(^**\).

Factors Enhancing or Possibly Increasing Transmission

- High maternal parasitic load

- T. cruzi parasites are composed of 6 genetic lineages (DTU TcI-TcVI). All have been observed in congenitally infected infants except TcIV. The role of lineage on transmission is not well characterized.

- HIV co-infection increases the risk for transmission.

- T. cruzi can “cluster” in families but there is no defined genetic predilection.

- Increasing maternal age could enhance transmission.

Congenital Chagas Disease

- An estimated 40,000 infected women of childbearing age live in the US; an estimated 63-315 infected infants are born each year*

- Most congenitally infected infants appear at healthy at birth; untreated, they are at risk for developing life-threatening cardiac or GI disease decades later

- 10% to 40% of infants are symptomatic at birth with findings that can include prematurity, hepatosplenomegaly, jaundice, anemia and thrombocytopenia; none is specific for Chagas disease

Congenital Chagas Disease

- The first report of congenital Chagas disease in the United States was a boy born in Virginia in 2010. His mother had moved recently to the United States from Bolivia.*

- The infant was born at 29 weeks of gestation by C-section for fetal hydrops. His birth weight was 1,840 g. APGAR scores were 6 at 1 and 9 at 5 minutes. By exam, he had ascites, pleural effusion and pericardial effusion.

- Blood smear in week 2 of life revealed *T. cruzi* trypomastigotes and *T. cruzi* PCR was strongly positive; serologic tests for anti-*T. cruzi* antibodies were positive.

- He received benznidazole for 60 days and was cured.

Challenges to Identifying Infants with Congenital Chagas Disease

- Many infants with congenital infection are asymptomatic at birth and symptoms, when present, are non-specific.
- Chagas disease in infants likely occurs more frequently than recognized; even when infants are symptomatic, the diagnosis is often not considered.
- Identifying maternal infection is a critical step to finding infants who should be monitored for congenital infection during the first year of life.
- The prevalence of infection among women of child-bearing age in the US is not known.
Chagas Disease in Southern Texas

- Cord blood or residual maternal blood obtained from 4,000 of 4,016 infants born consecutively at a single hospital in Houston (2011-2012) had serologic testing for Chagas disease performed at CDC

- >75% of mothers were born in Mexico, Central America or South America

- Samples from 28 of 4,000 women (0.7%) were screen positive by Chagatest ELISA

- Additional testing by IFA and/or TESA immunoblot confirmed Chagas disease in 10 women (0.25%)

Comparison of Features for Pregnant Women Based on *Trypanosoma cruzi* Serology

<table>
<thead>
<tr>
<th>Maternal feature</th>
<th>Positive (n = 10)</th>
<th>Negative (n = 3990)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean years of age</td>
<td>33.8 (25–41)(^b)</td>
<td>28.3 (13–46)</td>
<td>.007</td>
</tr>
<tr>
<td>Hispanic ethnicity</td>
<td>10 (100)</td>
<td>3376 (84.6)</td>
<td>NS</td>
</tr>
<tr>
<td>Birthplace</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mexico</td>
<td>3 (30)</td>
<td>2001(^c) (50.2)</td>
<td>NS</td>
</tr>
<tr>
<td>El Salvador</td>
<td>5 (50)</td>
<td>447 (11.2)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Honduras</td>
<td>2 (20)</td>
<td>357 (8.9)</td>
<td>NS</td>
</tr>
<tr>
<td>Guatemala</td>
<td>0</td>
<td>258 (6.5)</td>
<td>NS</td>
</tr>
<tr>
<td>Nicaragua</td>
<td>0</td>
<td>17 (0.4)</td>
<td>NS</td>
</tr>
<tr>
<td>Live birth (%)</td>
<td>10 (100)</td>
<td>3880 (97.2)</td>
<td>NS</td>
</tr>
</tbody>
</table>

\(^a\) Based on 4000 total women, 10 pregnant.

\(^b\) Mean (range).

\(^c\) Based on 3000 total women, 10 pregnant.

Maternal Interviews and Infant Evaluation

- 8 of 10 chronically infected mothers were interviewed
  - None had heard of Chagas disease
  - None knew of relatives with heart or GI problems

- None had known heart disease or arrhythmia; 1 had a year-long history of constipation

- All had lived in rural areas of Mexico or Central America
  - 6 had lived as children in a mud or adobe home
  - Several had lived in homes with thatched roofs

- 7 infants were term, 1 was a 25-week preterm infant; all had negative serologic tests by age 7 months

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Diagnosis of Congenital Chagas Disease

- **Direct detection**: Diagnostic if positive but less sensitive than PCR

- **PCR**: The most sensitive test for early diagnosis
  - PCR for *T. cruzi* is only available at the CDC laboratory; testing is under CLIA
  - Initial negative must be repeated at 1 month of age as parasites multiply in the first weeks of life

- **Serology**: Negative serology at 9-12 months of age excludes congenital infection
Diagnosis of Chagas Disease beyond the Neonatal Period

- **Step 1:** Perform *T. cruzi* antibody screening using a commercially available serologic test. The Wiener EIA is optimal, if available

- **Step 2:** Send screening test positive serum to CDC via the Texas Department of State Health Services Laboratory for confirmatory testing. Tests will include:
  - ELISA
  - Trypomastigote excreted antigen immunoblot (TESA)

- **Step 3:** Chagas disease is reportable in Texas. Report patients with confirmed *T. cruzi* infection to the Texas Department of State Health Services
Chagas Disease Screening in Blood Donors

- There are two blood donor screening tests:
  - ELISA (Ortho)
  - Chemiluminescent immunoassay (ChLIA) (Abbott)

- Some blood banks perform a second test for donors with a positive initial screen, usually the Abbott ESA, a recombinant antigen immunoblot

- Blood donor tests are screening tests. Donors screening positive are notified that they should contact a healthcare provider for further evaluation
Chagas Disease Treatment

- Nifurtimox or benznidazole
  - Not FDA-approved but approved by FDA for distribution by CDC
  - Shortages can occur
  - Nifurtimox, a nitrofurfurylidene derivative, directly inhibits *T. cruzi* nucleic acid synthesis

- Treatment is most effective during early infection

- Side effects are common and include:
  - Benznidazole: dermatitis, peripheral neuropathy, anorexia, bone marrow suppression
  - Nifurtimox: anorexia, nausea, weight loss, tremors, insomnia, peripheral neuropathy

Photo from CDC at http://www.cdc.gov/parasites/cme/chagas/index.html
Treatment of Chagas Disease in Infants

- Treatment early in life kills the parasite and prevents long-term complications from heart and intestinal disease; cure rates exceed 90%*
- Treatment is always recommended for infants with congenital infection and children up to age 18 years
- Treatment should be considered for all individuals younger than 50 years of age, especially women in the childbearing years**
- Infection can be transmitted in subsequent pregnancies among women chronically infected with *T. cruzi*

Prevention through Awareness

- Most physicians are not familiar with Chagas disease. A survey of Obstetrician-Gynecologists found:
  - 68% admitted to having “very limited” Chagas disease knowledge
  - Only 9% knew the risk of congenital infection

- Caregivers for mothers and infants must consider the diagnosis and request appropriate testing

- The perceived stigma that Chagas disease is a disease of poverty must be addressed

Chagas Disease Prevention

Chagas disease fact sheets for the public are available on-line in English and Spanish through CDC.

Other printable resources include, “Help protect mothers and their children from Chagas disease” and, “Chagas disease in the Americas”

www.cdc.gov/parasites/chagas/printresources.html
Chagas Disease Prevention

Chagas disease printable resources are available through CDC

This poster is available for free at this website, laminated with English on one side, Spanish on the other:

A course, “Chagas Disease: What U.S. Clinicians need to Know”, designed to educate clinicians about Chagas disease in the United States, is available online at:

http://www.cdc.gov/parasites/cme/chagas/index.html

Course content

- Lesson 1: Epidemiology and risk factors
- Lesson 2: Phases and manifestations of disease
- Lesson 3: Diagnosis, evaluation and treatment

The course is designated for a maximum of 1.25 AMA PRA Category 1 Credits
Future Directions

- Define the **extent and distribution** of Chagas disease in women of childbearing age in the United States
- Define **risk of domestic vector-borne transmission**
- Target high-risk pregnant women for screening to identify and treat those with Chagas disease
- **Screen infants** born to women with Chagas disease
- Develop **better performing diagnostic tests and validated screening tests**
- Develop **new drugs** that are effective, safe and readily available

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Selected References


I am grateful to Susan P. Montgomery, DVM, MPH, epidemiology team lead in the CDC’s parasitic disease branch for providing some of the slides in this presentation and for her helpful comments regarding content of the presentation.