Chagas for Ob/Gyn and Pediatrics: Screening and Diagnostics in Pregnant Women and Newborns

ECHO Chagas Session

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How would you describe your level of knowledge about congenital Chagas disease?

1. Excellent
2. Good
3. Limited
4. Very limited
5. I didn’t know that congenital infection could occur
Objectives

- Cite the population at risk for congenital Chagas disease in the United States
- Describe the clinical features of congenital Chagas disease
- Know how to establish the diagnosis of congenital 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.

Photo of Carlos Chagas in 1909 in his laboratory at the Instituto Oswaldo Cruz.
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)

**Triatomine Bug Stages**

1. Triatomine 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. Triatomine bug takes a blood meal (trypanostigotes ingested)
6. Epimastigotes in midgut
7. Multiply in midgut
8. Metacyclic trypomastigotes in hindgut

**Human Stages**

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.

1 = Infective Stage

4 = Diagnostic Stage
Blood smear with *T. cruzi* trypomastigote, the extracellular form of the parasite
Trypanosomiasis, American (Chagas disease)

**Triatomine Bug Stages**

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**Human Stages**

1. = Infective Stage

2. = Diagnostic Stage
The amastigote form of *T. cruzi* multiplies in infected tissues.
T. cruzi amastigotes in infected heart muscle tissue
Trypanosomiasis, American (Chagas disease)

**Triatomine Bug Stages**

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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. 

Panstrongylus megistus
Objectives

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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, usually, chronic infection can transmit infection to their infants

*Trypanosoma cruzi* parasite in a thin blood smear. CDC photo.
Who in the United States has Chagas Disease?

- Approximately 300,000 persons living in the United States have Chagas disease
- Among these, approximately 40,000 are women in the childbearing years
- The country of origin for at least 85% of these is Mexico, El Salvador, Guatemala or Honduras
- Infants born to women with Chagas disease are at risk for congenital Chagas disease

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

American Association of Blood Banks (AABB): Confirmed Positive Blood Donors 2007-2019*

*AABB Chagas Biovigilance Program.
Among 4,755 Latin American-born residents of Los Angeles County, 59 had Chagas disease for an overall prevalence of 1.24%.

Prevalence was highest among Salvadorans (3.45%) and, among those born in Mexico, from the states of Oaxaca (4.65%) and Zacatecas (2.2%).

>30,000 people living in Los Angeles county may have Chagas disease.

Objectives

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Chagoma or Romaña sign is thought to be from parasite penetration of the conjunctiva. The swelling is firm and lasts weeks.
Acute phase of Chagas disease ~4-8 weeks

T. cruzi infection

Chronic phase

Indeterminate form
No signs or symptoms of Chagas disease

- 60 - 80% remain indeterminate throughout life
- Can reactivate if immunosuppressed
- 20 - 40% progress over years - decades

Determinate forms
- Chagas cardiomyopathy &/or
- Gastrointestinal disease

Life-long infection if untreated
Time Course of Congenital Chagas Disease

Transmission
Transmission of *T. cruzi* from an infected mother to unborn baby occurs during the second or third trimester of pregnancy.

Diagnosis
Babies born with *T. cruzi* infection are in the acute phase of the disease for the first 4-8 weeks of life. Diagnosis is made by PCR detection of parasite or by finding trypomastigotes in circulating blood or CSF.

Treatment
Left untreated, babies will enter into chronic phase infection immediately following the acute phase. However, the cure rate is >90% when babies are treated with antiparasitic medication within the first year of life.

Mother-to-Child Transmission of *T. cruzi*

- Transmission occurs transplacentally in the 2nd or 3rd trimester of gestation. There is little evidence to suggest intrapartum or postpartum transmission.
- Mothers usually have chronic Chagas disease and are asymptomatic.
- **Mother-to-infant transmission rates are approximately 1% to 10%**
- Transmission rates are higher (5%) in countries where *T. cruzi* is endemic than in those where it is not (3%)*

*Howard et al. *BJOG* 2014; 121:22.*
Factors Enhancing or Possibly Increasing Transmission

- High maternal parasitic load
- **Genotype:** *T. cruzi* parasites are composed of 6 genetic lineages (DTU TcI-TcVI). 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
- **Maternal age:** 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 have findings that can include prematurity, hepatosplenomegaly, jaundice, anemia and thrombocytopenia. Infants with more severe infection can present with meningoencephalitis, pneumonitis, myocarditis, or hydrops fetalis; none is specific for Chagas disease

### Features of Congenital Chagas Disease among 91 Infants with Clinical Findings

<table>
<thead>
<tr>
<th>Feature</th>
<th>Frequency of Finding</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low birth weight (&lt;2500 g)</td>
<td>++</td>
</tr>
<tr>
<td>Prematurity</td>
<td>++</td>
</tr>
<tr>
<td>Respiratory distress</td>
<td>+++</td>
</tr>
<tr>
<td>Hepatomegaly</td>
<td>++++</td>
</tr>
<tr>
<td>Splenomegaly</td>
<td>+++</td>
</tr>
<tr>
<td>Sepsis</td>
<td>++</td>
</tr>
<tr>
<td>Cardiomegaly/heart failure</td>
<td>++</td>
</tr>
<tr>
<td>Myocarditis</td>
<td>++</td>
</tr>
<tr>
<td>Cardiac arrhythmia</td>
<td>++</td>
</tr>
<tr>
<td>Meningoencephalitis</td>
<td>++</td>
</tr>
<tr>
<td>Neurologic signs</td>
<td>++</td>
</tr>
<tr>
<td>Edema/anasarca</td>
<td>++</td>
</tr>
<tr>
<td>Petechiae</td>
<td>++</td>
</tr>
<tr>
<td>Anemia</td>
<td>+</td>
</tr>
</tbody>
</table>

*+++, noted in >50% of infants assessed; ++++, 25% to 50%; ++, 10% to 24%; +, <10%.*


Uncommon features of infection can include vitreitis or retinitis and intestinal megasymphdromes.

Approximately 5% of infants have a fatal outcome, usually in association with myocarditis or meningoencephalitis.

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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 key to identifying infants at risk but maternal screening is not routine.

- The prevalence of infection among women of child-bearing age in the US is not known.
Clinical Features of Congenital Chagas Disease

- Clinical features are found in 10% to 40% of infants.
- The common clinical features of congenital Chagas disease, such as low birth weight or hepatosplenomegaly, are also often seen in such infections as congenital syphilis or cytomegalovirus infection.
- Less common clinical features of congenital Chagas disease such as hydrops fetalis are also findings in such infections as parvovirus B19 infection.
- Clinical features of congenital Chagas disease, when present, suggest a congenitally-acquired infection. Many infants do not have clinical findings that prompt evaluation for congenital infection.
Objectives

- Cite the population at risk for congenital Chagas disease in the United States
- Describe the clinical features of congenital Chagas disease
- Know how to establish the diagnosis of congenital Chagas disease
Screening Pregnant Women and their Infants for Chagas Disease

- Chagas disease screening can identify women at risk for transmitting infection to their infants; screening is optimally performed during pregnancy.

- Women at risk are those who have migrated from an endemic region:
  - Risk is enhanced by having lived in a rural region.
  - Risk is also enhanced by having lived in a mud or thatched-roof home.

- Women who have visited and lived in an endemic region for 6 months or longer are at risk and should undergo *T. cruzi* screening.

- Neonates born to at-risk women who were not tested during pregnancy should be screened for *T. cruzi*. 
Screening for Chagas Disease during Pregnancy

- Screening for Chagas disease can be performed during any trimester of pregnancy
- A commercially-available ELISA should be ordered to test for *T. cruzi* IgG
- Chagas disease screening is a send-out test from most hospital laboratories. Results are available within days
- Cost (~$45) may be covered as an add-on to routine maternal screening
- It is not necessary or appropriate to screen for *T. cruzi* IgM
Diagnosis of Chagas Disease

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

- Chagas disease is reportable in Arizona, Arkansas, Louisiana, Mississippi, Tennessee, Texas and Utah as well as Los Angeles County
Algorithm for Evaluation of Chagas Disease in Pregnant Women

1. **Pregnant woman from a Chagas-endemic region?**
   - No
     - History of residence in U.S. areas where triatomine bugs are known to carry *T. cruzi* and there is concern for exposure to triatomines?
       - No
         - Chagas disease is unlikely; serologic testing has a low yield
       - Yes
         - T. cruzi serology through a commercial laboratory
           - Positive
             - Confirmatory *T. cruzi* serology at a reference diagnostic laboratory such as Parasitic Diseases Branch Laboratory of CDC
               - Positive
                 - Chagas disease excluded
               - Negative
                 - Clinical assessment and treatment after infant delivered
           - Negative
             - Chagas disease excluded
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 *T. 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)</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>2001c (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>

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

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 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
Chagas Disease Treatment

- Two medications are available:
  - Benznidazole is commercially available
  - Nifurtimox is approved by FDA for distribution by CDC

- **Duration:** 60 days (benznidazole) or 90 days (nifurtimox)

- Adverse effects include:
  - **Benznidazole:** dermatitis, peripheral neuropathy, anorexia, bone marrow suppression
  - **Nifurtimox:** anorexia, nausea, weight loss, tremors, insomnia, peripheral neuropathy

- Treatment is most effective during early infection

Photo from CDC at [http://www.cdc.gov/parasites/cme/chagas/index.html](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*

In a prospective study of 144 *T. cruzi* seropositive pregnant women, treated women were more likely to be PCR negative (92%) than were non-treated women (32%).

No infected infants were detected among treated mothers compared with 13.2% among untreated mothers (*P* = 0.019)

**Conclusion**: Treatment prevents congenital Chagas disease by reducing parasitemia

Case Study

An 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. Physical examination revealed ascites and pleural and pericardial effusions.

Do you think this infant is at risk for Chagas disease?

What additional information would be helpful?

Is his clinical presentation consistent with congenital Chagas disease?

What testing is indicated?

*MMWR 2012; 61:477*
Do you think this infant is at risk for Chagas disease?

1. Yes
2. No
What percent of infants with congenital Chagas disease have signs of infection?

1. <10%
2. 10-40%
3. 41-75%
4. >76%
5. I don’t know
What additional information would be helpful?

1. His mother’s place of birth
2. His mother’s *T. cruzi* IgG result
3. His mother’s information about her Chagas disease status
4. All of the above
What is the first test to order from the infant?

1. *T. cruzi* IgM
2. *T. cruzi* IgG
3. Examination of the placenta
4. Whole blood for PCR
An 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. He had ascites and pleural and pericardial effusions.

Do you think this infant is at risk for Chagas disease? Yes, he could be. He was born prematurely and has hydrops fetalis; he could be one of the 10% to 40% of infants with clinical signs of congenital Chagas disease.

What additional information would be helpful? Whether his mother has lived in a region endemic for Chagas disease. His mother had moved to the United States from Bolivia. During the infant’s second week of life, she recalled she had been told she had Chagas disease.

An 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. He had ascites and pleural and pericardial effusions.

Is the clinical presentation consistent with Chagas disease? Yes. Chagas disease should be a differential consideration in any infant presenting with nonimmune hydrops fetalis.

What testing is indicated? Blood smear revealed *T. cruzi* trypomastigotes and *T. cruzi* PCR was strongly positive; serologic testing for *T. cruzi* antibodies was positive. The infant received benznidazole for 60 days and was cured.

Algorithm for Evaluation of Congenital Chagas Disease:
Infant <3 Months of Age*

At time of birth, test cord blood (if no maternal blood contamination) or whole blood from infant for:
- Microscopic examination of blood (Giemsa stain for T. cruzi trypomastigotes)
- PCR
- Chagas disease serology if mother not tested during pregnancy to detect maternal antibody and determine whether infant at risk

Giemsa stain or PCR positive?

Yes  
Evaluate the infant for treatment*

No  
Repeat microscopic examination of blood smear and PCR at 4-6 weeks of age. Giemsa stain or PCR positive?

Yes  
Evaluate the infant for treatment

No  
Serology when infant >9 months of age

Serology positive
Evaluate the infant for treatment

Serology negative
Congenital Chagas disease excluded

*Infant born to mother with suspected or confirmed Chagas disease OR infant with symptoms of congenital Chagas disease in at-risk mother with serologic status unknown.

A positive PCR should be confirmed by repeat testing before treatment to exclude contamination from maternal blood.

https://www.cdc.gov/parasites/chagas/health_professionals/congenital_chagas.html
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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
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