Chagas Disease
Transmission
Sources and
Cardiac Outcomes
among Texas Blood
Donors

Melissa Garcia, MPH
Diseases in Nature Conference
26 June 2014
Agenda

• History of Chagas disease in Texas & US

• Seroprevalence estimates of Texans

• Houston area human disease transmission sources

• Cardiac manifestations of Chagas in Texas residents
Sylvatic vs Domestic Transmission Cycles

Mammalian Species → Triatomine Insects → Dogs → Humans → Triatomine Insects → Mammalian Species
Triatome Bug Stages

1. Triatome 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. Triatome bug takes a blood meal (trypomastigotes ingested)

6. Epimastigotes in midgut

7. Multiply in midgut

8. Metacyclic trypomastigotes in hindgut

CDC

http://www.dpd.cdc.gov/dpdx

Pediatrics

Baylor College of Medicine

Texas Children’s Hospital
>30% develop cardiac outcomes

Diagnosis

- Acute Phase
  - Microscopic examination
  - PCR

- Chronic Phase:
  - Two positive test results
  - ELISA (multiple), IB, IFA

- Clinical history & exposure
  - Locally acquired cases
Treatment

- Investigative Drug Protocol under CDC regulation
- Approved by CDC for distribution
- Treatment Failure in 19-97% of patients

<table>
<thead>
<tr>
<th>Drug</th>
<th>Age group</th>
<th>Dosage and duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benznidazole</td>
<td>&lt; 12 years</td>
<td>10 mg/kg per day orally in 2 divided doses for 60 days</td>
</tr>
<tr>
<td></td>
<td>12 years or older</td>
<td>5-7 mg/kg per day orally in 2 divided doses for 60 days</td>
</tr>
<tr>
<td>Nifurtimox</td>
<td>≤ 10 years</td>
<td>15-20 mg/kg per day orally in 3 or 4 divided doses for 90 days</td>
</tr>
<tr>
<td></td>
<td>11-16 years</td>
<td>12.5-15 mg/kg per day orally in 3 or 4 divided doses for 90 days</td>
</tr>
<tr>
<td></td>
<td>17 years or older</td>
<td>8-10 mg/kg per day orally in 3 or 4 divided doses for 90 days</td>
</tr>
</tbody>
</table>

Pinazo MJ et al. 2010. *Antimicrobial Agents and Chemotherapy*
History of Chagas Disease in Texas and the United States
Chagas Disease in a Domestic Transmission Cycle in Southern Texas, USA

Charles B. Beard,* Greg Pye,† Frank J. Steurer,* Ray Rodriguez,‡ Richard Campman,† A. Townsend Peterson,§ Janine Ramsey,¶ Robert A. Wirtz,* and Laura E. Robinson†

After three dogs died from acute Chagas cardiomyopathy at one location, an investigation was conducted of the home, garage, and grounds of the owner. A serologic study was conducted on stray dogs, and an ecologic niche model was developed to predict areas where the vector Triatoma gerstaeckeri might be expected.
An Estimate of the Burden of Chagas Disease in the United States

Caryn Bern and Susan P. Montgomery
Division of Parasitic Diseases, National Center for Zoonotic, Vector-Borne and Enteric Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia

Chagas disease causes the highest burden of any parasitic disease in the Western hemisphere. By applying published seroprevalence figures to immigrant populations, we estimate that 300,167 individuals with Trypanosoma cruzi infection live in the United States, with 30,000–45,000 cardiomyopathy cases and 63–315 congenital infections annually. T. cruzi causes a substantial disease burden in the United States.

Table 1. Calculated Prevalence of Trypanosoma cruzi Infections in Latin American–Born Persons living in the United States in 2005

<table>
<thead>
<tr>
<th>Country of origin</th>
<th>Immigrant population living in the United States</th>
<th>T. cruzi prevalence in country of origin, %</th>
<th>Estimated no. of immigrants with T. cruzi infection in the United States</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mexico</td>
<td>16,963,851</td>
<td>1.03</td>
<td>174,388</td>
</tr>
<tr>
<td>El Salvador</td>
<td>1,458,014</td>
<td>3.37</td>
<td>49,164</td>
</tr>
<tr>
<td>Guatemala</td>
<td>1,014,689</td>
<td>1.98</td>
<td>20,131</td>
</tr>
<tr>
<td>Honduras</td>
<td>567,002</td>
<td>3.05</td>
<td>17,311</td>
</tr>
<tr>
<td>Argentina</td>
<td>223,931</td>
<td>4.13</td>
<td>9246</td>
</tr>
<tr>
<td>Ecuador</td>
<td>345,204</td>
<td>1.74</td>
<td>6003</td>
</tr>
<tr>
<td>Colombia</td>
<td>554,821</td>
<td>0.96</td>
<td>5304</td>
</tr>
<tr>
<td>Brazil</td>
<td>501,036</td>
<td>1.02</td>
<td>5106</td>
</tr>
<tr>
<td>Bolivia</td>
<td>61,453</td>
<td>6.75</td>
<td>4149</td>
</tr>
<tr>
<td>Nicaragua</td>
<td>223,931</td>
<td>1.14</td>
<td>2553</td>
</tr>
<tr>
<td>Peru</td>
<td>371,980</td>
<td>0.69</td>
<td>2562</td>
</tr>
<tr>
<td>Venezuela</td>
<td>151,350</td>
<td>1.16</td>
<td>1754</td>
</tr>
<tr>
<td>Chile</td>
<td>92,761</td>
<td>0.99</td>
<td>914</td>
</tr>
<tr>
<td>Costa Rica</td>
<td>95,761</td>
<td>0.53</td>
<td>509</td>
</tr>
<tr>
<td>Paraguay</td>
<td>16,707</td>
<td>2.54</td>
<td>425</td>
</tr>
<tr>
<td>Uruguay</td>
<td>51,737</td>
<td>0.66</td>
<td>339</td>
</tr>
<tr>
<td>Belize</td>
<td>42,130</td>
<td>0.74</td>
<td>312</td>
</tr>
<tr>
<td>Panama</td>
<td>107,601</td>
<td>0.01</td>
<td>6</td>
</tr>
<tr>
<td>Total</td>
<td>22,843,939</td>
<td>1.31</td>
<td>300,167</td>
</tr>
</tbody>
</table>
• 23 autochthonous cases
• 28 states have vector
• 17 states have infected reservoir
AABB Chagas Biovigilance Network

Pediatrics
How many people have *T. cruzi* infection in Texas now?

And who are they?
Methods

• Blood center *T cruzi* testing
  - 2008-2012
  - Ortho or Abbott Repeat Reactive
  - RIPA confirmation

• Demographic info

• Zip code data from US Census
  - Percent Poverty & Rural Land Use
907,398 tested

261 repeat reactive

140 RIPA confirmation

1 per 6,500 confirmed positive for *T. cruzi* infection
*T. cruzi* RIPA positive per 100,000 blood donors by age

<table>
<thead>
<tr>
<th>Age Range</th>
<th>RIPA Positive per 100,000</th>
</tr>
</thead>
<tbody>
<tr>
<td>16-20</td>
<td></td>
</tr>
<tr>
<td>21-30</td>
<td></td>
</tr>
<tr>
<td>31-40</td>
<td></td>
</tr>
<tr>
<td>41-50</td>
<td></td>
</tr>
<tr>
<td>51+</td>
<td></td>
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</table>

Pediatrics
$T$ cruzi RIPA positive per 100,000 blood donors by Race/Ethnicity

<table>
<thead>
<tr>
<th>Race/Ethnicity</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>15</td>
</tr>
<tr>
<td>Hispanic</td>
<td>35</td>
</tr>
<tr>
<td>Caucasian</td>
<td>5</td>
</tr>
<tr>
<td>Mixed Races</td>
<td>35</td>
</tr>
<tr>
<td>Asian</td>
<td>5</td>
</tr>
<tr>
<td>African American</td>
<td>5</td>
</tr>
</tbody>
</table>
Percent Rural Land Use by Zip Code

- 75-100%
- 50-74%
- 25-49%
- 0-24%

p<0.00
Percent Poverty by Zip Code
p<0.04
Cost estimates for Texas Chagas cases

- Societal cost for healthcare & lost wages
  $2.7 million*

- Accrue 104 disability-adjusted life years lost
  as a result of chronic Chagas disease*

* $91,531 per case; 3.57 DALYs per year - Lee et al 2013 Lancet Infect Dis
Cost estimates: 30% RIPA confirmed
What is the human source of *T. cruzi* infection?

What are the routes of disease transmission?
Houston Pilot Study: Methods

• Invited RIPA + & RIPA – blood donors from GCRBC
  - 57% (17/30) of those who screened positive were confirmed

• The one-time assessment included:
  - 1) a questionnaire to evaluate risk factors for infection
    • Co-morbidities, travel history, source of disease transmission
  - 2) blood draw for biomarker evaluation
  - 3) an electrocardiogram
    • an echocardiogram for those with an abnormal ECG
36% (6/17) were locally acquired

<table>
<thead>
<tr>
<th>Study ID</th>
<th>Age</th>
<th>Race</th>
<th>Gender</th>
<th>Place of Birth</th>
<th>Occupational Exposure</th>
<th>Hunter</th>
<th>Camper</th>
<th>Travel to Endemic Rural Area</th>
<th>Report Seeing Vector Around TX Residence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tcruzi-002</td>
<td>75</td>
<td>Hispanic</td>
<td>Male</td>
<td>Robstown, Texas</td>
<td>No</td>
<td>No</td>
<td>Yes (10+ years)</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Tcruzi-004</td>
<td>54</td>
<td>White</td>
<td>Female</td>
<td>Halletsville, Texas</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Tcruzi-006</td>
<td>66</td>
<td>White</td>
<td>Male</td>
<td>Baycity, Texas</td>
<td>Yes (cotton farmer 23 years)</td>
<td>Yes (whole life)</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Tcruzi-007</td>
<td>75</td>
<td>White</td>
<td>Male</td>
<td>Rogers, Texas</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Tcruzi-012</td>
<td>68</td>
<td>Hispanic</td>
<td>Female</td>
<td>Cerralvo, Mexico</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Tcruzi-026</td>
<td>23</td>
<td>White</td>
<td>Male</td>
<td>Pasadena, Texas</td>
<td>No</td>
<td>No</td>
<td>Yes (15 years)</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>
Implications for Hunting as a High-risk activity for transmission

• Direct blood-to-blood transmission via skinning

• Inadequate lodging

• Increased exposure to vector

Photo credit: Victor Quispe-Machaca
Implications for High-risk Occupational Exposure in US

- 5 million with extensive time outdoors
- 178,000 working during nocturnal feeding time
Are those infected with *T. cruzi* in Texas developing cardiac disease?
• 41% (7/17) Abnormal ECG Finding
  - 72% (5/7) were major abnormalities
  - 57% (4/7) were potentially locally acquired
  - 14% (1/7) had ECHO abnormality
  - 57% (4/7) had Hypertension
  - 14% (1/7) had Diabetes
  - None have received treatment prior to study
Tcruzi-002 ECG

• 75 year old Hispanic Male

• Atrial paced with right bundle branch block

• Left anterior fascicular block

• 1st degree atrioventricular block
Tcruzi-014 ECG

- 43 year old Hispanic Female
- Right bundle branch block
- Left axis deviation
TcruzI-003

Control
Tcruzi-003   Control
Can we predict who is at risk for developing cardiac disease?
HsTnT biomarker levels by disease status

Controls (False Positive) vs. Chagas Disease (T. cruzi Positive)
High Sensitivity Troponin T could be an important biomarker for advanced Chagas cardiomyopathy.
Conclusions

• Substantial disease burden in Texas (1 per 6,500)

• *T. cruzi* infection can cause cardiac manifestations, even in persons without travel to Latin & South America

• High risk populations for transmission
  - Hunters (multiple sources)
  - Nocturnal occupations

• High Sensitivity Troponin T could be an important biomarker for stratifying cardiac disease severity
Acknowledgements

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  - Susan Rossmann

• American Red Cross
  - Rebecca Townsend, Susan Stramer

• Blood Systems Incorporated
  - Marjorie Bravo, Hany Kamel

• South Texas Blood & Tissue Center
  - Rachel Beddard

• Coffee Memorial Blood Center
  - Mary Townsend, Rebecca Oldham

• Research participants for their time