Treatment of Chagas Disease 100 years after its discovery: Little to Celebrate!

The experience of Medicos sin Fronteras

www.rompe-el-silencio.com
Estimated global population infected by *Trypanosoma cruzi*, 2009

Sources:
‘Médecins Sans Frontières’ (MSF)

• Humanitarian medical NGO, founded in 1971 by a group of French doctors

• Total independence

• Medical assistance to populations in need

• ‘Temoignage’
## MSF and Chagas: Evolution

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</thead>
<tbody>
<tr>
<td>Honduras</td>
<td>Under 5’s Rural</td>
<td>232 treated (0.9%)</td>
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<tr>
<td>Entre Rios - Bolivia</td>
<td>Under 15’s Rural</td>
<td>1450 treated (19.4%)</td>
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<tr>
<td>Nicaragua</td>
<td>Under 15’s Rural</td>
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<tr>
<td>Guatemala</td>
<td>Under 14’s Rural</td>
<td>124 treated (1.4%)</td>
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<tr>
<td>Sucre - Bolivia</td>
<td>Under 18’s Peri-urban</td>
<td>1100 treated (5.9%)</td>
<td>Rapid test</td>
<td></td>
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<tr>
<td>Cochabamba - Bolivia</td>
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<td></td>
<td></td>
<td></td>
<td>Under 50’s Urban and Peri-urban</td>
<td>600 treated to date</td>
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</table>
Chagas in Bolivia

- 60% of the country is endemic
- Population at risk: 4,000,000
- Population infected: >1 million
- Causes 15% of adult deaths
## Prevalence of Chagas

<table>
<thead>
<tr>
<th>Age Group (yrs)</th>
<th>Prevalence (%) -Sucre (n=19,400)</th>
<th>Prevalence (%) -Entre Rios (n=7,600)</th>
<th>Prevalence (%) -Cochabamba (n=6,500)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-4</td>
<td>1.9</td>
<td>5.9</td>
<td>2.0</td>
</tr>
<tr>
<td>5-9</td>
<td>4.1</td>
<td>14.8</td>
<td></td>
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<tr>
<td>10-14</td>
<td>8.6</td>
<td>31.0</td>
<td>5.4</td>
</tr>
<tr>
<td>&gt;15</td>
<td>14.2</td>
<td>51.7</td>
<td>27.5</td>
</tr>
<tr>
<td>Total</td>
<td>5.9</td>
<td>19.4</td>
<td>16.0</td>
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</table>
Field Evaluation of a Rapid Immunochromatographic Assay for Detection of *Trypanosoma cruzi* Infection by Use of Whole Blood

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*Médecins Sans Frontières*—Spain, Barcelona, Spain; *Centro Universitario de Medicina Tropical—Facultad de Medicina, Universidad Mayor de San Simón*, Cochabamba, Bolivia; and *Laboratório de Doenças Parasitárias, Instituto Oswaldo Cruz—Fiocruz, Rio de Janeiro, Brazil

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Laboratory and clinical diagnostic classification of seropositive individuals, followed by treatment and supportive therapy, is an established component of Chagas' disease control in areas where this disease is endemic. However, most Chagas' disease patients live in remote areas where neither equipped laboratories nor skilled human resources are widely available. Employing a rapid diagnostic test (RDT), when using whole blood samples, is the best option for Chagas' disease control. A high sensitivity and specificity for the Chagas Stat-Pak RDT (Chembio Diagnostic Systems, Inc., Medford, NY) has been reported for assays using serum and plasma, but its validity for the detection of antibodies to *Trypanosoma cruzi* infection in whole blood is unknown. This cross-sectional study measured the sensitivity and specificity of the Chagas Stat-Pak with whole blood, using conventional serological assays for comparison. The interobserver reliability in the interpretation of the Chagas Stat-Pak results and “ease-of-use” criterion needed to perform the Chagas Stat-Pak and conventional assays were also measured. The Chagas Stat-Pak yielded a high specificity (99.9%, 95% confidence interval [CI] = 98.4 to 99.4%) but a relatively low sensitivity (93.4%, 95% CI = 87.4 to 97.1%). The interobserver reliability was excellent (kappa [κ] = 1.913 = 0.999, P < 0.0001), and the quantified ease-of-use criterion suggested that the RDT is simple to perform. Despite the attributes of the Chagas Stat-Pak, it is not an ideal diagnostic test for the population investigated in the present study due to its relatively low sensitivity and high cost. The RDT manufacturer is called upon to improve the test if the international community hopes to make progress in controlling Chagas infections in areas where this disease is endemic.
## Side Effects in Sucre

<table>
<thead>
<tr>
<th>AGE GROUP</th>
<th>PATIENTS</th>
<th>CUTANEOUS</th>
<th>GASTROINTESTINAL</th>
<th>NEUROMUSCULAR</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>nº</td>
<td>%</td>
<td>nº</td>
<td>%</td>
</tr>
<tr>
<td>0 - 4 years</td>
<td>67</td>
<td>9</td>
<td>13,4%</td>
<td>0</td>
</tr>
<tr>
<td>5 - 10 years</td>
<td>297</td>
<td>64</td>
<td>21,5%</td>
<td>25</td>
</tr>
<tr>
<td>11 - 15 years</td>
<td>435</td>
<td>120</td>
<td>27,6%</td>
<td>31</td>
</tr>
<tr>
<td>&gt; 16 years</td>
<td>245</td>
<td>92</td>
<td>37,6%</td>
<td>25</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>1044</strong></td>
<td><strong>285</strong></td>
<td><strong>27,3%</strong></td>
<td><strong>81</strong></td>
</tr>
</tbody>
</table>
Adverse Events by Age Group,
Cochabamba, Bolivia Cohort

Age Group, Years

Adverse Event Rate, %

- Neuromuscular
- Gastrointestinal
- Cutaneous

<5 5-14 15-24 25-34 35-44 >45
Important Side Effects

- Mortality
  - 0/3300 patients

- Hospitalisation
  - 4/3300 patients (1 SJS, 1 TEN)

- Loss to Follow-Up
  - 0-15%
# Important Side Effects

<table>
<thead>
<tr>
<th></th>
<th>ENTRE RIOS &lt;15</th>
<th>SUCRE &lt;18</th>
<th>COCHA &lt;15</th>
<th>COCHA MALE &gt;15</th>
<th>COCHA FEMALE &gt;15</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Diagnosed Positive</strong></td>
<td>1464</td>
<td>1102</td>
<td>151</td>
<td>219</td>
<td>573</td>
</tr>
<tr>
<td><strong>Started Treatment</strong></td>
<td>1434 (97.9%)</td>
<td>1044 (94.7%)</td>
<td>109 (72.2%)</td>
<td>130 (59.3%)</td>
<td>264 (46%)</td>
</tr>
<tr>
<td><strong>Completed &gt;55 Days</strong></td>
<td>1356 (94.6%)</td>
<td>894 (85.6%)</td>
<td>82 (75.2%)</td>
<td>101 (77.7%)</td>
<td>174 (65.9%)</td>
</tr>
<tr>
<td><strong>Stop due to Side Effects</strong></td>
<td>28 (2.0%)</td>
<td>61 (5.8%)</td>
<td>12 (11.0%)</td>
<td>9 (6.9%)</td>
<td>56 (21.0%)</td>
</tr>
<tr>
<td><strong>Stop for Unknown Reason</strong></td>
<td>49 (3.4%)</td>
<td>83 (8.0%)</td>
<td>12 (11.0%)</td>
<td>20 (15.4%)</td>
<td>25 (9.5%)</td>
</tr>
</tbody>
</table>
BNZ (first-line) vs NFX (second-line): Adverse events in adults >15 years old

Moderate:
- 22.9% NFX vs 9.2% BNZ

Severe:
- 5.8% NFX vs 0.2% BNZ
Treatment Efficacy (% Seronegativisation)

- Entre Rios, Bolivia
  - 59 out of 1,101
  - 5.4% at 36-60 months

- Sucre, Bolivia
  - 0 out of 276
  - 0% at 18 months

- Yoro, Honduras
  - 87% at 18 months

- Olopa, Guatemala
  - 58% at 18 months
Impact of the projects?

- Prevention and Treatment
- Protocols
- Retained trained staff
- Publications
- In 5 health centres
  - 50% non-MSF staff are ‘involved’
  - 90% of treatment contacts by non-MSF doctors
  - 50% of screening done by non-MSF nurses
  - 30% of diagnosis done by non-MSF lab staff

- In Entre Rios:
  - Less than 100 children diagnosed and treated in 3 years since project closure

- In Sucre:
  - 1040 of 1080 children diagnosed before MSF departure remain untreated.

- In Bolivia:
  - >99% of adult need unmet
  - 95% of children need unmet
‘Pathology’ of Neglect

- Failure of Government
- Poverty *(Lack of human resources)*
- Few people *(..or too many people!)*
- Invisibility *(No symptoms, chronic effects, not photogenic, anonymous death)*
- Difficult/Costly prevention, diagnosis, treatment
- ‘Unsatisfying’ treatment
- Difficult research
- False beliefs and stigma
- No demand for treatment by community
‘...every study, every experience, points a finger towards a ...population which lives in extreme poverty, and produces irritation in their governments, being testament to their incapacity to resolve huge economic and social problems.’

Carlos Chagas
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What is needed?

• **Better tools**
  - Insecticides
  - Vaccine
  - Diagnostics
  - Drugs and Formulations
  - Test of Cure
  - **R&D system that is fit for purpose**

• **Better approaches**
  - Innovative Integrated Models
  - ‘Sustainability science’
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A ‘new’ model

• Community engagement and motivation
• Concept of ‘PLC’
• Treatment Preparedness
• Integrate prevention and treatment
• Compromise with reality
• ‘Task-shifting’ to mitigate human resource crisis
Muito obrigado

www.rompe-el-silencio.com
www.treatchagas.org
www.msf.org.br/chagas