Foodborne *Trypanosoma cruzi*: What is the disease burden?

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Foodborne pathogens…. Don’t forget the parasites – the neglected pathogens

- Generally, foodborne illness is equated with acute enteric disease – usually bacterial, sometimes viral.

- But what about parasites??
  - Some foodborne parasites can result in acute enteric disease.
  - But others may result in acute, non-enteric illness
  - Many more have a more insidious, long-term effect that can have a profound impact on human health, including fatalities

- It is important that the impact of foodborne parasites – the neglected pathogens – is not overlooked.
20 NTD

- 2 viral
- 5 bacterial or fungal
- 1 non infectious
- 12 parasitic

Of the 12 parasites, most (7) can be transmitted via food and/or water.
In 2007, WHO established Foodborne Disease Burden Epidemiology Reference Group (FERG)

Estimate burden of foodborne disease according to aetiology (globally and by region, etc.).

**Intention**: contribute to improvements in food safety throughout the food chain by incorporating estimates into policy development at national and international levels

2007-2015 – FERG-I: several papers published based on data from expert knowledge elicitation, systematic reviews, modelling…

- Chagas Disease (*Trypanosoma cruzi* infection) was not included
Due to resource limitations, it was not possible to consider all potentially foodborne parasites (for example, *Trypanosoma cruzi*).
But... IS Trypanosoma cruzi a foodborne pathogen?

Other less common routes of transmission include blood transfusions, organ transplantation, transplacental transmission, and foodborne transmission (via food/drink contaminated with the vector and/or its feces).
But… IS *Trypanosoma cruzi* a foodborne pathogen?

“Infection was confirmed in 103 of 1000 potentially exposed individuals. Of those infected, 75% were symptomatic, 20.3% required hospitalization, 59% showed ECG abnormalities, parasitemia was documented in 44, and 1 child died. Clinical features differed from those seen in vectorial transmission. The infection rate was significantly higher among younger children. An epidemiological investigation incriminated contaminated fresh guava juice as the sole source of infection.”
Foodborne transmission lifecycle

Note: none of the images are drawn to scale

The Neglected Problem of Foodborne Chagas Disease

PLOS NEGLECTED TROPICAL DISEASES

The importance of estimating the burden of disease from foodborne transmission of Trypanosoma cruzi

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Foodborne Chagas Disease

- **Trypanosoma cruzi**
  - Cause of Chagas Disease (can be fatal)
  - Around 7 million affected globally - largely limited to Latin America
  - Previously considered to be almost entirely vectorborne (reduviid bugs)
  - Increasing reports of foodborne transmission, including extensive outbreaks.

Reduviid bugs (*Rhodnius prolixus*) – nymphs and adults  From Wikimedia Commons, the free media repository

Açaí (palm berry) juice extractor in the streets of Belém, next to Ver-o-Peso market.  From Wikimedia Commons, the free media repository
One pathogen with several infection routes: How to estimate foodborne burden?

- Among previous WHO estimates, various hazards had a range of infection routes (e.g., via food or via: water, hand-to-mouth, zoonotic… etc.)

- To determine burden due to foodborne transmission, entire burden of disease estimated (SR); then decide proportion via each route (hazard-specific source attribution) using published data or EKE.

- E.g. Cryptosporidium (another protozoan parasite)

One pathogen with several infection routes: How to estimate foodborne burden?

- The approach described for *Cryptosporidium* has been investigated for *T. cruzi* \(^a\)

<table>
<thead>
<tr>
<th>Data estimate period</th>
<th>Burden in DALYS</th>
<th>Suggested proportion foodborne</th>
<th>Burden associated with foodborne transmission</th>
<th>Refs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Older data (2010)</td>
<td>546,000</td>
<td>50%</td>
<td>273,000</td>
<td>b, c</td>
</tr>
<tr>
<td>Newer data (2019)</td>
<td>275,377</td>
<td>50%</td>
<td>137,689</td>
<td>d</td>
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</tbody>
</table>

- The burden estimated is higher than published for more than 10 other foodborne hazards published in the WHO estimates in 2015

References:


One pathogen with several infection routes: How to estimate foodborne burden?

- HOWEVER:
  - Although the approach used for *Cryptosporidium* may provide a good estimate for most foodborne hazards, it is not suitable for *T. cruzi* due to the clinical disease differing by infection route.
    - Vectorborne route: largely associated with long-term/chronic effects (acute effects: usually mild)
    - Foodborne route: both acute and long-term/chronic effects, with notably higher morbidity and mortality than vectorborne infection.
Clinical Chagas disease by infection route

<table>
<thead>
<tr>
<th>Disease phase</th>
<th>Vectorborne transmission</th>
<th>Foodborne transmission</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute</td>
<td>Largely asymptomatic; 3% to 60% cases mild symptoms such as fever</td>
<td>Close to 100% experience fever. Other common symptoms include myalgia, headache, and oedema</td>
</tr>
<tr>
<td>Acute</td>
<td>Romaña’s sign or chagoma often seen</td>
<td>Facial oedema in around 90% of cases</td>
</tr>
<tr>
<td>Acute</td>
<td>Cardiac manifestation in up to 10% of cases, particularly children</td>
<td>Early myocardial involvement occurs frequently (up to 100%)—often severe; cardiac tamponade associated with mortality</td>
</tr>
</tbody>
</table>
| Chronic       | Symptomatic phase (years or decades after infection)  
• 60% to 70%: asymptomatic or indeterminate  
• 20% to 30% cardiac or digestive form (megaoesophagus/megacolon)  
• Both forms in 5% to 15% | Undefined—but rapid progression to long-term cardiac or gastrointestinal dysfunction indicated |
| Mortality     | Estimated 5% to 10% | Estimated 8% to 40% |
Why greater clinical severity with foodborne infection?

Still not entirely understood – likely multi-factorial

1) Greater parasitic load
   - Whole vector vs faecal deposit
   - Higher parasite survival with entry via digestive tract mucous membranes vs through skin

2) Differences in the mucosal pathways associated with infection site (immune response components)
   - Skin vs digestive tract
   - Oral cavity vs stomach entry (gavage) in mice – acute phase severity greater

3) Vector differences
   - *Panstrongylus geniculatus* more likely to be infected than other triatomine species and *T. cruzi* loads higher ($10^3 – 10^7$ per ml) – but not a good vector for vectorborne transmission (delayed defecation after blood meal)

4) Parasite lineages differ
   - Different (7) discrete typing units – different pathogenicities in mice and different vector preferences

5) Treatment susceptibility
   - Probably associated with parasite lineage, foodborne infections seem less susceptible to treatment than vectorborne
   - 10-year follow-up of patients following large foodborne outbreaks have shown ca. 70% treatment failure.

Mouse experiments: ID50 is 100-fold lower for oral challenge than for cutaneous
Inclusion of Chagas Disease in new WHO estimates

- Data on burden of Chagas Disease recently published (Gómez-Ochoa et al, 2022)\(^a\)
  - Does not consider infection route and relative infection route (source attribution) data is scarce.
  - Data synthesis from 2014 indicates that in some countries foodborne transmission is increasing and in Brazil predominates (Andrade et al, 2014)\(^b\)
  - Can use different possibilities in calculating proportion and also data from EKE

- For foodborne Chagas disease we need to propose a new disability weighting based on disease models for foodborne Chagas disease
  - Currently being developed

- As foodborne Chagas disease is almost entirely confined to South America, global weight may not be too shocking

- But relative to the population potentially exposed (population of S/C America) may provide vital clues to energise initiatives to combat this important issue.

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Trypanosoma cruzi in the food-chain

- Which foods?
  - Blood of infected animals
  - Food contaminated by infected vectors (whole vectors or their faeces)
  - Food contaminated by secretions of infected reservoir hosts (e.g., opossums).
  - Juices particularly associated, but also other foods reported in outbreaks (soup, salad)

- The infective stages can survive for prolonged periods in some food types
  - Experiments indicate survival of up to 72 h (motile trypomastigotes) in juice, acai pulp, coconut water
  - Also survive being frozen (around one day at -20°C)
  - Do not survive being heated to over >60°C
Which measures to consider to control *Trypanosoma cruzi* in the food-chain

- **Education**
  - Of relevant authorities at international and national levels
  - Of those involved in food preparation or sale
  - Of those working in agriculture (e.g., harvesting açaí)

- **Prevention of contamination of food**
  - Ensure freshly prepared food, particularly juices, are stored covered.
  - Reduce domiciliary / canteen (etc.) infestation with the reduviid bugs
  - Minimise access of potential reservoir hosts to places where food is stored or prepared

- **Inactivate parasites in food that maybe contaminated**
  - Pasteurisation of fruit juices
  - Meat, particularly game, cooked properly prior to eating.

- **HACCP, risk assessment, other standards to ensure safe food.**
Conclusions

- Chagas Disease is a neglected disease (one of WHO’s listed NTD)
  - The foodborne route of transmission is even more neglected
  - The relevance and relative importance of this transmission route requires international and national recognition
  - Foodborne Chagas disease is different and more serious than vectorborne Chagas disease – acute disease, greater severity, higher mortality
  - Will require establishment of new models (higher disability weighting) to determine burden
  - Although not included in FERG (2007-2015), foodborne Chagas Disease intended to be included in the current WHO estimates – providing data to promote and establish interventions
Thank you for your attention

- Many thanks to the WHO Foodborne Disease Burden Epidemiology Reference Group (FERG)
  - Parasitic Diseases Task Force (PDTF)
  - Source Attribution Task Force (SATF)

- WHO, particularly Yuki Minato and Charlee Roberts (moderating this webinar)

- Carlotta Di Bari (Sciensano, Belgium)

- Colleagues in South America, particularly Belkisyolé Alarcón de Noya and Oscar Noya González (Universidad Central de Venezuela, Caracas)