Chagas Disease ECHO Series

Extension for Community Healthcare Outcomes

Chagas Disease in the USA:
Screening, Diagnosis, and Treatment
for **Primary Care Patients**

Session 1 of 4 Part Series

December 6th, 2023 | 12:00 PM ET / 9:00 AM PT

Agenda

- Welcome
- Introductions and Announcements
  - ECHO Hub Team & Model
  - CDN Team
- Presentations
  - Dr. Eva Clark
  - Dr. Jill Weatherhead
- Q&A
- Closing Remarks

WHO WE ARE – THE ECHO HUB TEAM

Rockefeller University
- Jonathan Tobin, PhD

Clinical Directors Network
- Jonathan Tobin, PhD
- Marija Zeremski, PhD
- Melissa Samanoglu
- Monisa Nayim

Texas State University
- Zo Ramamanjiarvielo, PhD

San Diego State University
- Paula Stigler Granados, PhD
- Michael Vingiello, MPH

University of Texas Health Science Center (UTHealth), San Antonio
- Shreya Prasanna, BPTh., MSc.
- Keito Kawasaki

CHAGAS DISEASE 4-PART SERIES

Today's Session:

Chagas Disease in the USA: Screening, Diagnosis, and Treatment for Primary Care Clinicians

Upcoming Sessions:
- **January 10, 2024** - Congenital and Pediatric Chagas Disease in the USA
- **February 7, 2024** - Chagas Disease as a Migrant Health Issue
- **March 6, 2024** - Interprofessional Team Approaches to Chagas Disease Management

1.5 CME/CNE credit available for each session for total **6.0** credits for entire series provided by The American Academy of Family Physicians (AAFP)

DETAILS OF THE ECHO MODEL

Moving Knowledge, Not Patients

Principles of the model:

- **Technology to leverage resources** and create knowledge networks
- Improving **outcomes** by sharing and standardizing best practices
- **Case-based learning** to foster deep knowledge, skills, and self-efficacy
- **Data tracking** to monitor outcomes and inform quality improvement

CHAGAS DISEASE EDUCATIONAL SERIES FOR COMMUNITY-BASED CLINICIANS AND STAFF

www.CDNetwork.org

CONTINUING MEDICAL EDUCATION (CME) ACCREDITED EDUCATIONAL SERIES WITH EXTENSION FOR COMMUNITY HEALTHCARE OUTCOMES (ECHO) SESSIONS

CLINICAL DIRECTORS NETWORK
THE ROCKEFELLER UNIVERSITY CENTER FOR CLINICAL AND TRANSLATIONAL SCIENCE
Stavros Niarchos Foundation (SNF) Institute for Global Infectious Disease Research

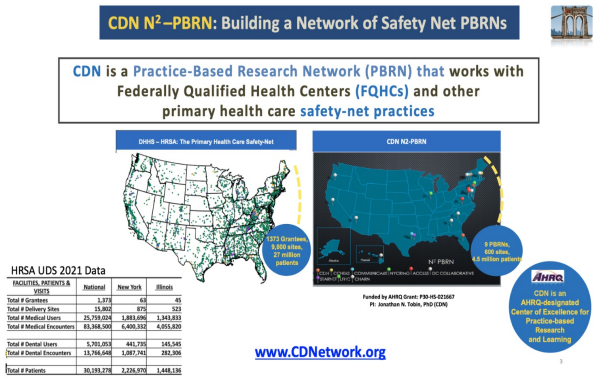
RU-SNF Pilot Project:
Chagas Disease as an Emerging Infectious Disease in the USA

Funded by: the SNF Institute for Global Infectious Disease Research,
NCATS NIH CTSA #UL1-TR-001866 and AHRQ grant #1P30-HS-021667

Clinical Directors Network, Inc. (CDN)

www.CDNetwork.org

Clinical Directors Network (CDN) is a New York City-based practice-based research network (PBRN) and is an AHRQ-designated Center of Excellence (P30) for Practice-based Research and Learning and a network of safety-net PBRNs ("N²-PBRN") dedicated to improving access to care and clinical outcomes for low income and medically underserved communities by creating community-academic partnerships around research, education/training, and service.



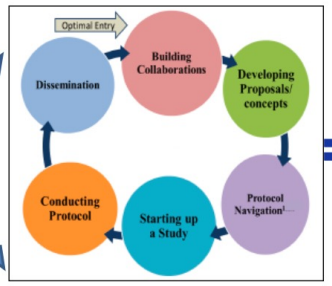
BUILDING COMMUNITY-ACADEMIC TRANSLATIONAL RESEARCH PARTNERSHIPS

www.CDNetwork.org

CDN/N² = PBRN INFRASTRUCTURE[1]
- Quality Improvement
- Clinical Outcomes
- Comparative Effectiveness Research
- Training Clinician Investigators
- Implementation Science
- Disseminating Methods & Clinical Outcomes Results

+

ROCKEFELLER = CTSA INFRASTRUCTURE
- Laboratory Investigation
- Mechanistic Questions
- Protocol Navigation
- Clinical Scholars
- Bioinformatics/ Phenotyping
- Disseminating Translational Research Methods



CEnR-Navigation Process (CEnR-Nav)²

=

CE
CEnR

CER/PCOR
+
Embedded Mechanistic Studies

Chagas Disease Specific Aims/Goals

- To build a full-spectrum translational research team that engages community-based practicing primary care clinicians with laboratory scientists to examine the emerging Chagas disease epidemic in the USA **(Community-engaged research aim)**
- To conduct bi-directional workforce training and development activities that bring together clinicians and investigators to build a learning community that will learn from each other as part of hybrid onsite/online CME-accredited trainings **(Education and training aim)**
- To evaluate the feasibility and utility of extracting electronic health records data to characterize the epidemiology and practice patterns related to testing and treatment of Chagas disease among participating FQHCs **(Descriptive epidemiologic aim)**

Funded by: The Stavros Niarchos Foundation (SNF) Institute for Global Infectious Disease Research
National Center for Advancing Translational Sciences, National Institutes of Health (NIH) Clinical and Translational Science Award (CTSA) at the Rockefeller University #UL1-TR-001866

Chagas Disease Educational Series for Community-based Clinicians and Staff

To Register or to view prior sessions, visit **www.CDNetwork.org**

Continuing Medical Education (CME) Accredited Educational Series with 4 Extension for Community Healthcare Outcomes (ECHO) sessions:

1. Chagas Disease in the USA: Screening, Diagnosis, and Treatment for Primary Care Clinicians
Date: Wednesday, December 6, 2023 at 12 PM ET/9 AM PT
Speakers: Eva Clark, MD, PhD[1], Jill Weatherhead, MD, PhD[1]
Introduction: Paula Stigler Granados, PhD[2]

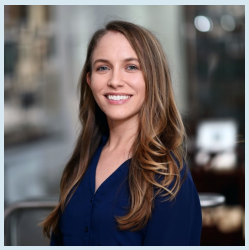
2. Congenital and Pediatric Chagas Disease in the USA
Date: Wednesday, January 10, 2024 at 12 PM ET/9 AM PT
Speakers: Morven Edwards, MD[1]
Introduction: Nancy Jenks, NP[3]

3. Chagas Disease as a Migrant Health Issue
Date: Wednesday, February 7, 2024 at 12 PM ET/9 AM PT
Speakers: Alyse Wheelock, MD[4], Colin Forsyth, PhD, MPH[5]
Introduction:

4. Interprofessional Team Approaches to Chagas Disease Management
Date: Wednesday, March 6, 2024 at 12 PM ET/9 AM PT
Speakers: Maja Carrion, DrPH[4], Paula Stigler Granados, PhD[2]
Introduction: Deliana Garcia, MA[6]

[1]Baylor College of Medicine
[2]San Diego State University
[3]Sun River Health
[4]Boston University
[5]Drugs for Neglected Diseases Initiative (DNDI)
[6]Migrant Clinicians Network (MCN)

PRESENTER



Dr. Eva Clark, MD, PhD

- Dr. Eva Clark is an Assistant Professor in the Departments of Medicine (Section of Infectious Diseases) and Pediatrics (Division of Tropical Medicine) at Baylor College of Medicine (BCM) in Houston, Texas.
- She is a co-leader of the United States Chagas Disease Providers' Network, the Director of Clinical Education at BCM's National School of Tropical Medicine, and the Medical Director of the Harris Health System's Tropical Medicine clinic.
- Her current research interests include studying the epidemiologic, immunologic, and clinical consequences of tropical infectious diseases on the development of chronic diseases in underserved communities.

PRESENTER

Dr. Jill Weatherhead, MD, PhD

- Dr. Weatherhead is an Assistant Professor of Pediatrics and Medicine in the Sections of Pediatric Tropical Medicine, Pediatric Infectious Diseases and Adult Infectious Diseases at Baylor College of Medicine (BCM) and Texas Children's Hospital.
- She is board certified in pediatrics, internal medicine, pediatric infectious diseases, and adult infectious disease with a sub-specialty certificate in tropical medicine and travelers' health and a PhD in immunoparasitology.

DISCUSSION FACILITATOR

Dr. Paula Stigler Granados, PhD

- Dr. Paula Stigler Granados is an Associate Professor in the School of Public Health and Division Head of the Environmental Health Division.
- She is a subject matter expert in Chagas disease and has been the PI for the last 8 years on a Center for Disease Control funded cooperative agreement award to raise awareness among healthcare providers in the U.S. about Chagas disease. She also works with the U.S. military on Chagas disease surveillance activities and helped launch the Texas Chagas Taskforce in 2015.

REMINDERS

Click "Live Transcript" button to enable Closed captioning

Complete evaluation survey upon exit

Use Zoom Q & A to ask a question

Session is being recorded

- Will be posted to our website within 1 week
- Available with our previous recordings https://wp.uthscsa.edu/echo/echo-programs/chagas-disease/

Use Zoom chat feature for comments/reactions/intros

CME/CNE Evaluation

- **To obtain Continuing Medical Education (CME) and Continuing Nursing Education (CNE) credit, you must complete the evaluation form**
- **1.5 CME/CNE credits available for each session for total 6.0 credits for entire series**
- **CME/CNE Evaluation Link:** www.proprofs.com/quiz-school/ugc/story.php?title=chagas-disease-echo-educational-series-session-1-12623ey

Clinical Directors Network, Inc. (CDN) is accredited by The American Academy of Family Physicians (AAFP) to provide Continuing Medical Education (CME) credits and the American Nurses Credentialing Center (ANCC) for Continuing Nursing Education (CNE) credits

Thank You!

- CME certificates will be issued within 3 weeks following this session
- Recordings of the sessions will be made available for CME/CNE
- If you have any questions, please reach out to **chagasus@gmail.com**

This work is supported by the Cooperative Agreement Number, 6 NU2GGH002323-01-01, funded by the Centers for Disease Control and Prevention. The contents of this webinar are solely the responsibility of the presenters and do not necessarily represent the official views of the Centers for Disease Control and Prevention or the Department of Health and Human Services.

Chagas Disease in the US:
Screening, Diagnosis, & Treatment

Eva H Clark, MD, PhD, CTropMed
Baylor College of Medicine
US Chagas Disease Providers' Network (USCN)

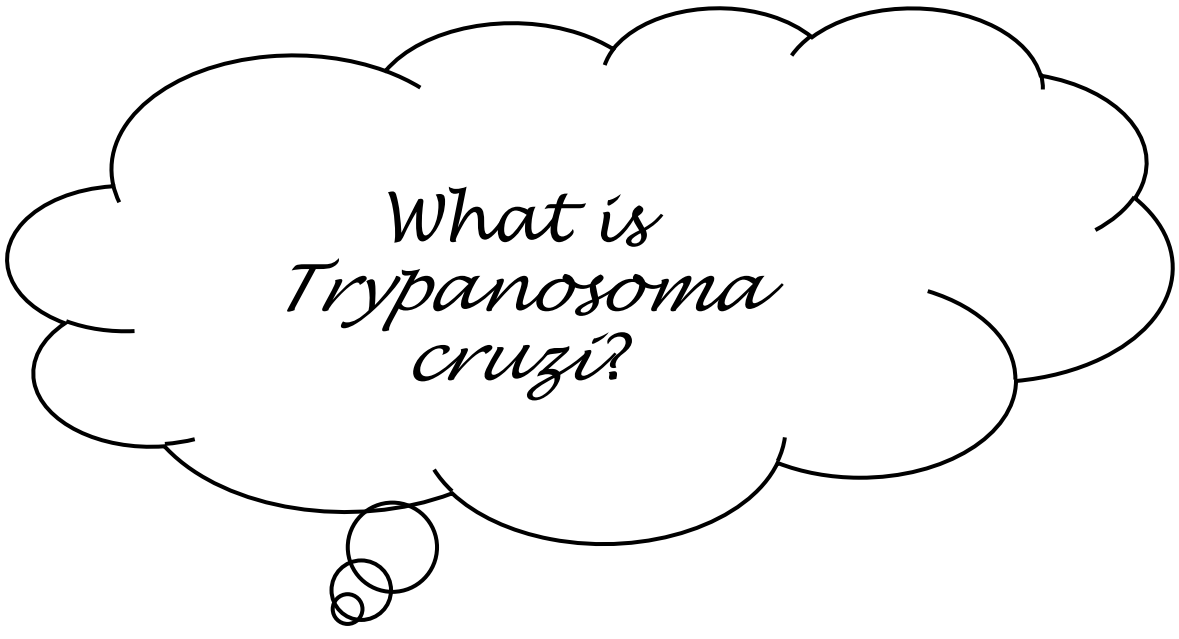
Jill Weatherhead, MD, PhD, CTropMed
Baylor College of Medicine
National School of Tropical Medicine

Objectives & Disclosures

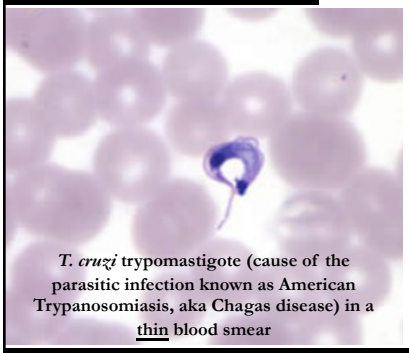
- **Objectives:**
  - Review the epidemiology of Chagas disease in the US including risk factors for exposure to *Trypanosoma cruzi*
  - Understand how to screen at-risk people living in the US for Chagas disease and how to follow up the screening test with appropriate diagnostic test(s)
  - Discuss available treatments for *T. cruzi* infection and appropriate management strategies
- **Disclosures:**
  - Eva Clark, none
  - Jill Weatherhead, none

What is Chagas Disease & Who is at risk?

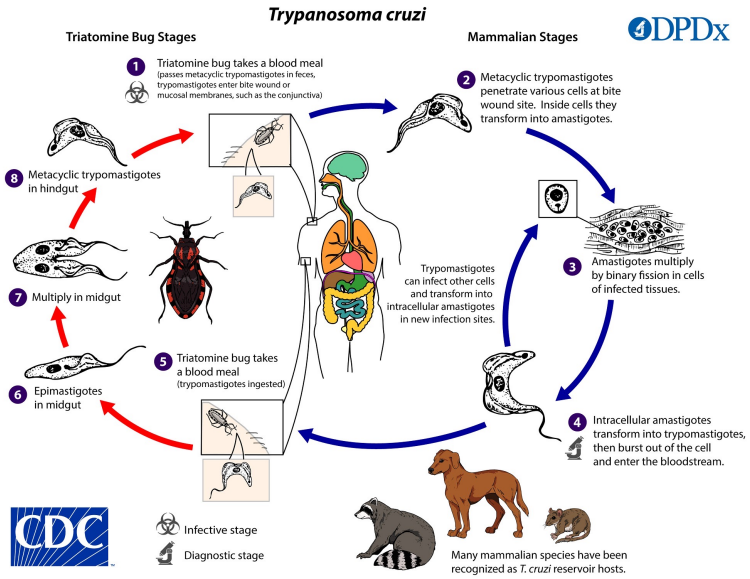
A brief introduction to Chagas disease in the United States



T. cruzi Life Cycle



***T. cruzi* trypomastigote (cause of the parasitic infection known as American Trypanosomiasis, aka Chagas disease) in a thin blood smear**



CDC Dpdx:
https://www.cdc.gov/dpdx.html
https://www.cdc.gov/dpdx/trypanosomiasisamerican/index.html

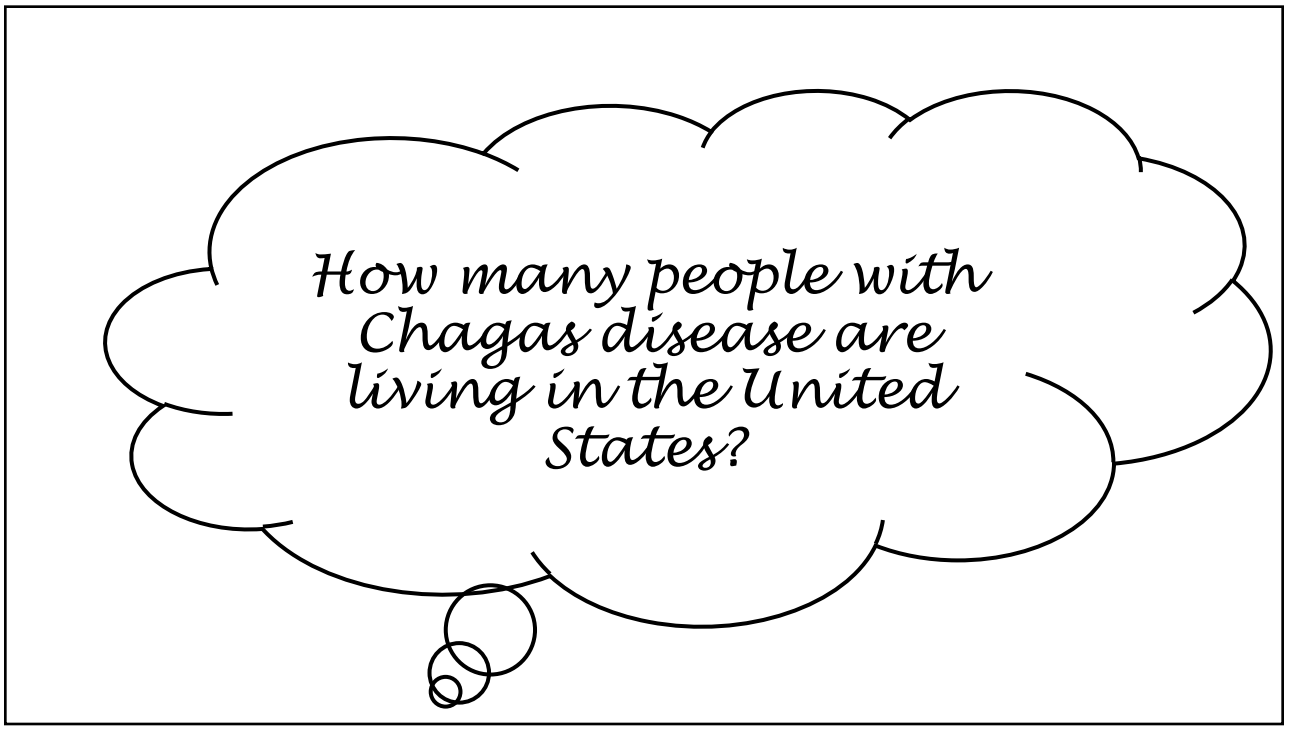
https://www.youtube.com/watch?v=79bVKq_vTR0

How is *T. cruzi* transmitted?

T. cruzi Exposure Risk Factors

***T cruzi* can be transmitted by:**

- Feces of Triatomine vector (endemic areas)
- Mother-to-baby (congenital)
- Contaminated blood products (transfusions)
- An organ transplanted from an infected donor
- Laboratory accident (rare)
- Contaminated food or drink (rare?)



Chagas Disease: *Trypanosoma cruzi* Epidemiology

- 6-8 million people globally (LA!)
- Estimated 288,000 people (LA immigrants) with chronic Chagas disease in US
- 76 domestically-acquired cases documented in the US, 2000-2018
- US blood donor screening since 2007
  - ~1 in 27,500 donors test positive
  - Only ~11% seek treatment!

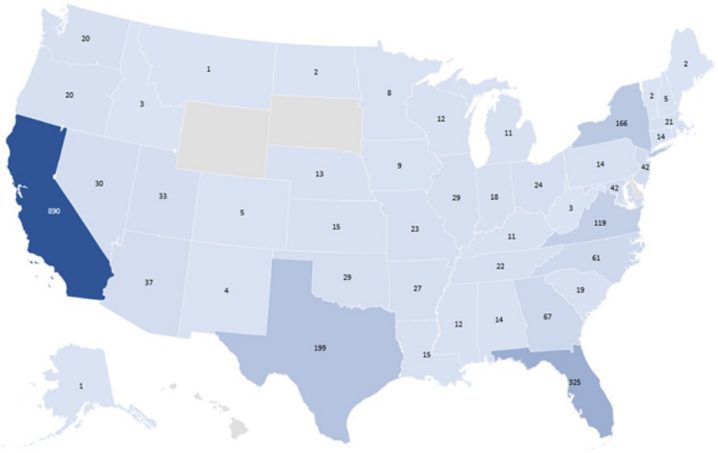
Table 1. Studies on Prevalence of Chagas Disease in Latin American-born Populations in the U.S. (2010-2020)*

Study	*Population*	*prevalence (%)*
Castro et al. 2020	1,514 people in the greater Washington, DC metropolitan area (community screening program)	3.8
Hernandez et al. 2019	189 relatives of 86 previously diagnosed patients with CD	7.4
Manne-Goehler et. al. 2019	5,125 people from endemic regions screened in primary care setting in East Boston	1.0
Meymandi et al. 2017	4,755 Latin American-born residents of Los Angeles (community screening program)	1.2
Traina et al. 2017	327 hospital patients with electrocardiogram abnormalities	5.2
Park et al. 2017	80 patients with pacemakers	7.5
Traina et al. 2015	135 hospital patients with nonischemic cardiomyopathy	19.0
Kapelusznik et al. 2013	39 hospital patients with nonischemic cardiomyopathy	13.0

*All study populations consist of people who were born or lived a significant amount of time in endemic countries of Latin America.

Bern C et al. CMR. 2019 Nov 27;33(1):e00023-19.
Lynn MK et al. Acta Trop. 2020 May:205:105361.
Forsyth C et al. JID. 2021 Oct 8.
Irish A et al. EID. 2022 Jul;28(7):1313-1320.

Chagas Biovigilance Network: Confirmed Positive Chagas Donations by States: 2007 - 2019



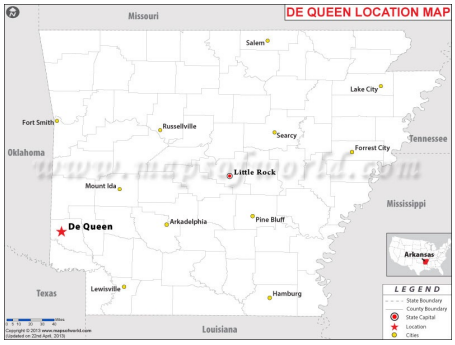
https://www.aabb.org/news-resources/resources/hemovigilance/chagas-biovigilance-network

Case

17-year-old male with controlled asthma, allergic rhinitis and nasal polyposis (Flonase, Flovent, albuterol) presenting to pediatric infectious disease in Arkansas Children's Hospital for a positive Chagas IgG (he tested positive during a routine blood donation as part of a school fundraiser). He is asymptomatic.

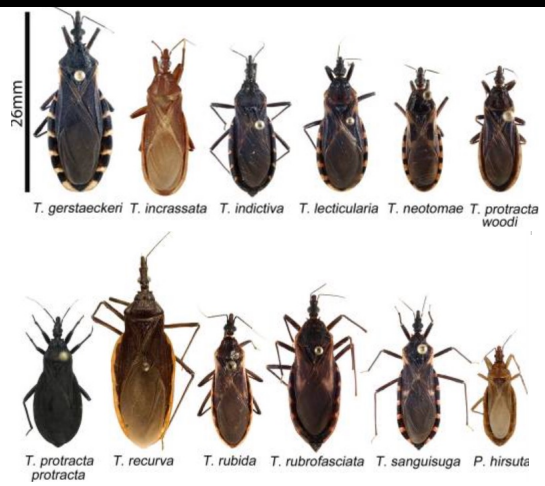
Exposures:

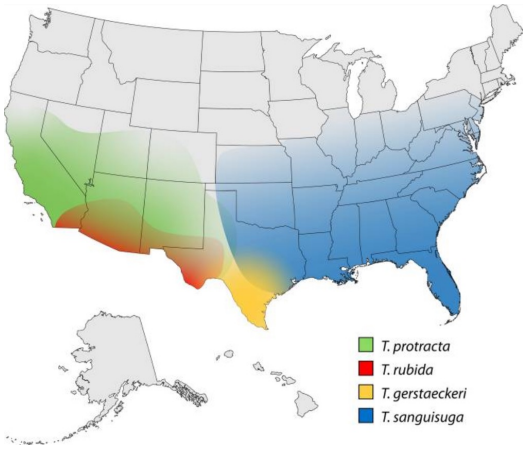
- Born in De Queen, Arkansas
- No domestic travel outside of Arkansas
- Travelled to Cozumel, Mexico on a cruise in 2013
- Mother has never lived outside of US
- No international visitors
- Animals: lives on a farm, has dog and cat
- Lots of bug bites but was not able to recognize a reduviid bug
- No raw or unpasteurized drink/food, buys all food in grocery store
- Active outdoorsman: hunting, camping, fishing



Could this patient have Chagas disease?

Triatomine Species in the US





Bern C et al. Clin Microbiol Rev. 2019 Nov 27;33(1):e00023-19.

Autochthonous Chagas Disease in the US

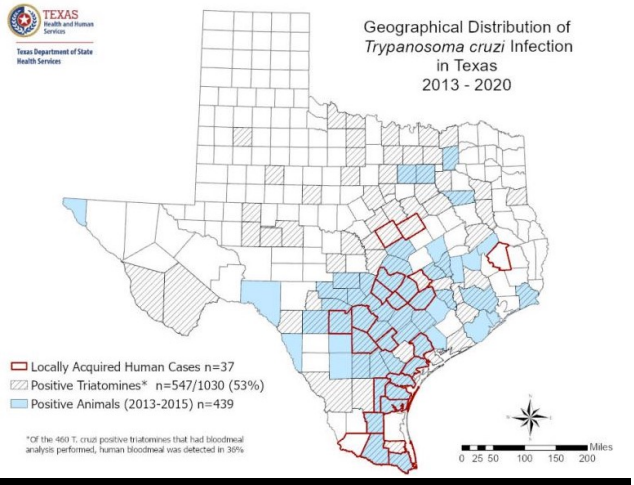


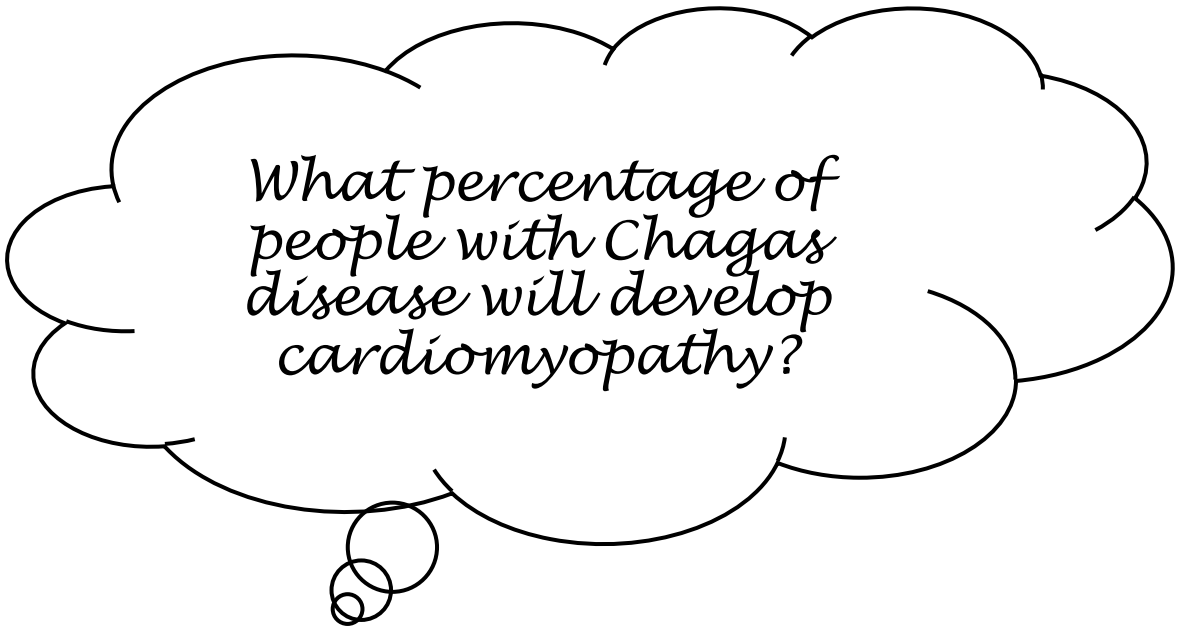
Table 1. Distribution of confirmed or suspected locally acquired cases of Chagas disease in the USA. **(2000-2018), Lynn MK et al. Acta Trop. 2020 May:205:105361.**

State	# Confirmed	# Suspected	Total Case Count	References
Texas	26	22	48	(Garciaetal., 2016; Curtis-Roblesetal., 2017b; Webberetal., 2017; Garciaetal., 2015a; ServicesTDoSH; Guntheretal., 2017; Leibyetal., 2000; Bernetal., 2011; Walker,2003)
Louisiana		7	7	(Bernetal., 2011; LOPH.2018; Dornetal., 2007)
Arkansas	2		2	*pers. comm.*
California		1	1	(Hernandezetal., 2016;)
Arizona	1	1	2	(Harrisetal., 2017; Beattyetal., 2018; *pers. comm.*)
Mississippi		1	1	(Canteyetal., 2012;)
State not provided		15	15	(Canteyetal., 2012)
Total Cases USA			76	

https://www.dshs.state.tx.us/IDCU/disease/chagas/Chagas-Disease-Data.aspx

Clinical Manifestations, Diagnosis, & Screening

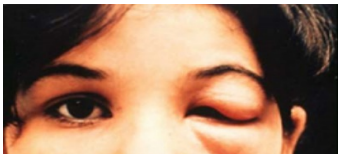
How to screen for and diagnose Chagas disease in the United States



Presentations of Chagas Disease

- **Congenital:** 1-5% of infected mothers transmit to fetus; usually asymptomatic but can manifest in infants as low birth weight, prematurity, hepatosplenomegaly; rarely severe disease/death
- **Acute:** 2-4 weeks post exposure to *T cruzi*; usually asymptomatic but may have fever and non-specific symptoms due to active parasitemia
- **Chronic:** Typically asymptomatic; 20-30% develop cardiac or GI disease decades after initial infection
- **Disseminated/Reactivation:** Rare; only occurs in immunocompromised hosts, e.g. post-organ transplant or AIDS; >70% mortality

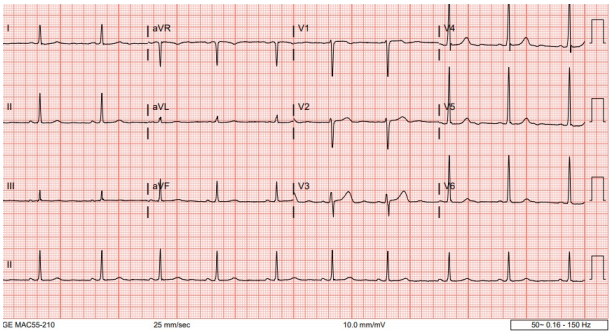
First baby diagnosed with congenital Chagas in US (2010)
MMWR Morb Mortal Wkly Rep. 2012 Jul 6;61(26):477-9.



Romaña's sign of acute Chagas disease
WHO/TDR,https://www.cdc.gov/parasites/chagas/gen_info/vectors/index.html#list

Because chronic Chagas disease is usually asymptomatic, ALL people from endemic regions should be screened…and the earlier in their life they are screened the better!

Chronic Chagas Disease: Indeterminate → End-organ Damage



2017 TTE: Unremarkable; LVEF is estimated at 60-64%.
2023 TTE: Left ventricle is moderately dilated. Normal wall thickness. Severely reduced systolic function. Estimated ejection fraction of 25 - 29%.

Chagas Cardiomyopathy CASE:

32 yo woman from Mexico who presented to her PCP in 2017 with bilateral pedal edema.

TH: Grew up in Mexico (Guerrero) but moved to Houston in 2003.

SH: Lives in Houston and works in a restaurant

PMH: Unremarkable

- EKG showed sinus bradycardia (HR 59)
- TTE was unremarkable
- Diagnosed with hypertension (BP 136/100) and started on amlodipine, lost to follow-up
- Presented to ER with dyspnea and bilateral lower extremity edema in 2023, EF=25-29%, *T. cruzi* IgG+

Because chronic Chagas disease is usually asymptomatic, ALL people from endemic regions should be screened…and the earlier in their life they are screened the better!

Chronic Chagas Disease: Indeterminate → End-organ Damage

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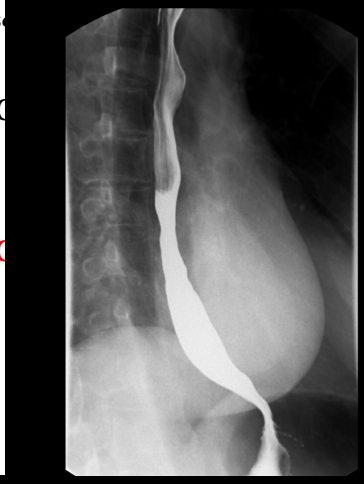


Because chronic Chagas disease is usually asymptomatic, ALL people from endemic regions should be screened…and the earlier in their life they are screened the better!

Chagas GI Disease CASE:

45 yo woman from Santa Cruz, Bolivia presented to PCP with years of worsening dysphagia

TH: Grew up in Bolivia but went to school in Brazil. She emigrated to the US in 2005.

SH: Lives in Houston and works as a nanny (though she was a lawyer before emigrating)

PMH: Unremarkable

- EGD showed mildly atrophic gastric mucosa, biopsy + *H. pylori*
- Underwent esophageal manometry which showed disorganized tertiary contractions consistent with esophageal dysmotility
- Diagnosed with achalasia

USCN · National School of Tropical Medicine · Harris Health System · Texas Children's Hospital · Baylor College of Medicine

Case

Summary: 17-year-old asymptomatic male from De Queen Arkansas, Chagas disease IgG positive via blood donation.

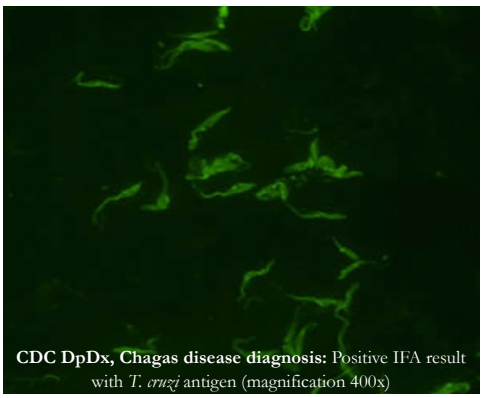
At the time the CDC parasitology lab was closed and TCH Tropical Medicine was consulted for additional guidance.

What do you recommend next?

How many serologic tests are needed to diagnose chronic Chagas disease?

Diagnosis of Chronic Chagas Disease

- Per PAHO (2018) and CDC guidelines, need at least two different serologic tests to result +.
- For confirmatory testing, CDC uses:
  - EIA based on recombinant *T. cruzi* antigens plus immunoblot (TESA) as the first-line tests.
  - If initial EIA and TESA results are discordant, an immunofluorescence assay (IFA) is used as a "tie-breaker."
- FDA-approved tests: (1) Hemagen *T. cruzi* IgG EIA, (2) Wiener *T cruzi* IgG EIA, (3) InBios rapid test*, (4) Ortho (only blood donors)



CDC DpDx, Chagas disease diagnosis: Positive IFA result with *T. cruzi* antigen (magnification 400x)

Diagnosis of congenital, acute, and reactivation/disseminated *T cruzi* infection differ and includes blood smear microscopy and *T cruzi* PCR!

FDA-Approved Chagas Serologic Tests

TABLE 1
Characteristics of FDA-cleared assays for Chagas disease

	Testing platform	Antigen protein base	Sample type	Sensitivity performance characteristics from the FDA 510(k)	Specificity performance characteristics from the FDA 510(k)	Sensitivity within a U.S. population based on consensus reference	Specificity within a U.S. population based on consensus reference	Notes on performance characteristics
ORTHO *T. cruzi* ELISA (ORTHO Clinical Diagnostics)	ELISA	Native parasite	Serum and plasma	100% (CI: 96.6–100) compared with IFA (n = 106); 98.9% compared with IFA (n = 1,074)[12]	99.4% (CI: 98.7–99.8) compared with IFA (n = 1,074 patients)[12]	95.3% (CI: 93/0–97.0)[21]	99.7% (CI: 98.3–100.0)[21]	High rate of cross-reactivity with *Leishmania* (79/100 samples from India tested positive)[12]
Hemagen Chagas' kit ELISA (Hemagen Diagnostics, Inc)	ELISA	Native parasite	Serum	100% (CI: 97.7–100) compared with "commercial ELISA" (n = 160)[13]	98.7% (CI: 96.2–99.6) 226/229 compared with "commercial ELISA" comparator test (n = 394 kits)[13]	90.70% (CI: 87.8–93.1)[21]	99.68% (CI: 98.3–100.0)[21]	In the United States, testing has lower sensitivity but higher specificity
Wiener Chagatest Recombinante v.3.0 ELISA (Wiener Laboratories)	ELISA	Recombinant parasite proteins (shed acute-phase antigen)	Plasma or serum	97.9% (CI: 95.6–99.1) compared with IHA, IFA, or ELISA (n = 330)[14]	97.8% (CI: 97–98.5), compared with IHA, IFA, or ELISA (n = 1,507)[14]	96.3% (CI: 94.2–97.8)[21]	98.1% (CI: 95.9–99.3)[21]	There was a recall of this test in 2018 based on device not reaching expiration dates
InBios Chagas Detect *Plus* Rapid Test (InBios International, Inc)	Lateral flow immuno chromato graphic assay	Recombinant parasite proteins	Serum or whole blood (includes finger-prick)	96.6% (CI: 94.5–97.9) for serum, 97.0% (CI: 95.0–98.2) for finger-prick compared with IFA (n = 473)[15] 100.0% (CI: 95.2–100.0) for serum; 98.7% (CI: 93.0–99.8) for finger prick (n = 108 highly endemic Bolivian population)[15]	100% for both serum and whole blood (CI: 98.1–100) (n = 200 non-endemic U.S. population)[15] 87.1% (CI: 71.1–94.9) for serum and 96.8% (CI: 83.8–99.4) (n = 108 highly endemic Bolivian population)[15]	99.2% (CI: 97.9–99.8)[21]	90.5% (CI: 86.7–93.5)[21]	Finger-prick option has potential for screening in settings without trained phlebotomists. Based on U.S. testing, this has lower specificity and higher sensitivity[21]

Case

Summary: 17-year-old asymptomatic male from De Queen Arkansas, Chagas disease IgG positive via blood donation.

At the time the CDC parasitology lab was closed and TCH Tropical Medicine was consulted for additional guidance.

Blood specimen was tested via:

- ARUP (Hemagen IgG test) = positive
- Quest (Wiener IgG test) = positive

What is his official diagnosis?
What do you recommend next?

Case

Summary: 17-year-old asymptomatic male from De Queen Arkansas, Chagas disease IgG positive via blood donation.

At the time the CDC parasitology lab was closed and TCH Tropical Medicine was consulted for additional guidance.

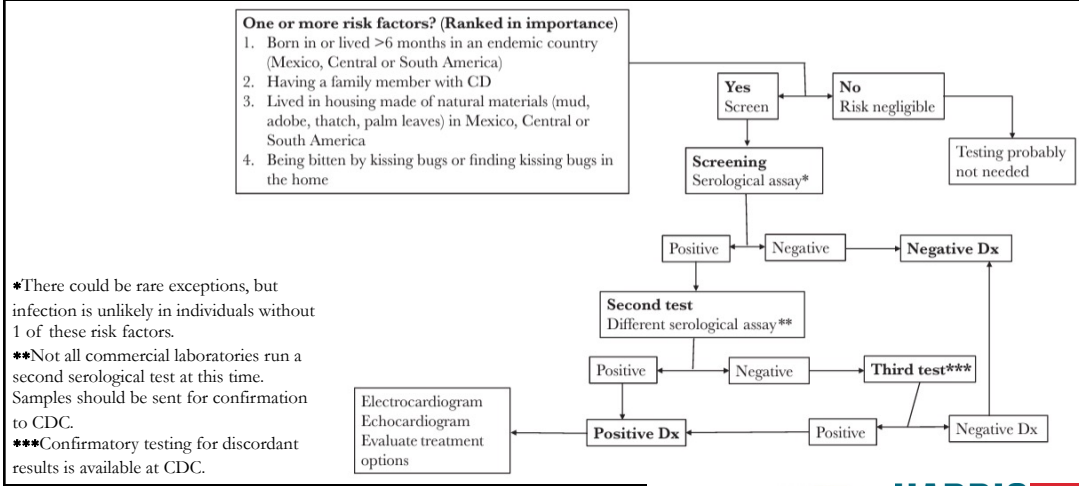
Blood specimen was tested via:

- ARUP (Hemagen IgG test) = positive
- Quest (Wiener IgG test) = positive

- **EKG = sinus rhythm, normal rate**
- **TTE = unremarkable**

DIAGNOSIS = Chronic Chagas Disease (indeterminate stage)

Algorithm for Chagas Disease Screening/Diagnosis in US



Forsyth C et al. JID. 2021 Oct 8.

Challenges of Chagas Disease Screening & Diagnosis

1. Lack of a gold standard to evaluate test performance characteristics
2. Sensitivity of available tests varies depending on geographic origin of the infection

TABLE 3 Sensitivity of *T. cruzi* IgG serological tests by blood donor region of birth

	% sensitivity (CI)					
	Blood donor status			Consensus status (at least 2 current tests positive)		
Test	Mexico	Central America[a]	South America[b]	Mexico	Central America[a]	South America[b]
Hemagen	82.98 (74.13, 89.24)	88.64 (80.33, 93.71)	93.15 (84.95, 97.04)	86.67 (78.13, 92.21)	89.66 (89.66, 94.46)	93.15 (84.95, 97.04)
Ortho	85.11 (76.54, 90.92)	95.45 (88.89, 98.22)	97.26 (90.55, 99.51)	88.89 (80.74, 93.82)	96.55 (90.35, 99.06)	97.26 (90.55, 99.51)
Wiener	91.49 (84.10, 95.62)	96.59 (90.45, 99.07)	98.63 (92.64, 99.93)	93.33 (88.84, 91.12)	96.55 (90.35, 99.06)	98.63 (92.64, 99.93)
InBios	97.87 (92.57, 99.62)	98.86 (93.84, 99.94)	98.63 (92.64, 99.93)	100.00 (95.91, 100.00)	100.0 (95.77, 100.00)	98.63 (92.64, 99.93)

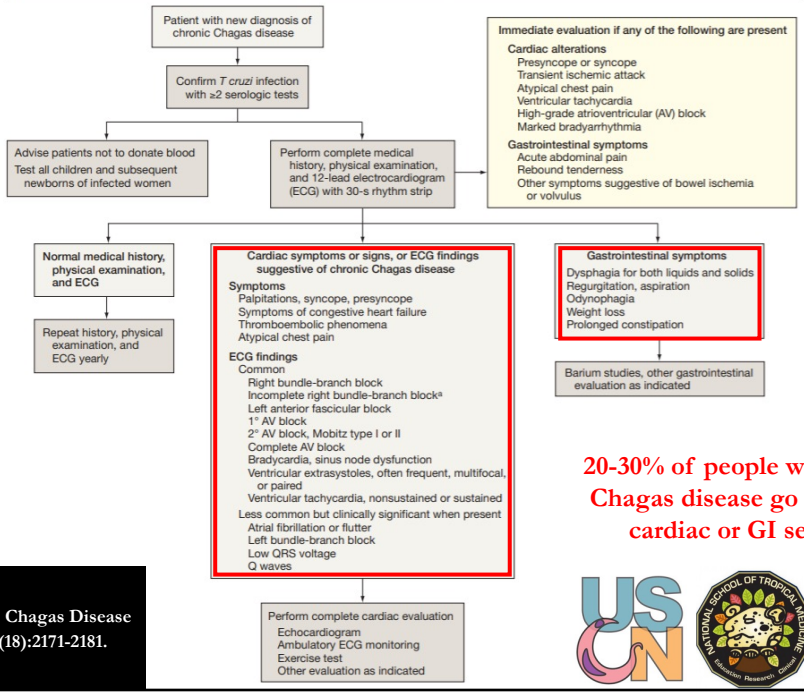
[a]Data represent blood donors born in El Salvador (n = 67), Guatemala (n = 10), Honduras (n = 7), Costa Rica (n = 1), Nicaragua (n = 1), or an unspecified location in Central America (n = 2).
[b]Data represent donors born in Bolivia (n = 32), Argentina (n = 13), Chile (n = 5), Paraguay (n = 2), Uruguay (n = 1), Brazil (n = 6), Colombia (n = 9), Ecuador (n = 2), or an unspecified location in South America (n = 3).

Whitman et al. J Clin Microbiol. 2019 Nov 22;57(12):e01217-19.

Treatment & Management

How to manage Chagas disease in the United States

Management of Chronic Chagas Disease



20-30% of people with chronic Chagas disease go on to have cardiac or GI sequelae

Bern et al. Evaluation and Treatment of Chagas Disease in the United States. *JAMA*. 2007;298(18):2171-2181.

Baylor College of Medicine

Are drug treatments available for Chagas disease?

To Treat or Not to Treat?

All people diagnosed with chronic Chagas disease should receive a baseline EKG and TTE and be given appropriate subspecialty follow-up.

Table 2. Recommendations for Antitrypanosomal Drug Treatment According to Chagas Disease Phase and Form, Patient Age, and Clinical Status

Antitrypanosomal Drug Treatment by Chagas Disease Phase, Form, and Demographic Group	Strength of Recommendation and Quality of Supporting Evidence[a]
Should always be offered	
Acute *Trypanosoma cruzi* infection	AII
Early congenital *T cruzi* infection	AII
Children aged ≤12 y with chronic *T cruzi* infection	AI
Children aged 13-18 y with chronic *T cruzi* infection	AIII
Reactivated *T cruzi* infection in patient with HIV/AIDS or other immunosuppression	AII
Should generally be offered	
Reproductive-age women	BIII
Adults aged 19-50 y with indeterminate form, or mild to moderate cardiomyopathy (Kuschnir grades 0, I, or II)	BII
Impending immunosuppression[b]	BII
Optional	
Adults aged >50 y without advanced cardiomyopathy (Kuschnir grades 0, I, or II)	CIII
Patients with Chagas gastrointestinal tract disease but without advanced cardiomyopathy[c]	CIII
Should generally not be offered	
Advanced chagasic cardiomyopathy with congestive heart failure (Kuschnir grade III)	DIII
Megaesophagus with significant impairment of swallowing	DIII
Should never be offered	
During pregnancy	EIII
Severe renal or hepatic insufficiency	EIII

Bern et al. Evaluation and Treatment of Chagas Disease in the United States. *JAMA*. 2007;298(18):2171-2181. doi:10.1001/jama.298.18.2171

Chagas Disease Pharmacologic Treatment Options in the US

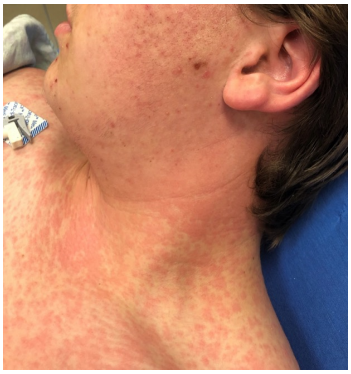
- **Benznidazole**
  - FDA approved in 2017 for use in children ages 2-12 years old
  - Common SEs: allergic dermatitis, peripheral neuropathy, anorexia, insomnia
  - Adults: 5-7mg/kg PO divided BID for **60 days**
  - Children: Weight-based dosing
  - Only available in US via Exeltis! (www.benznidazoletablets.com)
- **Nifurtimox (Lampit)**
  - FDA approved in 2020 for use in children from "birth to less than 18 years of age and weighing at least 2.5 kg"
  - Common SEs: anorexia, N/V, polyneuropathy, H/A, dizziness/vertigo
  - Adults: 8-10mg/kg PO divided TID-QID for **60 days**
  - Children: Weight-based dosing
  - Only available in US via CDC!

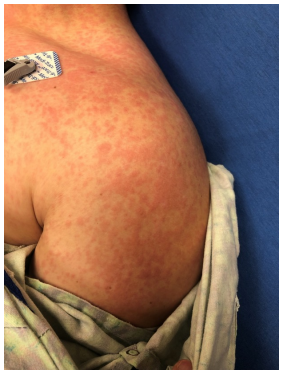
Monitor clinical picture & laboratory values at baseline every 2 weeks during treatment: CBC/diff, CMP

Treatment guidelines vary greatly by country!
Recommend monitoring every 2 weeks during treatment

Case

- Summary: 17-year-old asymptomatic male from De Queen Arkansas, Chagas disease IgG positive via blood donation, confirmed by two different commercial lab tests. Unremarkable EKG and TTE.
- Prescribed benznidazole 150 mg BID for 60 days
- On Day 10 of treatment presented to an ED in Texarkansas:
  - Diffuse rash not relieved with Benadryl, no mucosal involvement
  - Febrile





Case

- Lab workup in ED:

WBC 6.7 (64.2% N, 5.3% E)
Hgb 16.8
Platelets 184

Na135
K 3.7
BUN/Cr 11/0.9

Prot 7.7
Alb 4.9
Tbili 0.3
Dbili 0.4
AST 13
ALT 15
Alk phos 158
Lactic acid 1.4

What would you recommend at this point?

Case

- Benznidazole was stopped
- Prednisone taper was started
- Upon resolution of the rash he was re-started on benznidazole plus prednisone…
- After the first dose he developed the rash again!

Case

- Started Nifurtimox 180 mg daily (approximately 8 mg/kg, maximum dose) QID for 60 days.
  - Increased frequency of drug administration has been associated with fewer adverse events.
- Patient was given 120 mg daily (error) and tolerated for 12 days. Subsequently increased to 180 mg daily.
- 4 days later he developed fever and rash, requiring cessation of medication

Total Treatment: 10 days of Benznidazole + 4 days of Nifurtimox

Chagas Disease Treatment Trials

Table 1. Prospective Controlled Trials of Benznidazole or Nifurtimox for Chronic Chagas Disease in the Published Literature

Source	Chagas Form	Study Design	Age, y	Length of Treatment, d	Comparison Groups	Sample Size, No.	Primary Outcome of Interest, %	Major Adverse Events or Adverse Effects >5%
de Andrade et al,[87] 1996[a]	Indeterminate (n = 120) Early Chagas heart disease (n = 9)[b]	Randomized, double-blinded	7-12	60			Negative seroconversion at 36 mo by AT-ELISA	Maculopapular rash and pruritus
					Benznidazole, 7.5 mg/kg per d	64	58	12.5
					Placebo	65	5	3.1
Sosa Estani et al,[88] 1998	Indeterminate	Randomized, double-blinded	6-12	60			Negative seroconversion at 48 mo by F29-ELISA	Intestinal colic
					Benznidazole, 5 mg/kg per d	55	62	NR
					Placebo	51	0	NR
							Xenodiagnosis-positive at 48 mo	
					Benznidazole, 5 mg/kg per d	55	5	NR
					Placebo	51	51	NR
Coura et al,[89] 1997[c]	Indeterminate with ≥2 of 3 pretreatment xeno-diagnoses positive[d]	Randomized but apparently not double-blinded	Adults[d]	30	Benznidazole, 5 mg/kg per d	26	Posttreatment xeno-diagnosis positive 1.8	NR
					Nifurtimox, 5 mg/kg per d	27	9.6	NR
					Placebo	24	34.3	NR
Viotti et al,[90] 2006[d]	Indeterminate and nonsevere determinate	Alternate assignment to benznidazole or no treatment; nonrandomized, unblinded	Mean, 39.4	30			Progression	Severe allergic dermatitis prompting discontinuation 13.0
					Benznidazole, 5 mg/kg per d	283	4.2	NR
					No treatment	283	14.1	
					Benznidazole, 5 mg/kg per d	283	Mortality 1.1	NR
					No treatment	283	4.2	NR

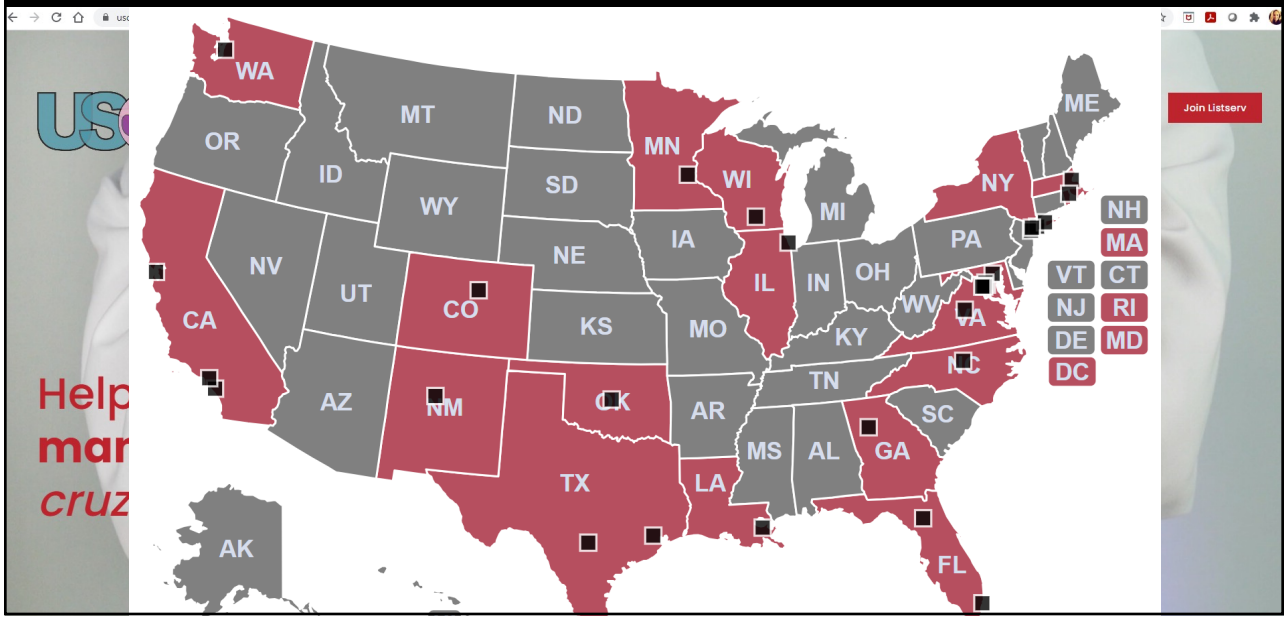
Bern et al. Evaluation and Treatment of Chagas Disease in the United States. *JAMA*. 2007;298(18):2171-2181. doi:10.1001/jama.298.18.2171

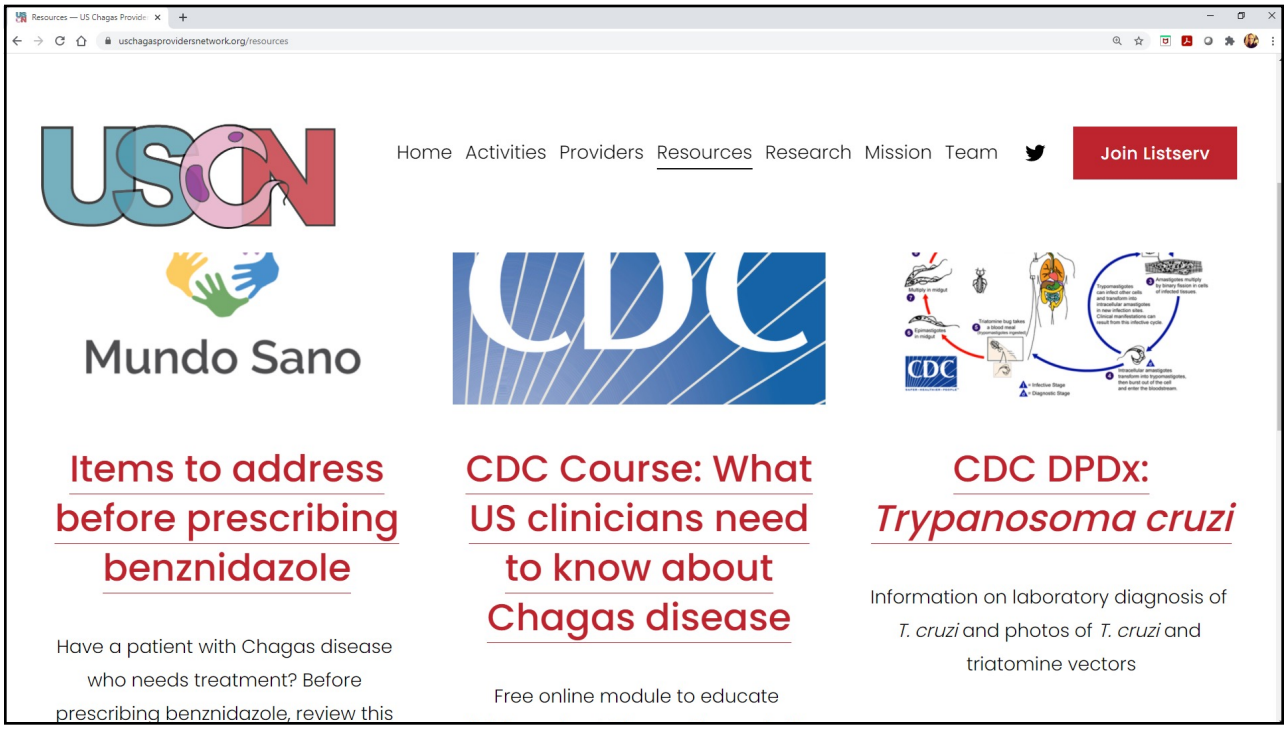
Pivotal Adult Chronic Chagas Disease Treatment Studies

- **BENDITA Trial** (2016-2017, published 2021)
  - Phase 2 double-blind RCT, 210 adults, Bolivia (Cochabamba, Tarija, and Sucre)
  - **Arms:** (1) BNZ 300mg daily for 8 wks, (2) 4 wks, or (3) 2 wks, (4) BNZ 150mg daily for 4 wks, (5) BNZ 150mg daily for 4 wks plus fosravuconazole, (6) BNZ 300 mg once wkly for 8 wks plus fosravuconazole, or (7) placebo (12-month follow-up period)
  - **Primary endpoints:** (1) sustained parasitological clearance at 6 mos (i.e., persistent negative qPCR from end of treatment) and (2) incidence and severity of adverse events
  - **Results:** 2 wks (83%) and 4 wks (89%) non-inferior to 8 wks of BNZ (89%)
- **MULTIBENZ Trial** (NCT03191162, Hospital Universitari Vall d'Hebron Research Institute [Spain])
  - Phase 2 RCT comparing BNZ 300mg/day for 60d, 150mg/day for 60d, and 400mg/day for 15d); Spain, Brazil, Argentina, and Colombia
- **BETTY Trial** (NCT03672487, Tulane, UCSD, ICMHP)
  - Phase 3 RCT comparing BZN 150mg/day for 30d vs BZN 300 mg/day for 60d; Argentina

Torrico et al. Lancet Infect Dis. 2021 Aug;21(8):1129-1140.

US Chagas Providers Network





What is Chagas disease?

Chagas disease is caused by the parasite *Trypanosoma cruzi* and is spread by infected bugs called triatomines.

Where is Chagas found?

Endemic throughout much of Mexico, Central America, and South America

Who is at risk?

- Persons living in the U.S. who have migrated from endemic areas
- Estimates of 300,000 or more infected Latin Americans living in the U.S.

How is the disease transmitted?

- Triatomines thrive in poorly constructed and usually rural housing, typically living within cracked mud walls and thatched roofs
- During the night, the bugs emerge from their hiding places to feed, defecate, and thus inoculate
- Also transmitted by:
  - Blood transfusion
  - Organ transplantation
  - Congenitally
  - Lab accident (rare)
  - Food or drink (rare)
- Screening for Chagas disease instituted in early 2007

Chagas disease may be life-threatening in both the acute and chronic phases of the infection.

CS293359A June 18, 2018

What are the phases of the disease?

Acute

- 4–8 weeks
- Asymptomatic or characterized by mild illness

Chronic

Indeterminate

- Typically asymptomatic for years or decades

Symptomatic

- 20-30% of chronically infected persons develop symptomatic disease
- Cardiac disease beginning with conduction abnormalities may be followed by apical aneurysm and thrombus formation
- Gastrointestinal manifestations
- Increased risk of stroke

Diagnosing Chagas Disease

- Detailed patient history including having seen the bug and having stayed within mud walls or thatched roofs, in a country with known Chagas risk
- Hispanic patients may be familiar with other names for the insect such as "kissing bug," "benchuca," "vinchuca," "chinche" or "barbeiro"
- Serum samples may be sent to CDC through your state health department
- Patients should be reassured that contact for testing or treatment will have no effect on immigration status

Treatment of Chagas Disease

- Two drugs, nifurtimox and benznidazole, are worldwide standard antiparasitic treatment
- For more information, please visit the Chagas website at www.cdc.gov/parasites/chagas and click "Resources for Health Professionals" or call 404.718.4745 for clinical consults
- Fact sheets and contact information provided on the web

CDC U.S. Department of Health and Human Services Centers for Disease Control and Prevention

Thank you! Questions?

Stay in touch!

https://uschagasnetwork.org/

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HARRIS HEALTH SYSTEM

Texas Children's Hospital

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