Congenital Chagas Disease in the United States: Screening, Diagnosis and Treatment Challenges

ECHO: Extension for Community Healthcare Outcomes
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Texas Children's Hospital

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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

Medical News & Perspectives

Putting Chagas Disease on the US Radar Screen

Bridget M. Kuehn, MSJ

- "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 6 million people in the Americas have Chagas disease
- An estimated 20% to 30% of those with chronic infection develop Chagas cardiomyopathy

Carlos Chagas in 1909 in his laboratory at the Instituto Oswaldo Cruz

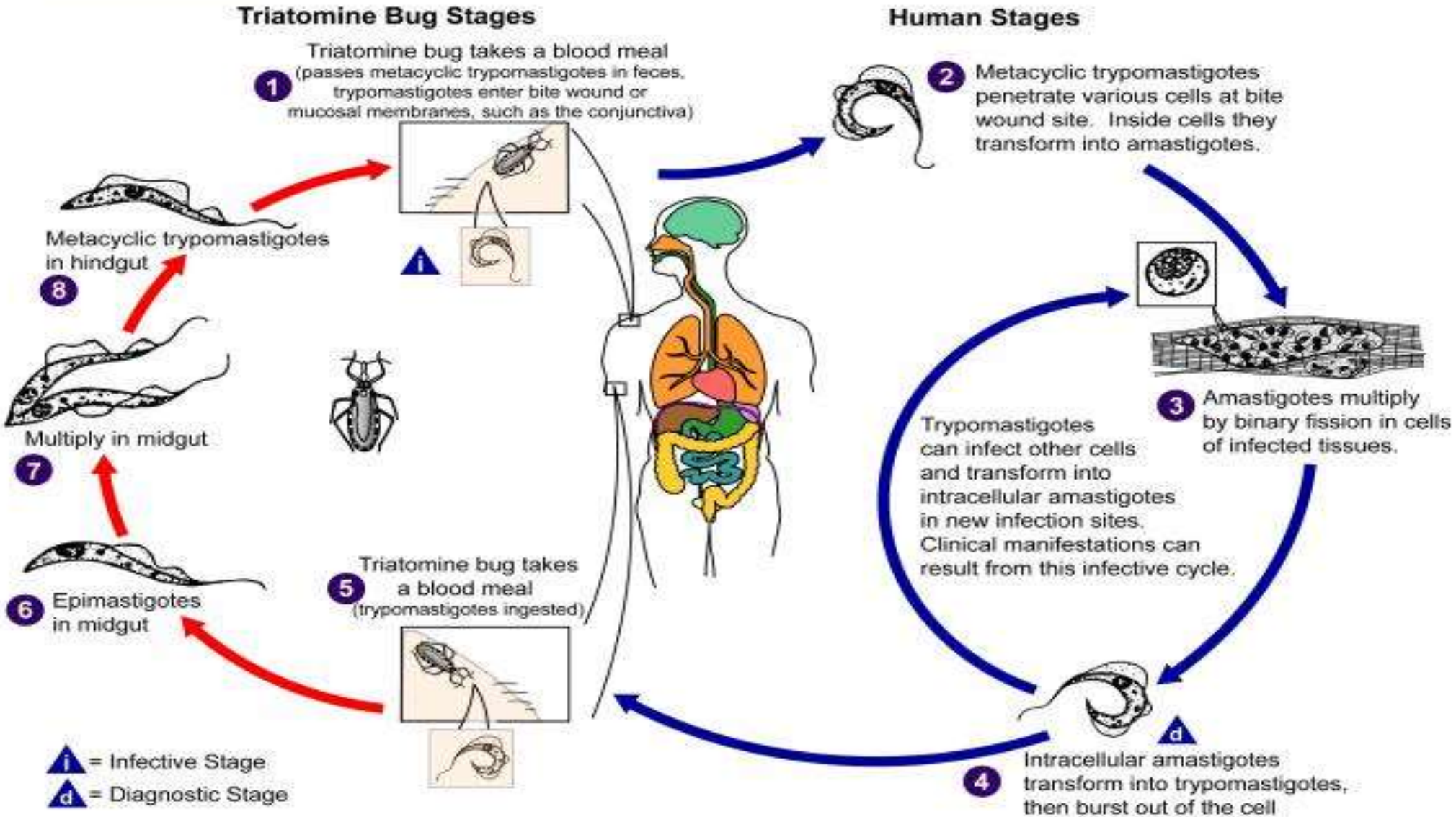
The triatomine bug, sometimes known as the "kissing bug" is the vector for Chagas disease. The bug becomes infected after biting an animal or a person who is already infected with *T. cruzi*. They are also called "benchuca", "vinchuca" or "chinche".

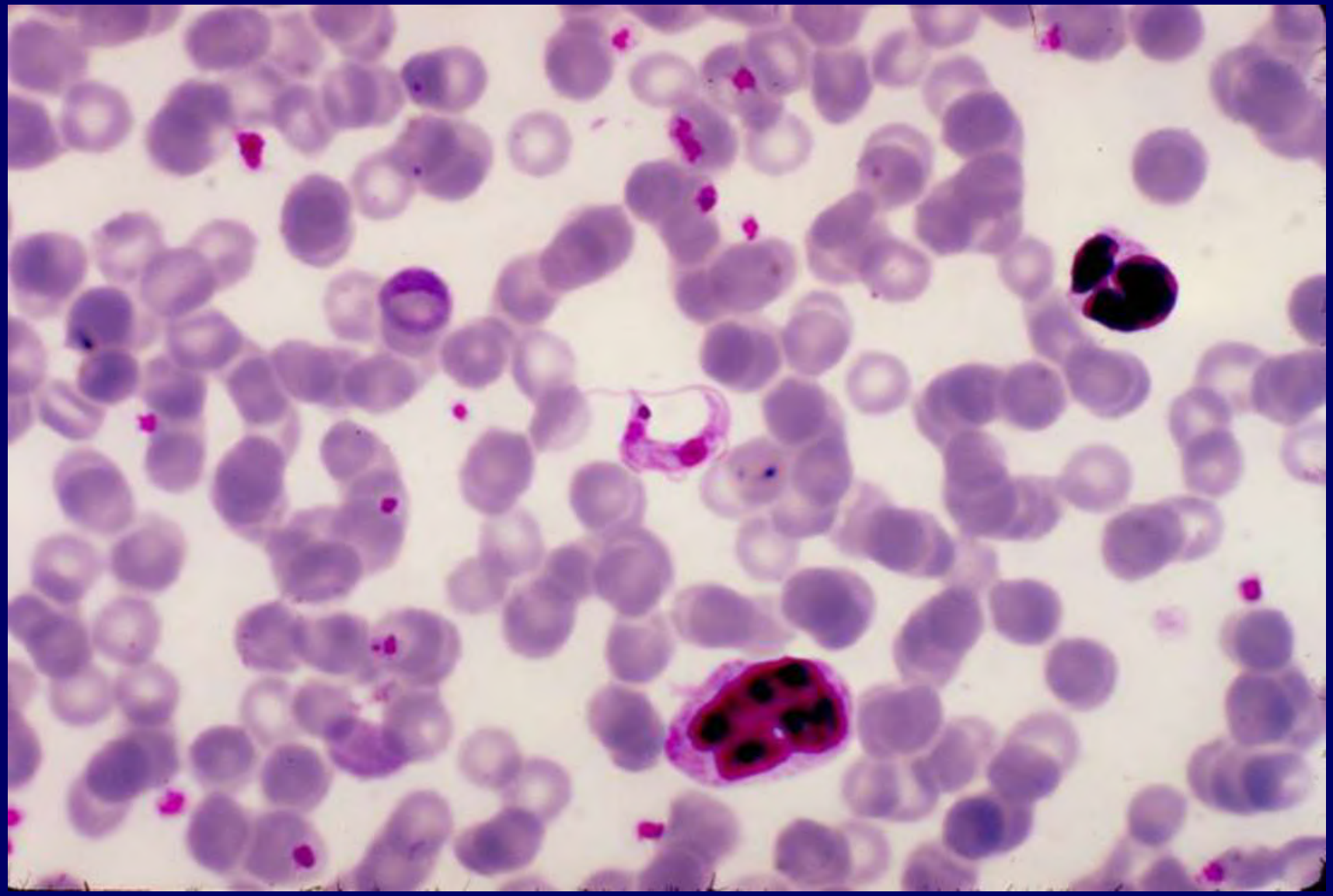
Triatomines defecate during or after taking a blood meal. A person bitten is inoculated by rubbing insect feces into the bite or on mucous membrane.

CDC Public Health Image Library

Trypanosomiasis, American (Chagas disease)

(Trypanosoma cruzi)



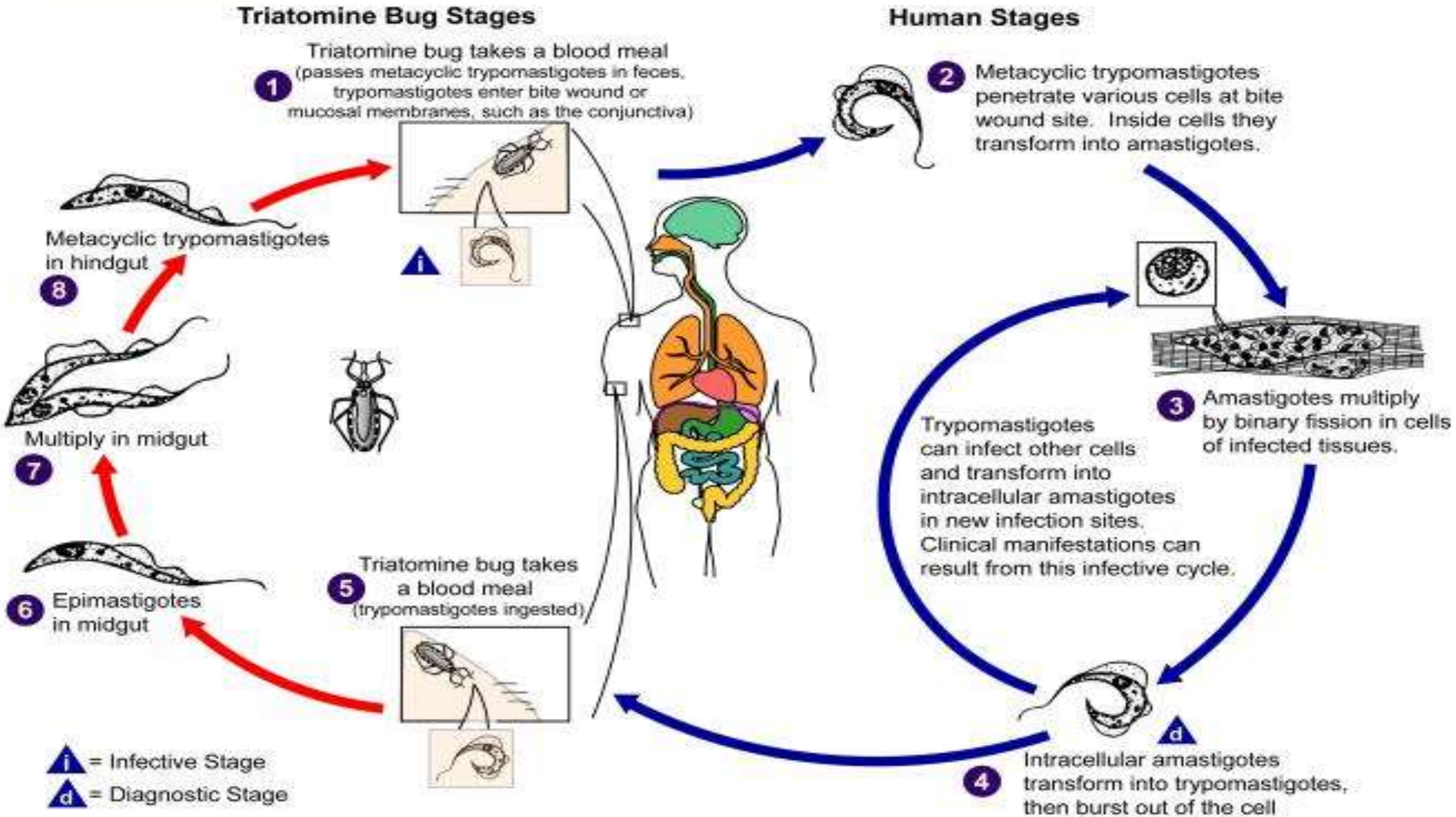


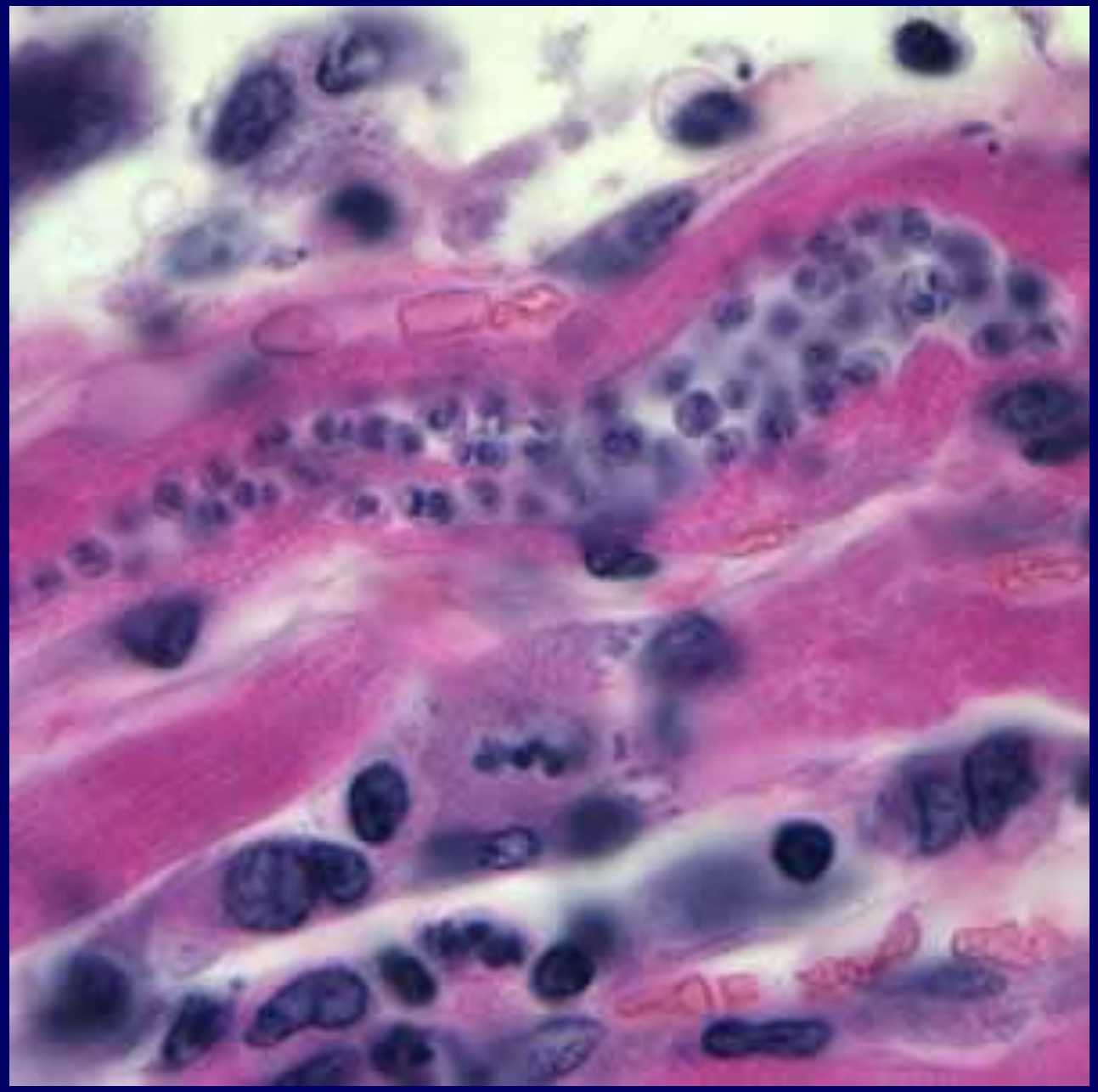
Blood smear with *T. cruzi* trypomastigote, the extracellular form of the parasite

CDC Public Health Image Library

Trypanosomiasis, American (Chagas disease)

(Trypanosoma cruzi)

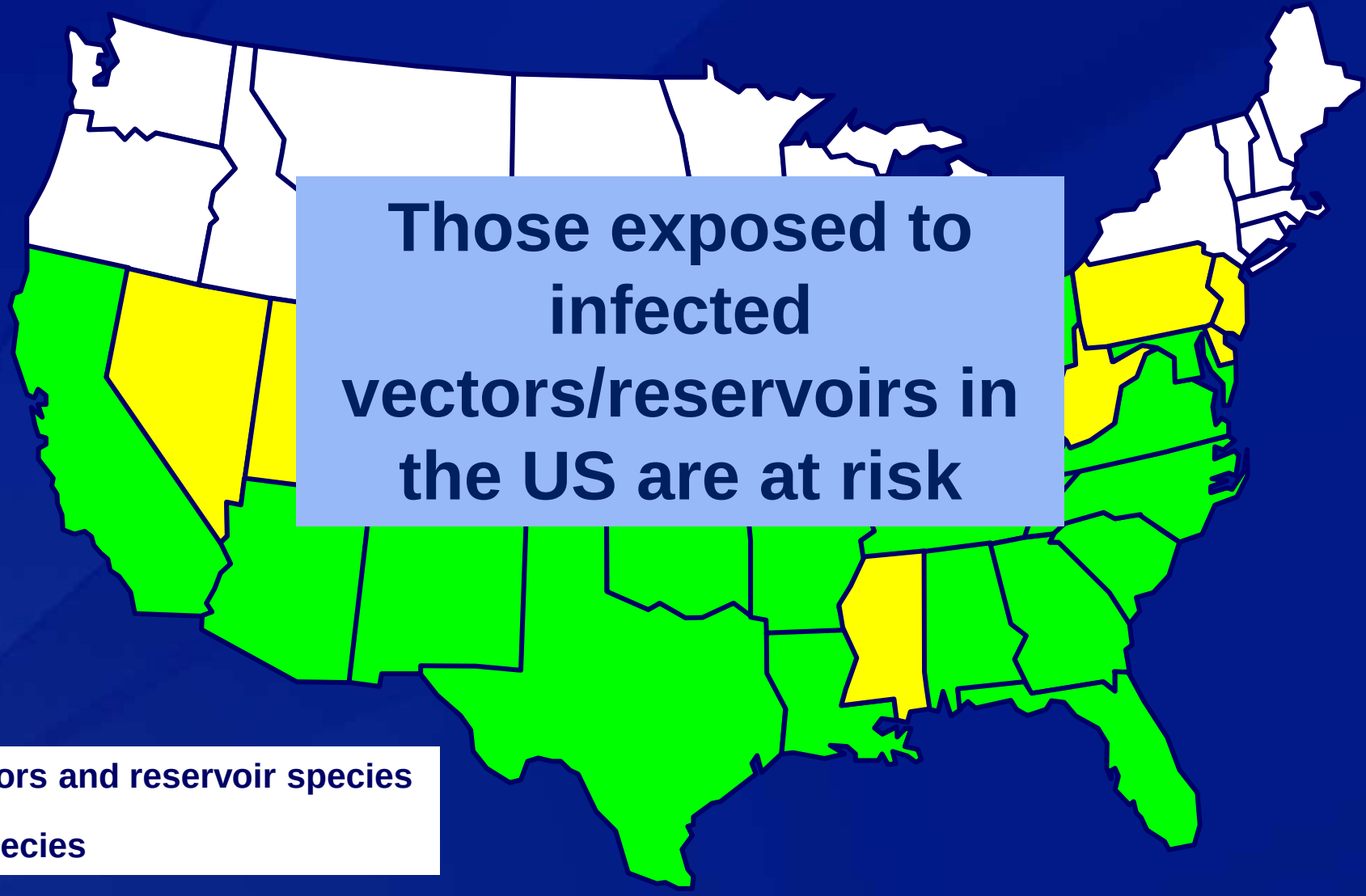




T. cruzi amastigotes in infected heart muscle tissue

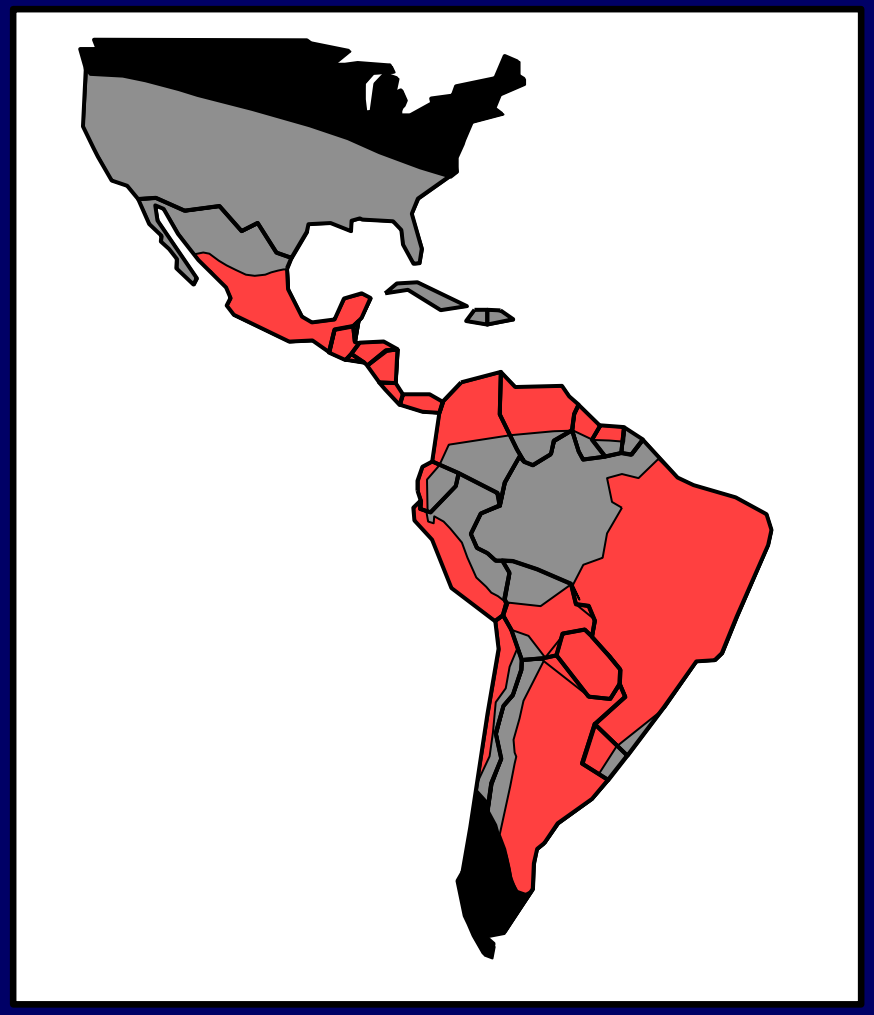
CDC DPDx-Laboratory Identification of Parasites of Public Health Concern. Available at: https://www.cdc.gov/dpdx/trypanosomiasisamerican/index.html

States with documented vectors and mammalian reservoirs



> 18 infected reservoir species identified

Distribution of Vectors and Disease



- Endemic for human Chagas disease
- Infected vectors, nonhuman mammals*

Panstrongylus megistus

***Including opossums, raccoons, foxes, armadillos, skunks, squirrels, dogs.**

Launch Poll

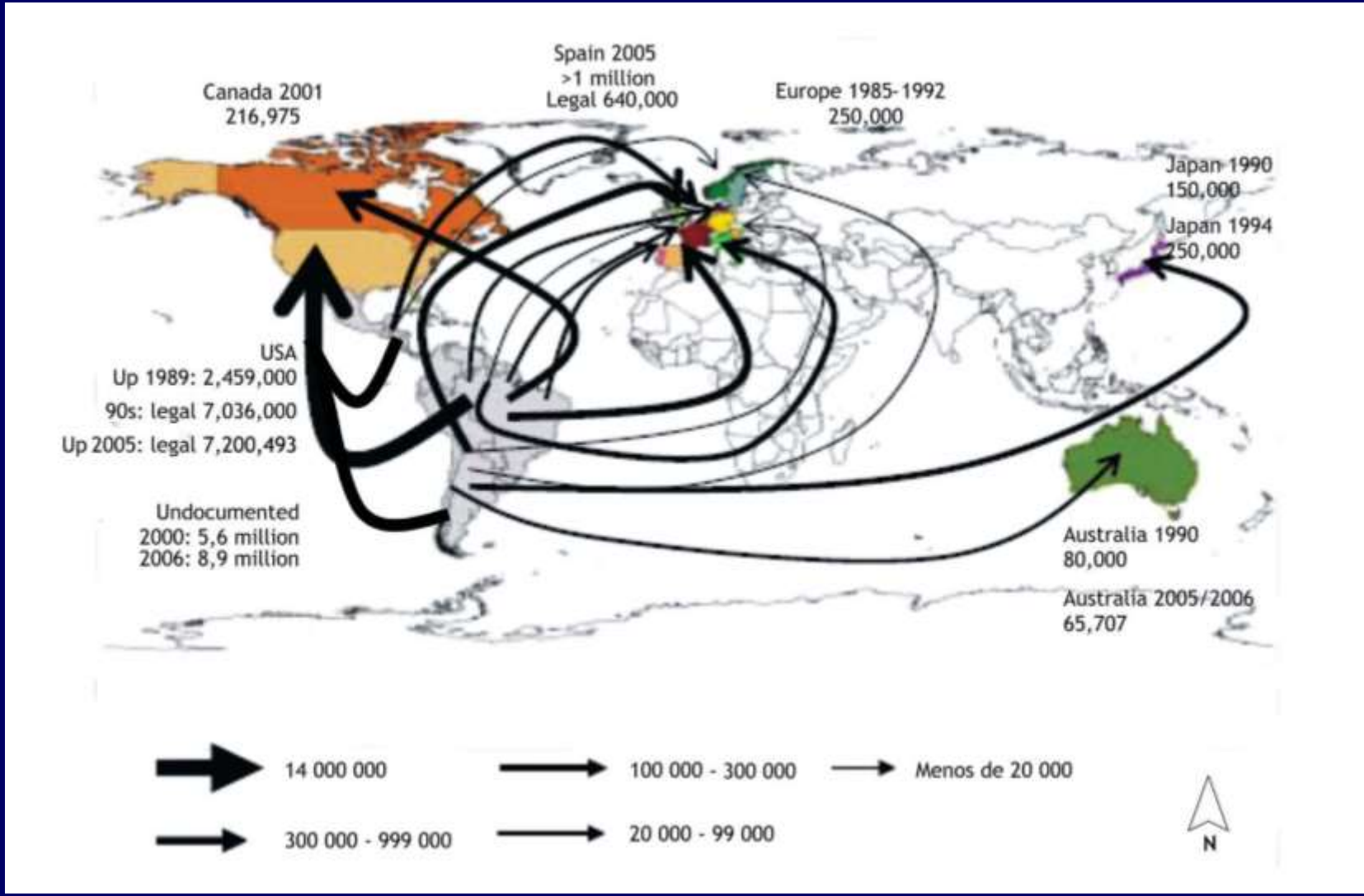
Question 1

Who in the United States has Chagas Disease?

- An estimated 288,000 to 300,000 persons living in the United States have Chagas disease
- The country of origin for at least 85% of these is Mexico, El Salvador, Guatemala or Honduras
- Southern states have established enzootic cycles of *T. cruzi.* Transmission of infection within the United States is well-documented but is rare

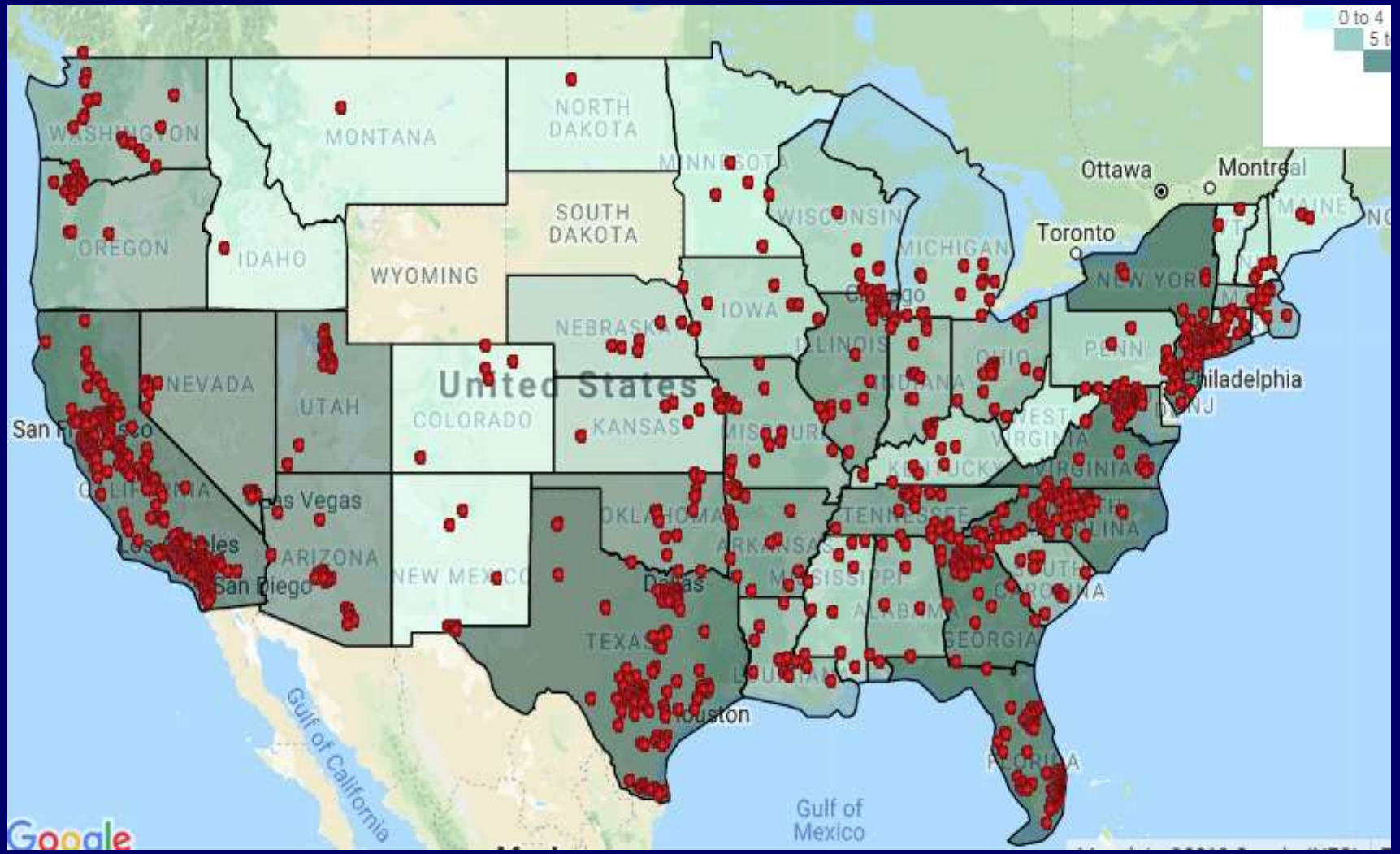
Bern C, Montgomery SP. *Clin Infect Dis* 2009; 49:e52.
Irish A, et al. *Emerg Infect Dis* 2022; 28:1313/
Cantey PT et al. *Transfusion* 2010; 52:1922.

18 Million People in the US were Born in Mexico, Central or South America



Schmunis et al. Mem Inst Osw Cruz 2007.

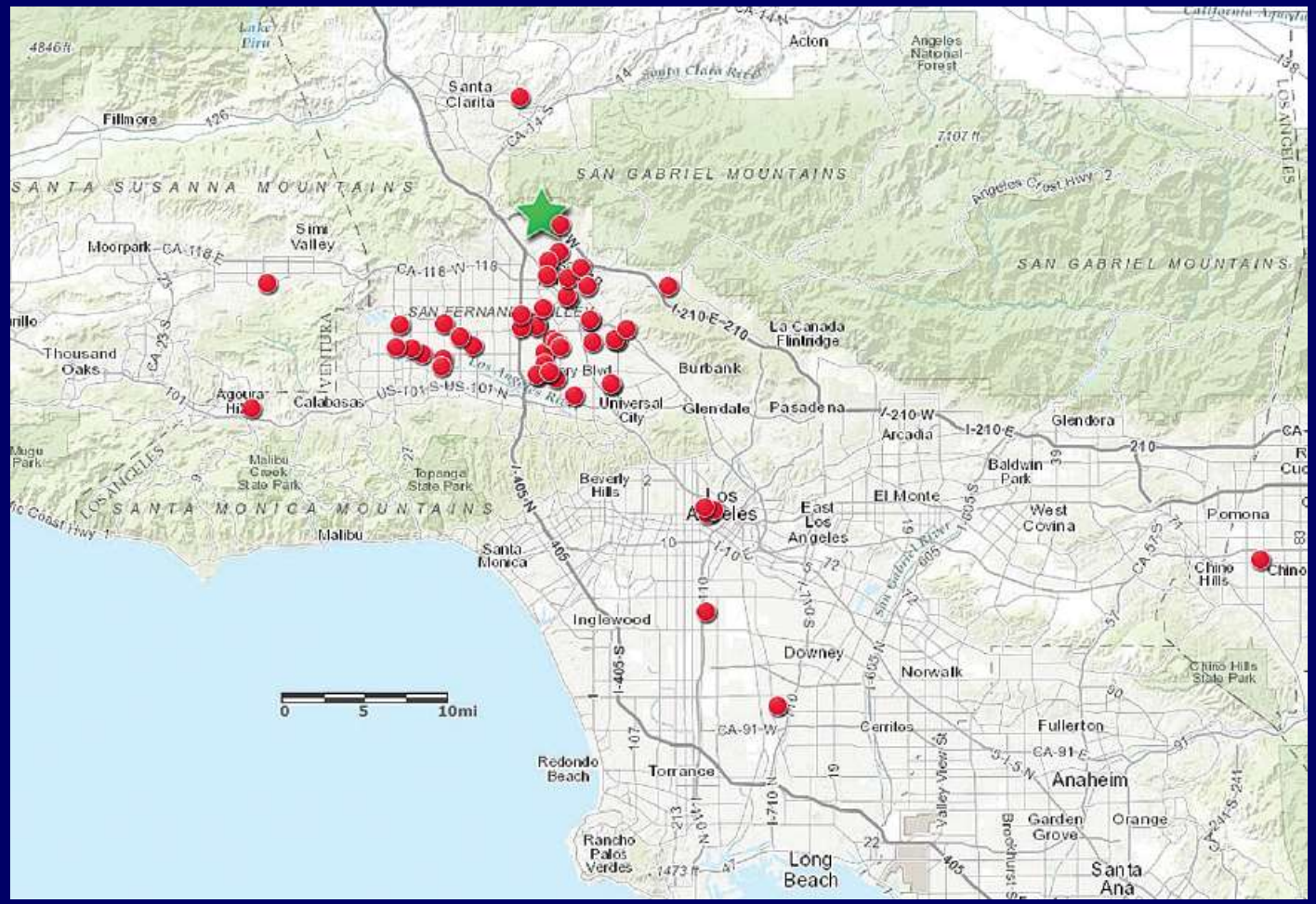
American Association of Blood Banks (AABB): 2,437 Confirmed Positive Blood Donors 2007-2020*



Chagas disease is reportable in:
Arizona
Arkansas
Louisiana
Mississippi
Tennessee
Texas
Utah
Los Angeles Co, CA

***AABB Chagas Biovigilance Program**

Chagas Disease Positive Persons in Los Angeles County, 2008-2014

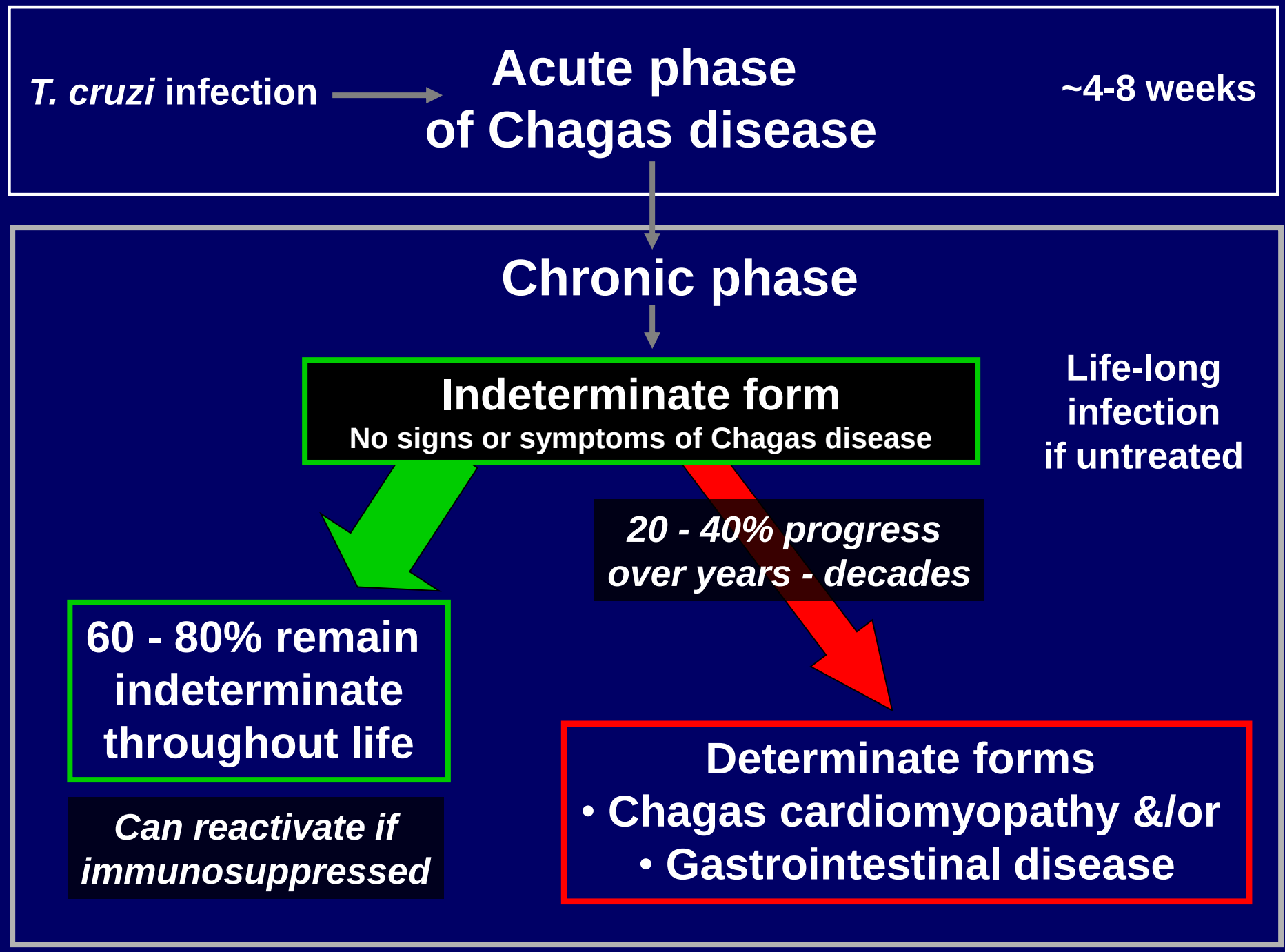


Among 4,755 Latin American-born residents of Los Angeles County, 59 had Chagas disease for an overall prevalence of 1.24%.

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.

Meymandi SK et al. *Clin Infect Dis* 2017; 64:1182.


T. cruzi infection
Acute phase of Chagas disease
~4-8 weeks
Chronic phase
Indeterminate form
No signs or symptoms of Chagas disease
Life-long infection if untreated
20 - 40% progress over years - decades
60 - 80% remain indeterminate throughout life
Can reactivate if immunosuppressed
Determinate forms
• Chagas cardiomyopathy &/or
• Gastrointestinal disease

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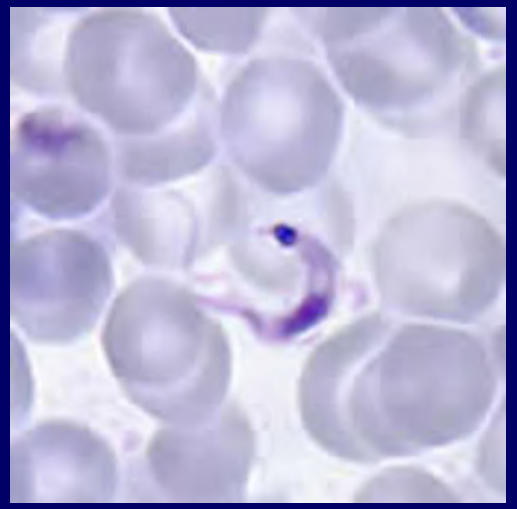
Modes of Transmission



- 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 Chagas disease can transmit infection to their infants. An estimated 23% of infections occur through congenital transmission

Bern C et al. *Clin Microbiol Rev* 2020; 33:e00023-19.
Photo: *Trypanosoma cruzi* parasite in a thin blood smear. CDC photo.

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
- Mother-to-infant transmission rates are 1% to 5%. Mothers are usually asymptomatic
- Transmission rates are higher (5%) in countries where *T. cruzi* is endemic than in those where it is not (3%)*
- Factors such as a high maternal parasitic load and HIV co-infection enhance transmission**

***Howard et al. *BJOG* 2014; 121:22.**
****Beukens et al. *Mat Child Health* 2008; 12:283.**

Launch Poll

Question 2

Congenital Chagas Disease

- An estimated 40,000 to 43,000 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 clinical signs at birth with findings that can include prematurity, hepatosplenomegaly, jaundice, anemia and thrombocytopenia; none is specific for Chagas disease

*Irish et al estimate that there are 22 to 108 congenital infections occurring annually in the United States

Bern & Montgomery. *Clin Infect Dis* 2009; 49:e52.
Irish A, et al. *Emerg Infect Dis* 2022; 28:1313.
Beukens et al. *Mat Child Health* 2008; 12:283.

Congenital Chagas Disease: Initial U.S. Report

- Congenital Chagas disease in the United States was first reported in a boy born in Virginia in 2010. His mother had moved recently to the United States from Bolivia.*
- The infant was born at 29 weeks' 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
- Blood smear in week 2 of life revealed *T. cruzi* trypomastigotes and *T. cruzi* PCR was strongly positive; serologic tests for *T. cruzi* antibodies were positive
- He received benznidazole for 60 days and was cured

***CDC. Congenital transmission of Chagas disease- Virginia, 2010. *MMWR* 2012; 61:477.**

Signs of Congenital Chagas Disease in 91 Infants

Feature	Frequency of Finding[b]
Low birth weight (<2500 g)	++++
Prematurity	++
Respiratory distress	+++
Hepatomegaly	++++
Splenomegaly	+++
Sepsis	++
Cardiomegaly/heart failure	++
Myocarditis	++
Cardiac arrhythmia	++
Meningoencephalitis	++
Neurologic signs	++
Edema/anasarca	++
Petechiae	++
Anemia	+

[a]Adapted from references 33, 43, 45, and 46. Not all infants had each feature assessed. The remaining 110 infants infected with *T cruzi* had no clinical signs of Chagas disease.
[b]++++, noted in >50% of infants assessed; +++, 25% to 50%; ++, 10% to 24%; +, <10%.

Edwards MS et al. *J Pediatr Infect Dis Soc* 2019; 8:461.

Objectives

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Pregnancy-Based Screening for Chagas Disease Benefits Mother and Infant

- Pregnancy is the optimal access point for identifying Chagas disease at risk family units because delivery is the most likely time for contact with the healthcare system

- Women at risk have migrated from an endemic region
  - ➔ Risk is enhanced by having lived in a rural region
  - ➔ Having lived in a mud or thatched-roof home also increases risk

- Women who have visited and lived in an endemic region for 6 months or longer also at risk

- Women at risk for Chagas disease should have pregnancy-based screening for *T. cruzi* IgG

Challenges to Identifying Mothers and Infants with Chagas Disease

- Identifying maternal infection is key but mothers have no symptoms
- None of the findings in infant infection are specific for Chagas disease
- The diagnosis must be considered
- Screening during pregnancy or at delivery is key to identifying women and infants at risk but maternal screening is not standard of care
- The prevalence of infection among women of child-bearing age in the US is not known

Chagas Disease in Southern Texas

- Cord blood or residual maternal blood obtained from 4,000 infants born consecutively at a Houston hospital (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 confirmed Chagas disease in 10 women (0.25%)

Edwards et al. *J Ped Infect Dis* 2015; 4:67.

Comparison of Features for Pregnant Women Based on *T. cruzi* Serology

Maternal feature	*Trypanosoma cruzi* Serologic Status[a] Positive (n = 10)	Negative (n = 3990)	*P* Value
Mean years of age (range)	33.8 (25–41)[b]	28.3 (13–46)	.007
Hispanic ethnicity	10 (100)	3376 (84.6)	NS
Birthplace			
Mexico	3 (30)	2001[c] (50.2)	NS
El Salvador	5 (50)	447 (11.2)	<.001
Honduras	2 (20)	357 (8.9)	NS
Guatemala	0	258 (6.5)	NS
Nicaragua	0	17 (0.4)	NS
Live birth (%)	10 (100)	3880 (97.2)	NS

Edwards et al. *J Ped Infect Dis* 2015; 4:67.

Triatomine Bug Infestation of a House in Mexico

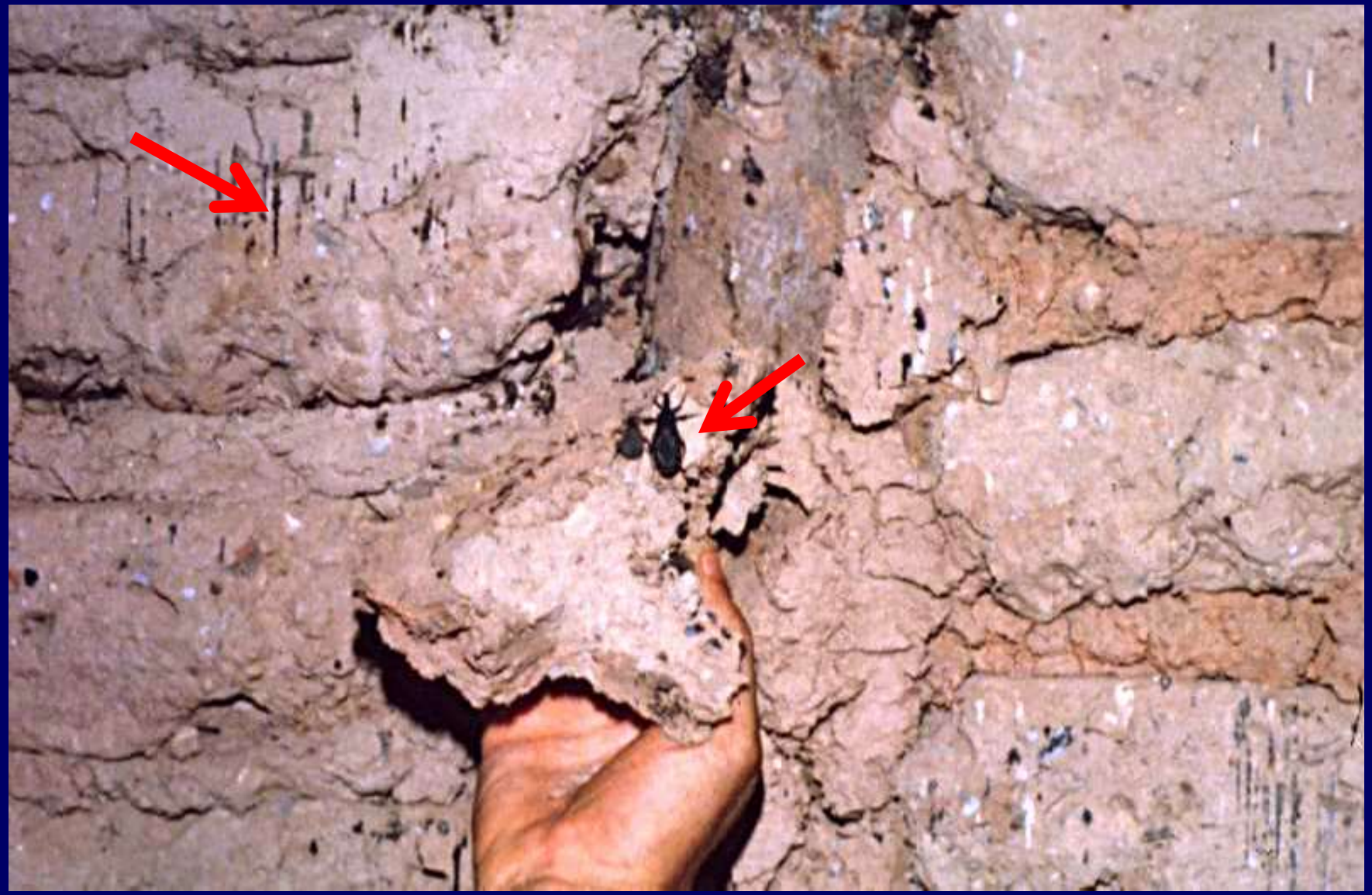


Photo from WHO at http://www.who.int/chagas/resources/photo_gallery/en/

Screening for Chagas Disease during Pregnancy

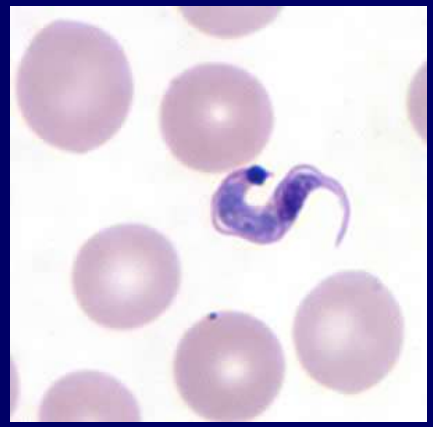
- Screening for Chagas disease can be performed during any trimester
- A commercially-available ELISA should be ordered to test for *Trypanosoma cruzi* IgG
- Chagas disease screening is a send-out test from most hospital laboratories. Results are available within days
- Chagas screening can be included with routine maternal screening
- It is not necessary or appropriate to screen for *T. cruzi* IgM

Pregnancy-Based Screening for Chagas Disease is Cost-Saving

- Pregnancy-based screening has the advantage that results are known at delivery. Screening at admission for delivery or screening of neonates are alternative approaches
- At current costs, targeted screening, including the cost of treatment, would result in savings of $1,314 per birth and $670 million in lifetime savings per birth-year cohort
- Universal screening and treatment would also be cost-saving

Perez-Zetune V et al. *Am J Trop Med Hyg* 2020; 102;1086

Evaluation for Suspected Congenital Chagas Disease



- Direct detection: Diagnostic if positive; less sensitive than PCR
- PCR: The most sensitive test for early diagnosis
  - ➔ PCR for *T. cruzi* is available through the CDC; testing is under CLIA
  - ➔ Initial negative should be repeated as parasites multiply in the first weeks of life
- Maternal Serology: Order *T. cruzi* IgG if not performed during pregnancy
- Infant Serology: If PCR is negative and maternal serology is positive, follow infant's *T. cruzi* IgG. Negative serology at 9-12 months of age excludes congenital infection

Treatment of Chagas Disease

- Treatment is always indicated for congenital Chagas disease. Treatment early in life kills the parasite and prevents long-term complications from heart and intestinal disease; cure rates exceed 90%*
- If a woman is diagnosed with Chagas disease, her other children should have serologic testing; treatment is always indicated for children <18 years of age
- Treatment is always indicated for women in the childbearing years**, both for the health of the woman and for the sake of her children
- Infection can be transmitted congenitally in sequential pregnancies among women chronically infected with *T. cruzi*

*** *MMWR* 2012; 61:477-9.**

****Bern C. Antitrypanosomal therapy for chronic Chagas' disease. *N Engl J Med* 2011; 364:2527.**

Chagas Disease Treatment

- All infants and children with confirmed *T. cruzi* infection should receive treatment
- Two medications are available, both administered orally:*
  - ➔ Benznidazole: approved by FDA for use in children 2–12 years of age and is available from www.benznidazole.com
  - ➔ Nifurtimox (Lampit®): approved by FDA for treatment of children from birth to younger than 18 years and is commercially available for pharmacies to purchase from several drug wholesalers
- Duration: 60 days
- Consultation with an infectious diseases specialist is advisable

*** https://www.cdc.gov/parasites/chagas/health_professionals/tx.html**

Acknowledgements

I am grateful to Susan P. Montgomery, DVM, MPH, epidemiology team lead in the CDC's parasitic disease branch for providing some of the slides in this presentation and for her helpful comments regarding content of the presentation.

Selected References

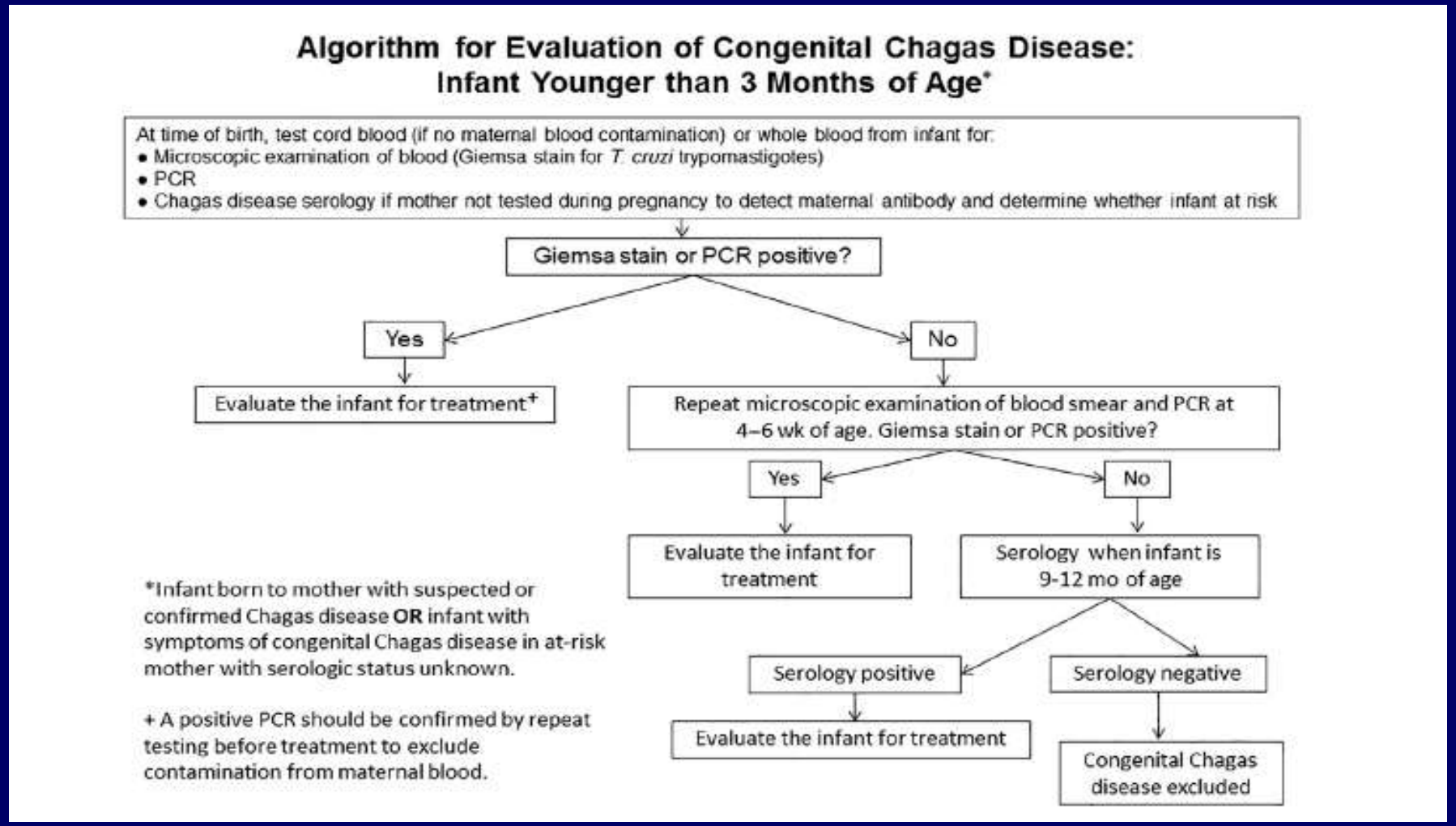
Bern C et al. Chagas disease in the United States: a public health approach. *Clin Microbiol Rev* 2020; 33(1):e00023-19. Comprehensive and current review.

Centers for Disease Control and Prevention. Access at: http://www.cdc.gov/parasites/chagas/index.html Excellent source for general information and diagnosis and treatment information.

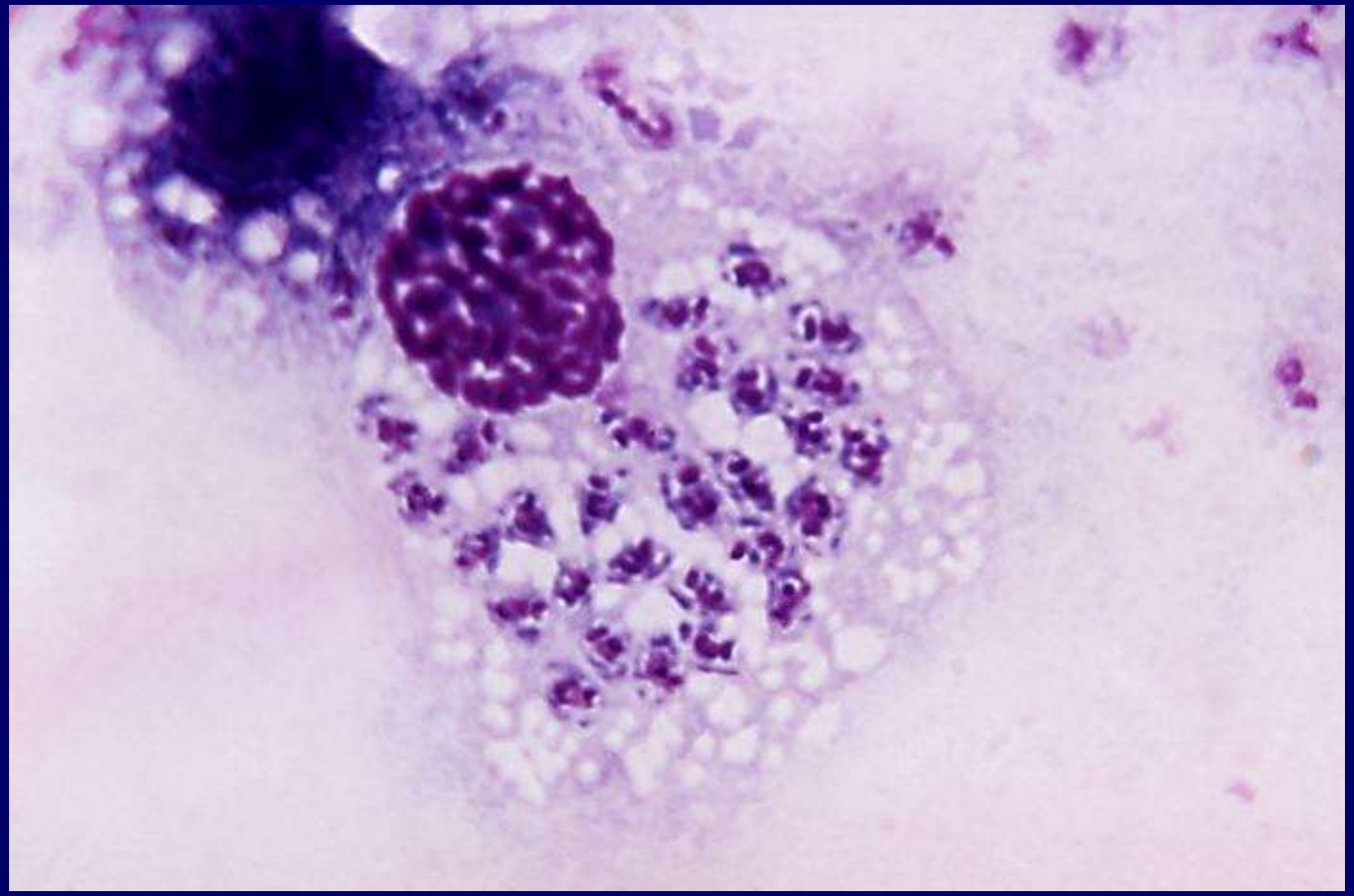
Edwards MS et al. Evaluation and management of congenital Chagas disease in the United States. Provides algorithms for evaluation of mothers and infants. *J Pediatr Infect Dis Soc* 2019; 8:461.

Perez-Zetune V et al. Congenital Chagas disease in the United States: The effect of commercially priced benznidazole on costs and benefits of maternal screening. *Am J Trop Med Hyg* 2020; 102:1086. Maternal screening is cost saving, whether targeted to at-risk pregnant women of performed universally.

Evaluation for Congenital Chagas Disease

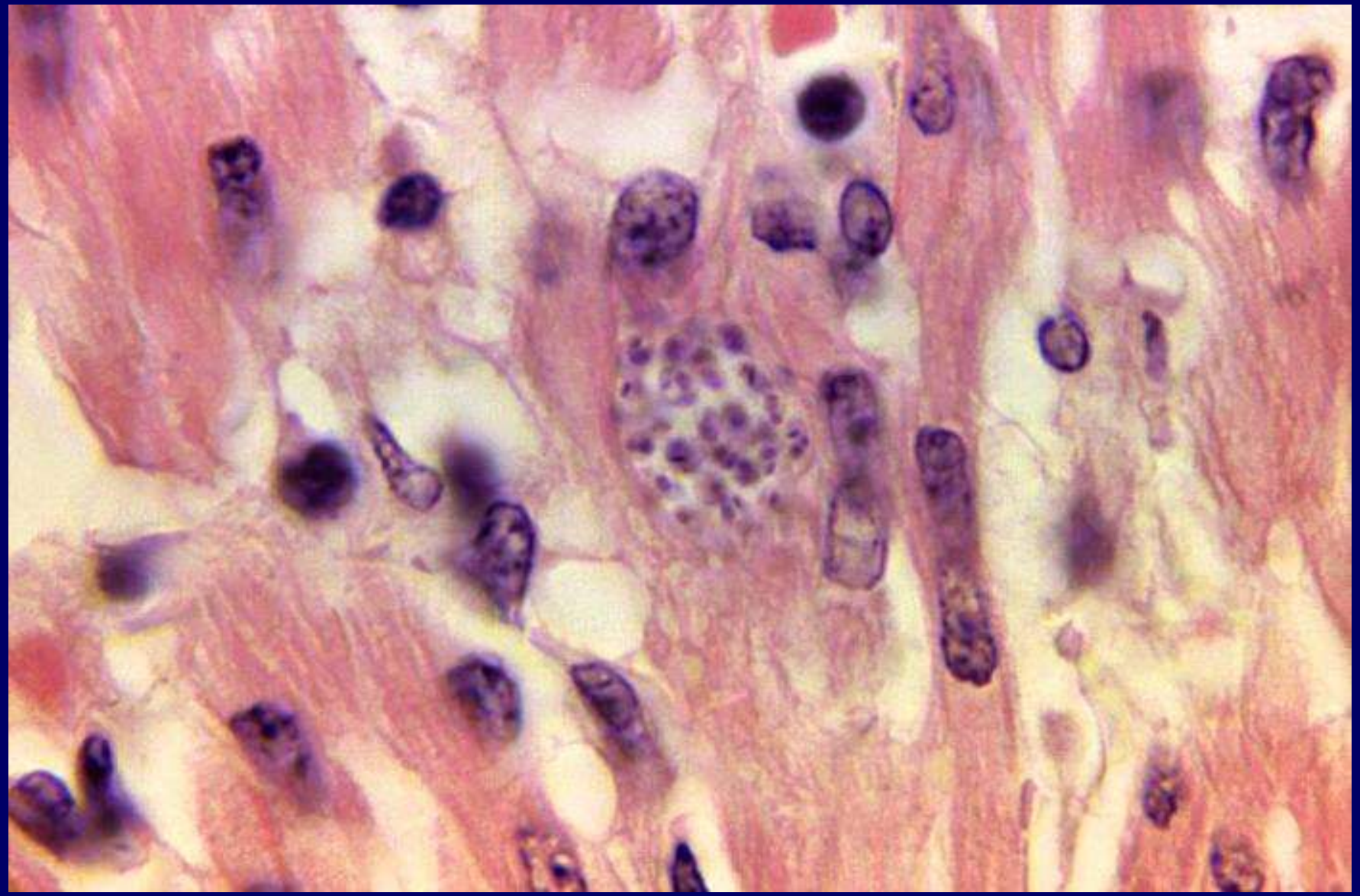


https://www.cdc.gov/parasites/chagas/health_professionals/congenital_chagas.html



The amastigote form of *T. cruzi* multiplies in infected tissues.

CDC Public Health Image Library

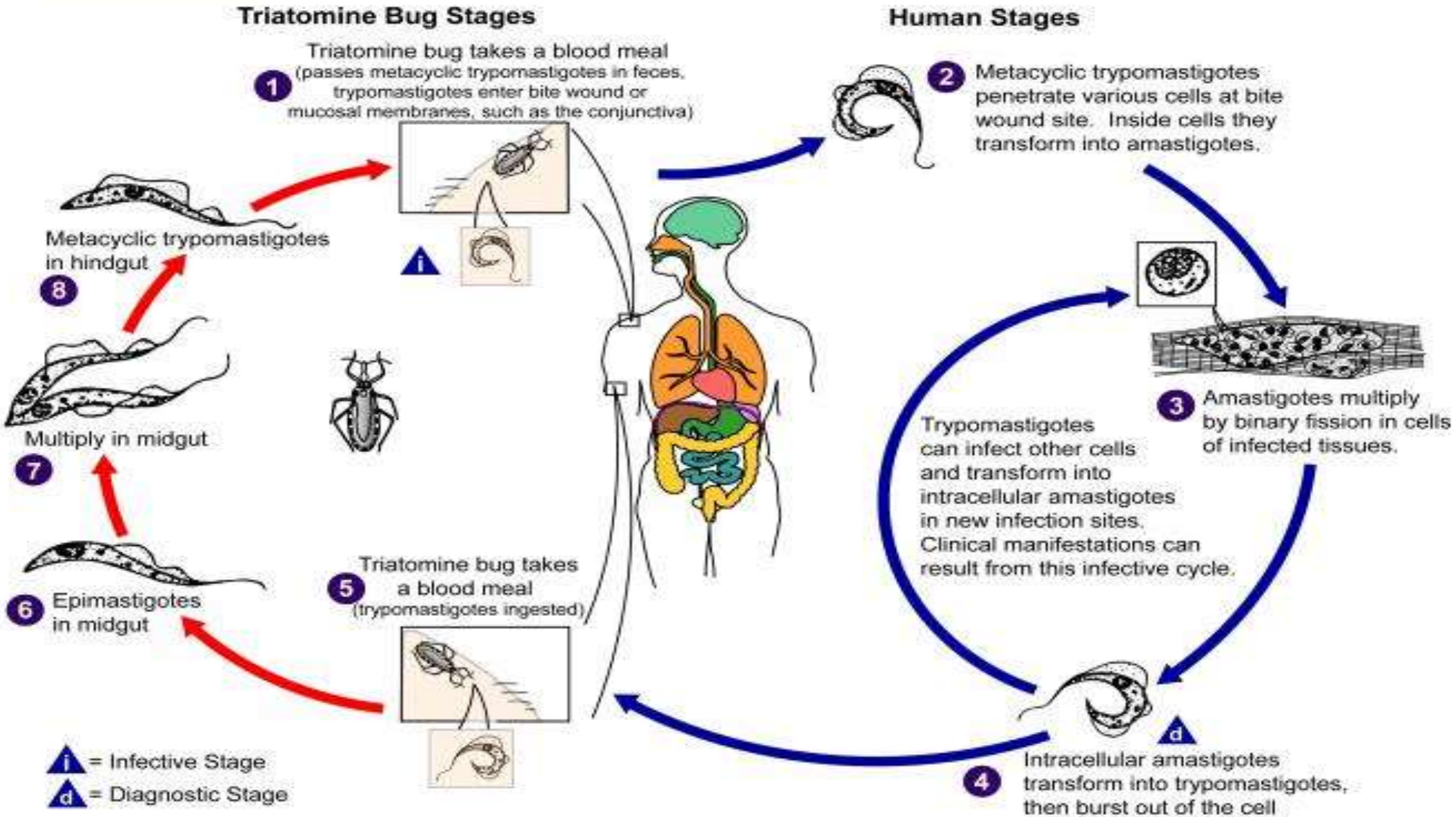


T. cruzi amastigotes in infected heart muscle tissue

CDC Public Health Image Library

Trypanosomiasis, American (Chagas disease)

(Trypanosoma cruzi)



Factors Enhancing or Possibly Increasing Transmission

- High maternal parasitic load
- Genotype: *T. cruzi* parasites are composed of 6 genetic lineages or discrete typing units (DTUs [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

Beukens et al. Mat Child Health 2008; 12:283.

A Great Imitator

An infant was born vaginally at 36 weeks' gestation to a 28-year old mother with no prenatal care. She had come to the United States from El Salvador two years earlier.

The birth weight was 2,600 grams. Exam revealed mild jaundice, an enlarged liver and spleen and petechiae. Initial testing revealed elevated bilirubin, normal WBC and a low platelet count.

In this infant, the "usual suspects" include congenital syphilis, cytomegalovirus and toxoplasmosis.

Could this be congenital Chagas disease?

A Great Imitator

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The birth weight was 2,600 g. Exam revealed mild jaundice, an enlarged liver and spleen and petechiae. Initial testing revealed mildly elevated bilirubin, normal WBC and a low platelet count.

This infant had congenital syphilis. He received a 10-day course of IV penicillin and clinical signs of infection resolved. Urine PCR for cytomegalovirus, toxoplasmosis serology and *T. cruzi* serology on infant blood were negative.

Congenital Chagas Disease: The Other U.S. Report

- A male infant was born at 30 weeks' gestation to a 37 year-old mother from Bolivia in 2015. In utero ultrasound revealed pericardial effusion and ascites, concerning for hydrops fetalis
- His birth weight was 1,785 g. He required intubation and ventilator support. He had cardiomegaly and additional study showed hypoplastic tricuspid valve and right ventricle
- Examination of the placenta revealed intracellular parasites. The infant's blood was positive for *T. cruzi* by PCR at the CDC
- He received benznidazole for 60 days. He had residual focal endocardial fibroelastosis of the right ventricle at 7 months of age

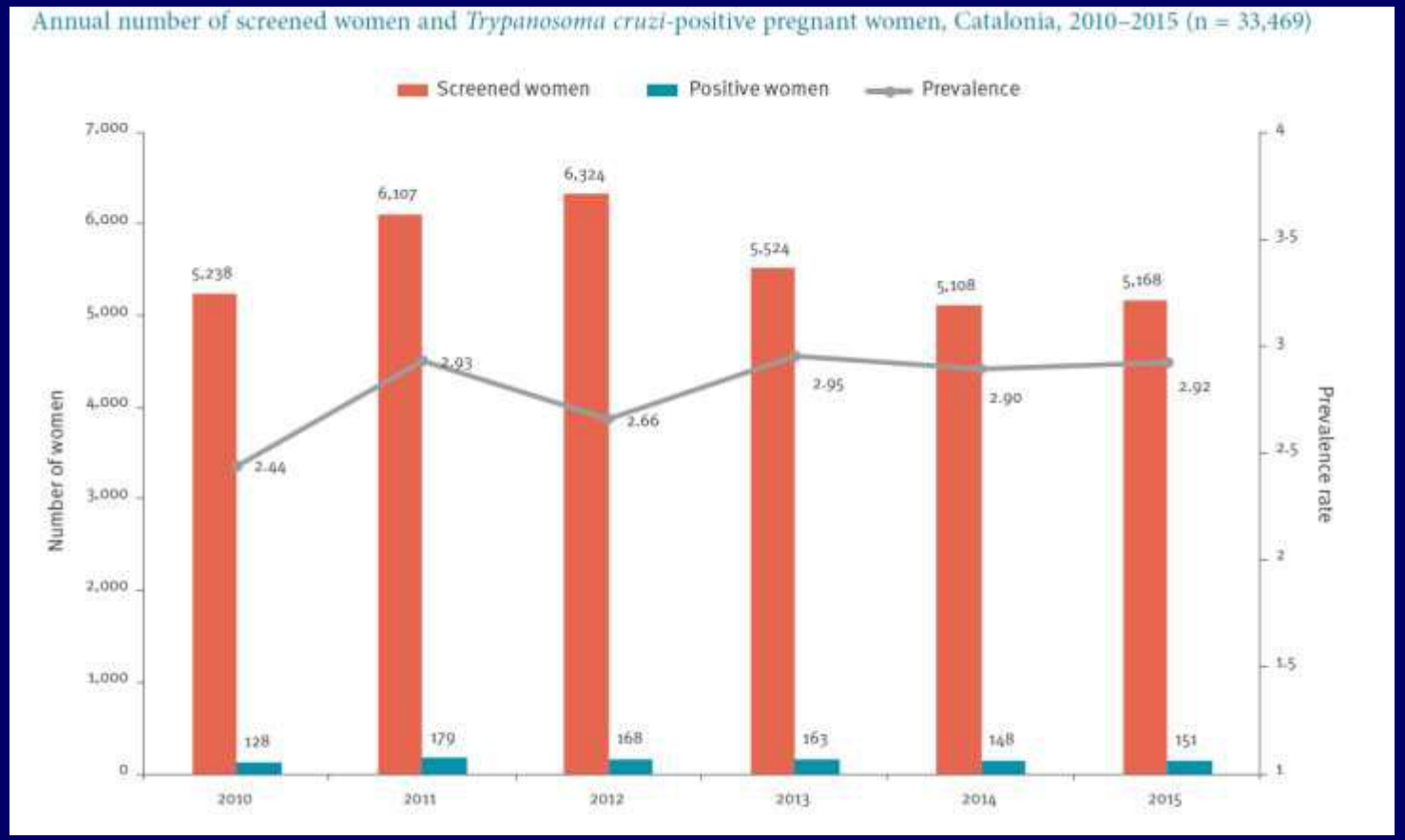
Alarcon A, et al. Diagnosis and treatment of congenital Chagas disease in a premature infant. *J Pediatr Infect Dis Soc* 2016; 5:e28.

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

Edwards et al. *J Ped Infect Dis* 2015; 4:67.

Epidemiology of congenital Chagas disease 6 years after implementation of a public health surveillance system, Catalonia, 2010 to 2015



33,469 pregnant women from endemic countries and those who had lived in a rural area of an endemic country were screened

The overall prevalence of maternal Chagas disease was 2.8%. Rates were highest in women from Bolivia (15.8%), El Salvador (1.4%) and Paraguay (1.2%)

28 infants were diagnosed with congenital Chagas disease (transmission rate 4.2%)

Basile L et al. *Euro Surveill.* 2019;24(26):pii=1900011. https://doi.org/10.2807/1560-7917.ES.2019.24.26.19-00011

Epidemiology of congenital Chagas disease 6 years after implementation of a public health surveillance system, Catalonia, 2010 to 2015

- Children born to *T. cruzi*-positive women before the current pregnancy were screened
- Among 178 children, 14 (7.9%) were diagnosed with Chagas disease. The children ranged in age from 3-18 (median 10) years of age
- Siblings of an index case of Chagas disease should also undergo screening

Basile L et al. *Euro Surveill.* 2019;24(26):pii=1900011. https://doi.org/10.2807/1560-7917.ES.2019.24.26.19-00011

Chagas Disease Prevention

Chagas disease printable resources are available through CDC

This poster is available without charge at this website, laminated with English on one side, Spanish on the other:

https://www.cdc.gov/parasites/chagas/printresources.html

Prevention through Awareness

- Many physicians are not familiar with Chagas disease. In one survey:
  - ➔ 68% admitted to having “very limited” Chagas disease knowledge
  - ➔ Only 9% knew the risk of congenital infection
- Caregivers for mothers and infants are optimally positioned to consider the diagnosis and request appropriate testing
- Barriers to pregnancy-based screening, such as mothers’ lack of knowledge of the morbidity of Chagas disease can be addressed

Verani et al. *Am J Trop Med* 2010; 83:891.

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

Protect Your Baby from Chagas Disease

Chagas disease is an illness that can lead to serious heart and stomach problems, and even death. Chagas disease can be life threatening even though you may not feel sick now. In fact, people usually don't feel sick until many years after they have been infected.

Who can get Chagas disease?

Anyone. However, people have a much greater chance if at some point in their lives they have:

- Lived in rural areas of Mexico, Central America, or South America
- Stayed in a house in Mexico, Central America, or South America with walls that have cracks or crevices
- Seen this bug

How can someone get Chagas disease?

People usually get Chagas disease from contact with a triatomine bug (also called "kissing bug"). However, there are other ways the disease can be spread, including from an infected mother to her unborn baby.

What should I do if I think I might have Chagas disease?

If you think you might have Chagas disease, you should see your OB/GYN or other health care provider, who will examine you. He or she may take a sample of your blood for testing.

If I have Chagas disease, does it mean my baby is infected?

No, not necessarily. The risk of an infected mother spreading Chagas disease to her unborn baby is less than 1 in 10.

If I have Chagas disease, should my baby be tested?

Yes. If you have been told you have Chagas disease, all of your children should be tested, regardless of their ages.

Is there treatment for Chagas disease?

Yes, there is treatment for the disease. Your baby can be treated any time after birth, and treatment is very effective for newborns and children. You can be treated after your baby is born and you have finished breastfeeding.

Many people who have tested positive are leading healthy lives with the help of their health care providers.

For more information on Chagas disease, please visit www.cdc.gov/parasites/chagas or call **404.718.4745.**

Center for Global Health
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