Chagas Disease Case Classification and Testing

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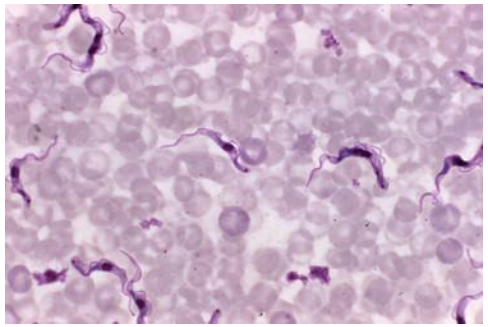
Chagas Disease (AKA American Trypanosomiasis)

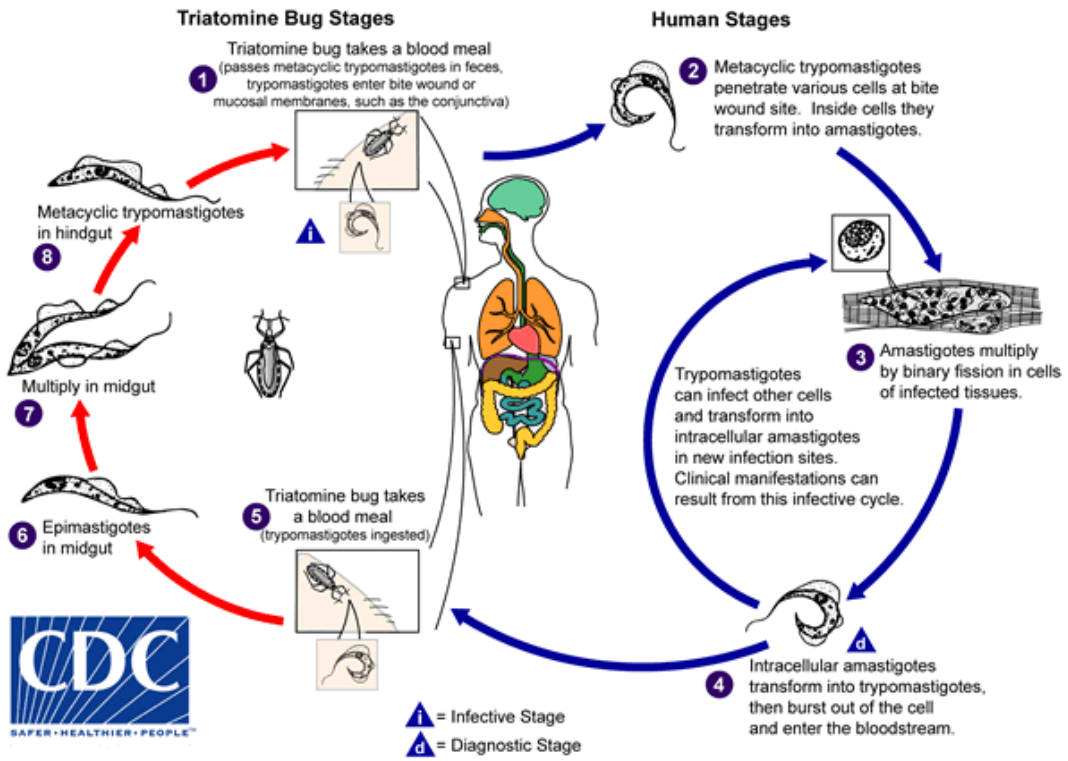
Named after the Brazilian physician Carlos Chagas, who discovered the disease in 1909



- **Causative Agent:**
  - ➢ *Trypanosoma cruzi*, a hemoflagellate protozoan parasite
- **Distribution**:
  - ➢ Endemic in the Americas - known range extends from north of the Patagonia region of South America to approximately the southern 1/2 of the U.S.
- **Prevalence**:
  - ➢ An estimated 8 million people are infected in Mexico, Central and S. America
  - ➢ CDC estimates that >300,000 persons with Chagas disease live in the U.S. (*most acquired infections in endemic countries*)

Chagas Disease - Lifecycle

A sylvatic lifecycle is maintained between multiple mammalian wildlife hosts (*rodents, opossums, raccoons, and armadillos in particular in the southwestern U.S.*) and multiple species of triatomines



- Infection typically occurs when feces (containing the parasite) from an infected triatomine enters through a bite wound or mucosal membrane

- Infection can also occur from:
  - mother-to-baby (congenital),
  - contaminated blood products (transfusions),
  - an organ transplanted from an infected donor,
  - laboratory accident, or
  - contaminated food or drink (rare)

Chagas Disease - Vector

Triatomine bugs (also called reduviid bugs, “kissing” bugs, assassin bugs, cone-nosed bugs, and blood suckers)

DSHS, in conjunction with CDC, provides free testing of triatomine bugs for the parasite *Trypanosoma cruzi* (http://www.dshs.state.tx.us/idcu/health/zoonosis/Triatominae/)

http://kissingbug.tamu.edu/found-a-bug/#non-kissing-bugs

Three species of triatomines ("kissing bugs") that can be found in Texas:

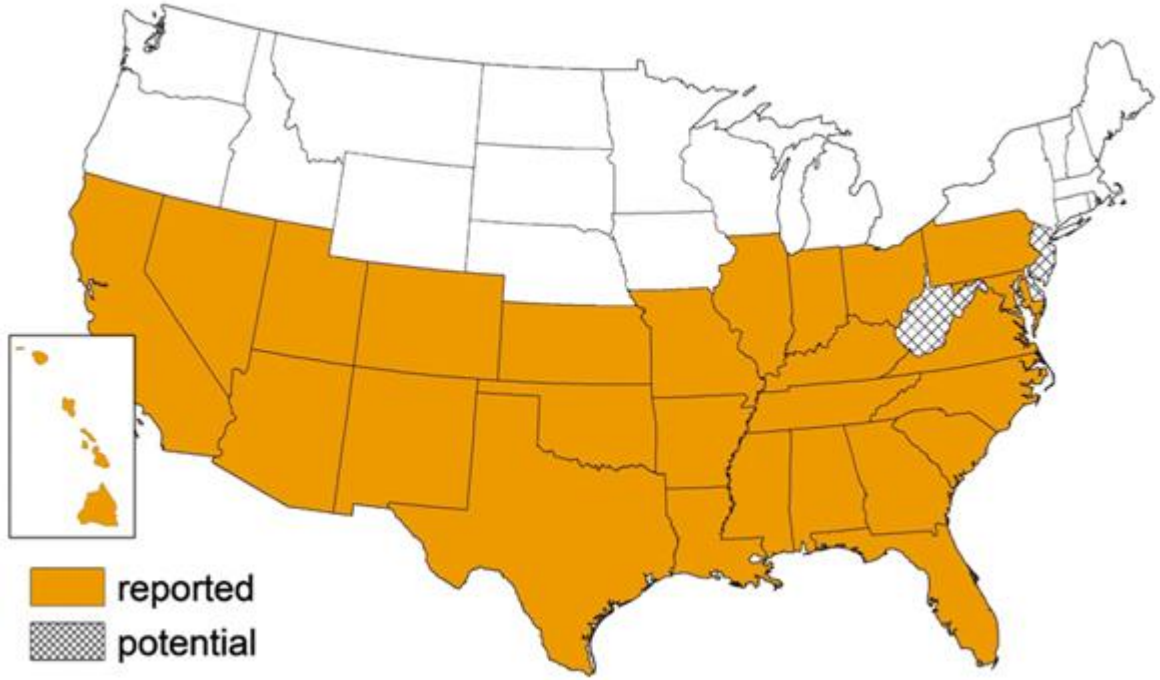
- *Triatoma sanguisuga*
- *Triatoma gerstaeckeri*
- *Triatoma protracta*

wheel bug

squash bug

assassin bug

leaf-footed bug



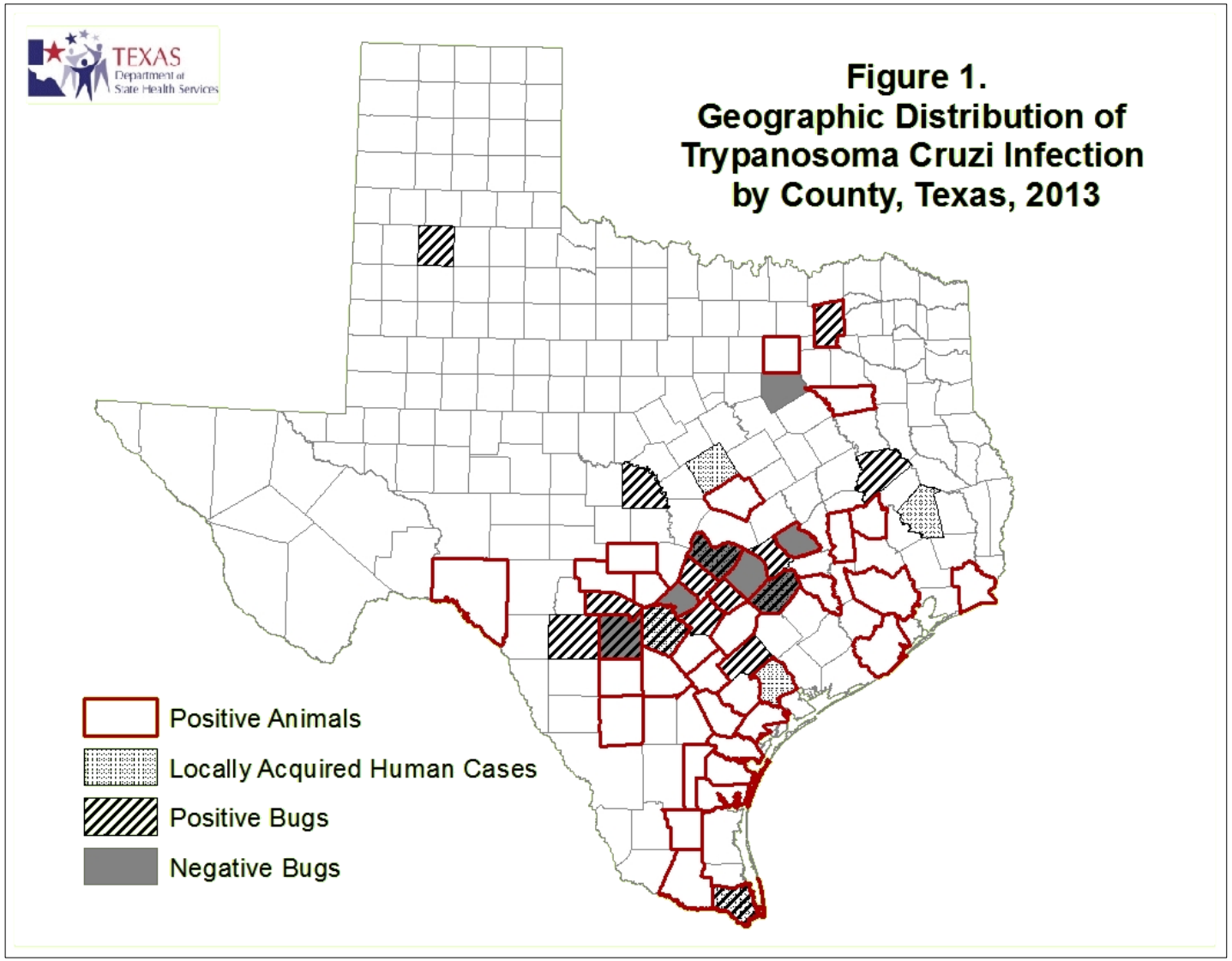
Chagas Disease - Data

Chagas disease became reportable in Texas in 2013
http://www.dshs.state.tx.us/idcu/disease/chagas/data/

Human Chagas *Cases Reported, by County and Acquisition Method, Texas, 2013-2014				
County	Locally Acquired	Imported	Unknown	Grand Total
Atascosa County	1			1
Bexar County	3	1	1	5
Brooks County	1			1
Cameron County	1	3		4
Coryell County	1			1
Dallas County		7		7
Fayette County	1			1
Fort Bend County		1		1
Harris County		7	1	8
Hidalgo County		2	1	3
Lee County	1			1
McLennan County		1		1
Polk County	1			1
Shelby County		1		1
Travis County	1			1
Victoria County	1	1		2
Total	12	24	3	39

*33 chronic indeterminate and 6 chronic symptomatic

Chagas Disease – Reported Case Distribution, 2013



- Triatomines collected from 20 counties
- 5 species of triatomines were collected
- Approximately 60% were positive for *T. cruzi*
- 207 animals, mainly dogs

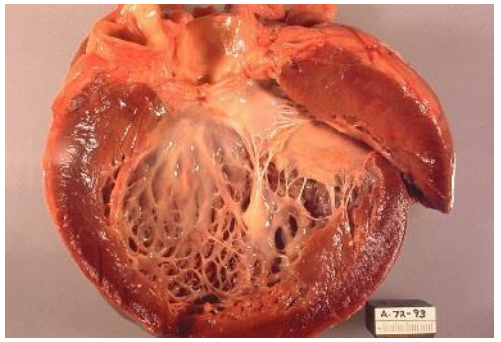
Clinical Course of Chagas Disease

Three clinical phases:

- Acute Phase: often asymptomatic or mild and non-specific symptoms
  - Signs and symptoms may include:
    - Fever, hepato/splenomegaly, subQ edema, non-pruritic rash
    - Rarely, acute myocarditis, meningoencephalitis, or pneumonitis
    - Chagoma (localized swelling) at the site of parasite entry
    - Romaña's sign (swollen eyelid in the inoculated eye) in cases of conjunctival entry of the parasite; this is the most recognized marker of acute infection
  - If present, symptoms usually resolve spontaneously in 3-8 weeks
  - Detectable parasitemia on blood smears and/or by PCR testing of blood sample

Clinical Course of Chagas Disease

- Chronic Indeterminate Phase: Asymptomatic
  - Latent infection; parasitemia below detectable levels
  - Antibodies detectable via serologic tests
  - 70-80% of these patients will remain asymptomatic for life



- Chronic Symptomatic Phase: Symptomatic
  - 20-30% of latent infections will progress to symptomatic chronic infection
  - Typically manifests as heart conduction abnormalities/heart failure and/or less often intestinal motility and megasyndromes, particularly megaesophagus and megacolon
  - Parasitemia below detectable levels
  - Antibodies detectable via serologic tests

Laboratory Diagnosis of Chagas Disease

- **Acute Phase**

  - Definitive Tests:
    - Blood Smear, observation of trypomastigotes – NOT highly sensitive and a negative result won't rule out infection (not recommended)
    - Polymerase Chain Reaction (PCR) – performed only at CDC

  - Suggestive Tests:
    - Serology – antibodies may not be present *early, but testing still recommended; samples that test positive at a commercial lab can be forwarded to CDC for confirmation
      - *not likely to be detected if less than two weeks after exposure to a triatomine; best if blood drawn ~6-8 weeks following vector exposure

- **Chronic Indeterminate Phase/Chronic Symptomatic Phase**

  - Serology – negative results do not rule out diagnosis because of poor test sensitivity, especially during this phase

Major Commercial Labs that Currently Perform Chagas Ab Testing

- **Mayo Medical Lab**
  - IFA for *T. cruzi* IgM: http://www.mayomedicallaboratories.com/test-catalog/Overview/58041 (performed at ARUP)
  - ELISA for *T. cruzi* IgG: http://www.mayomedicallaboratories.com/test-catalog/Overview/86159

- **ARUP**
  - IFA for *T. cruzi* IgM: http://ltd.aruplab.com/tests/pub/0051075
  - ELISA for *T. cruzi* IgG: http://ltd.aruplab.com/Tests/Pub/0051076

- **Quest/Focus Diagnostics**
  - Total *T. cruzi* Ab Immunoassay: http://www.questdiagnostics.com/testcenter/TestDetail.action?tabName=OrderingInfo&ntc=90827 (performed at Focus)

Treatment for Chagas Disease

- Pharmacologic treatment using either of two efficacious drugs which are available under Investigational New Drug (IND) status only through the CDC
  - Benznidazole or Nifurtimox
    - Treatment course is lengthy (60 days for Benznidazole and 90 days for Nifurtimox)
    - Significant drug side effects are common
    - http://www.cdc.gov/parasites/chagas/health_professionals/tx.html
  - Antiparasitic treatment is indicated for:
    - all acute infections
    - chronic infections in children up to 18 years of age
    - chronic infections in adults up to age 50 who have no indication of advanced cardiomyopathy
    - reactivated infections in immunocompromised patients
- Cardiac and gastrointestinal abnormalities can be managed with symptomatic treatment

Chagas Disease, Acute
Case Definition/Case Classification

- Chagas disease is a parasitic infection caused by *Trypanosoma cruzi*. The acute phase is characterized by the first 8 weeks of infection, detectable parasitemia, and asymptomatic (most common) or symptomatic manifestations of disease which can include any of the following:
  - Fever, malaise, rash, body aches, headache, loss of appetite, vomiting, diarrhea, hepatomegaly, splenomegaly, lymphadenopathy, Chagoma (nodular swelling at site of inoculation), Romaña's sign (unilateral swelling of the eyelid) and rarely, acute myocarditis and/or meningoencephalitis.
- ***Confirmed***: A case (asymptomatic or symptomatic) that has confirmatory laboratory testing
- ***Probable****:* A clinically compatible case with supportive laboratory testing* and documented exposure** within 8 weeks of illness onset or diagnosis
  - *Supportive laboratory testing includes**:**
    - Positive diagnostic serology for *T. cruzi* antibodies
      - **OR**
    - Positive blood donor screening test PLUS a positive supplemental test

**Documented exposure may include history of travel to an endemic country

Chagas Disease, Acute
Laboratory Confirmation Tests

Identification of *T. cruzi* by microscopy including:

Microscopic examination of *T. cruzi* by:

Wet mount – motile trypanosomes OR

Thick & thin smears - Giemsa stain

OR

Isolation of the agent by

Culture (specialized media - NNN, LIT) OR

Inoculation into mice OR

*Xenodiagnosis

OR

Detection of *T. cruzi* DNA by polymerase chain reaction (PCR)

***Xenodiagnosis** is a diagnostic method used to document the presence of infectious disease microorganisms or pathogens by exposing possibly infected tissue to a vector and then examining the vector for the presence of the microorganisms or pathogens it may have ingested*

Chagas disease, chronic indeterminate
Case Definition/Case Classification

Following the acute phase, most infected people enter into a prolonged, asymptomatic form of disease (called “chronic indeterminate”) during which few or no parasites are found in the blood. During this time, most people are unaware of their infection. Many people remain asymptomatic for life and never develop chronic Chagas-related symptoms.

***Confirmed**:* An asymptomatic case >9 months of age with confirmatory lab results obtained more than 8 weeks after documented exposure*

***Probable**:* An asymptomatic case >9 months of age with supportive laboratory testing obtained more than 8 weeks after documented exposure. Supportive laboratory testing includes**:**

Positive diagnostic serology for *T. cruzi* antibodies

OR

Positive blood donor screening test PLUS a positive supplemental test

**Documented exposure may include history of travel to an endemic country*

Chagas disease, chronic symptomatic
Case Definition/Case Classification

Much like the chronic indeterminate phase, the chronic symptomatic phase of disease (more than 8 weeks post infection) is characterized by undetectable parasitemia. However, an estimated 20 - 30% of infected people will develop debilitating and sometimes life-threatening medical problems over the course of their lives. Complications of chronic Chagas disease may include: heart rhythm abnormalities that can cause sudden death, a dilated heart that doesn't pump blood well and/or a dilated esophagus or colon, leading to difficulties with eating or passing stool.

***Confirmed**:* A physician-diagnosed case of chronic Chagas disease in a patient > 9 months of age with confirmatory laboratory results obtained more than 8 weeks after documented exposure* or symptom onset

***Probable**:* A physician-diagnosed case of chronic Chagas disease > 9 months of age with supportive laboratory results obtained more than 8 weeks after a documented exposure* or symptom onset. Supportive laboratory testing includes**:**

Positive diagnostic serology for *T. cruzi* antibodies

OR

Positive blood donor screening test PLUS a positive supplemental test

**Documented exposure may include history of travel to an endemic country*

Chagas disease
Laboratory Confirmation Tests

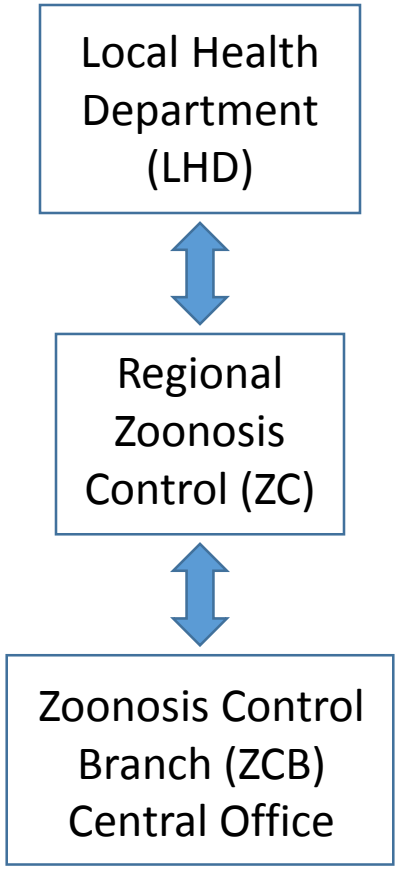
- Detection of antibody specific to *T. cruzi* by TWO distinct diagnostic tests
- Tests must be performed at Centers for Disease Control and Prevention (**CDC**)
- Tests currently in use at CDC include:
  - Trypanosoma cruzi AB EIA
  - Trypanosoma cruzi AB IB (TESA)

Note: No single supportive test has the sensitivity and specificity to be relied on alone, thus two different methods or antibodies specific to *T. cruzi* are used.

Chagas Disease Case Investigation

- Almost all cases are *T. cruzi* positive blood donors
  - repeat testing at a commercial lab recommended
  - if positive at a commercial lab, should be confirmed at CDC
- Most important component of investigation is determining where transmission likely occurred ⟹ local versus imported cases
  - having resided outside of US for longer than 30 days/travel history
  - history of contact with Triatomines
- Medical information – if patient is symptomatic, need to obtain medical records
- Make sure all required fields are completed in NEDSS (*refer to Data Entry Guidelines – Quick Reference section for patient demographics/lab report*)

Disease Reporting/Communication



- **Regional ZC should be the liaison between the LHDs and ZCB – if responsible jurisdiction is LHD, information should flow through regional ZC office**
  - Completed case investigation forms
  - Questions
  - Issues with classification or missing documentation/information
- **Regional ZC all have different preferences and are involved to varying degrees**
- **If ZCB communicates directly with LHD, regional ZC should at least be notified (cc'd if email)**

DSHS Chagas Disease (*Trypanosoma cruzi*) Exposure Assessment and Testing Guidance

Rev. 02-16

1

Person exposed/potentially exposed to a triatomine, and the bug or photo of bug is available for identification

- Have individual email digital photo to DSHS: david.florin@dshs.texas.gov and bonny.mayes@dshs.texas.gov
  - If bug is NOT a triatomine, the person is NOT at risk for Chagas disease
- If bug appears to be a triatomine or no photo is available, individual should send bug to DSHS for testing at CDC: www.dshs.state.tx.us/idcu/disease/chagas/
  - If bug tests **positive** for *T. cruzi*, go to 2 or 3 (depending on timeframe)
  - If bug tests **negative** for *T. cruzi*, the person is NOT at risk for Chagas disease
- If bug appears to be a triatomine but is not available for testing, and person is asymptomatic but concerned, go to scenario 2 or 3 (based on timeframe)

2

Person tests positive at a blood bank
OR
Person exposed or potentially exposed to a triatomine >8 weeks prior
OR
Person with onset of cardiac disease compatible with chronic Chagas disease
OR
Person with Chagas positive mother or sibling
OR
Person potentially exposed to blood from an infected animal >8 weeks prior
(e.g. needlestick injury)

- Have person contact their provider regarding need for Chagas disease testing
- Perform serology at a commercial lab

Negative serology – person NOT at risk for Chagas disease

Positive serology – request that sample be forwarded from commercial lab or collect a new sample and send directly to CDC

3

Person exposed or potentially exposed to a triatomine ≤8 weeks prior
OR
Person traveled to Chagas disease endemic area and has acute symptoms (Chagoma, etc)
OR
Person potentially exposed to blood from an infected animal ≤8 weeks prior
(e.g. needlestick injury)

- Have person contact their provider regarding need for Chagas disease testing (PCR at CDC or serology at a commercial lab)
- Have person give provider your contact information
- Give provider CDC contact information so they can consult directly with CDC regarding most appropriate testing for specific scenario (tell provider to mention they have consulted with DSHS)
- If CDC agrees to test by PCR, sample should be sent directly to CDC
- If CDC recommends serology, sample should be sent to a commercial lab

Positive PCR

Negative Serology** – person NOT at risk for Chagas disease

- **If person tests POSITIVE at CDC, provider will need to consult with CDC staff regarding clinical evaluation, management, and treatment* of Chagas disease:**
  - **CDC Parasitic Diseases Public Inquiries:**
  - **404-718-4745 or chagas@cdc.gov**
- **If person tests NEGATIVE at CDC, person is NOT at risk for Chagas disease**

**Investigational drugs are available only through CDC*

** *CDC may recommend convalescent sample be tested*

Technical Resources

- DSHS Zoonotic Control Branch Subject Matter Experts – David Florin or Bonny Mayes, 512-776-6545 or 2888.
- DSHS Laboratory Subject Matter Expert- Cathy Snider, DSHS Medical Parasitology Team, 512-458-7560.
- CDC Subject Matter Experts- Susan Montgomery, DVM, MPH, Parasitic Disease Branch; 404-718-4731; zqu6@cdc.gov (epi and technical consultation); Frank Steurer; 404-718-4175; fsteurer@cdc.gov (laboratory testing)
- "Evaluation and Treatment of Chagas Disease in the United States: A Systematic Review," Bern, Caryn et al, JAMA, November 14, 2007, Vol. 298, No. 18.
- "Chagas Disease," by Yves Carlier et al on the eMedicine website, http://www.emedicine.com/MED/topic327.htm
- CDC Chagas Disease website, http://www.cdc.gov/chagas/
- Infectious Diseases of the Dog and Cat, Craig E. Greene, 3rd Edition, Saunders, 2006, Chapter 72. "Trypanosomiasis." Pp. 676-681.
- DSHS Zoonosis Control Chagas Disease website http://www.dshs.state.tx.us/idcu/disease/chagas/