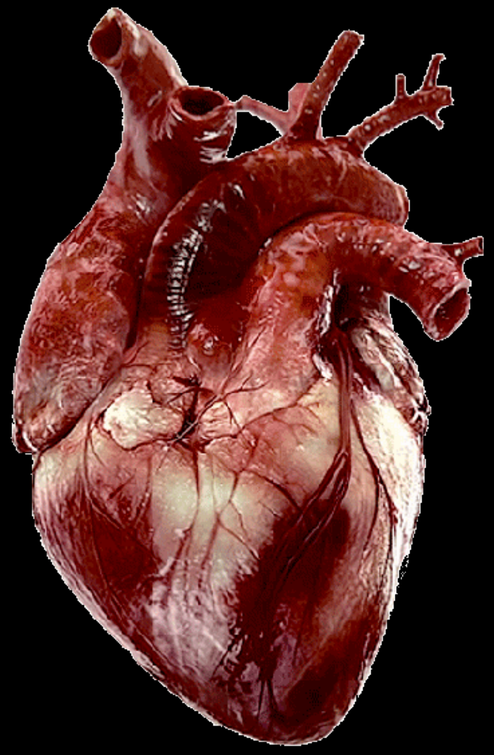
Deep In the Heart of Texas

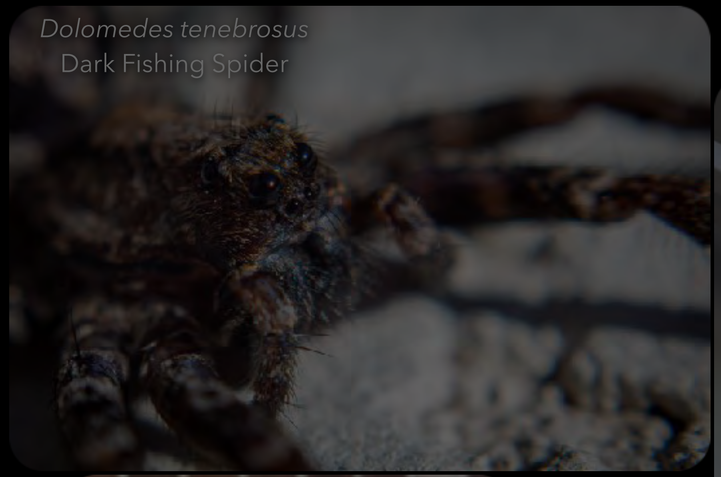
"By my troth, I kiss thee with a most constant heart."
Shakespeare, King Henry IV Part II



Polistes carolina Red Paper Wasp

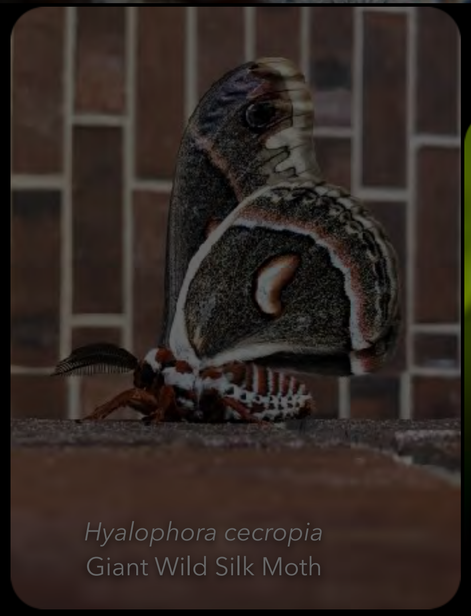
Craig Sisson, MD, MBA, AEMUS, RDMS, FACEP
San Antonio, Texas

Let’s see what we can find…



Dolomedes tenebrosus
Dark Fishing Spider

Neobarrettia spinosa
Giant Texas Katydid



Hyalophora cecropia
Giant Wild Silk Moth

Zelus longipes
Milkweed Assassin Bug
reduviidae family

Cybister fimbriolatus
Predaceous Diving Beetle

San Antonio, Texas

Zelus longipes
Milkweed Assassin Bug
reduviidae family

Oncopeltus fasciatus
Milkweed Bug

San Antonio, Texas

Arthropoda

phyllum

Arachnomorpha

Trilobita

Chelicerata

Mandibulata

Myriapoda

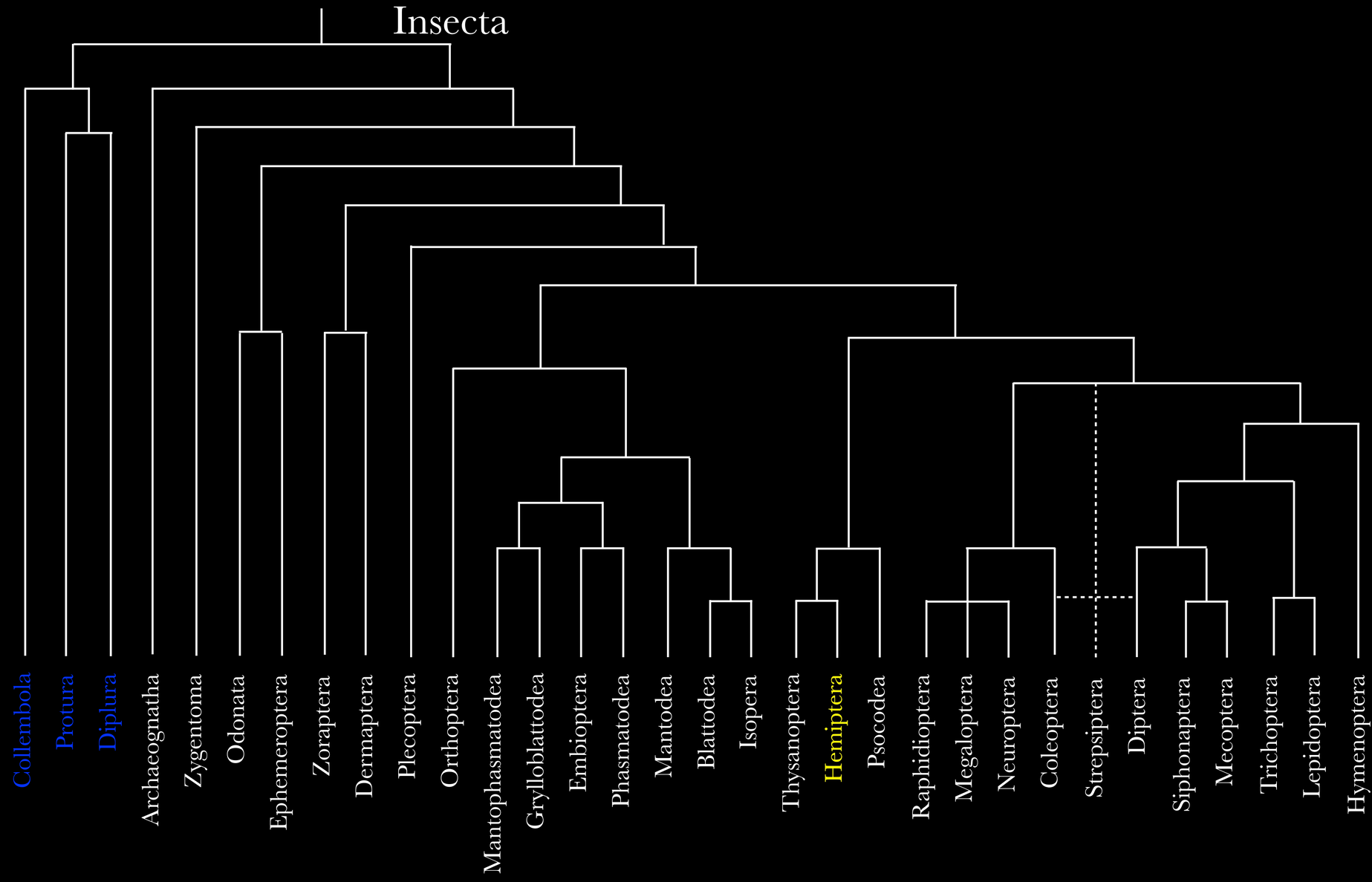
Pancrustacea

Hexapoda

class

Crustacea

Hexapoda


Insecta
Collembola
Protura
Diplura
Archaeognatha
Zygentoma
Odonata
Ephemeroptera
Zoraptera
Dermaptera
Plecoptera
Orthoptera
Mantophasmatodea
Grylloblattodea
Embioptera
Phasmatodea
Mantodea
Blattodea
Isopera
Thysanoptera
Hemiptera
Psocodea
Raphidioptera
Megaloptera
Neuroptera
Coleoptera
Strepsiptera
Diptera
Siphonaptera
Mecoptera
Trichoptera
Lepidoptera
Hymenoptera

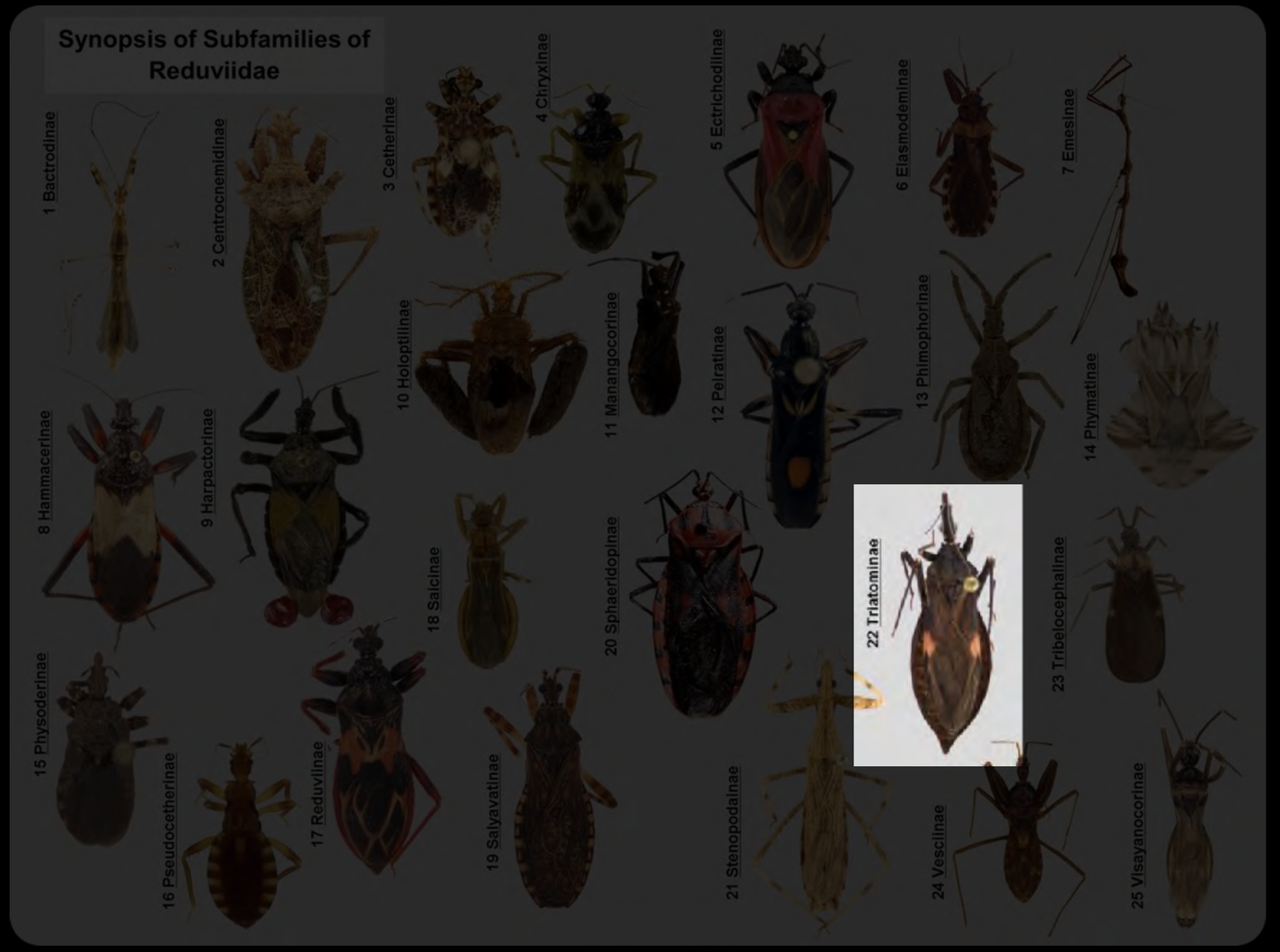
Hemiptera = “True Bugs”, all have piercing sucking mouth parts

Order

Sternorrhyncha Auchenorrhyncha Coleorrhyncha Pentatomomorpha Reduviidae Cimicidae

Reduviidae = The “Assassin” bugs

Family



Latin American Local Names

barbeiros

vinchucas

chinches

pito

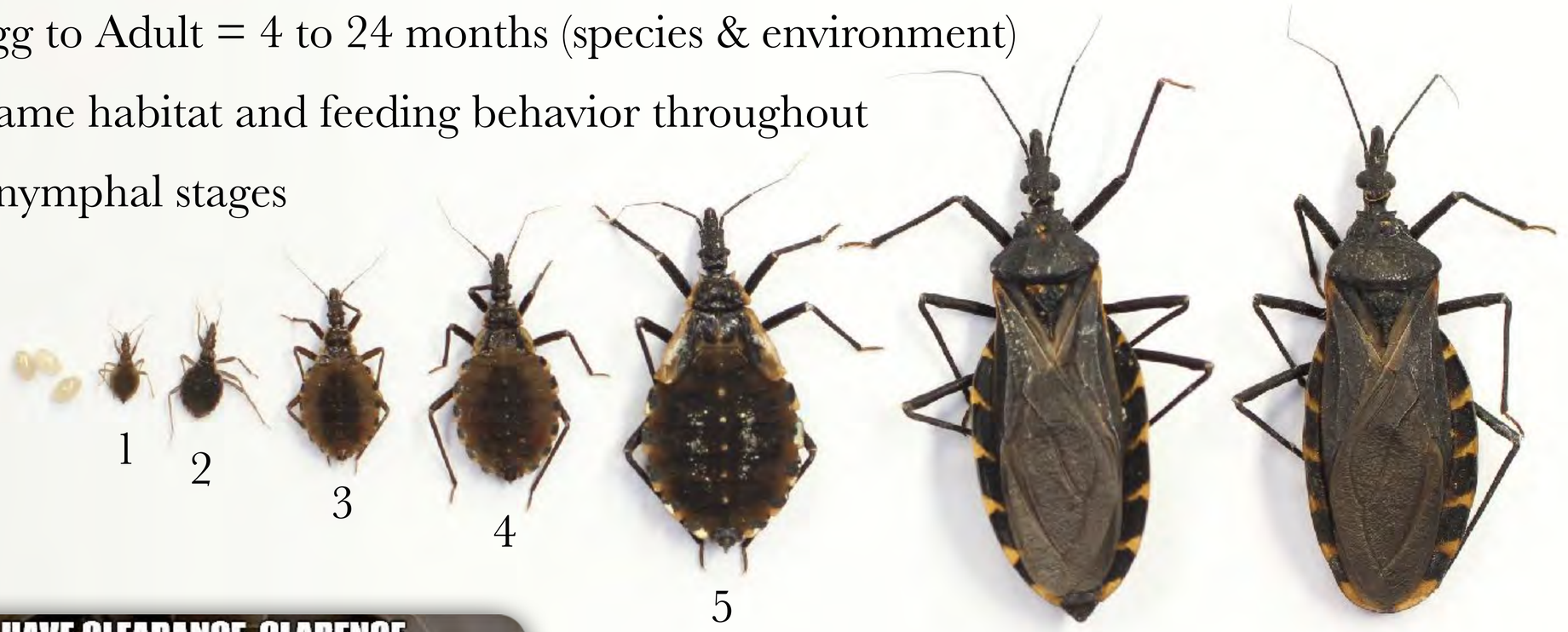
Triatominae

San Antonio, Texas

Egg to Adult = 4 to 24 months (species & environment)

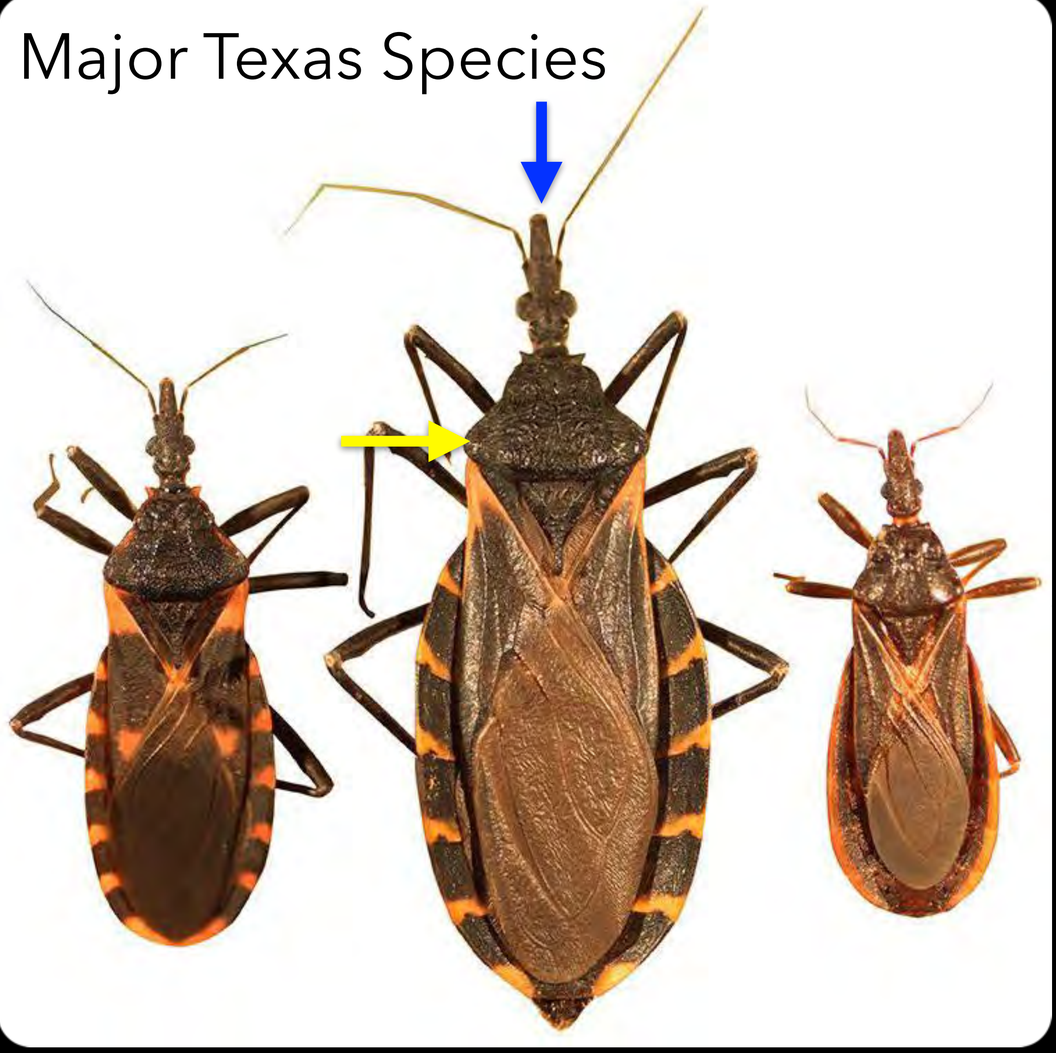
*Same habitat and feeding behavior throughout

5 nymphal stages



NOT born with *T. cruzi* in their gut

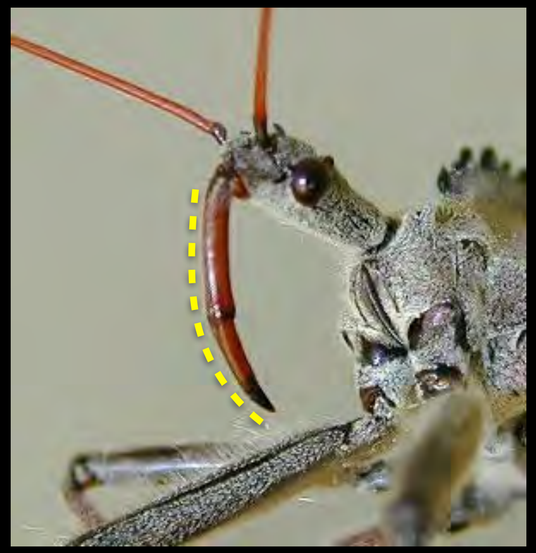
Major Texas Species

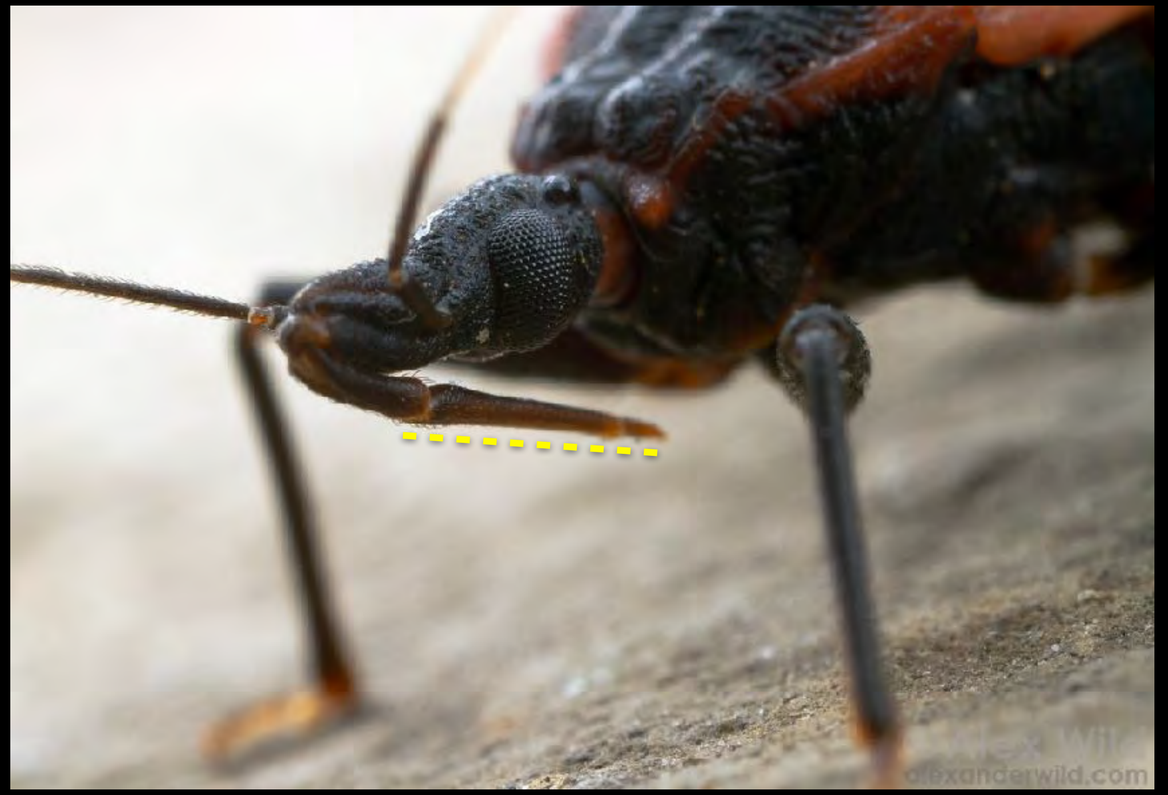


Triatoma sanguisuga

Triatoma gerstaeckeri

Triatoma protracta





Triatominae

Triatominae Insect Mimics in Texas

Leptoglossus brevirostris
Leaf Footed Bug
coreoidae family

Arilus cristatus
Wheel Bug
reduviidae family

Zelus longipes
Milkweed Assassin Bug
reduviidae family

Harpactorinae subfamily
(not *Triatominae*)

San Antonio, Texas

Vector Born Diseases = 17% of infectious disease worldwide

<u>Vectorial Capacity</u>

1. Vector Density
2. Vector Longevity
3. Host Preference
4. Feeding Behavior
5. Vector Competence = Ability of vector to become infected
    - Susceptibility to Infection
    - Permissiveness for Reproduction & Development
    - Transmission Efficiency
    - Incubation Period or Cycle

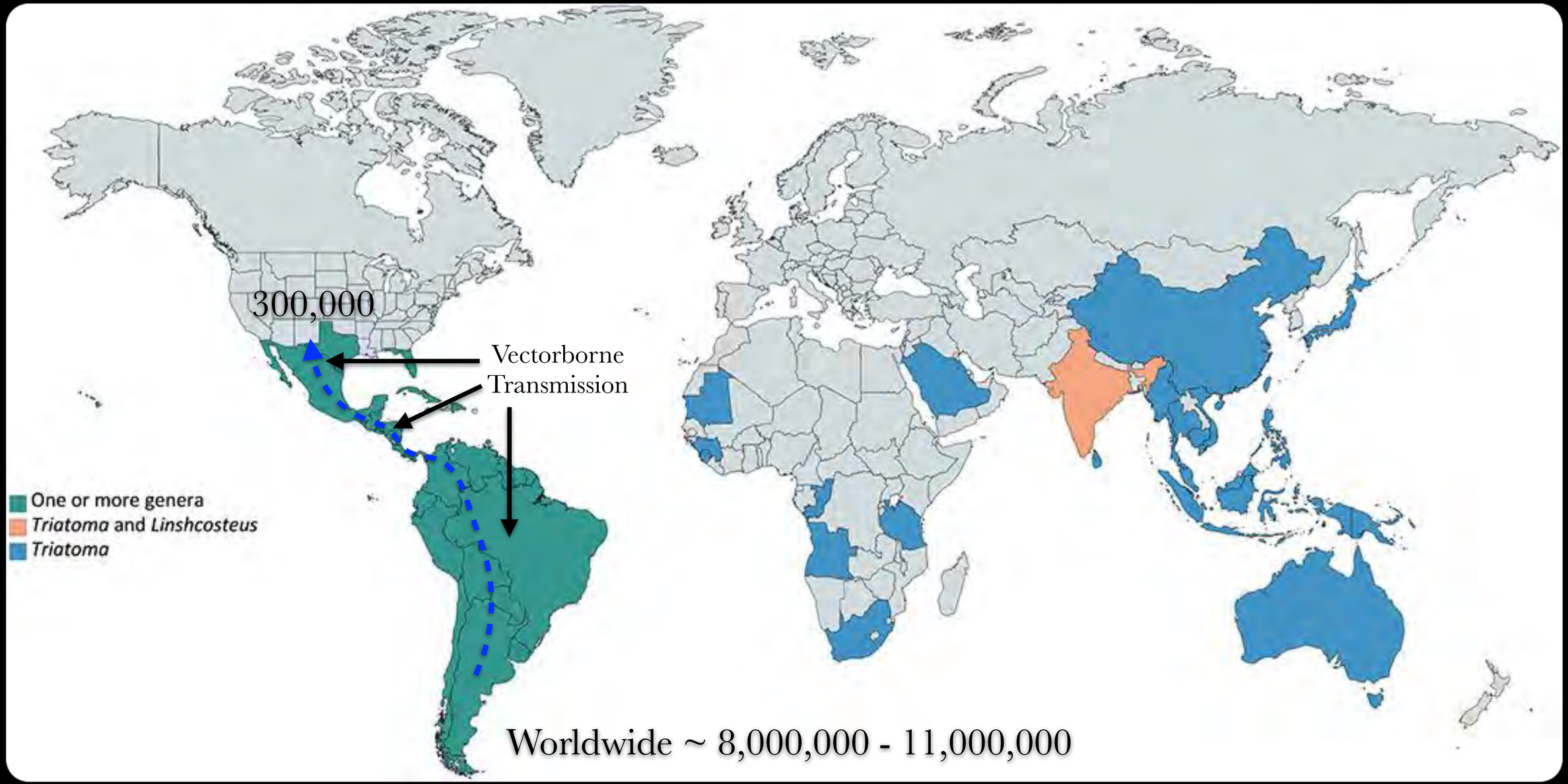
Obligate Hematophagous Insects

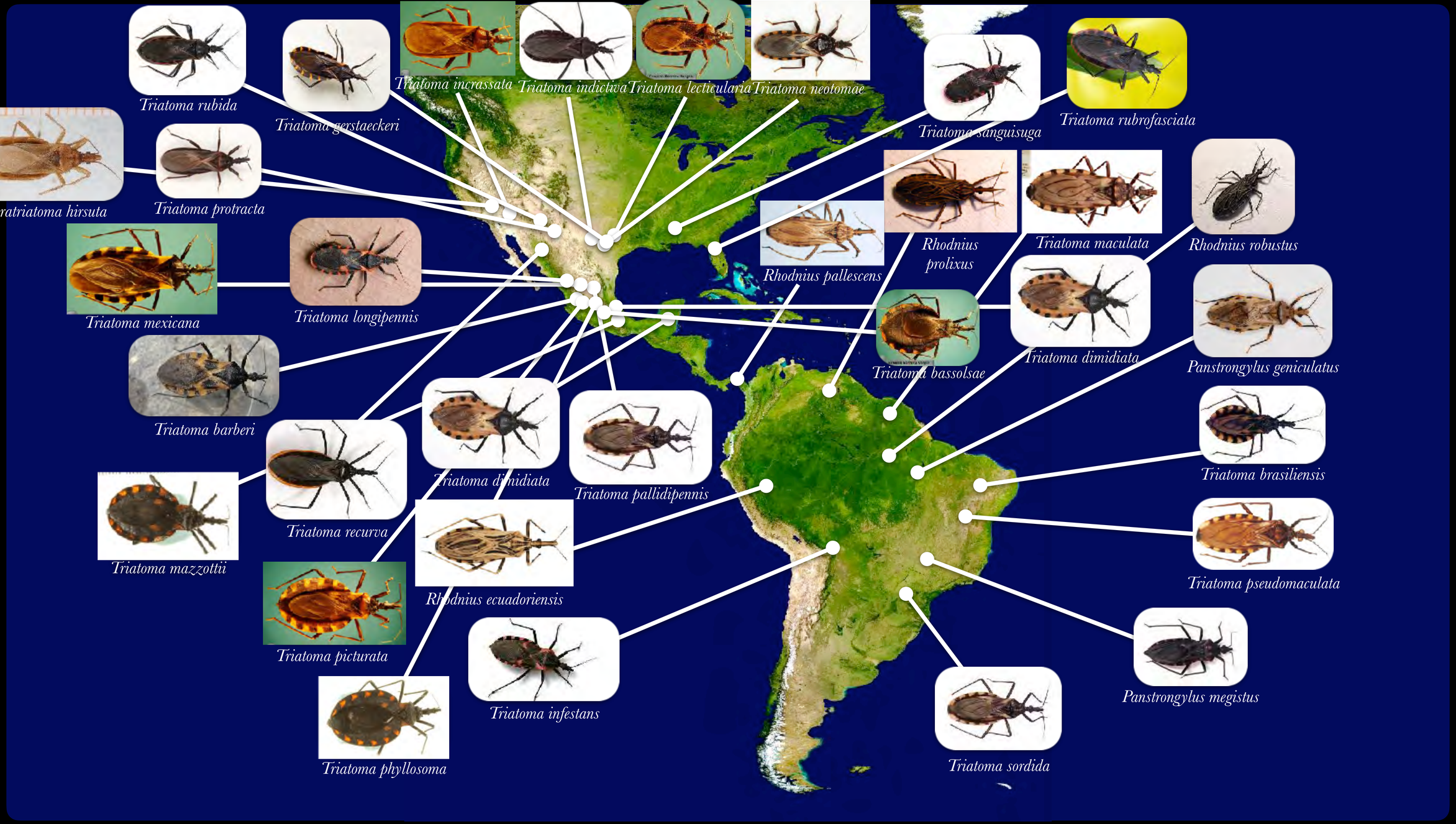
Rest during the day, close…feed at night while victim sleeps

Triatoma sanguisuga

San Antonio, Texas

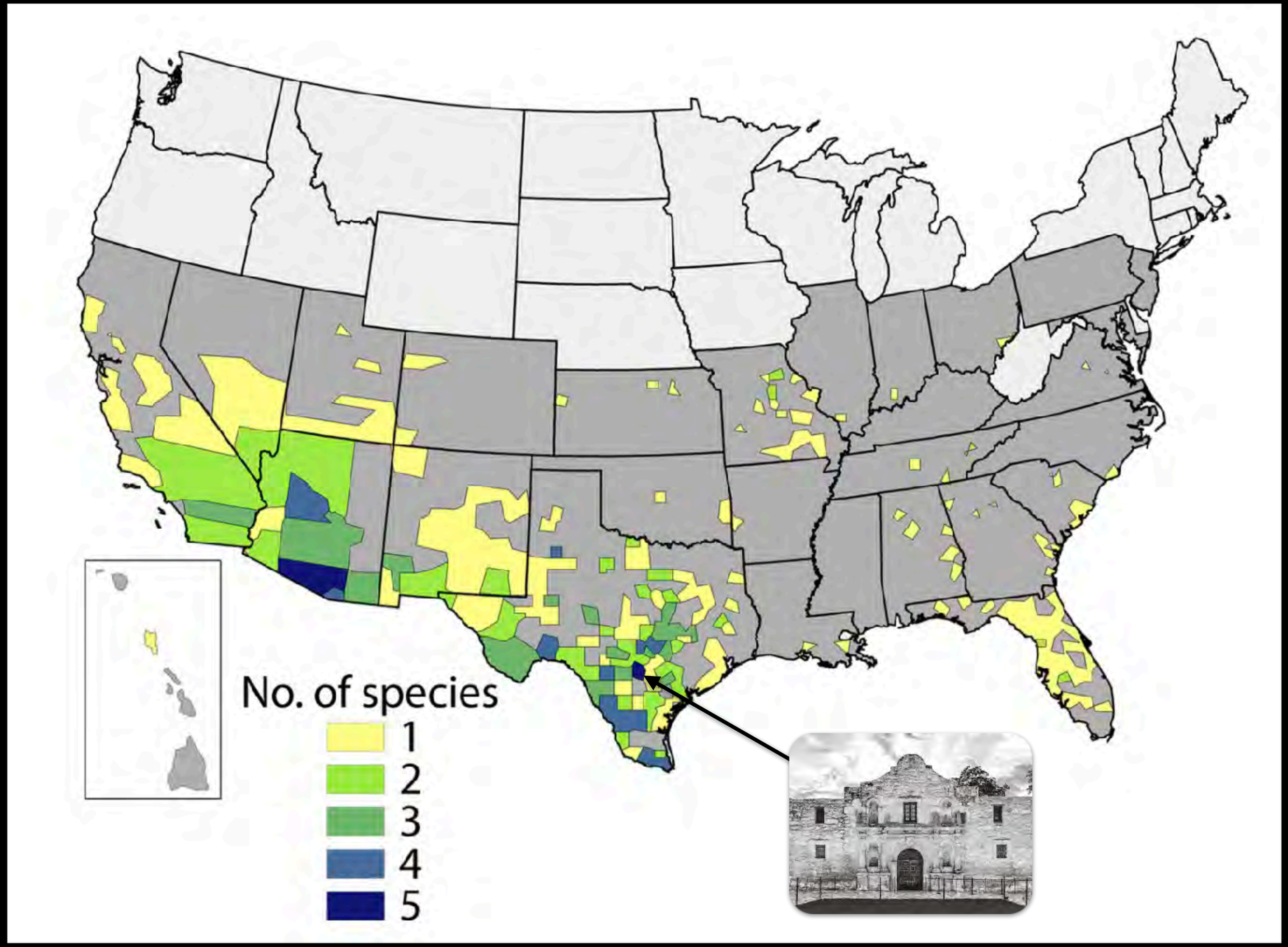
Majority of species occur in *Americas* (South, Central, North)



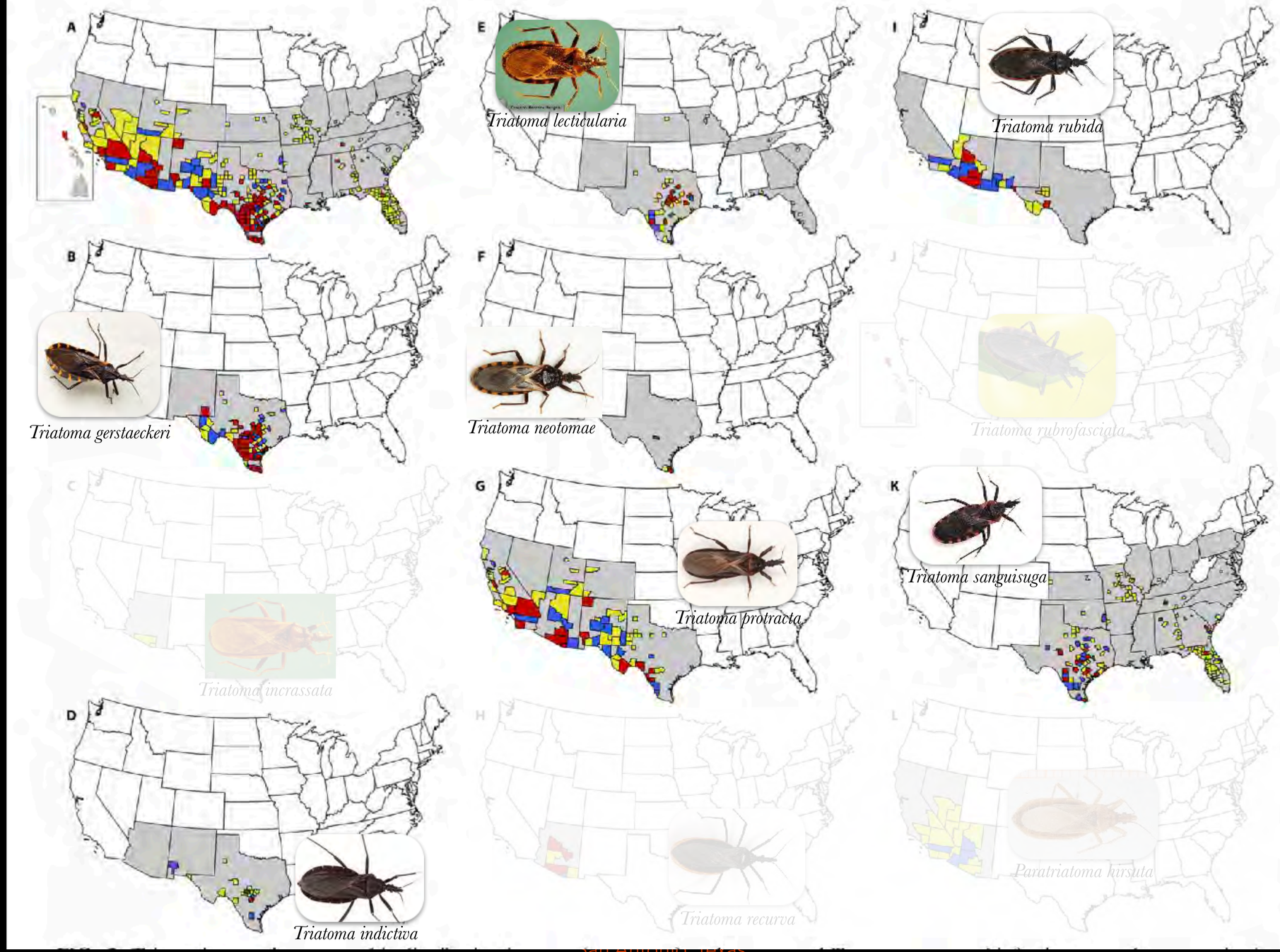


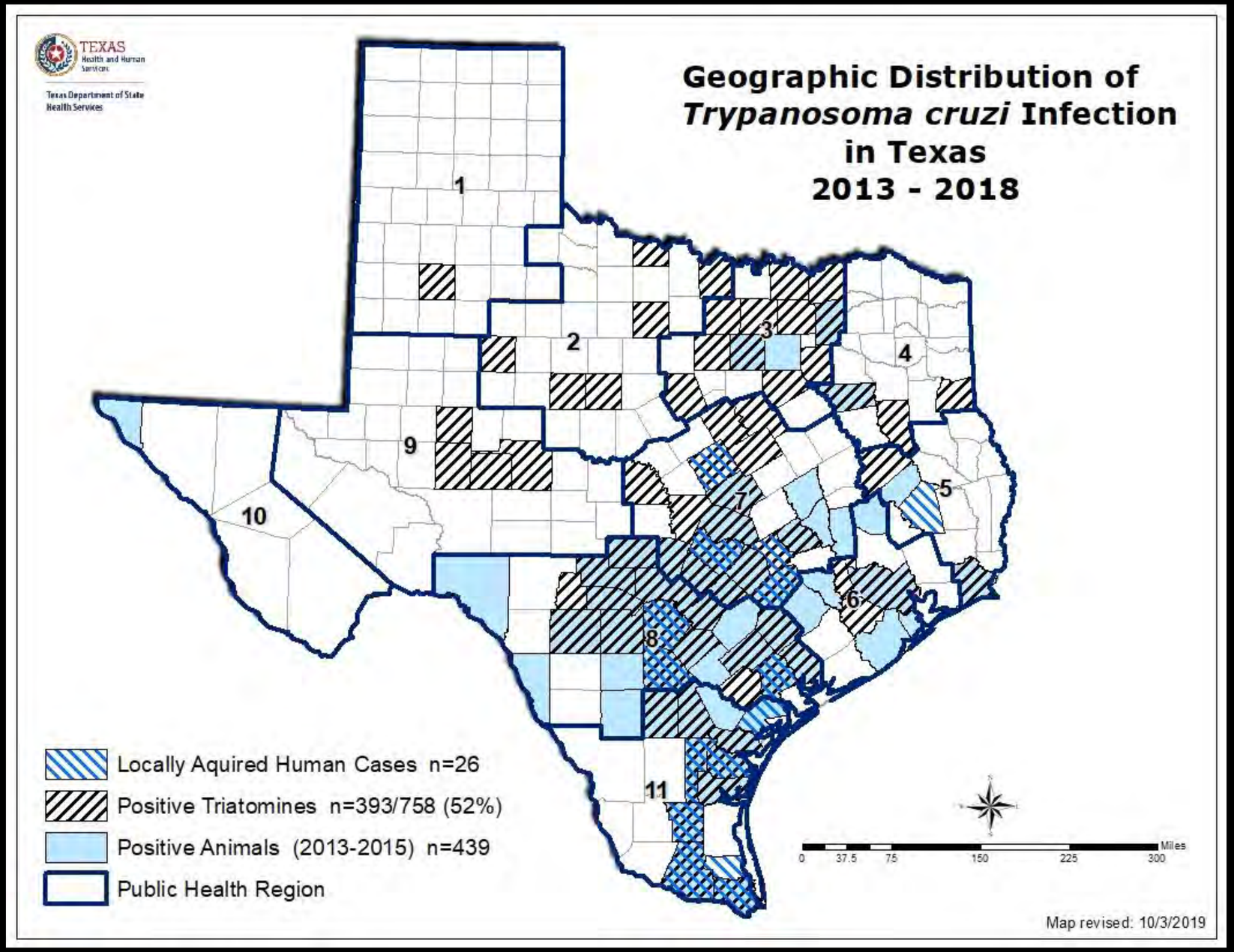
San Antonio, Texas

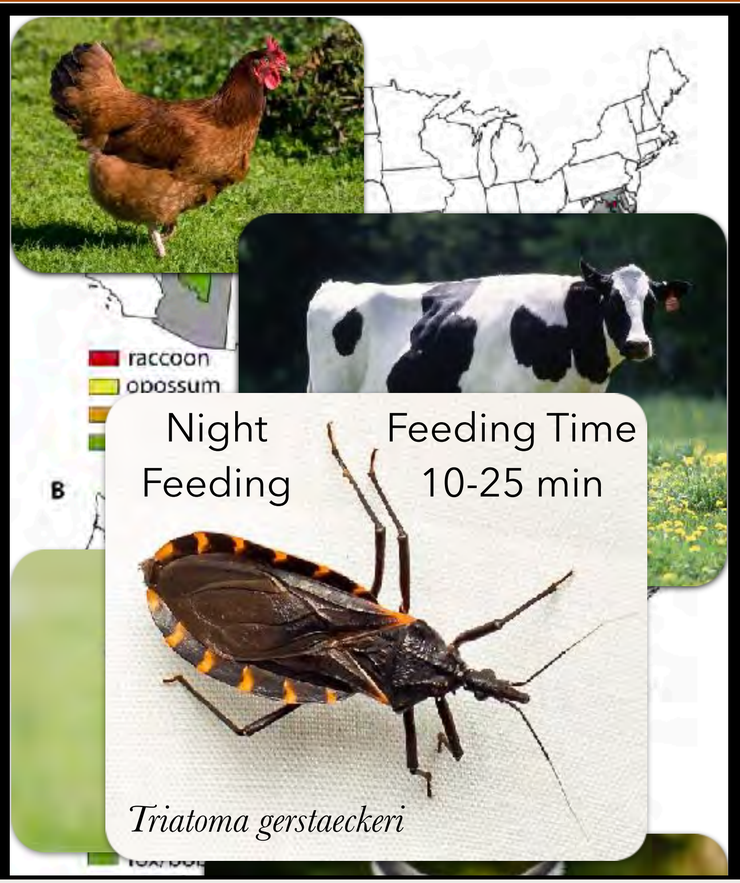
All species have ability to transmit *Trypanosoma cruzi*

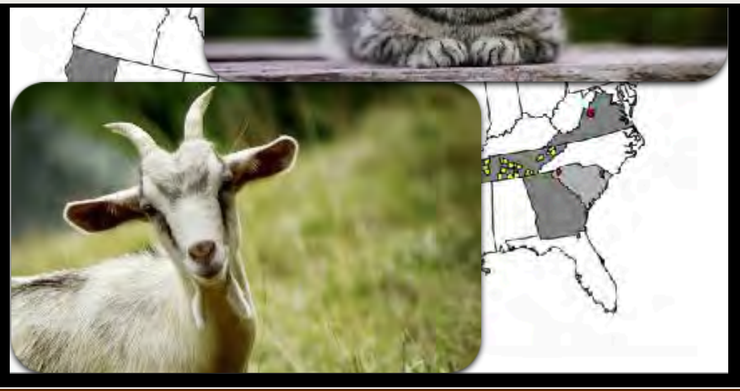


San Antonio, Texas


A
B
Triatoma gerstaeckeri
C
Triatoma incrassata
D
Triatoma indictiva
E
Triatoma lecticularia
F
Triatoma neotomae
G
Triatoma protracta
H
Triatoma recurva
I
Triatoma rubida
J
Triatoma rubrofasciata
K
Triatoma sanguisuga
L
Paratriatoma hirsuta


TEXAS
Health and Human Services
Texas Department of State Health Services
Geographic Distribution of
Trypanosoma cruzi Infection
in Texas
2013 - 2018
1
2
3
4
5
6
7
8
9
10
11
Locally Aquired Human Cases n=26
Positive Triatomines n=393/758 (52%)
Positive Animals (2013-2015) n=439
Public Health Region
0 37.5 75 150 225 300
Miles
Map revised: 10/3/2019





Domiciliated vs. Peridomiciliary vs. Sylvatic

Most important parasitic disease in Western Hemisphere

Disease Burden = 7.5x that of Malaria

Dr. Carlos Chagas

Oswaldo Cruz Institute, Brazil

Central Railroad Company

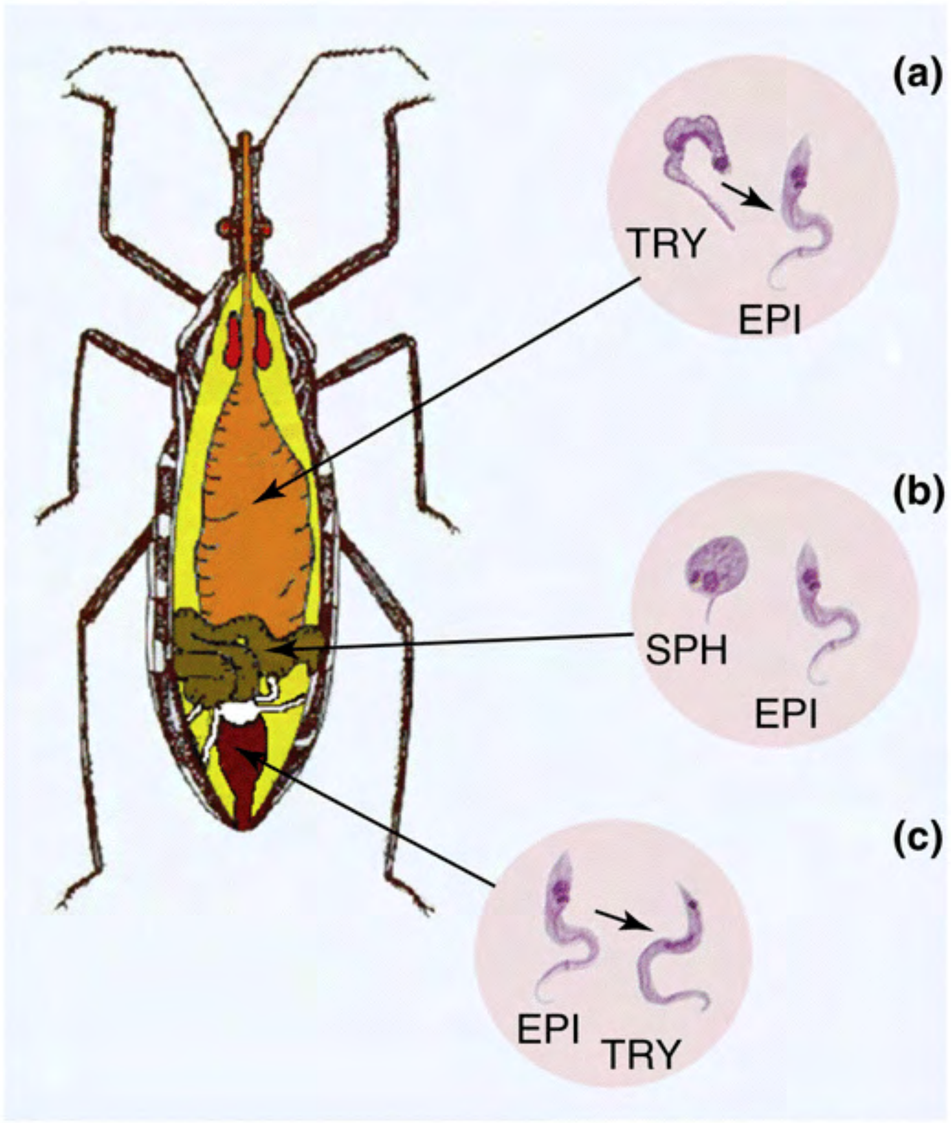
Rio de Janeiro

“The Barber”

The Parasite

The Mentor “Oswaldo Cruz”

The “American Trypanosomiasis”



Trypanosoma cruzi = Protozoan Parasite

Order: Kinetoplastida

└ Family: Trypanosomatidae

Transmission Mechanisms

Vector Zoonosis (Americas)

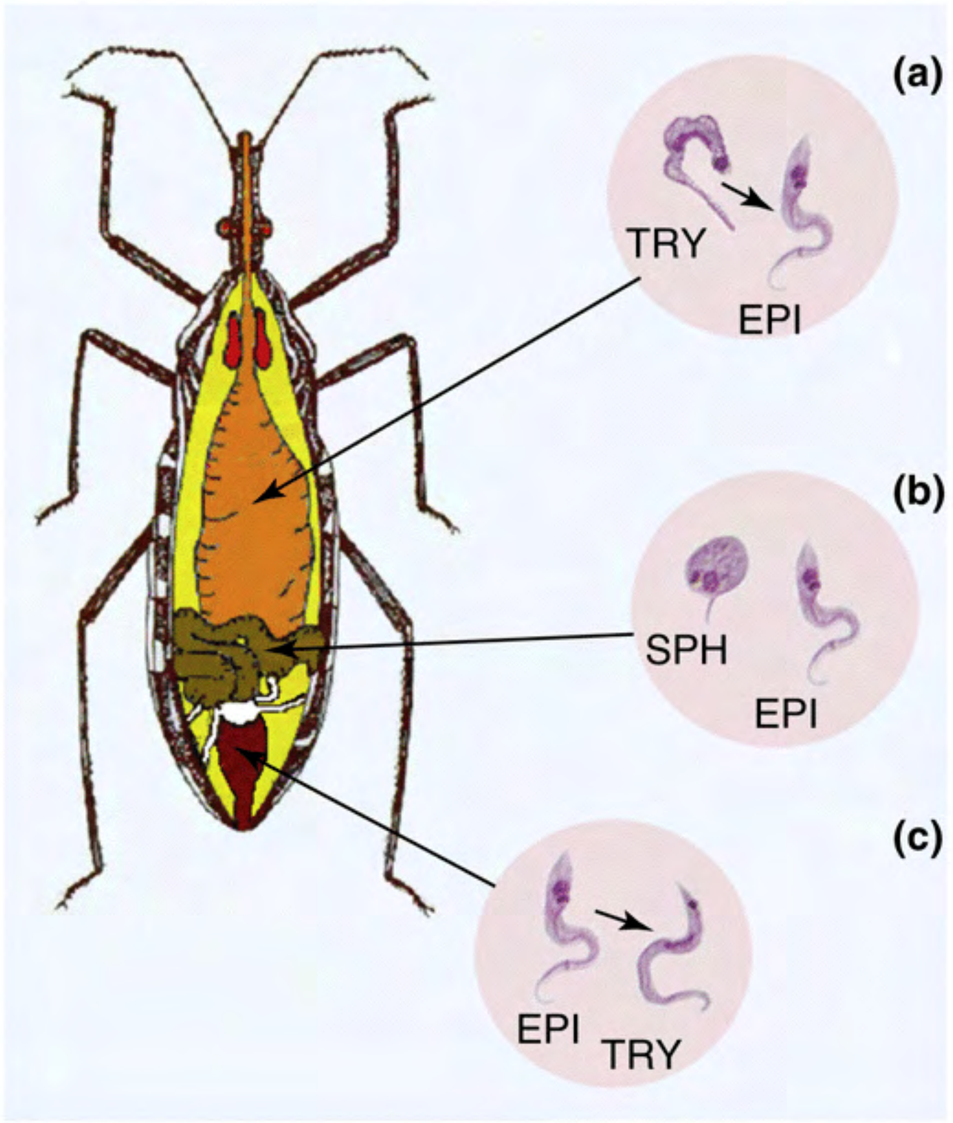
Blood Transfusion

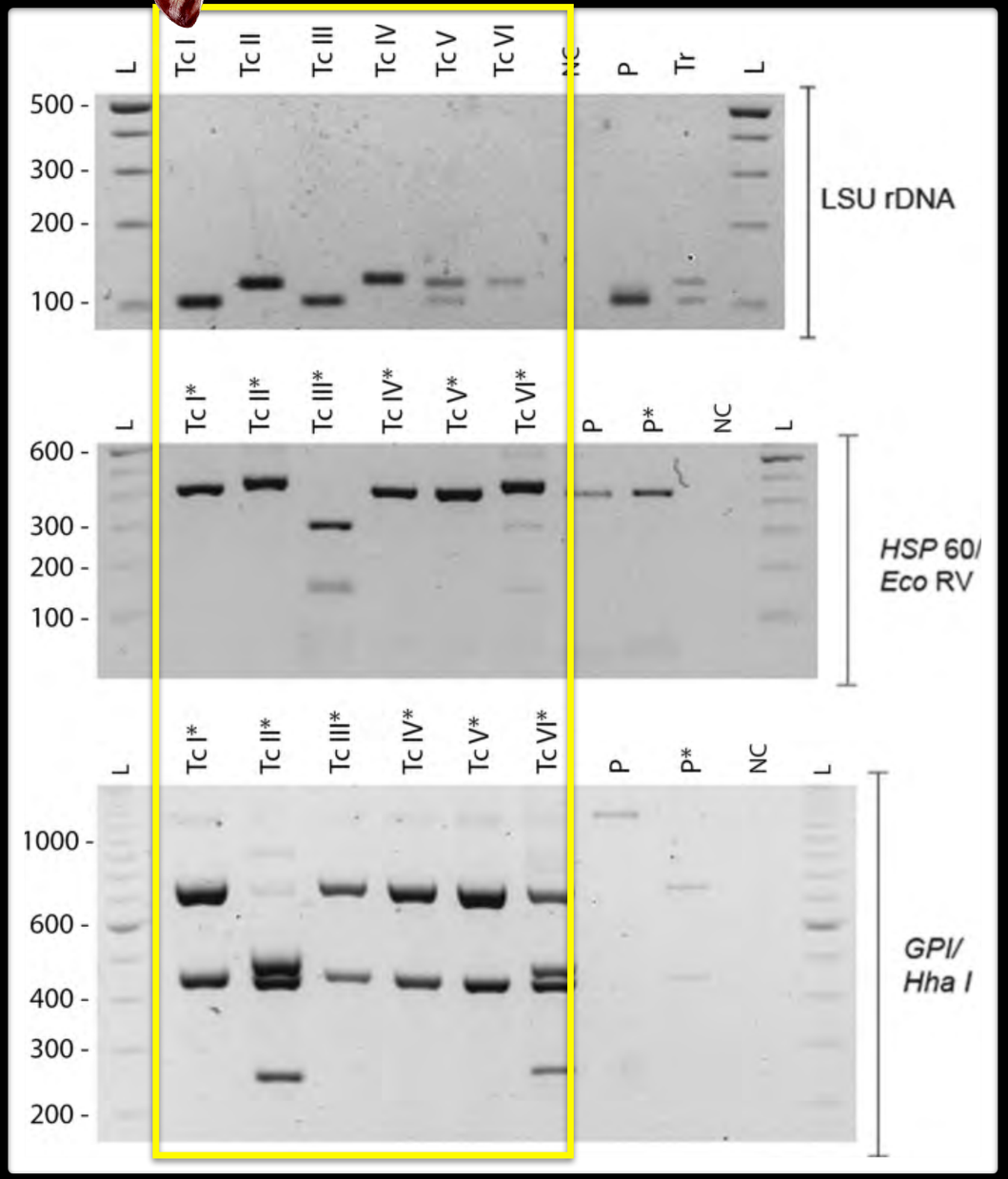
Organ Transplantation

Congenital

Contaminated Food & Water Higher Case Fatality

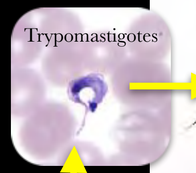
Infection is *lifelong* unless treated appropriately.

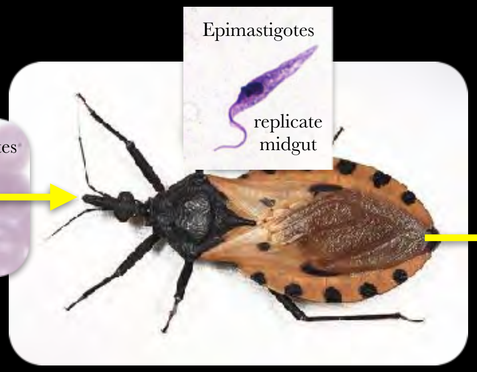

(a)
TRY
EPI
(b)
SPH
EPI
(c)
EPI
TRY
TRENDS in Parasitology

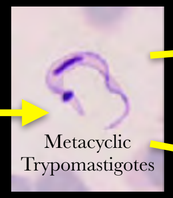

L
Tc I
Tc II
Tc III
Tc IV
Tc V
Tc VI
P
Tr
500 -
300 -
200 -
100 -
LSU rDNA
Tc I*
Tc II*
Tc III*
Tc IV*
Tc V*
Tc VI*
P*
NC
600 -
300 -
200 -
100 -
HSP 60/
Eco RV
1000 -
600 -
400 -
300 -
200 -
GPI/
Hha I

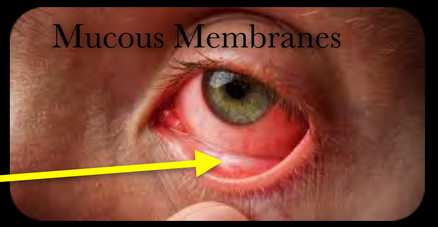
Stercorarian Transmission

Very Inefficient Transmission (<1%/year)









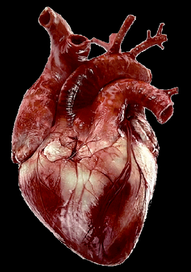
Rubbing or Scratching

Acute Reaction

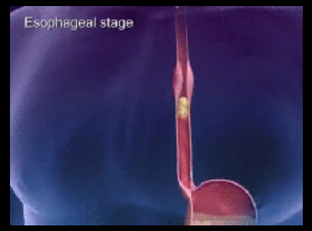
Swelling Fever

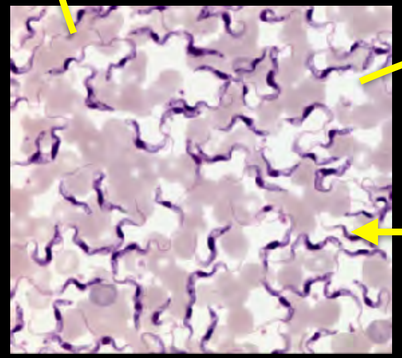
Itching Anaphylaxis

Hepatosplenomegaly

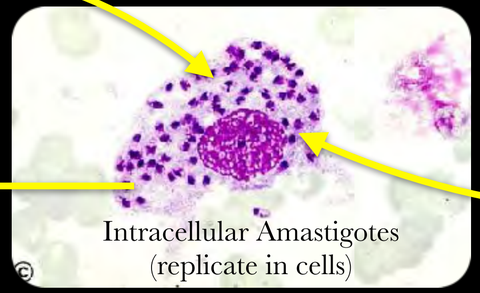


Chronic Infection Risks



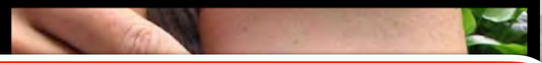


Amastigote to Trypomastigote and cell rupture



San Antonio, Texas

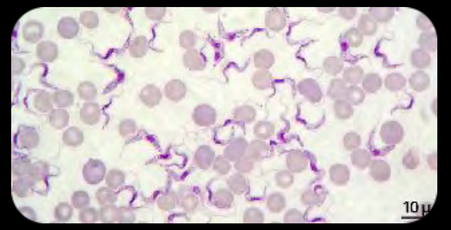
Acute Phase of Infection



90% of acute infections go undiagnosed

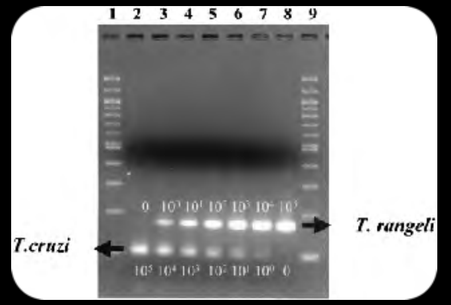
Ramaña Sign

Chagoma



+ Peripheral Smear

Giemsa Staining



+ PCR

Trypomastigote	Amastigote
Blood and intracellular spaces of vertebrate-host and cells culture	Inside the cells of vertebrate-host and cells culture

+ Hemoculture

Chronic Phase of Infection

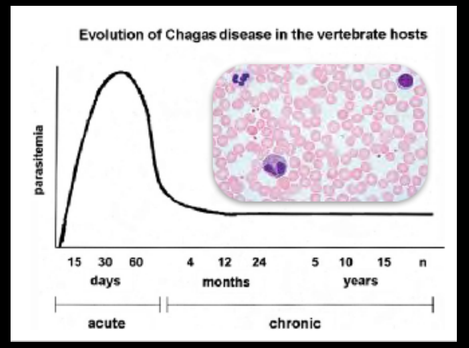
Worldwide ~ 8-11 Million People

Indeterminate Form

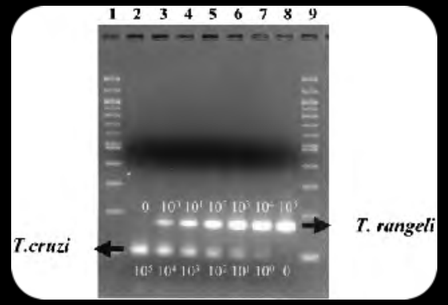
No Signs or Symptoms

Chronic Phase

No individual test has a high enough sensitivity and specificity to be used alone.



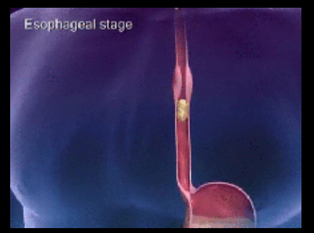
\- Peripheral Smear

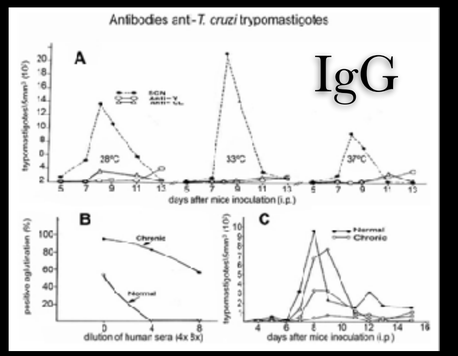


\+ PCR (20-70%)

70-80% stay indeterminate for lifetime

Determinate Form





Dx = Serology

San Antonio, Texas

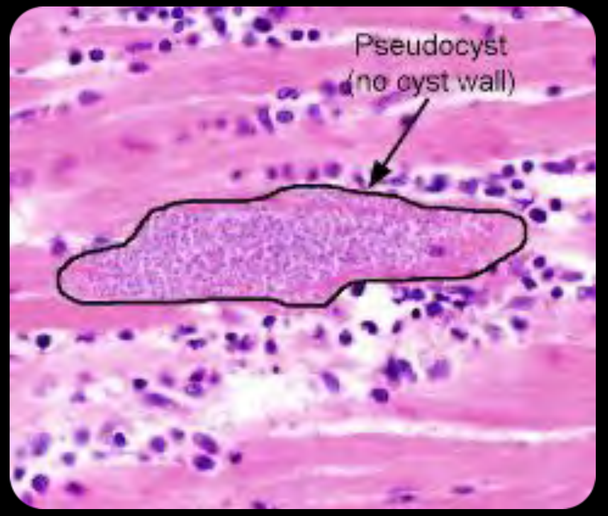
Chagas (American Trypanosomiasis) Cardiomyopathy

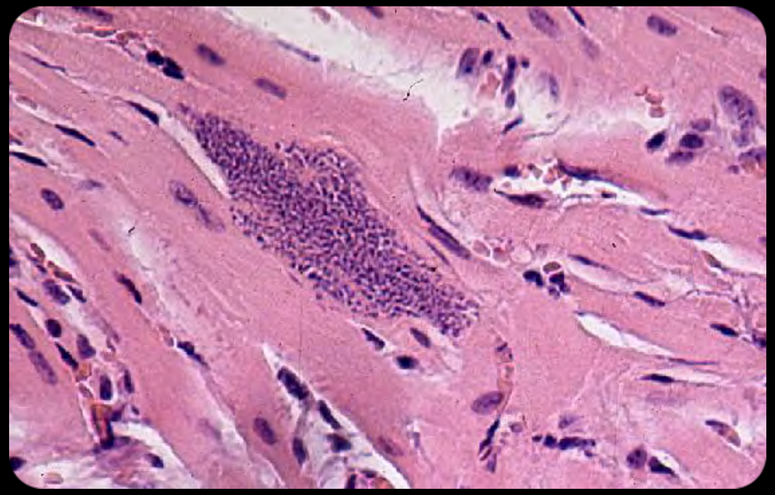
Actual pathological cause unknown

Likely related to parasitic persistence (chronic inflammation)

Areas where vector control obtained…decreased incidence

Repeated infections (chronic inflammation)

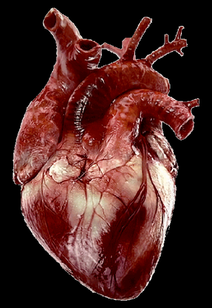




Trypanosoma cruzi reinfections in mice determine the severity of cardiac damage

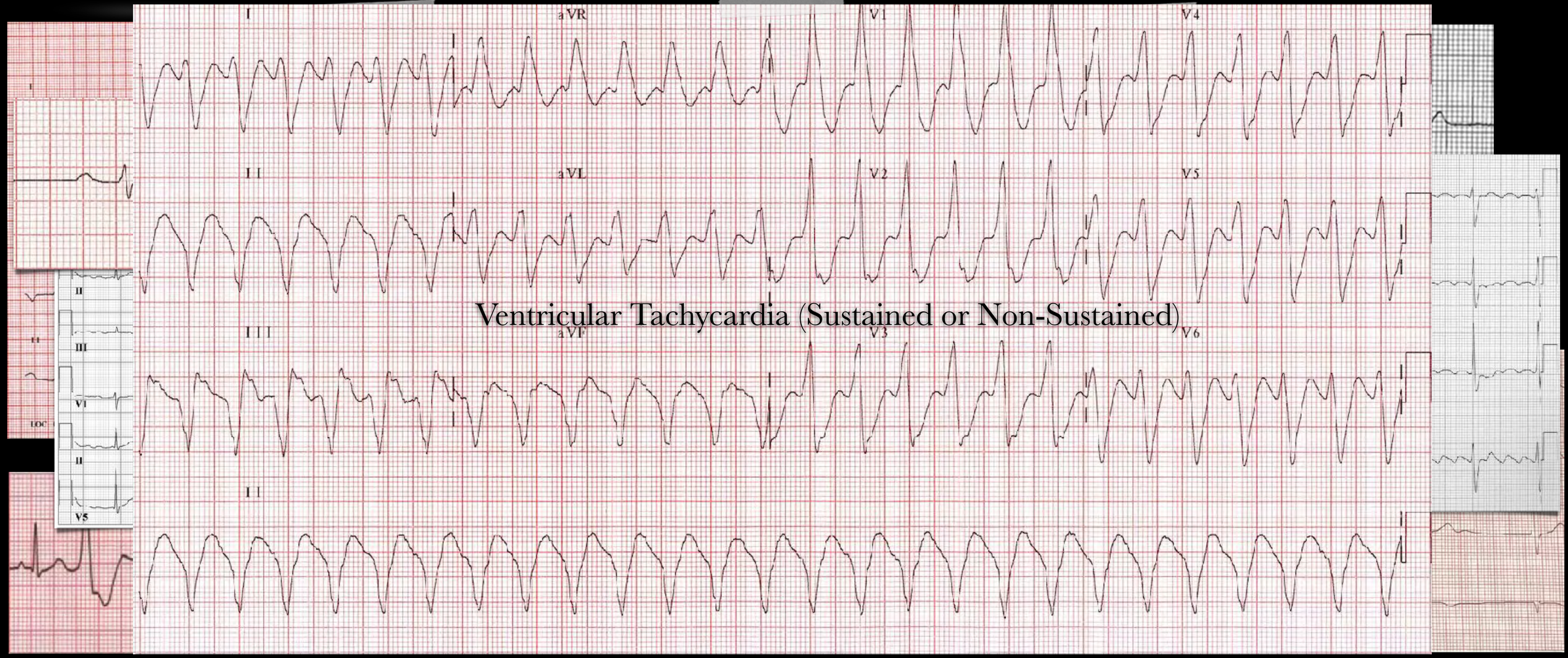
Juan M. Bustamante[a], Héctor W. Rivarola[a], Alicia R. Fernández[a,b], Julio E. Enders[a], Ricardo Fretes[c], José A. Palma[a], Patricia A. Paglini-Oliva[a,*]

International Journal for Parasitology 32 (2002) 889–896

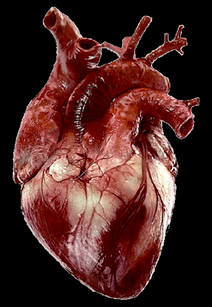


Chaga's (American Trypanosomiasis) Cardiomyopathy

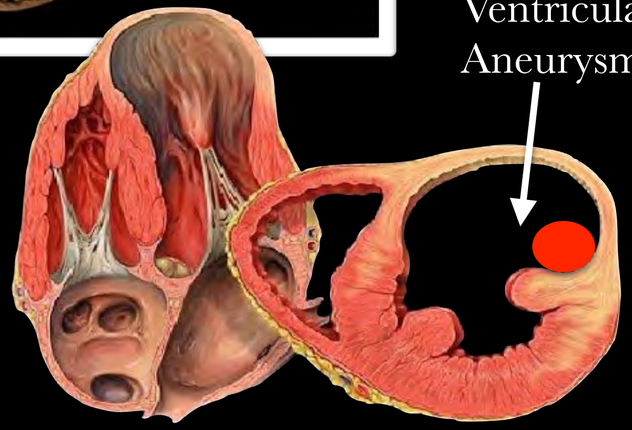
Highly Arrhythmogenic



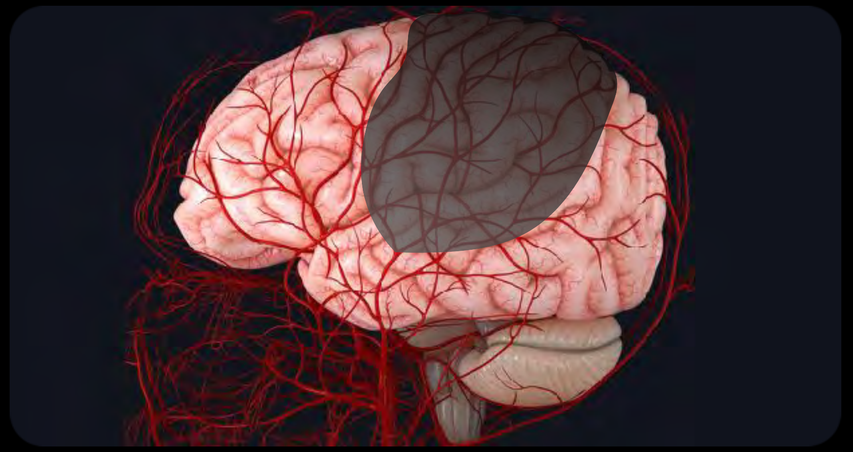
San Antonio, Texas

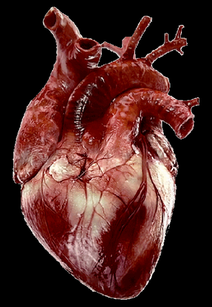


Chaga's (American Trypanosomiasis) Cardiomyopathy



Dilated Cardiomyopathy





Chagas (American Trypanosomiasis) Cardiomyopathy

Chaga's (American Trypanosomiasis) Gastrointestinal

Damage to gastrointestinal intramural neurons

Megaesophagus


Achalasia

Dysphagia

Odynophagia

GERD

Aspiration

Cough


Megacolon

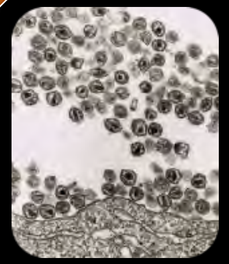
Constipation

Fecaloma

Volvulus

Bowel Ischemia

Bowel Perforation



Chagas (American Trypanosomiasis) Immunocompromised

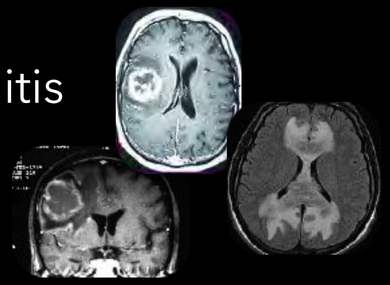
Reactivation of Chronic Disease

HIV Co-infection

#1

Meningoencephalitis

Brain Abscess



#2

Acute Myocarditis
(even in chronic cardiomyopathy)

Rare

Skin Lesions

Peritoneum
Stomach
Intestine

Organ Transplantation

Patient's who receive heart transplant do as well or *better* than those receiving heart for other reasons

Reactivation can happen, but is more rare

CNS infection not common in reactivation

Consider reactivation in febrile patient or those showing signs of rejection

Chagas (American Trypanosomiasis) Congenital

First Congenital Chagas Case in U.S. Reported

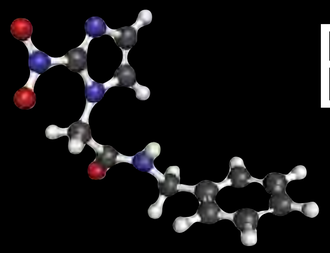
-A Virginia boy born in August, 2010 is the first case of congenital Chagas disease reported in the U.S., according to the CDC.

by Michael Smith, North American Correspondent, MedPage Today July 6, 2012

Non-vector transmission***

Potential congenital exposure: Repeat testing at 9 months of age once maternal antibodies have cleared

Treatment

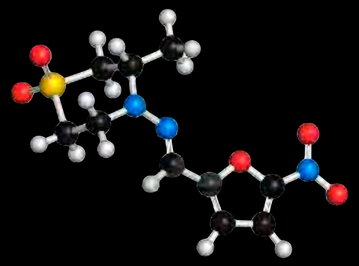


Benznidazole

Rochagan
Radanil
(nitroimidazole)

(fda.gov)

2017
Pediatric Infections
2 - 12 y.o.



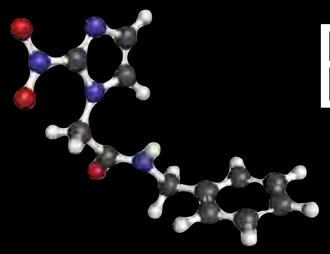
Nifurtimox

Lampit
(nitrofuran)

(fda.gov)

2020
Pediatric Infections
Birth - 18 y.o.

Treatment

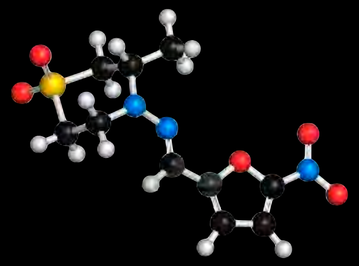


Benznidazole

Rochagan
Radanil
(nitroimidazole)

(fda.gov)

12.5mg or 100mg tablet



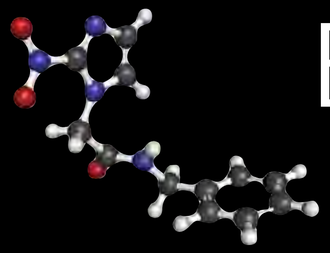
Nifurtimox

Lampit
(nitrofuran)

(fda.gov)

30mg or 120mg tablet

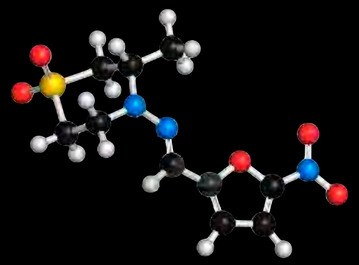
Treatment



Benznidazole

Rochagan
Radanil
(nitroimidazole)

(fda.gov)



Nifurtimox

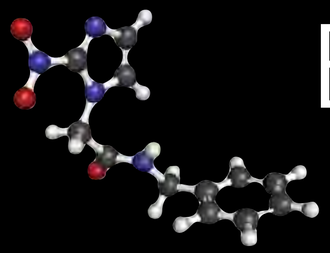
Lampit
(nitrofuran)

(fda.gov)

Contraindications

Pregnancy
Severe Liver Disease
Severe Kidney Disease

Treatment



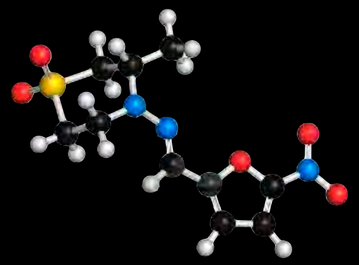
Benznidazole

Rochagan
Radanil
(nitroimidazole)

(fda.gov)

- Genotoxicity
- Carcinogenicity
- Headache
- Allergic Dermatitis
- Peripheral Neuropathy (dose dependent, not permanent)
- GI Effects (anorexia, nausea/vomiting, weight loss)
- Neutropenia

**adverse reactions far less common in children



Nifurtimox

Lampit
(nitrofuran)

(fda.gov)

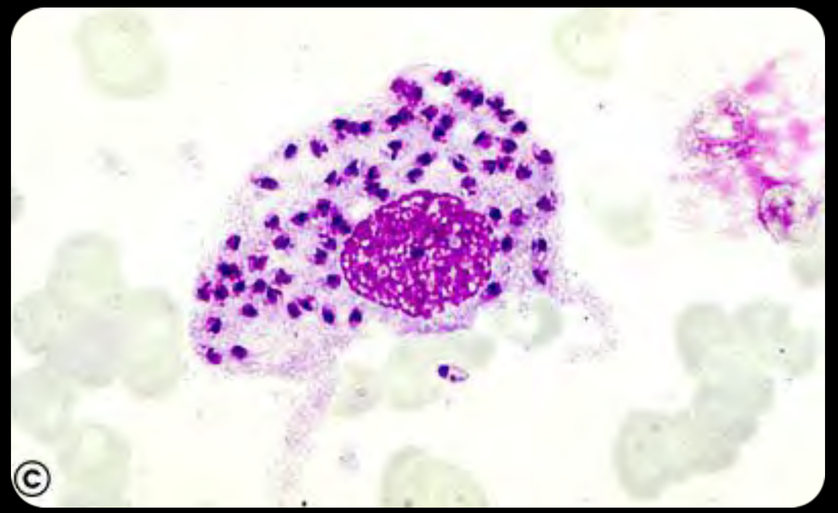
- Genotoxicity
- Carcinogenicity
- Worsening of Neurological/Psychiatric Disease
- GI Effects (anorexia, nausea/vomiting, weight loss)
- Hypersensitivity (angioedema, hypotension, severe skin reactions, dyspnea)
- Porphyria (nitrofuran derivative)

San Antonio, Texas

Spontaneous dormancy protects *Trypanosoma cruzi* during extended drug exposure

Fernando J Sánchez-Valdéz[1†‡], Angel Padilla[1,2†], Wei Wang[1], Dylan Orr[1], Rick L Tarleton[1,2*]

Sánchez-Valdéz *et al.* eLife 2018;7:e34039. DOI: https://doi.org/10.7554/eLife.34039

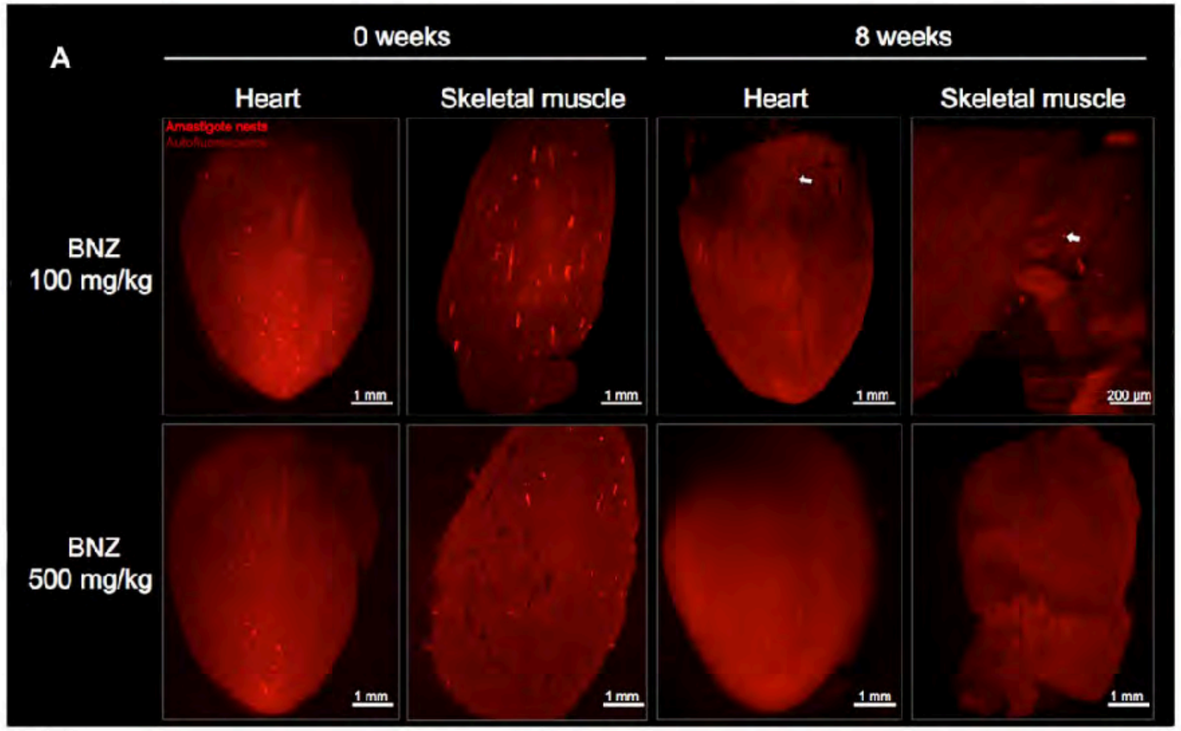


Non-replicating Amastigotes can survive therapeutic [drug] for ~30 days

A modified drug regimen clears active and dormant trypanosomes in mouse models of Chagas disease

Juan M. Bustamante[1]*, Fernando Sanchez-Valdez[1,2]*, Angel M. Padilla[1], Brooke White[1], Wei Wang[1], Rick L. Tarleton[1,3†]

Bustamante *et al.*, *Sci. Transl. Med.* **12**, eabb7656 (2020) 28 October 2020



B

Parasite-infected cells detected at weeks post-treatment

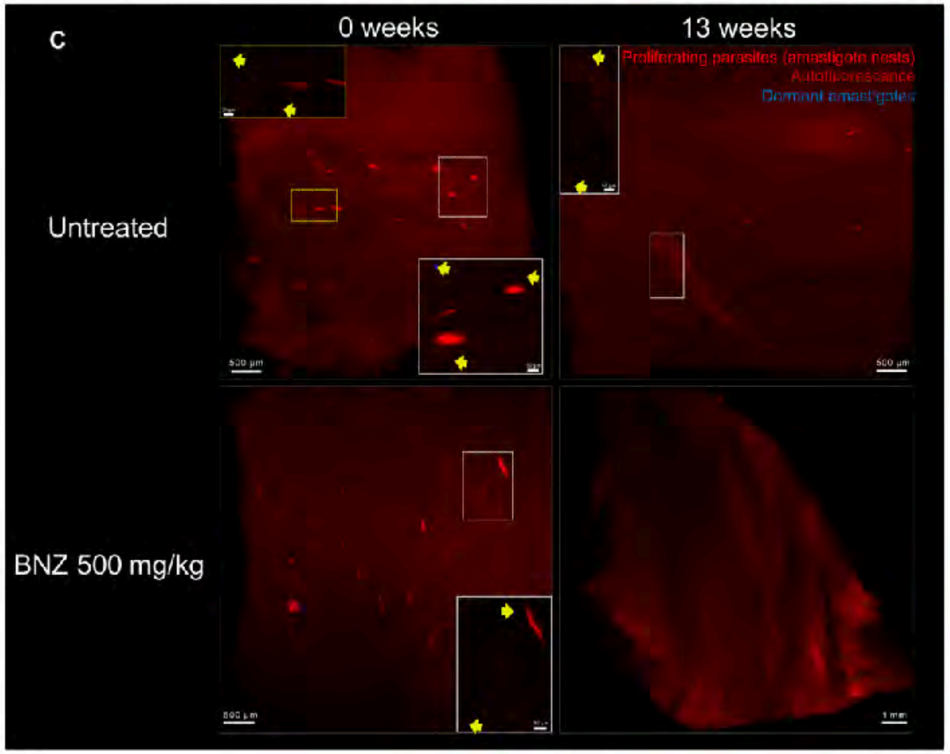
		0	2	4	6	8
BNZ 100 mg/kg	Heart	56	ND	1	2	5
	Muscle	79	2	5	3	6
BNZ 500 mg/kg	Heart	64	ND	0	0	0
	Muscle	48	2	2	0	0

A Proliferating parasites

		Weeks 0	3	6	9	13
Untreated	Heart	2.6	0.3	0	1	0
	Muscle	24.6	27	11	2.3	1
	Intestine	3.3	2.3	6	2.6	2
BNZ 500 mg/kg	Heart	4	0	0	0	0
	Muscle	29	4	0	0	0
	Intestine	7	2.6	0	0	0

B Dormant parasites

		Weeks 0	3	6	9	13
Untreated	Heart	1.3	2.3	0	0.6	0
	Muscle	3	5	0.6	0.6	1
	Intestine	11.3	4.6	2.3	0	0.6
BNZ 500 mg/kg	Heart	9.6	0	0	0	0
	Muscle	2.3	2.3	0	0	0
	Intestine	8.3	5.6	0	0	0



Treatment Efficacy

Chagas' Disease

Caryn Bern, M.D., M.P.H.

N ENGL J MED 373;5 NEJM.ORG JULY 30, 2015

Acute & Congenital Infections = 80-100%

Treatment Efficacy

Chagas' Disease

Caryn Bern, M.D., M.P.H.

N ENGL J MED 373;5 NEJM.ORG JULY 30, 2015

Early Chronic Infections (≤18 y.o.) = ~60%

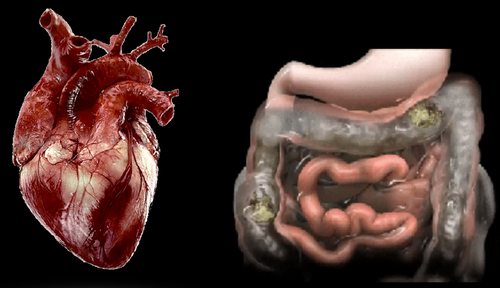
Treatment Efficacy

Chagas' Disease

Caryn Bern, M.D., M.P.H.

N ENGL J MED 373;5 NEJM.ORG JULY 30, 2015

Other Chronic Infections (>18 y.o.)



No evidence of, or unknown, treatment efficacy

Screening in the United States

1. Born or lived for >6 months in endemic area

Screening in the United States

2 Close (first-degree) relative of someone diagnosed

Screening in the United States

3 Exposure to traitomine species capable of transmitting *Trypanosoma cruzi*…including in the U.S.A.

San Antonio, Texas

Screening in the United States

4 Traveled to endemic areas with confirmed exposure to triatomines

Screening in the United States

5 Women of childbearing age who lived in endemic areas

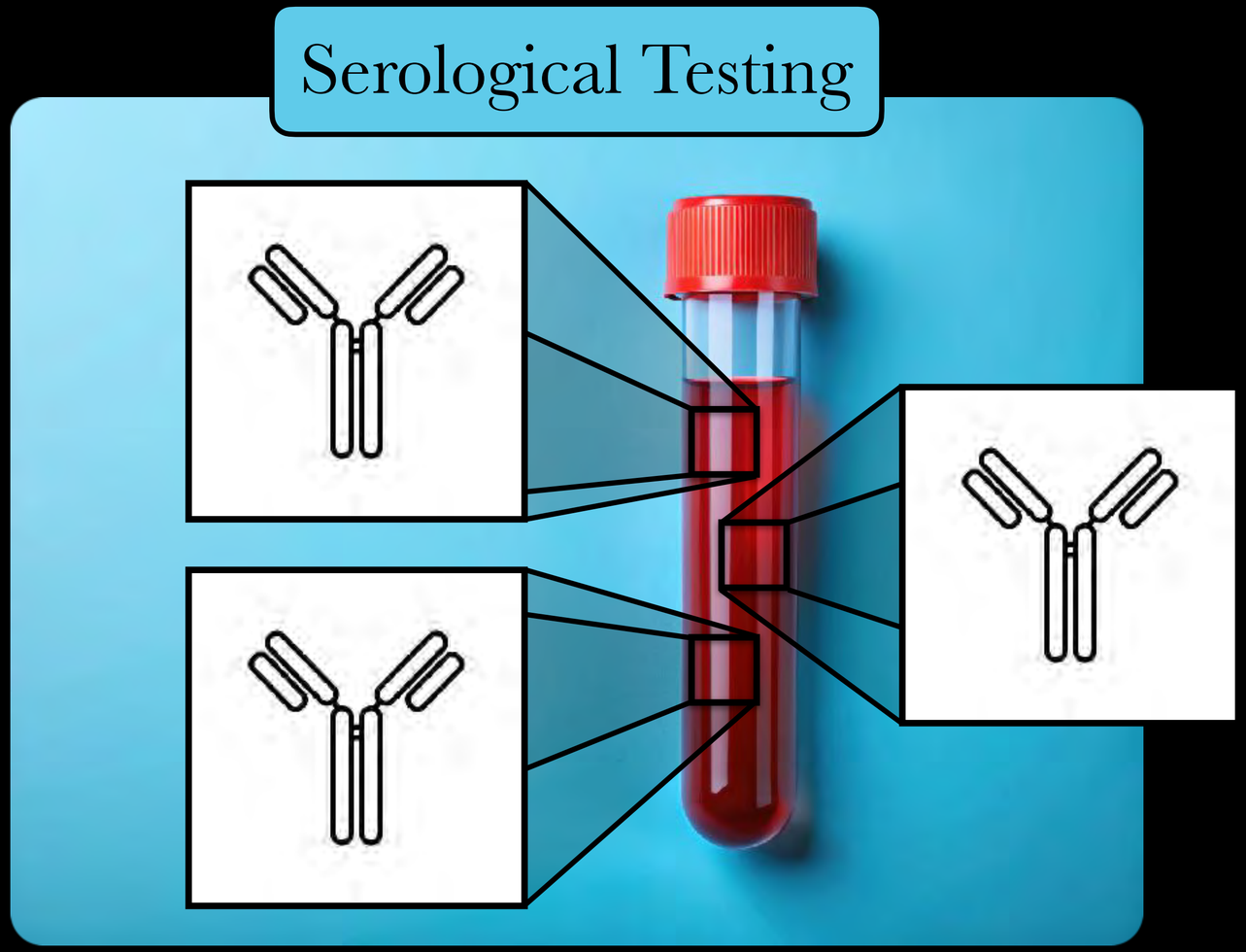
**Pregnancy

Screening in the United States

6 Epidemiologic Risk Factors and…

- ECG abnormalities
- Regional Wall Motion Abnormalities
- Thromboembolic Phenomenon
- Reduced Ejection Fraction/CHF
- Megacolon/Megaesophagus

Screening in the United States



4 FDA Approved Serological Tests:

Ortho *T. cruzi* ELISA

Hemagen Chagas' kit ELISA

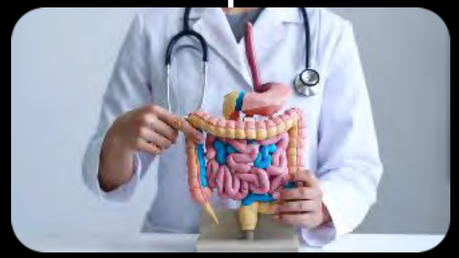
Weiner Chagatest Recombinante 3.0 ELISA

InBios Chagas Detect Plus

CDC Contact Information for Chagas Testing:

parasites@cdc.gov (404) 718-4745

What to do if someone is positive…



San Antonio, Texas

If Immune Compromise…

Chagas Disease: "The New HIV/AIDS of the Americas"

Peter J. Hotez[1,2*], Eric Dumonteil[3], Laila Woc-Colburn[2,4], Jose A. Serpa[2,4], Sarah Bezek[2,5], Morven S. Edwards[2,6], Camden J. Hallmark[2,7], Laura W. Musselwhite[8], Benjamin J. Flink[8], Maria Elena Bottazzi[1,2]

PLoS NEGLECTED TROPICAL DISEASES

www.plosntds.org

May 2012 | Volume 6 | Issue 5 | e1498

…a burden of disease in the Latin American & Caribbean region…approximates or even exceeds that resulting from HIV/AIDS.

…prevalence (of Chagas) exceeded only by hookworm and other soil-transmitted helminth infections.

…especially high burden of disease in ***Texas*** and along the Gulf coast…

Bed Bugs (*Cimex lectularius*)

Bed Bugs (*Cimex lectularius*) as Vectors of *Trypanosoma cruzi*

Renzo Salazar, Ricardo Castillo-Neyra, Aaron W. Tustin, Katty Borrini-Mayorí, César Náquira, and Michael Z. Levy*
Chagas Disease Field Laboratory, Universidad Peruana Cayetano Heredia, Arequipa, Peru; Department of Epidemiology, Johns Hopkin Bloomberg School of Public Health, Baltimore, Maryland; Center for Clinical Epidemiology and Biostatistics, University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania

Am. J. Trop. Med. Hyg., 92(2), 2015, pp. 331–335

Murine (mouse) model

Bidirectional transmission of *T. cruzi*

Fecal quantitative *T. cruzi* levels similar

Bed Bugs (*Cimex lectularius*)

Survival and Transstadial Persistence of *Trypanosoma cruzi* in the bed bug (Hemiptera: Cimicidae)

Brittny N. Blakely,[1] Stephen F. Hanson,[1] and Alvaro Romero[1,2]

Journal of Medical Entomology, 55(3), 2018, 742–746

Both nymphs and adults can carry *T. cruzi*

T. Cruzi persisted across stadia (molts)

T. Cruzi persisted in adults postinfection *at least* 97 days

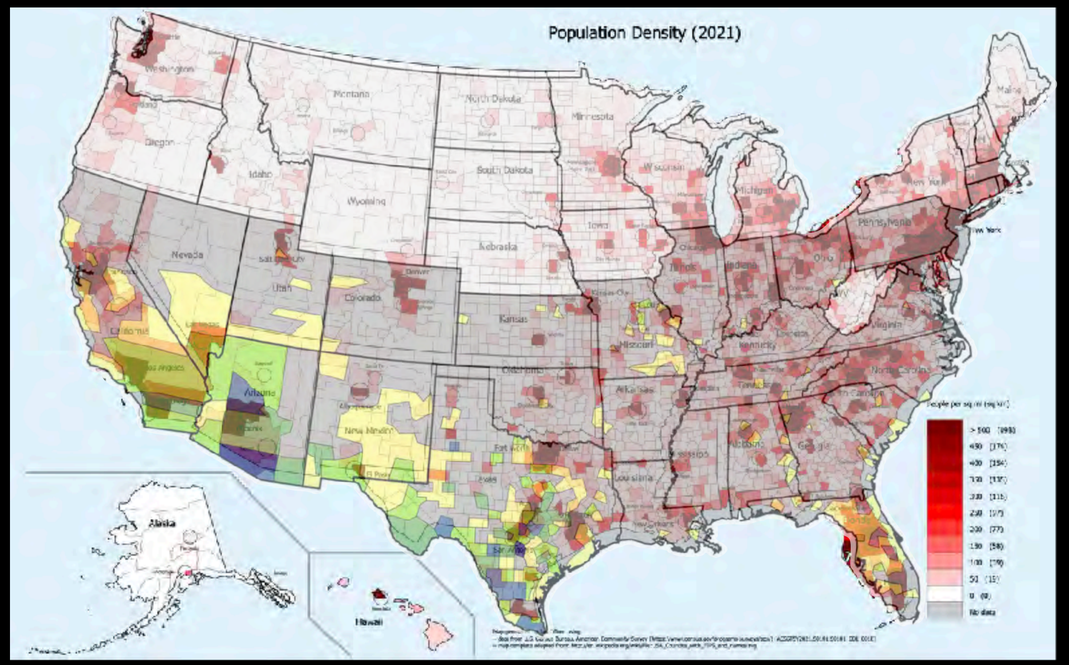
Bed Bugs (*Cimex lectularius*)

Most Common Places Pest Control Companies find Bed Bugs:

Single Family Homes	91%
Apartments/Condominiums	89%
Hotels/Motels	68%
Nursing Homes	59%
Schools & Day Care Centers	47%
Office Buildings	46%
College Dorms	45%
Hospitals	36%
Public Transportation	19%

Bed Bugs (*Cimex lectularius*)

They feed on mammals, including cats & dogs, but *PREFER HUMANS*.



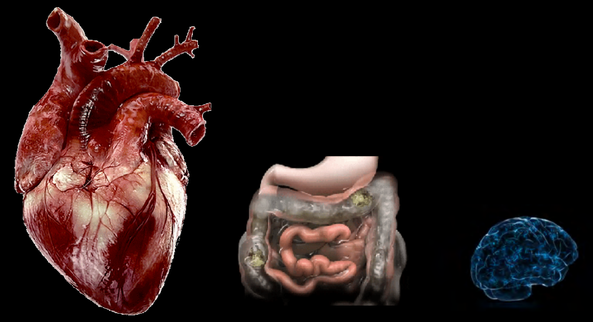
Texas State Hospital (1861)…Austin, TX

Ardzroony Packchanian (U.S. Public Health Service)

Summarizing Chagas (American Trypanosomiasis)

Triatominae “bug”

Trypanosoma cruzi



Benznidazole

Rochagan
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Nifurtimox

Lampit
(nitrofuran)

San Antonio, Texas

Sphecius speciosus
Cicada Killer Wasp
"Cicada Hawk"

Just in case you don't want to sleep now.

Remember, everything is bigger in Texas.

Questions?