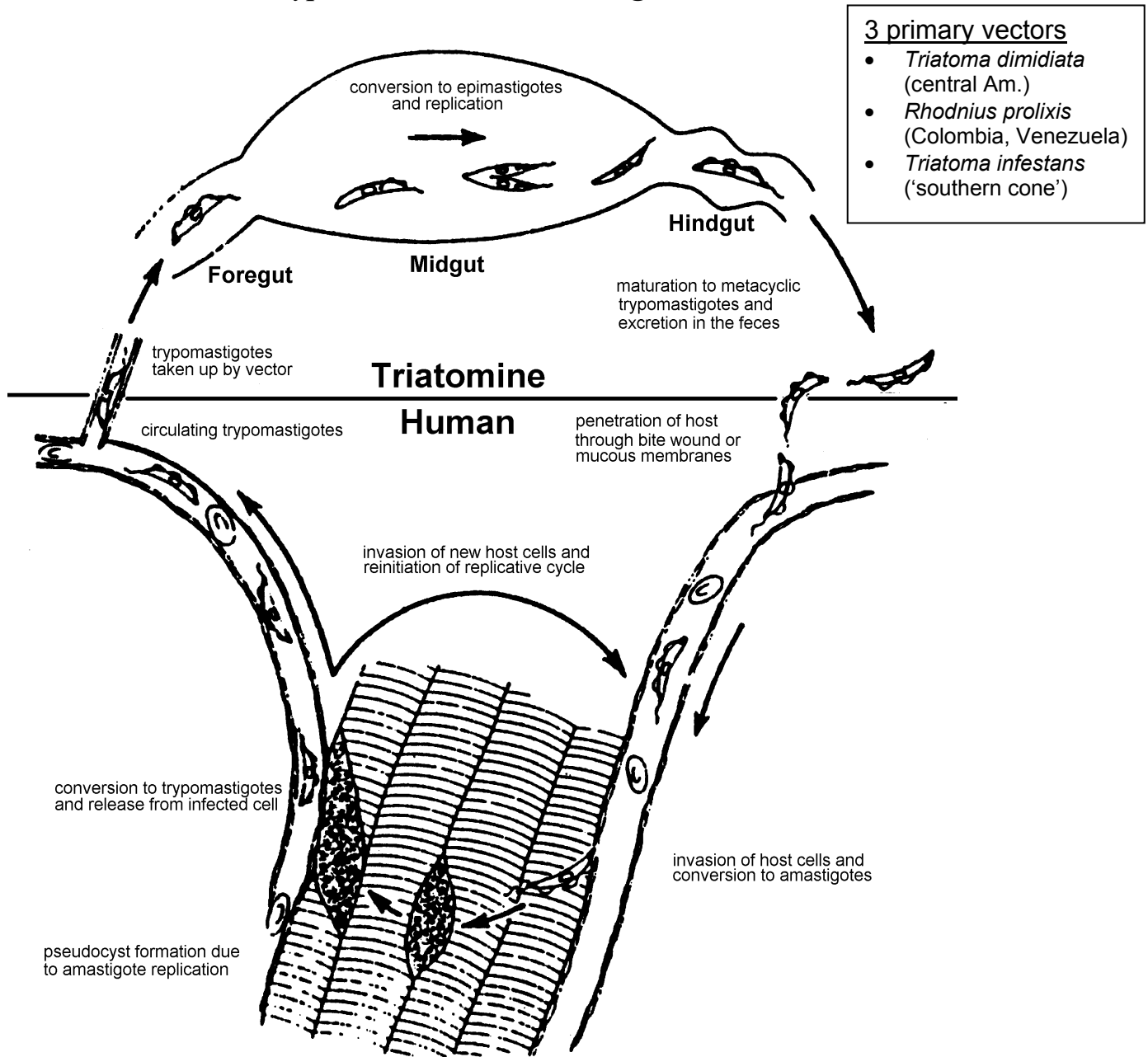


Trypanosoma cruzi and Chagas Disease



***Trypanosoma cruzi* life cycle.** *T. cruzi* is transmitted to the vertebrate host by three different species of the Reduviidae family (*Triatoma*, *Rhodnius*, *Panstrongylus*) commonly called triatomine bugs. While taking a blood meal the triatomines will defecate and infective **metacyclic trypomastigotes** are excreted with the feces. The trypomastigotes can gain access to the vertebrate host by entering through the bite wound, mucous membranes, or hair follicles. Infection is often associated with rubbing the infected fecal material into the bite wound or eyes while sleeping. The trypomastigotes invade a host cell and transform into **amastigotes**, which replicate by binary fission within the cytoplasm of the host cell. This mass of amastigotes within an infected cell is sometimes called a **pseudocyst**. The amastigotes will differentiate into back into trypomastigotes and be released from the infected cell. These trypomastigotes can invade another cell and repeat the replicative process, or enter the circulatory system and be taken up by a triatomine bug during feeding. Within the vector's midgut the parasite differentiates to an

epimastigote and undergoes multiple rounds of binary fission. The epimastigotes quit dividing and differentiate back into metacyclic trypomastigotes in the hindgut.

Modes of Transmission

SOURCE	COMMENTS
Vector	Natural transmission by triatomine bugs through contamination by post-prandial infected feces.
Transfusion	A prevalent mode of transmission in urban areas. Gentian violet treatment (24 hr) eliminates parasites in blood.
Congenital	Occurs during any stage of <i>T. cruzi</i> infection. Can result in premature labor, abortion neonatal death.
Accidental	Ingestion of food contaminated with triatomine feces. Laboratory accidents.

Types of Vector Transmission

Salivarian	Stercorarian
<ul style="list-style-type: none"> • transmission via mouth parts • very efficient • infection rate in vector is low 	<ul style="list-style-type: none"> • hind gut station • acquired from feces or eating vector • inefficient • infection rate in vector is high

Factors Influencing Human Transmission

- ‘early’ defecation (i.e., during triatomine feeding)
- colonization of human habitats
 - adobe walls
 - thatched roofs
- para-domiciliary cycles
 - animal stalls adjacent to domicile
- proximity to sylvatic cycle

CHAGAS CONTROL

- improvement of human dwellings
- separation of animal stalls from house
- insecticides: residual sprays, fumigant canisters, etc.
- health education
- gentian violet in blood for transfusions

Clinical Course of Chagas

- **acute phase**
 - ◆ active infection
 - ◆ 3-4 months
 - ◆ majority asymptomatic
- **indeterminate phase**
 - ◆ 10-30 years of latency
 - ◆ no detectable parasitemia
 - ◆ relatively asymptomatic
 - ◆ seropositive
- **chronic phase**
 - ◆ 10-30% of infected persons
 - ◆ myocarditis, cardiomyopathy
 - ◆ congestive heart failure
 - ◆ megasyndromes
 - ◆ paucity of parasites

Chronic Chagas' Cardiomyopathy

Clinical Presentation

- arrhythmias[†]
- conduction defects
- congestive heart failure[†]
- thromboembolic phenomenon

Pathology

- cardiomegaly
- apical aneurysm (left ventricle)
- hypertrophy*
- extensive fibrosis*
- cellular infiltration

[†]typical cause of death

*correlates best with clinical symptoms

MEGAVISCERAE

- prevalence varies by geographical zones
- colon and esophagus most frequently affected
- megaesophagus: painful swallowing, regurgitation
- megacolon: severe constipation
- destruction of parasympathetic neurons → dilation

Basis of Pathogenesis?

- autoimmunity?
 - few (if any) parasites
 - anti-self responses (both antibody and cellular)
 - slow development
 - organ specificity
- altered immune response?
 - Th1 → Th2 switch correlated with severe disease
- chagasic factor or toxin?
 - proposed, but not found
- parasite-mediated destruction?
 - persistent low level parasitemia
 - correlation between parasites and inflammation
 - exacerbated by immune suppression
 - successful treatment of chronic patients

DIAGNOSIS

- history of living in infested house
- bug bite, chagoma, Romana's sign
- cardiac or gastrointestinal symptoms

- detection of parasite (acute)
 - ◆ direct examination
 - ◆ stained blood smears
 - ◆ inoculation into mice
 - ◆ in vitro culture
 - ◆ xenodiagnosis
 - ◆ biopsy

- serology (chronic)
 - ◆ complement fixation
 - ◆ immunofluorescence
 - ◆ ELISA

TREATMENT

- acute stage
 - ◆ nifurtimox (8-16 mg/kg/day, 60-90 days)
 - ◆ benznidazole (5-7 mg/kg/day, 30-120 days)
 - ◆ allopurinol (experimental)

- chronic stage
 - ◆ treat symptoms

Viotta et al (1994) *Am. Heart J.* 127:151

Sero-positive patients were treated with benzidazole (5 mg/kg/day, 30 days) and followed for 8 years.

% of patients exhibiting

	treated (131)	control (70)
electrocardiogram changes	4%	30%
deterioration in clinical condition	2%	17%
sero-negative conversion	19%	6%

Lauria-Pires et al (2000) *AJTMH* 63:111

- Brasilia street cleaners ± treatment
 - standard treatment with nifurtimox or benznidazole
 - 10 year follow up
- treated vs. untreated:
 - no parasitological cure (PCR)
 - no sero-negative conversion
 - no ECG improvements
- administration of nitroderivatives
 - severe side effects
 - compliance problems