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Understanding Chagas Disease: Essential Insights for U.S. Military Health

Learning Objectives:

- Describe the epidemiology and pathophysiology of Chagas cardiomyopathy
- Review the current Chagas screening programs throughout the military
- Describe military-unique challenges to diagnosing and treating Chagas disease

Discussion Facilitator:

Paula Stigler Granados, PhD

Division of Environmental Health
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School of Public Health



The South Coastal Area Health Education Center (SCAHEC) is accredited by the Texas Medical Association (TMA) to provide continuing medical education for physicians. South Coastal Area Health Education Center designates this live educational activity for a maximum of 4 AMA PRA Category 1 credit(s)[™] (1 per session). Physicians should only claim credit commensurate with the extent of their participation in the activity.



Presenters:

MAJ Joseph Marcus, MD

Infectious Disease Physician
Brooke Army Medical Center
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Rachel Marcus, MD

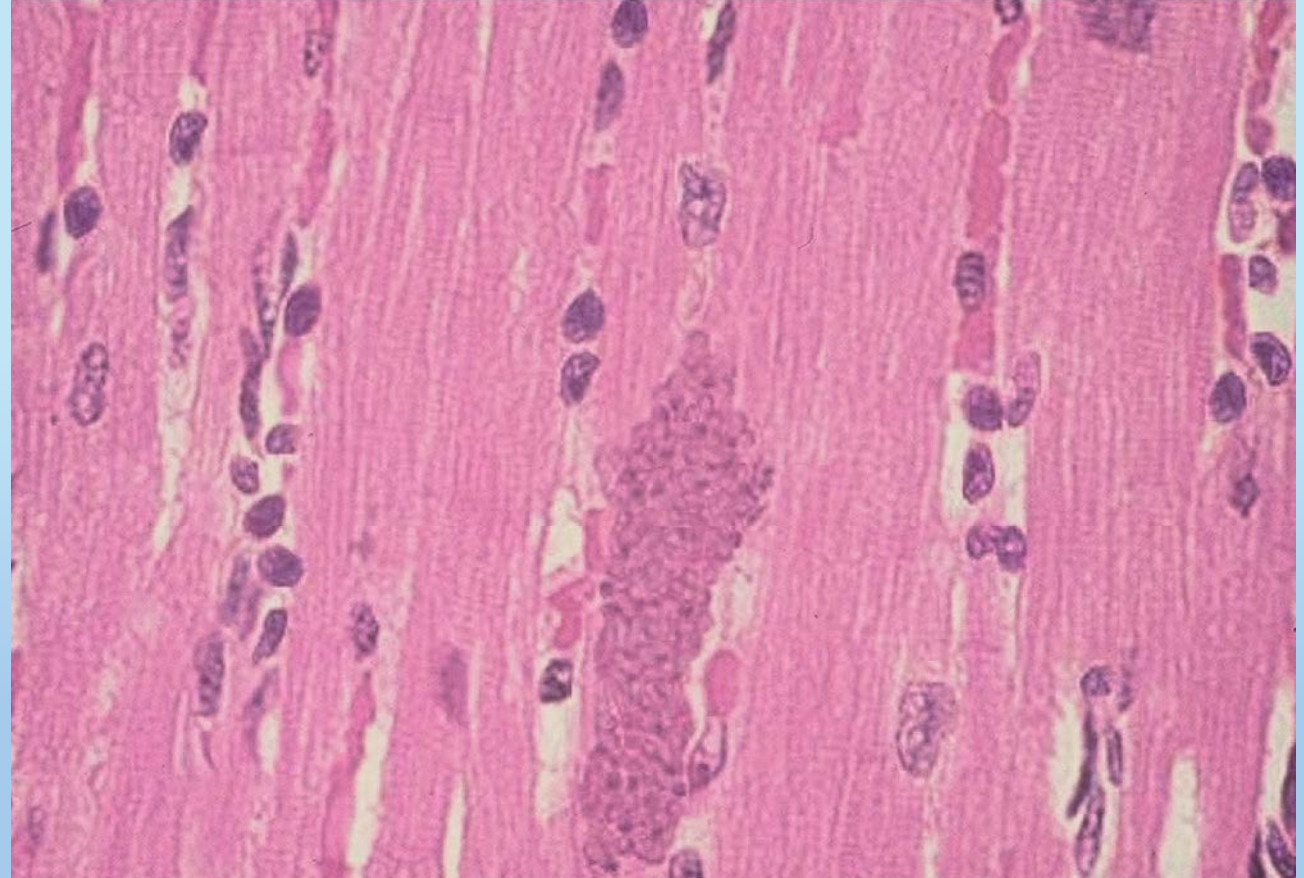
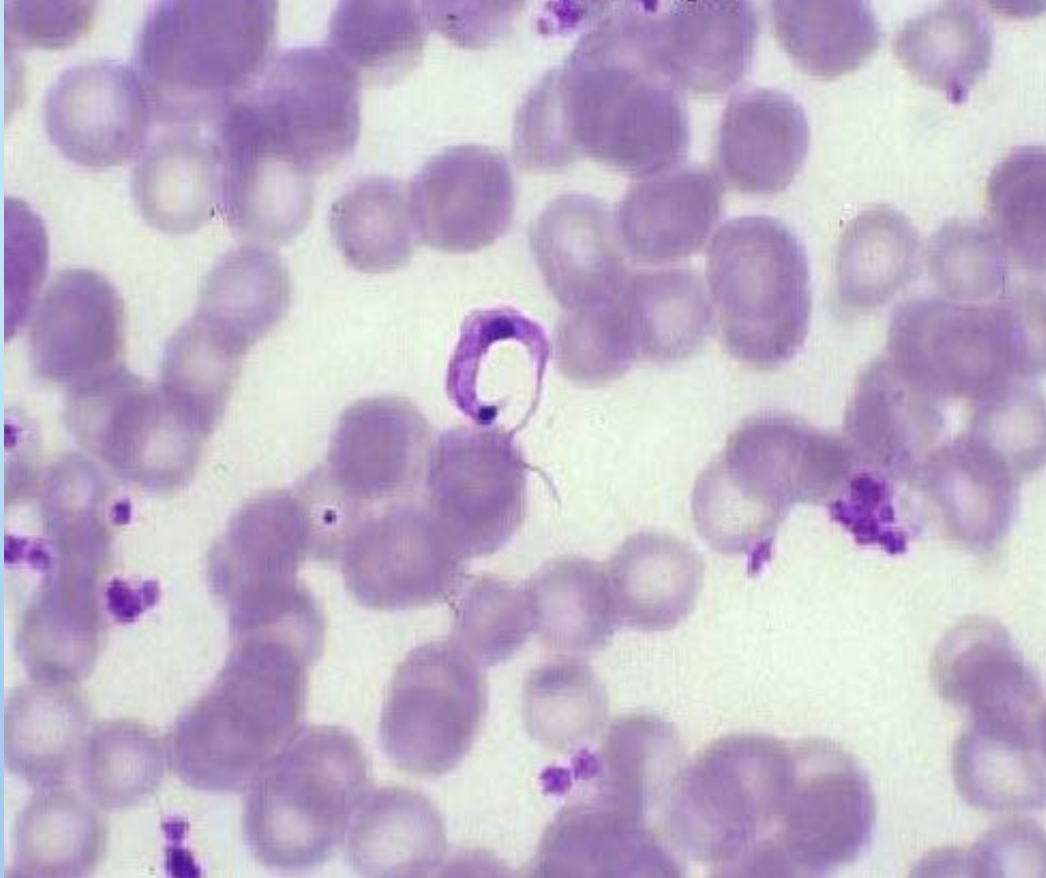
Cardiologist
Regional Director of Echocardiography,
Medstar North

Learn more at: [UTHealth ECHO - Chagas Disease](#)



NTD: Nothing to Disclose

What is Chagas Disease?

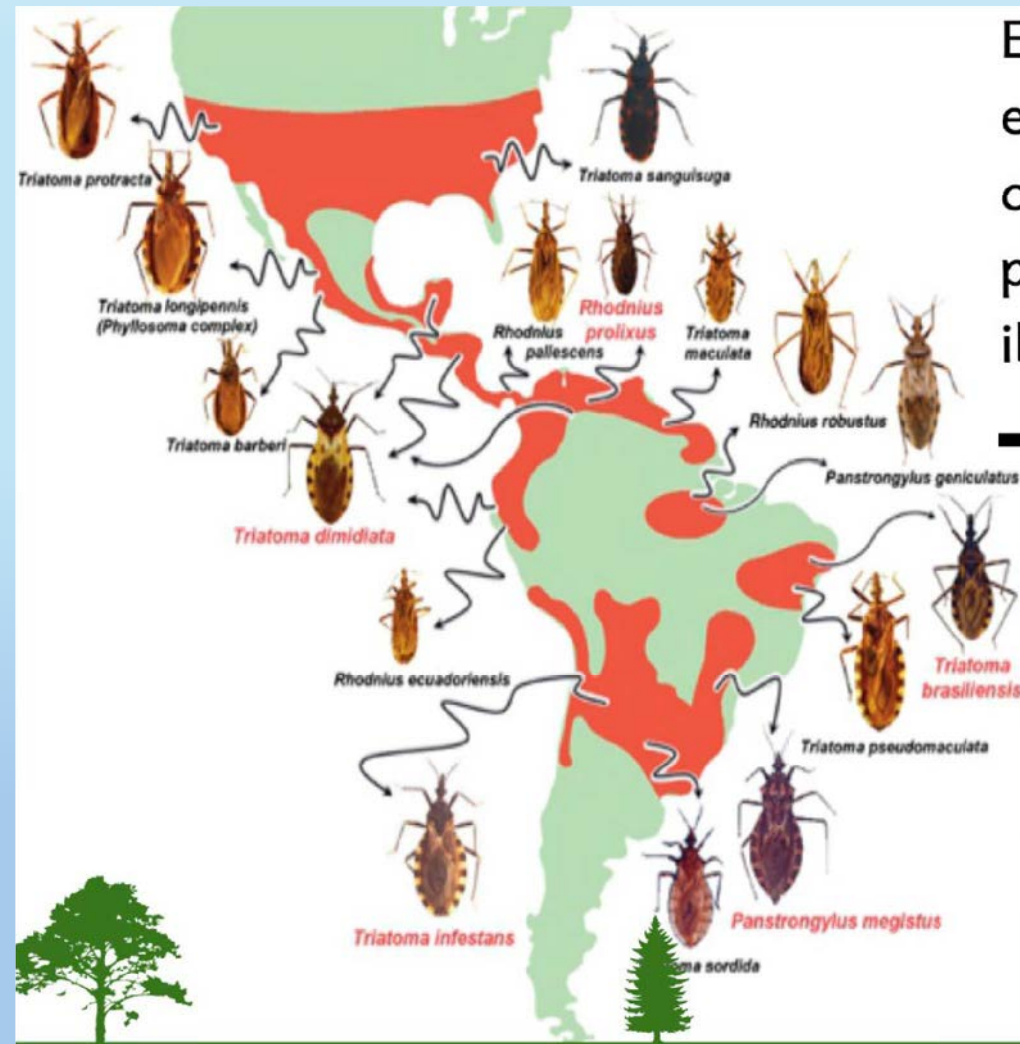




Courtesy of World Health Organization

Vector: Triatomine Insect, Reduviid Bug

- Kissing Bug
- Insecto asesino
- Vinchuca
- Chinche
- Barbeiro
- Chipo
- Pito



Triatomine having dinner



Clinical Course: Acute Phase

- Non-specific symptoms: malaise, adenopathy. Frequently not remembered as an adult. Lasts 6-8 wks.
- 5-10% clinically important presentation with myocarditis/meningoencephalitis which in <5% can be fatal.
- Parasitemia is present/treatment with antiparasitic medications effective for “cure” in 70-90%
- 10% leave childhood with an ECG abnormality suggesting chronic cardiac disease



World Health Organization

Romaña's sign

Other Acute Presentations

- **Congenital Chagas**: asymptomatic, premature, hepatosplenomegaly, anemia, hydrops.
 - Can't use antibody tests to diagnose
- **Reactivation**:
 - Disease induced: HIV, malignancy: neuro
 - Medication induced: transplant immunosuppression : skin, cardiac
- Oral: unpasteurized juice
- Transfusion/**Donor Organ**

Clinical Course: Indeterminate Phase

- Without treatment, virtually everyone passes to this stage, no end organ manifestations except for subclinical autonomic dysfunction.

- Positive serology(2 forms)* PCR



- End of significant manifestations of illness for 70-80% of patients, 2%/year progress*.

Clinical Course: Chronic Phase

- At a minimum defined as positive serology and an abnormal ECG*.
- Presents 15-30 years after time of likely infection
- 20-30% of patients progress, not clear who, although more men have significant cardiac impairment. Degree of parasitemia? Reinfection? Manual labor? Strain type? Genetic factors in immune response.
- GI manifestations in 10%, more common in South America

Cardiac Pathophysiology

- **Parasite Persistence:** PCR evidence of parasite DNA in areas of lymphocytic infiltrate.
- **Immune and inflammation-mediated injury/dysregulation**
- **Microvascular abnormalities:** intimal proliferation/endarteritis, abnormal vasodilation: watershed ischemia
- **Autonomic derangements**

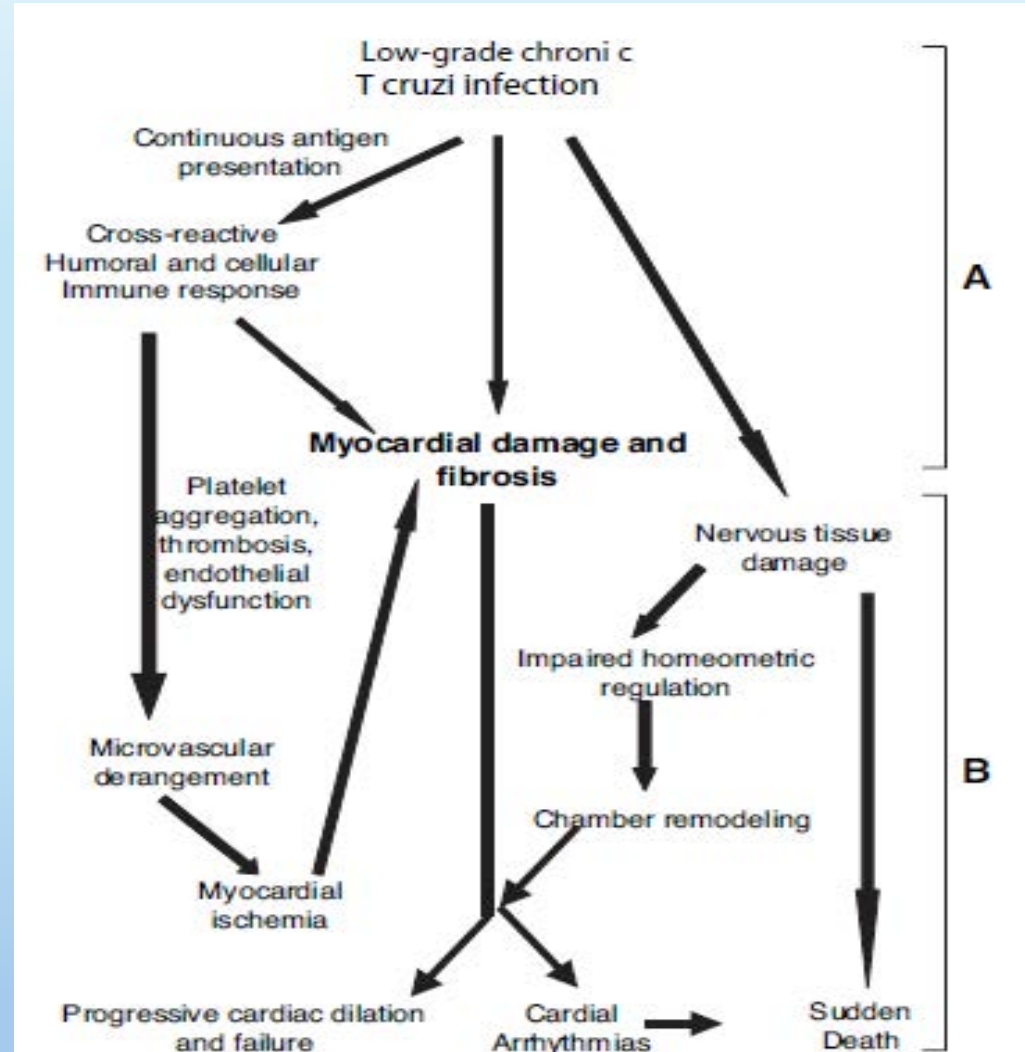


Figure 7. Schematic view of main pathogenetic mechanisms in chronic Chagas cardiomyopathy.

Cardiac Pathology

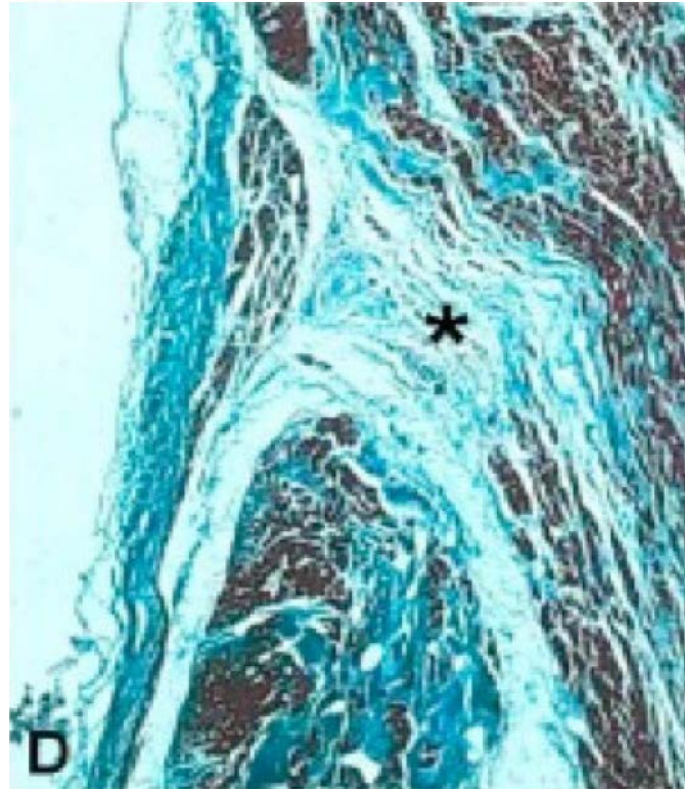


Fig. 3. Macroscopic and microscopic chagasic features, emphasizing the segmental myocardial fibrosis. (A) A chronic chagasic heart exhibits severe dilation of left and right ventricles plus thinning, fibrosis and thrombosis of the left ventricular apex (arrow). (B) A moderately dilated and hypertrophic left ventricle showing segmental fibrosis on the apex (arrow), considered to be a pathognomonic lesion of Chagas heart disease. (C) Fibrotic thinning of the myocardium adjacent to the mitral valve at the posterior wall of the left ventricle (arrow). (D) Microscopic view of the bifurcation of the His bundle showing segmental fibrosis (asterisk) at the origin of the right bundle branch (Masson trichrome, objective magnification: 2.5 \times).

Symptoms of Chronic Phase: Cardiac

- **Angina**, from microvascular disease
- **Exertional intolerance**: chronotropic incompetence
- **Palpitations/Syncope**: autonomic issues/brady/tachyarrhythmias*
- **CHF**: LV/RV dysfunction
- **Stroke**: apical aneurysm, afib*

Table 2. Recommendations for Screening and Diagnosis of Chagas Disease in the United States

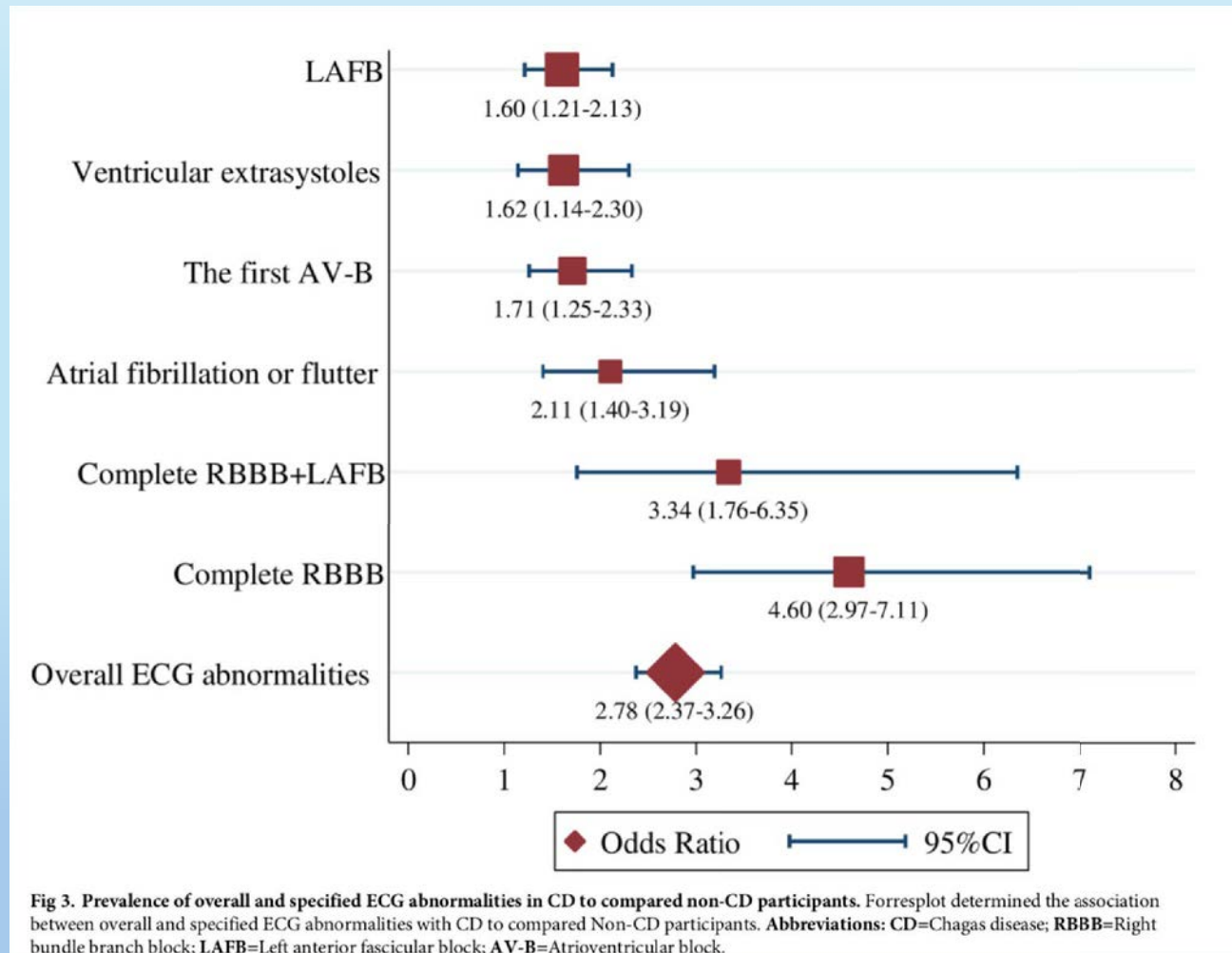
Recommendation	Strength	Quality of Evidence
Who should be screened for Chagas disease in the United States?		
People who were born or lived for a prolonged period (> 6 mo) in areas of Mexico, Central or South America with endemic Chagas disease	Strong	Low
Close (first-degree) relatives of people previously diagnosed with Chagas disease	Strong	Low
People with entomologically confirmed or highly suspected exposure (bites and/or triatomines/kissing bugs found in the home), in states with known presence of triatomine species capable of transmitting <i>Trypanosoma cruzi</i>	Conditional	Low
Travelers with confirmed exposure to triatomines or associated risk factors in regions of Latin America where Chagas disease is endemic	Conditional	Low
Women of childbearing age who have lived in a region of Mexico, South or Central America with endemic Chagas disease	Strong	Moderate

ECG with 30 second rhythm strip

- The main diagnostic criteria for chronic phase.

Meta-analysis of ECG findings

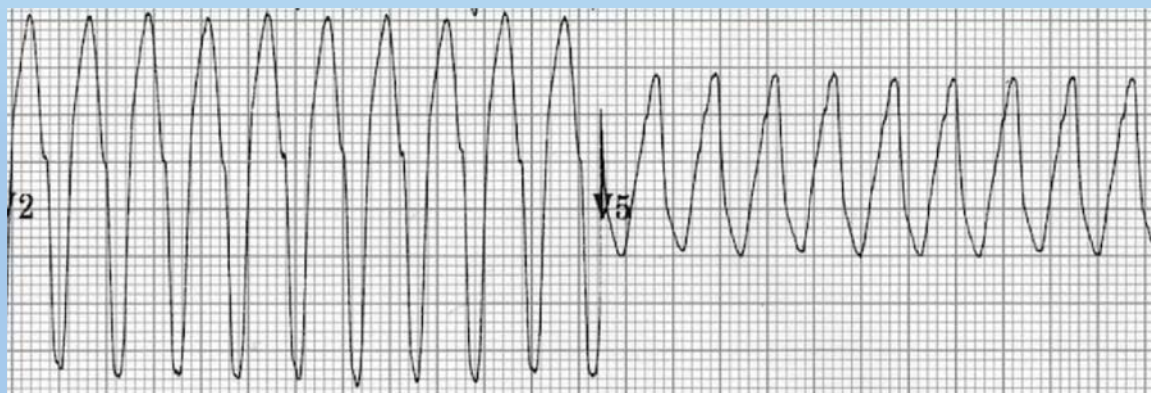
PLoS Negl Trop Dis 12 June 13, 2018(6): e0006567





Rhythm Monitoring

- Not necessary with normal ECG/Echo/asymptomatic
- Frequent brady/tachyarrhythmias, signs of autonomic dysfunction
- NSVT poor prognostic sign



Echo in Chagas

Table 1 Stages of ChHD

Acute Phase	Chronic Phase				
	Indeterminate Form, A	Chagas Cardiomyopathy			
		B1	B2	C	D
Infected by <i>T. cruzi</i> and findings of acute ChD	Positive serology Normal ECG findings No heart disease or HF	Structural cardiomyopathy (abnormal ECG or echocardiographic findings) but normal LV function No HF	LV dysfunction No HF	LV dysfunction HF (current or prior)	Refractory HF despite optimal medical therapy

Normal*

WMA

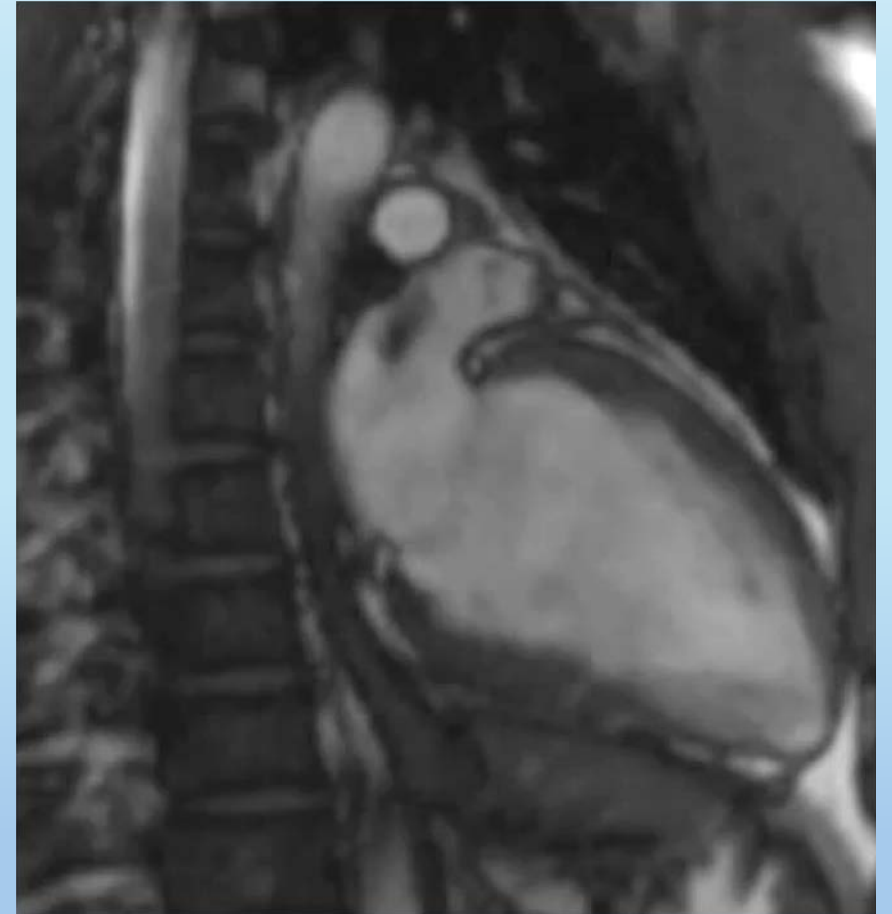
WMA +low EF

Wall motion: Basal inferior, inferolateral, apical aneurysm

Diastology, strain

MRI in Chagas disease

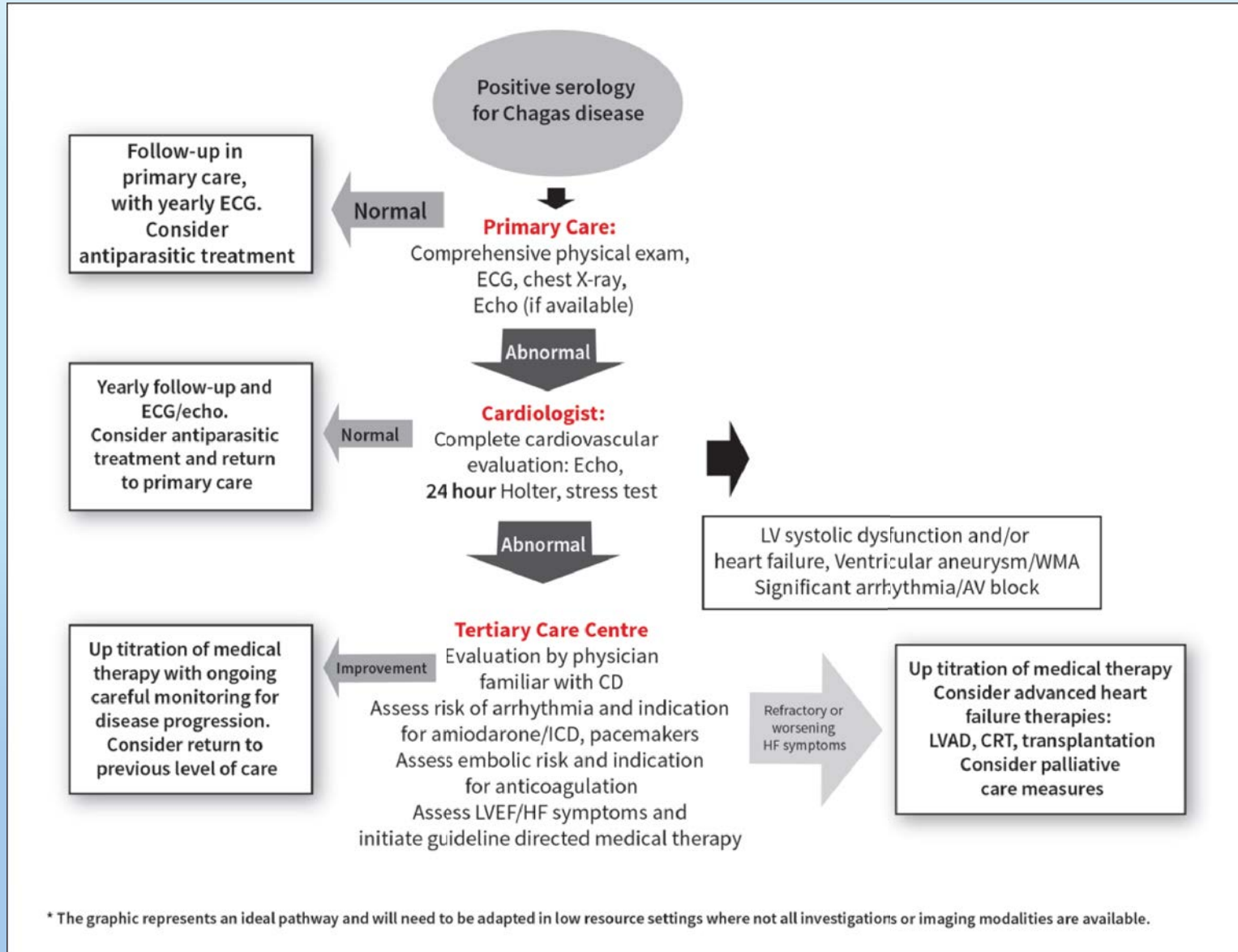
- Many studies have shown association of LGE with Chagas
- Indeterminate phase patients can have scar, significance is not yet known: 8-40%.
- Magnitude of scar is associated with worse outcomes, role in risk stratification for AICD?



How do I treat my patient?

Diagnostic/Treatment Algorithm

WHF Roadmap Chagas Disease



What's the data for antiparasitic treatment?

- Seronegativization from rx in children*
- Observational data suggests significant decrease in risk of transplacental passage in women of childbearing age
- Randomized trial evidence in indeterminate phase only looks at serologic/PCR endpoints, none have assessed impact on disease progression.

Category	PAHO recommendation	Recommendation level	Strength of evidence
Acute infection	Administer anti-trypanosomal treatment	Strong	Moderate
Congenital infection	Administer anti-trypanosomal treatment	Strong	Moderate
Children with chronic infection	Administer anti-trypanosomal treatment	Strong	Moderate
Females of childbearing age (15-44)	Administer anti-trypanosomal treatment	Strong	Moderate
Adults with chronic infection, no organ involvement	Offer anti-trypanosomal treatment	Conditional	Low
Adults with chronic infection, moderate to severe organ involvement	Do not offer any anti-trypanosomal treatment	Conditional	Moderate
Reactivation in immunocompromised patients*	Administer anti-trypanosomal treatment	Strong	Low
Cases of laboratory or surgical accidents	Administer anti-trypanosomal treatment	Strong	Low

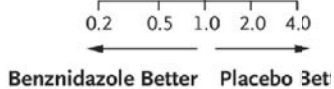
Figure 10: Anti-trypanosomal Treatment Recommendation. Adapted from Guidelines for the diagnosis and treatment of Chagas disease. Washington, DC: PAHO; 2019.

Antiparasitic therapy

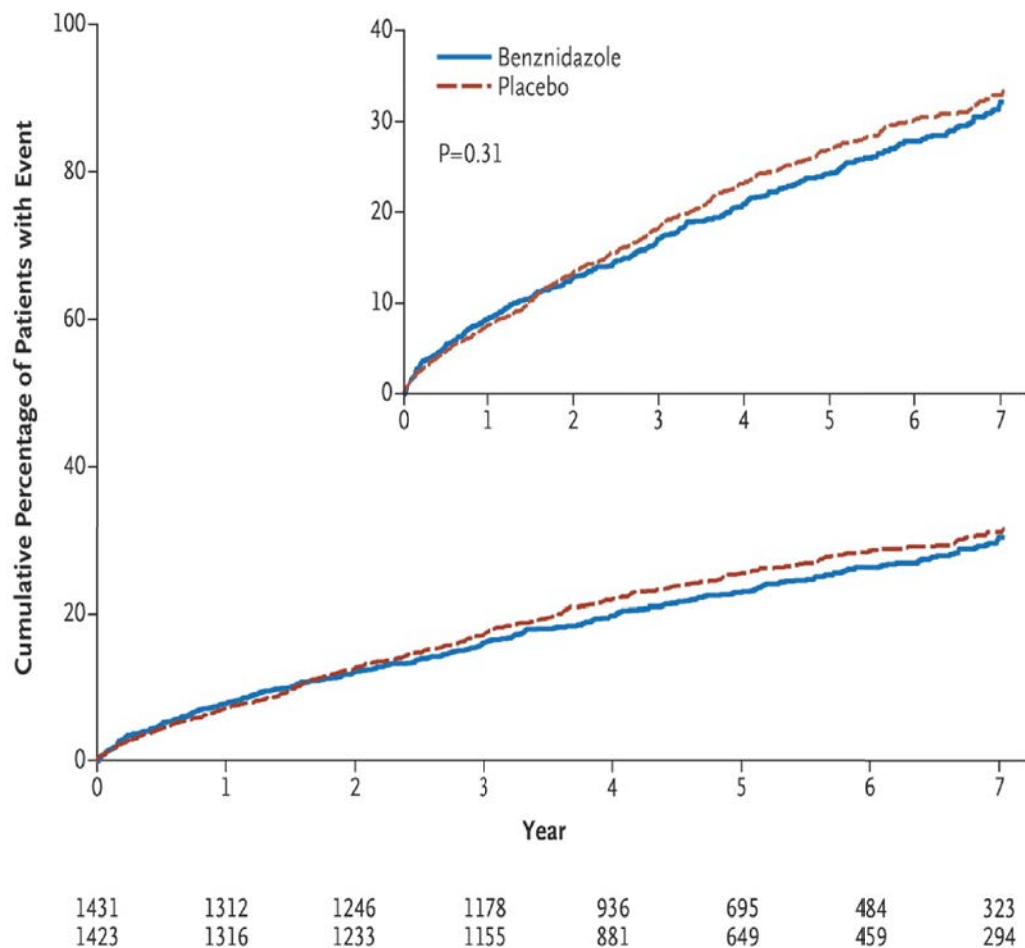
- **Benznidazole:** 2 nitro-imidazole
 - 5-7mg/kg po in divided doses 60 days*.
 - Frequent **rash**/wt loss/HA/late polyneuropathy
 - 65-85% finish Rx
- **Nifurtimox:** 5-nitrofurran
 - 8-10mg/kg divided TID-QID po x 90 days
 - Only 50% complete course
 - Skin, GI, psychiatric

Help in CCC?

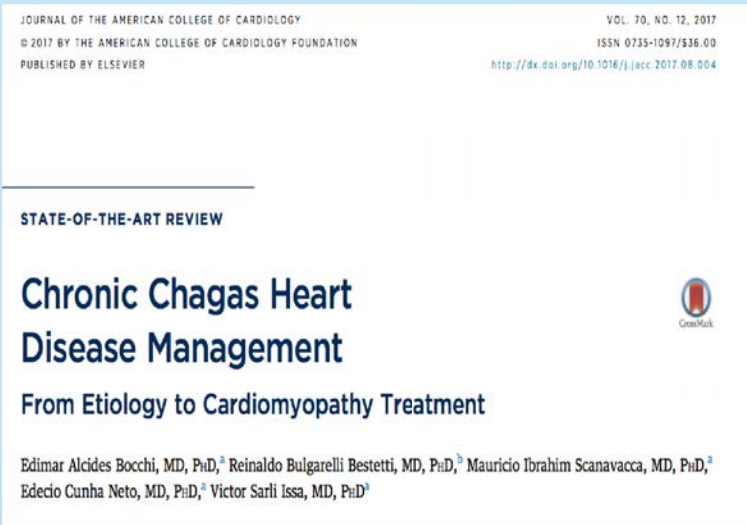
Subgroup	No. of Patients	Benznidazole % of patients	Placebo % of patients	Hazard Ratio (95% CI)	P Value for Interaction
Country					0.16
Colombia or El Salvador	580	24.1	25.6	NEJM 2015;373:1295-1306	
Brazil	1358	33.2	37.6		
Argentina or Bolivia	916	21.4	18.5		
PCR status at baseline					0.96
Positive	1148	24.6	26.9		
Negative	748	23.7	25.3		
Age					0.56
≤56 yr	1428	22.8	25.6		
>56 yr	1426	32.1	32.7		
Sex					
Female	1445	24.1	25.1		
Male	1409	30.8	33.4		
Disease-severity score					
Low	1309	16.8	16.2		
Intermediate	890	29.9	33.3		
High	655	45.1	50.0		
Left ventricular ejection fraction					
<40%	389	62.5	63.0		
≥40%	2465	21.8	23.9		
Left ventricular end diastolic diameter					
<50 mm	674	13.7	17.9		
≥50 mm	1548	34.6	36.6		
Use of amiodarone					
No	2302	24.7	24.1		
Yes	551	39.1	50.9		
Use of spironolactone					
No	2375	21.6	23.5		
Yes	478	56.8	57.0		
Regional wall-motion abnormality					
No	1397	21.2	22.4		
Yes	853	41.1	43.6		
Low QRS voltage					
No	2342	28.7	29.9		
Yes	341	25.8	28.2		
RBBB and left anterior fascicular block					
No	1946	28.6	29.2		
Yes	907	25.4	29.0		



No. at Risk
Benznidazole
Placebo



Management of Chagas Heart Disease



Circulation

AHA SCIENTIFIC STATEMENT

Chagas Cardiomyopathy: An Update of Current Clinical Knowledge and Management

A Scientific Statement From the American Heart Association

Endorsed by the Inter-American Society of Cardiology

Marin-Neto, Rassi Jr et al.
Diretriz da SBC sobre Diagnóstico e Tratamento de Pacientes com Cardiomiopatia da Doença de Chagas – 2023

Diretrizes

Diretriz da SBC sobre Diagnóstico e Tratamento de Pacientes com Cardiomiopatia da Doença de Chagas – 2023

SBC Guideline on the Diagnosis and Treatment of Patients with Cardiomyopathy of Chagas Disease – 2023

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