

# Case Study

- Jose
- 46 years old
- California, USA
- Admitted to hospital with chest pain, shortness of breath
- Diagnosed with advanced heart failure

Chagas Disease

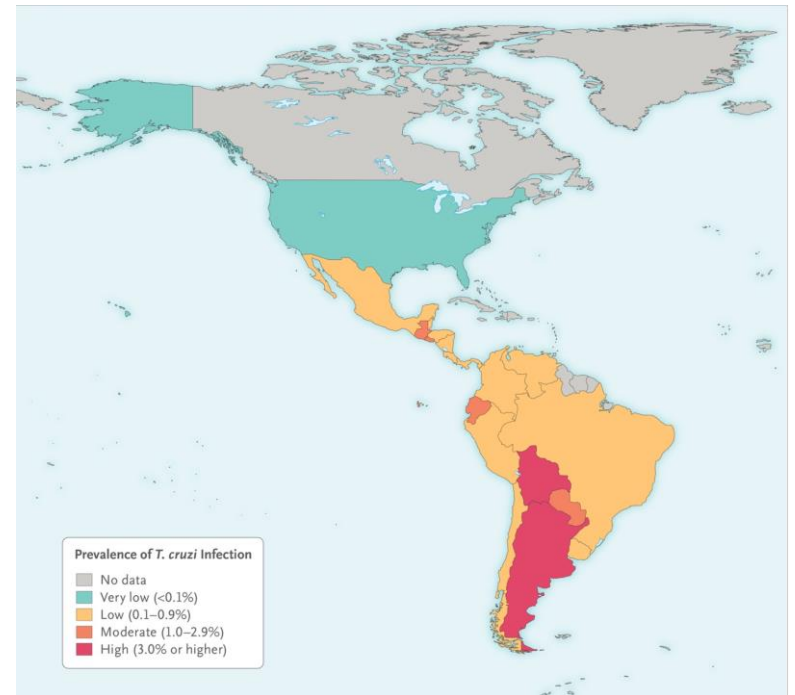
# History

- *Trypanosoma cruzi* (*T. cruzi*) was first discovered in a Chinchorro mummy (9000 years old)
- Miguel Diaz Pimenta recorded symptoms similar to Chagas disease in his book in 1707
- **Carlos Chagas** discovered Chagas disease in 1909



# Epidemiology

- Predominant in the continental part of Latin America
- Vectors prefer inhabiting the mud structures of villages and huts
- Infection rate: less than 1% per year
- Occurance rate has decreased: 18 million in 1991 vs 5.7 million in 2010



# Transmission

- Contact through feces of infected vector (*Triatoma infestans* → “kissing bugs”)
- Congenital contraction
- Contact with contaminated blood transfusions or donated organs
- Rarely with contaminated food/drink



Triatoma definition/meaning. (n.d.). Retrieved January 31, 2018, from <http://imagict.com/en/words/triatoma>



World Thalassaemia Day: 10 facts you must know about blood transfusion. (2015, May 08). Retrieved January 31, 2018, from <http://www.thehealthsite.com/diseases-conditions/ten-facts-you-need-to-know-about-blood-transfusion/>



Nadeau, M. (2016, August 03). *Healthy Alternatives for Junk Food*. Retrieved January 31, 2018, from <https://www.nautilusplus.com/healthy-alternatives-junk-food/>

# Symptoms of Chagas Disease

## Acute Phase

- After infection
  - Lasts first few weeks to months
- Swelling/redness at infection site
- Swollen lymph nodes
- Skin rash
- Fever
  - 95% of cases do not show symptoms



**Romana's sign:**  
Swelling of the eyelid

Swelling at the  
bite site



# Symptoms of Chagas Disease Cont'd...

## **Indeterminate Phase**

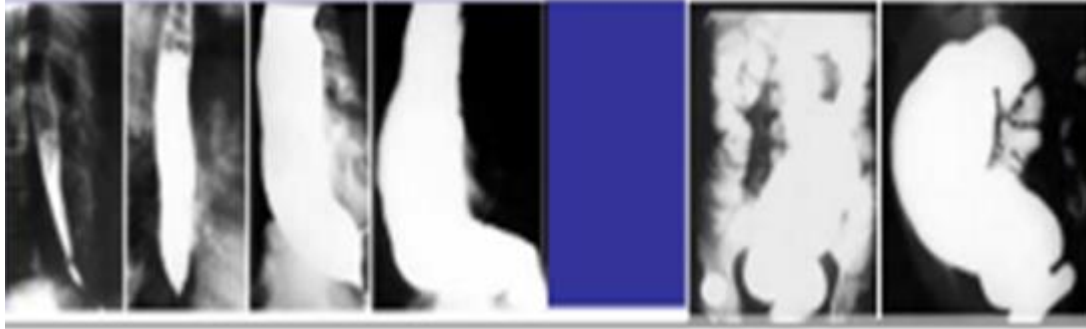
- No symptoms
- Lasts 10-20 years in patient's lifetime

## **Chronic Phase**

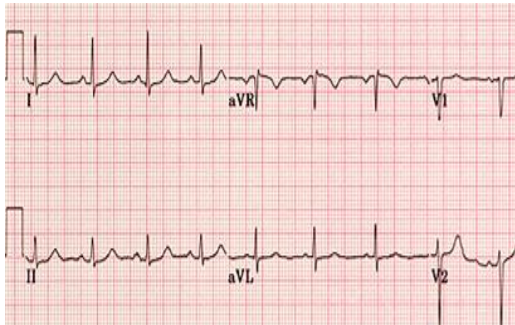
- Palpitations
- Cardiomyopathy
- Congestive Heart Failure (CHF)
- Chronic constipation
- Shortness of breath
- Emphysema
- Fainting

# Chronic Phase Signs

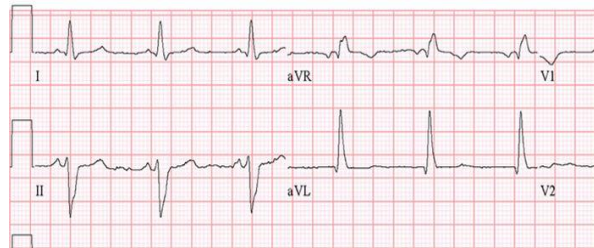
Rassi, A., (2014, July) Chagas' Heart Disease. World Congress of Cardiology Scientific Sessions, Australia.



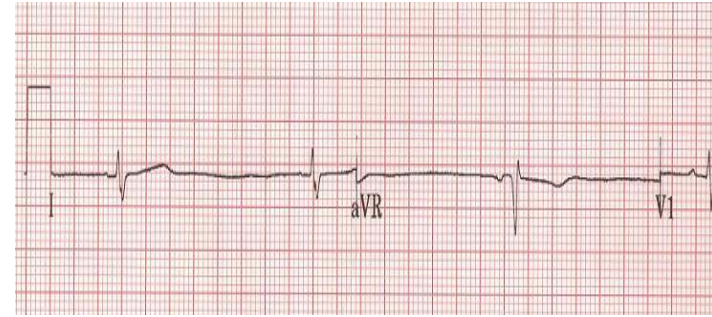
Associated megaesophagus and megacolon



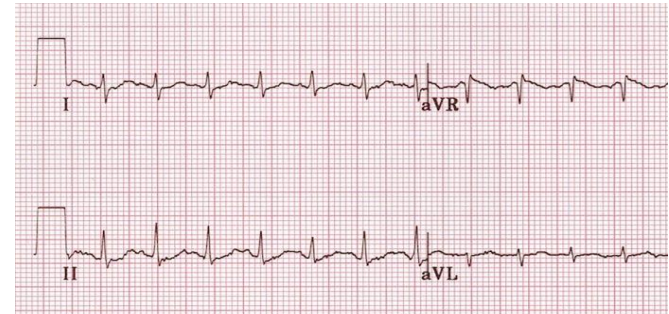
Normal ECG



Abnormal Q waves, AV blocks, a low QRS voltage, Sick Sinus Syndrome



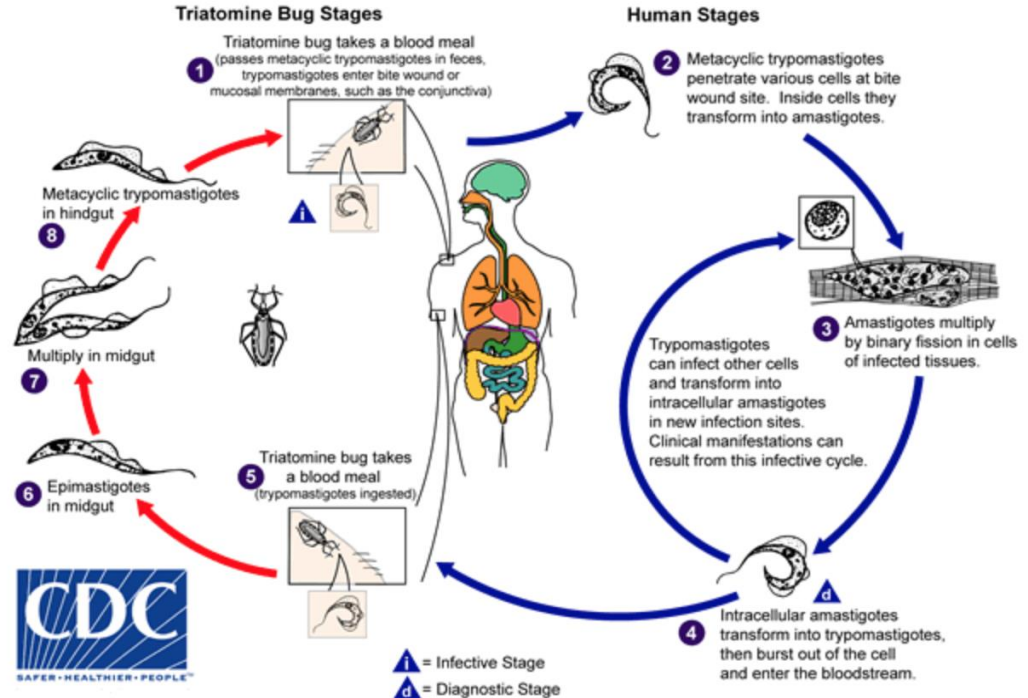
Bradyarrhythmia



Tachycardia

# Life Cycle of *T. cruzi*

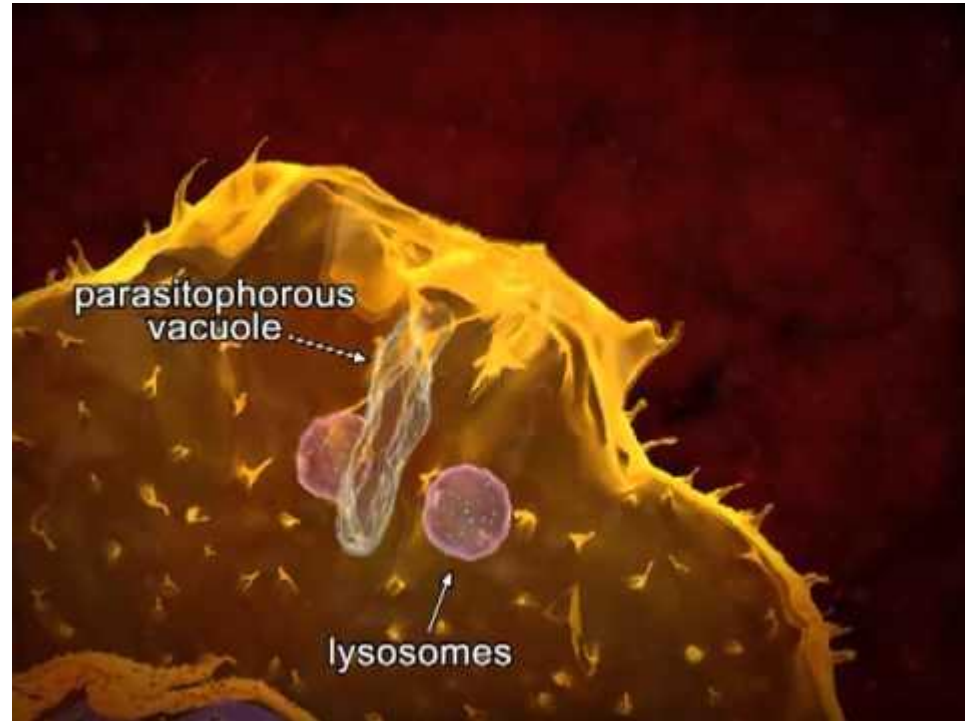
- Amastigotes = no flagella
- Trypomastigotes = has flagella
- Replicate inside the cells as amastigotes
- Burst out of the cells as trypomastigotes



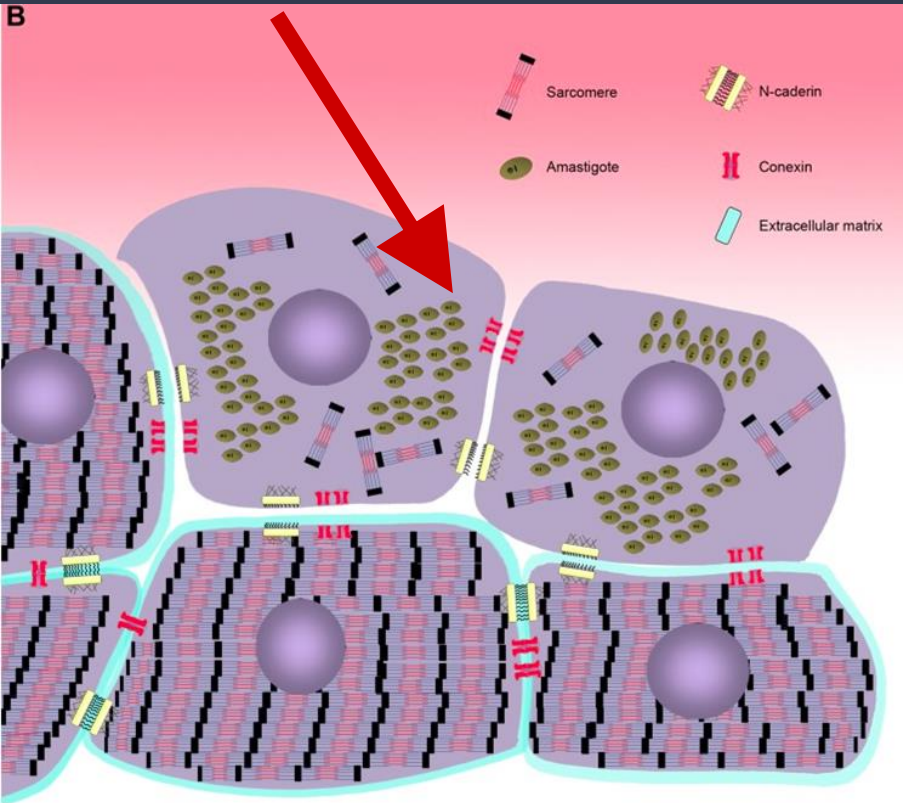


# Mechanisms - Step 1

- Recognition and recruitment of the immune system's macrophages
  - Internalization of the trypomastigote and amastigote at the site of insect bite via phagocytosis



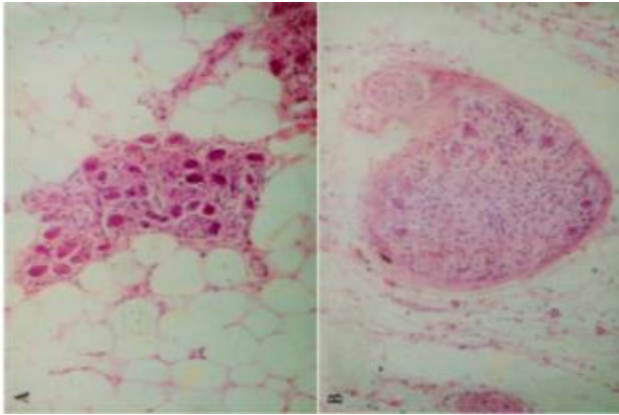
# Mechanisms - Step 2



- Internalization mechanism of cardiomyocytes
  - Microfilament rearrangement
- Result: Cardiac Arrhythmias

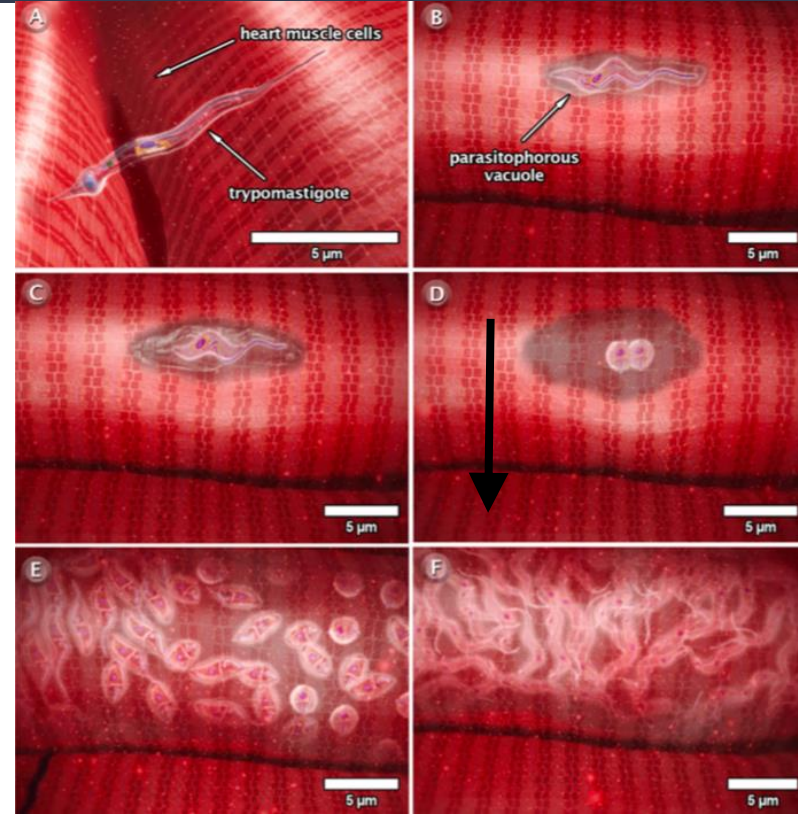
# Pathophysiology

- Accumulation of immune response cells
  - Cytokines, chemokines, nitric oxide
- Necrosis of myofibrils
- Results in cardiac fibrosis, hypertrophy and cardiac denervation (below)



Normal neuronal population

Degenerative neuronal population



# Pathophysiology

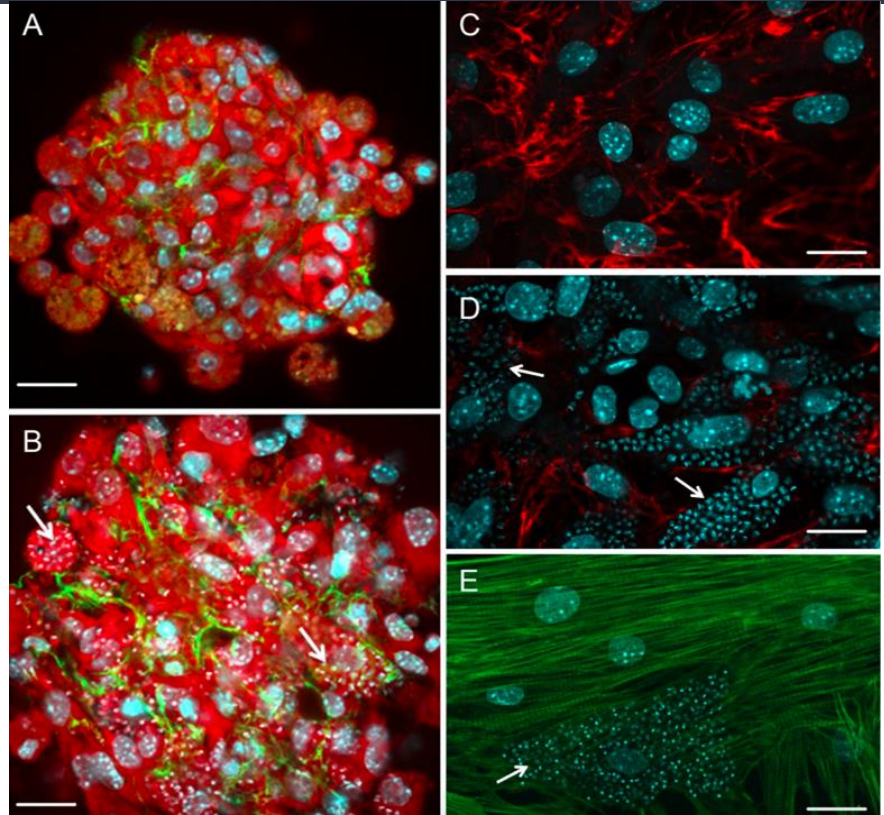
A → uninfected cardiomyocyte

B → infected cardiomyocyte

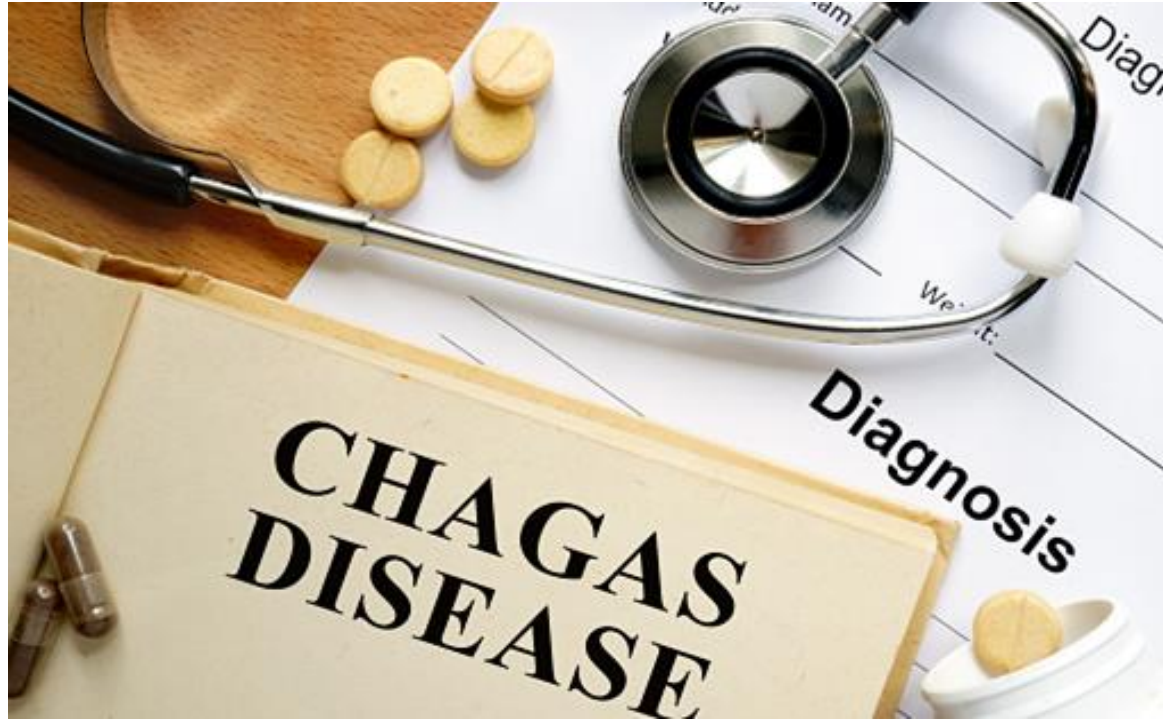
C → normal distribution of fibronectin

D → abnormal distribution of fibronectin

E → disorganization of myofibrils

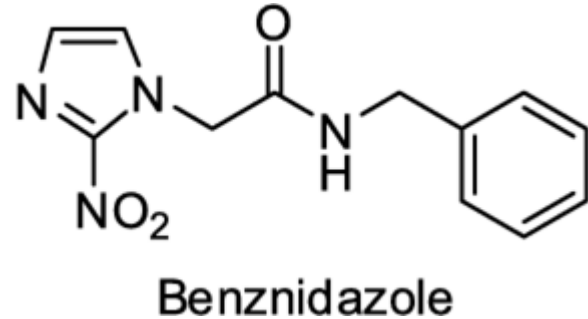


# But Can You Be Cured Of Chagas Disease?



# Treatment: Benznidazole

- Released in 1972 at La Roche Laboratories
- **Approved by FDA in August 2017**
  - **Only for ages 2-12**
- Nitroimidazole antiparasitic
  - Acute infection
- Unable to treat chronic cases
- Severe side effects
  - Harmful for pregnant women



Chemical structure of Benznidazole

# Side effects: Benznidazole

- Allergic dermatitis
- Peripheral neuropathy
- Anorexia and weight loss
- Insomnia



Popular drug for Benznidazole

# Treatment: Nifurtimox

- Alternative to Benznidazole
- **Not approved by FDA**
- Mechanism: intracellular nitro reduction with the generation of the nitro radical, followed by redox cycling against T.cruzi
- Not recommended for pregnant women or patients with kidney problems

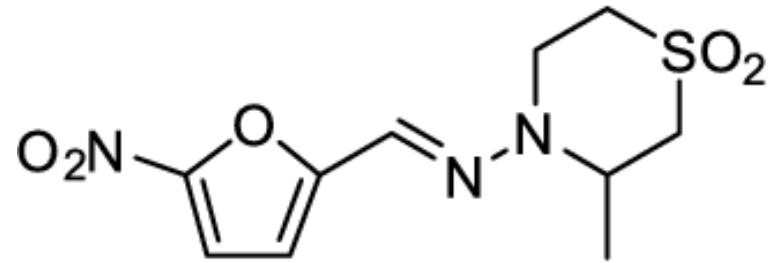


Popular drug for Nifurtimox



# Side effects: Nifurtimox

- Anorexia and weight loss
- Polyneuropathy
- Nausea
- Vomiting
- Headache
- Dizziness or vertigo



Nifurtimox

Chemical structure of Nifurtimox

# Back to the Case Study

- Put on donor list
- Doctor contacted Centers for Disease Control and Prevention (CDC) when she remembered learning about Chagas Disease in med school
  - CDC physician hotline
- Blood tests
- Complicated treatment plan
  - Waited 2 months post-surgery for treatment medications

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# Question 1

Which one of the following methods of transmission is the LEAST likely to occur for Chagas disease?

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- B. Congenital contract from mother to baby
- C. Contact with contaminated blood transfusions or contaminated organs from donors
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## Question 2

How can amastigotes bind to macrophages at the site of infection without transforming into trypomastigote?

- A. Amastigotes have a flagella so they travel to the macrophages
- B. Macrophages are recruited to the site due to an immune response
- C. Amastigotes send signals to recruit macrophages
- D. They do not bind

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