# *Chagas Disease*

## *Ancient, Exotic, Endemic, Deadly*

# *My Experience with Chagas Disease*

Simon Bolivar Visiting Professor,
National University, Caracas, Venezuela
1970

*Additional Experience*

# Progress in Cardiovascular Diseases

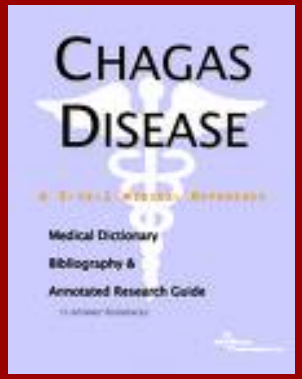
**1970**

## Uncommon Causes of Heart Failure (With a Section on Chagas Disease)

**Joseph K. Perloff, Keith M. Lindgren and Bertron M. Groves**

Osler called syphilis the great imitator because the signs and symptoms were similar to so many other diseases.

Another Great Imitator:




South American Trypanasomiasis, (*Trypanosoma Cruzi).*

# *How Ancient is Ancient ?*

Chagas disease began millions of years ago as an enzootic (non-human) disease of wild animals.

DNA evidence of *Trypanosoma Cruzi* has been found in 4000 year old South American mummies.

# *Exotic*

Caused by *a hemoflagelate* that enters the bloodstream after a bite of the *reduvid sandfly*.

# *Endemic & Deadly*

Chagas disease is endemic In Mexico, Central and South America. Annual death toll is 50,000. 18 million are already infected, and 100 million--25% of the population--are at risk of acquiring the infection.

*Types of Trypanosomiasis:*

***African Trypanosomiasis***

Sleeping Sickness

***American Trypanasomiasis***

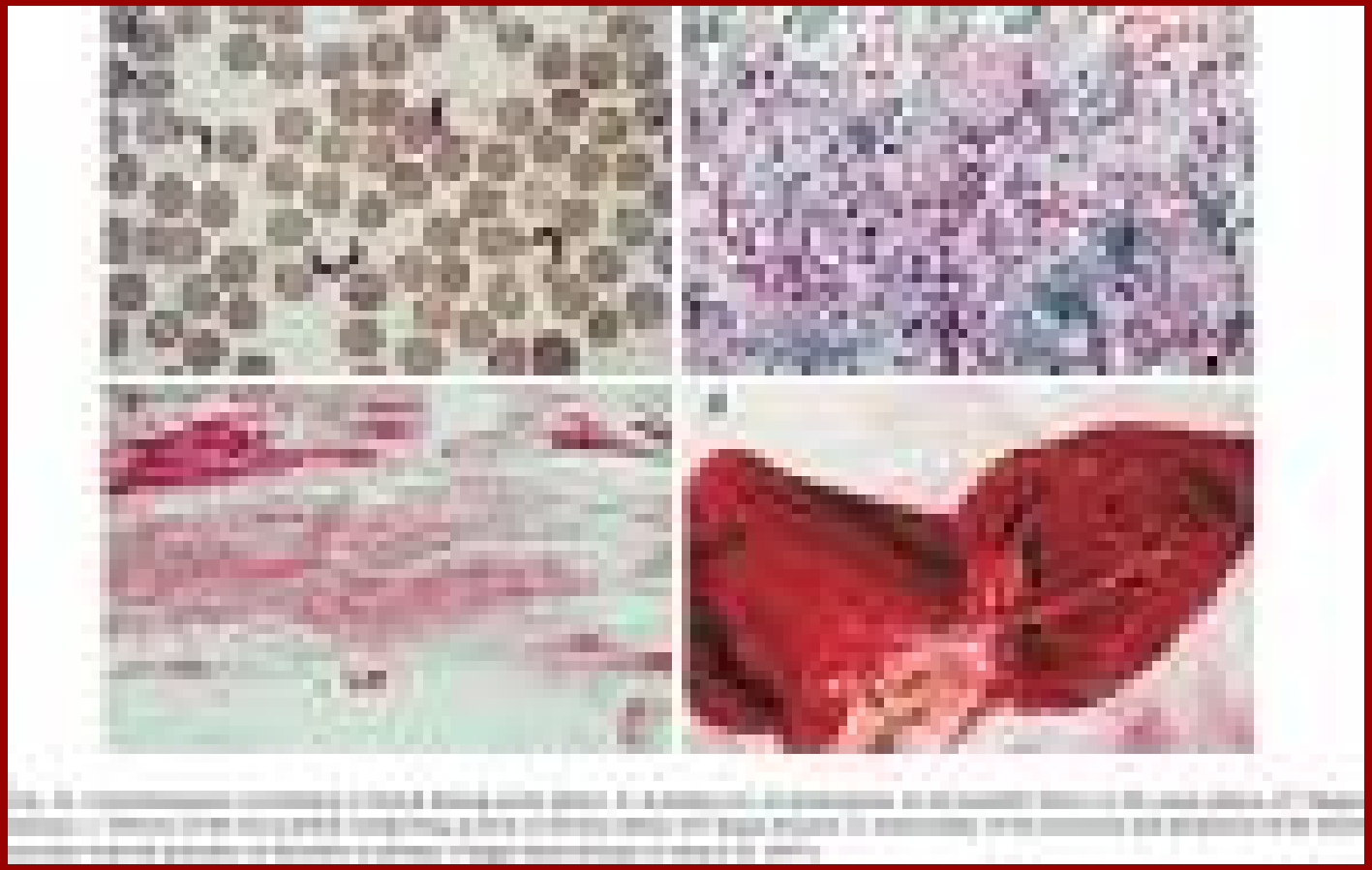
Chagas Disease

# *African Trypanosomiasis*

Caused by the parasite *Trypanosoma brucei* that enters the bloodstream after a bite by the Tsetse fly.

# *American Trypanasomiasis*
# *Chagas Disease*

**Animal-to-human and human-to human transmission by a blood sucking reduvid bug---the phlebotomine sandfly.**



Upper left--circulating flagellates.
Upper right--pseudocysts light blue
Lower left--myocardial fibrosis.
Lower right--dilated cardiomyopathy.

# *Who Was Chagas?*

# Carlos Justiniano Rubiero Chagas

Was 29 years old when he described the parasite in the blood stream, the cycle of the vector in the digestive tract, cultivation in agar-blood, and transmission to vertebrates by the bite of the infected reduvid sandfly.

In 1911, Oswaldo Cruz announced Chagas' discovery at the National Academy of Medicine in Rio de Janeiro. In 1922, Chagas was awarded the Pasteur Prize.

Chagas was born on a Brazilian coffee farm in July 1879. His father died when the boy was four years old. An uncle urged young Carlos to study medicine. In 1908, while investigating malaria in the Amazon, Carlos learned of the existence of “kissing bugs,” so-called because of their habit of biting (kissing) sleeping human beings on the face. In 1909, Chagas described the case of a nine month old infant with the kissing bug disease.

# *Who Was Cruz ?*

The mentor of Carlos Chagas

Oswaldo Goncalves Cruz's great work was the eradication of malaria and yellow fever in Rio de Janeiro.

At age 15, Cruz began his studies at the Rio de Janeiro Faculty of Medicine, and in 1892 he graduated. Inspired by Louis Pasteur, Cruz wrote a thesis on water as a vehicle for the propagation of microbes.

# *A Paradigm of Scientific Deduction*

Chagas proposed that the kissing bug---a sandfly---transmitted a parasite to human beings and to other vertebrates. He recovered flagellates in the hindgut of the bug and in the bloodstream of domestic animals, and soon announced “a new species different from any other species of the same genus.”

The parasite was first named *Schyzotrypanum Cruzi* in honor of Oswaldo Cruz, and was later renamed *Trypanasoma Cruzi*.

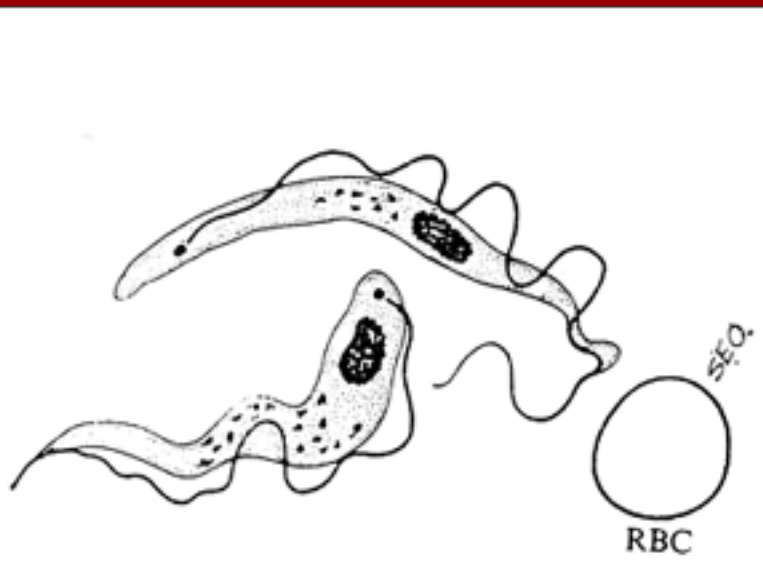



그림 5-2. 크루스파동면모충

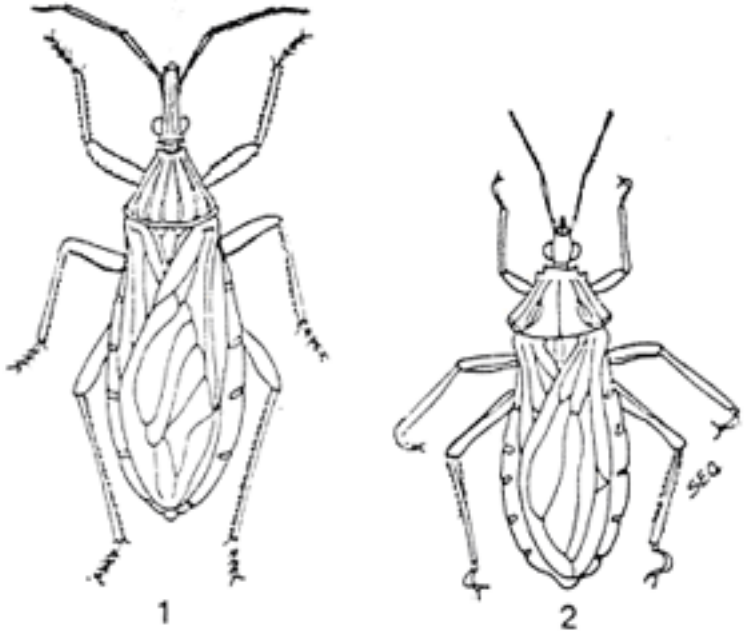



그림 5-3. 크루스파동 편모충의 매개곤충)

1. *Rhodnius Prolixus*
2. *Panstrongylus megistus*

The Parasite

The Vector

# *Transmission of Chagas Disease*

The insect is found in palm fronds of roofs and in cracks of the mud or adobe walls of thatched houses of the poor.

# *Congenital Chagas Disease*

An infected mother passes the disease onto her baby either by placental transmission (chronic placentitis) or at delivery or from breast milk.

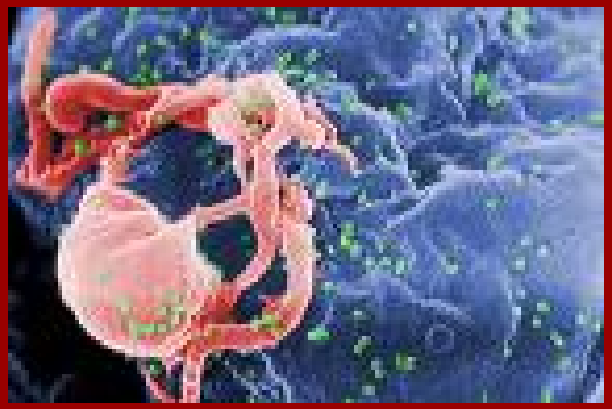
# *Chagasic Fetal Hydrops*

Intrauterine Heart Failure Detected by Ultrasound.

# *Additional Forms of Transmission*

Blood transfusion

Organ transplantation



Chagas Disease is an opportunistic infection among patients with HIV and other types of immunosuppression.

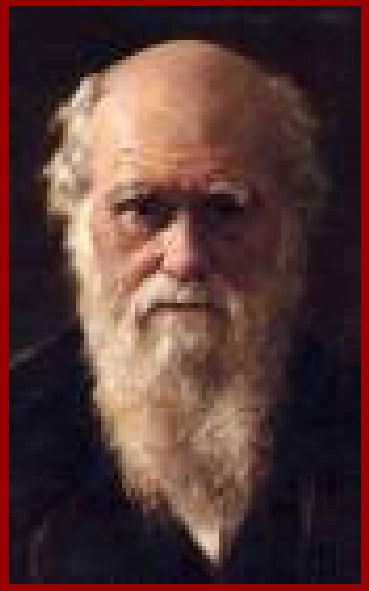
# *The Kissing Bug Kissing*

# *Bed Net*

*Simple, effective, cheap, but not cheap enough for the poor.*

# *A Good Night Kiss*


During the nocturnal bite, the infected bug deposits feces laden with parasites. Transmission is enhanced when the skin is scratched at the bite site.



Charles Darwin is believed to have contracted Chagas disease during his 1833
South American expedition.

# Genetics

Within the clinical spectrum of Chagas Disease, the role of parasitic genetic variability is emerging. *T Cruzi is now* divided into two divergent subgroups isolated from human beings, from insect vectors, and from sylvatic (wild) mammals. The two lineages diverged 37 to 88 million years ago. It has been hypothesized that lineage two is indigenous to South America, while lineage one was introduced more recently with North American placental mammals.

## *Symptomatic Chagas in Newborns and Young Children*

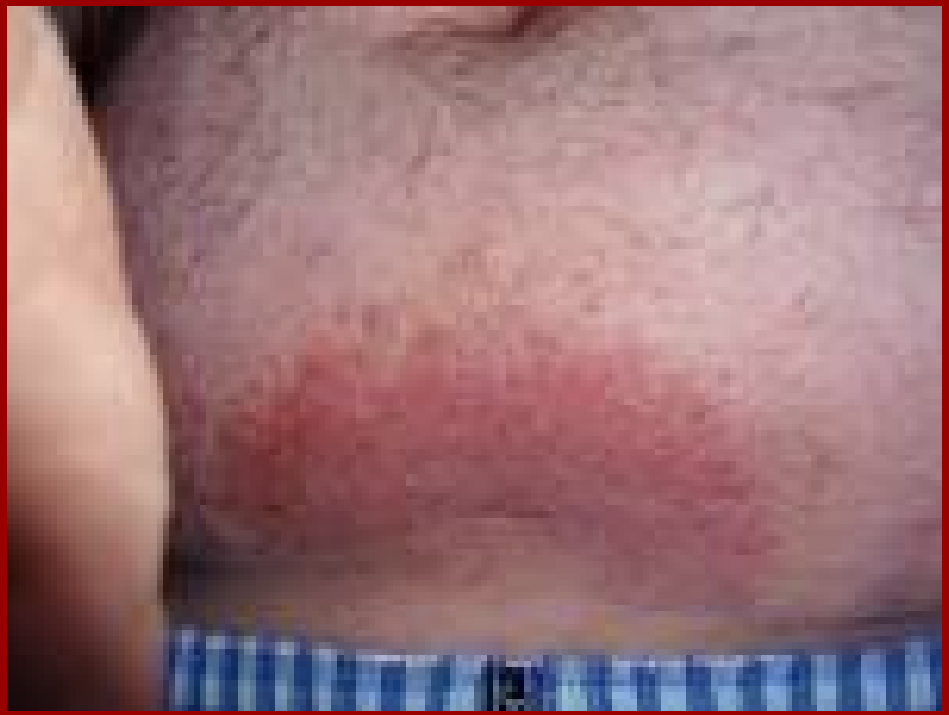
*Chagoma*—reddish area at bite site.
*Rash*
*Romana's sign*---Unilateral periorbital edema.
*High fever*
*Inappropriate (disproportionate) tachycardia.*
*Myocarditis/pericarditis*
*Meningoencephalitis*
*Hepatomegaly*
*Lymphadenopathy*

# CHAGAS DISEASE

## *Chagoma*


(Courtesy of Dr. R. Pinckney, U. of Wisconsin)

# *Chagasic Rash*



# *Romana's Sign*

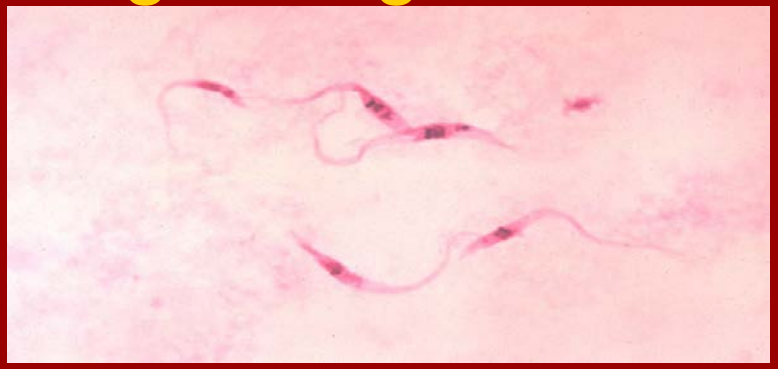

Painless unilateral periorbial edema

# Laboratory Tests

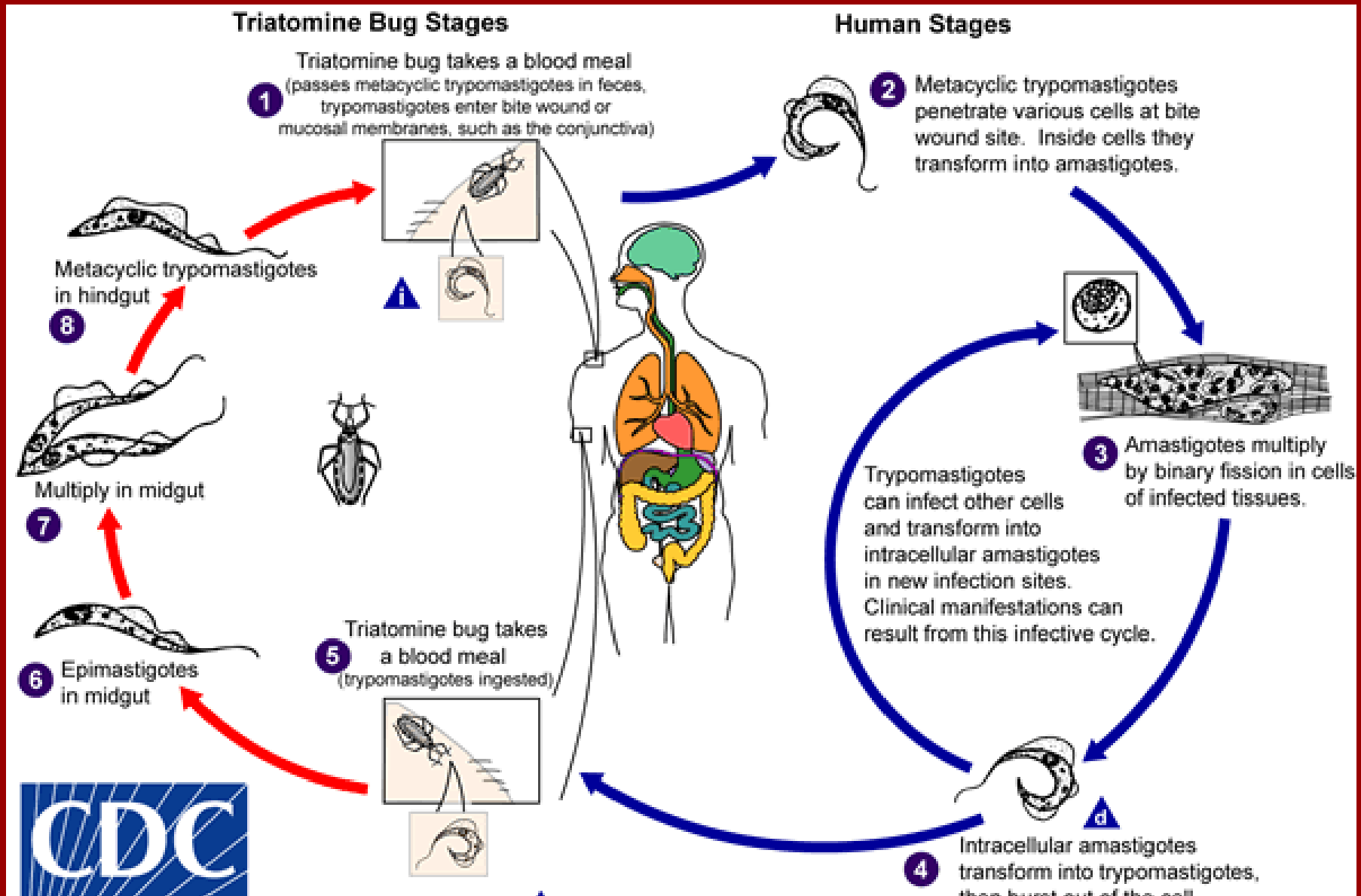
*Complement fixation* —1913

*Xenodiagnosis* (1914) exposure of an infected individual or tissue to a clean vector (laboratory -bred mosquito or tick).

*Sero-diagnosis*---1970. Detection of antibodies against the parasite. Of limited value in diagnosing the acute phase.



# *Life Cycle*


Triatomine Bug Stages
Human Stages
Triatomine bug takes a blood meal
(passes metacyclic trypomastigotes in feces, trypomastigotes enter bite wound or mucosal membranes, such as the conjunctiva)
1
2
Metacyclic trypomastigotes penetrate various cells at bite wound site. Inside cells they transform into amastigotes.
Metacyclic trypomastigotes in hindgut
8
Multiply in midgut
7
3
Amastigotes multiply by binary fission in cells of infected tissues.
Trypomastigotes can infect other cells and transform into intracellular amastigotes in new infection sites. Clinical manifestations can result from this infective cycle.
Triatomine bug takes a blood meal
(trypomastigotes ingested)
5
6
Epimastigotes in midgut
4
Intracellular amastigotes transform into trypomastigotes,
CDC

When host cells rupture, flagellated parasites are released into the lymphatics and bloodstream through which they spread to distant sites and invade new host cells. The process continues for the life of the host.

# *Acute to Chronic Disease*

***Acute Phase*** -- Most acute cases escape medical attention because symptoms are non-specific (fever, malaise, vague signs of infection). Flagelates vanish from the blood stream as symtoms disappear.

***Latent Period*** ---As long as 20 years.

***Cardiac Involvement*** ---Conduction defects (RBBB/left anterior hemiblock, sudden death (complete heart block, ventricular tachyarrhythmias), cardiomyopathy, heart failure, unique LV apical aneurysm, mural thrombus.

***Involvement of Hollow*** *Viscera*---Esophagus, stomach, colon.

Despite a century of research, the pathogenesis of chronic Chagas cardiomyopathy remains incompletely understood.

# *Pathogenetic Mechanisms of Chagas Heart Disease*

1) Cardiac dysautonomia
2) Microvascular involvement
3) Parasite-dependent myocardial damage
4) Immune mediated myocardial injury

# *Dysautonomia*

Disease or malfunction of the autonomic nervous system

In 1922, Carlos Chagas and Eurico Vilella reported a blunted chronotropic response to atropine. Cardiac neuronal damage was described in 1949.

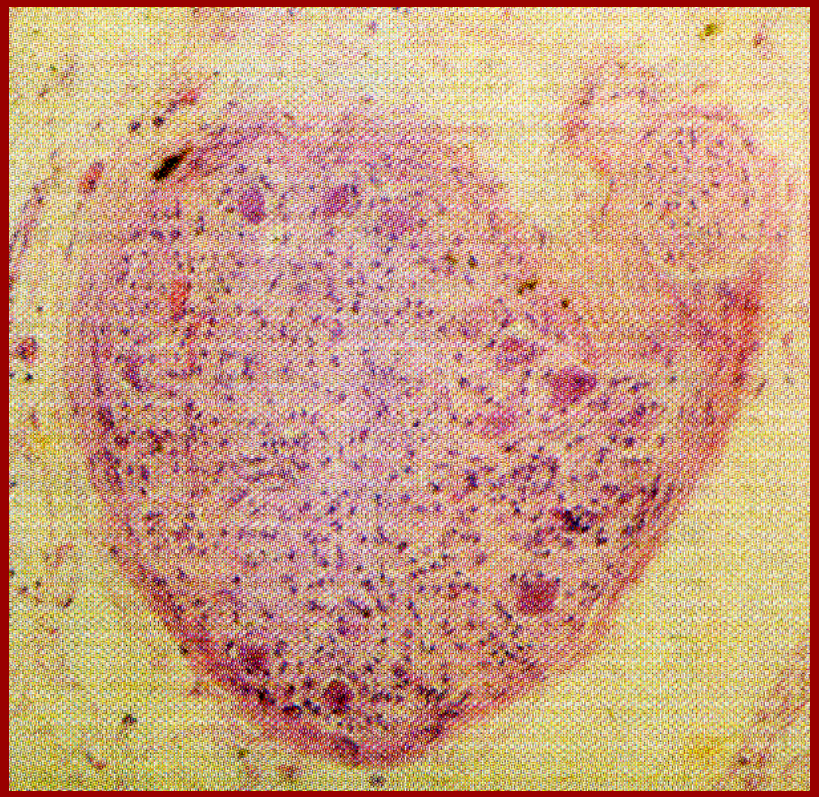
*Oria and Ramos. Arq Bras Cardiol.*

# *The Autonomic Nervous System.*
# Parasympathetic Denervation

Major neuronal damage of the heart with parasympathetic denervation confirmed morphologically. Abnormal cardiac reflexes (Valsalva maneuver). Denervation of the sinus node with lack of parasympathetic inhibitory action, and lack of vagally mediated response to changes in blood pressure and venous return.

# Neuronal Depopulation With Degenerative Changes

## *Atrial Ganglia*



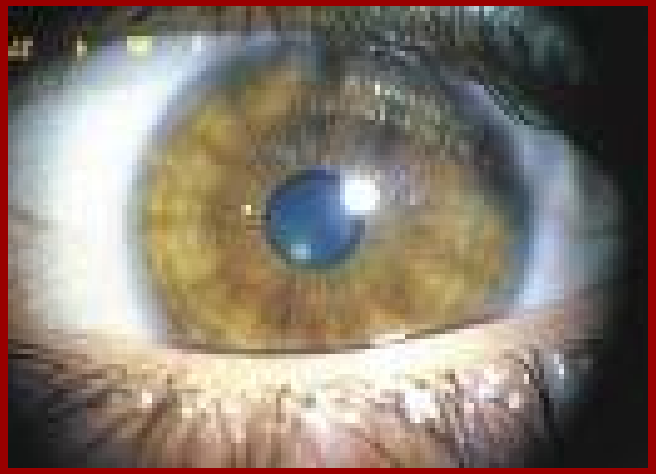
# *Parasympathetic Denervation*

*Heart---*Abnormal cardiac reflexes. Sinus node denervation. Neuronal damage at necropsy.

*Urethra/Bladder*—Abnormal function

*Iris*—Exaggerated pupillary responses

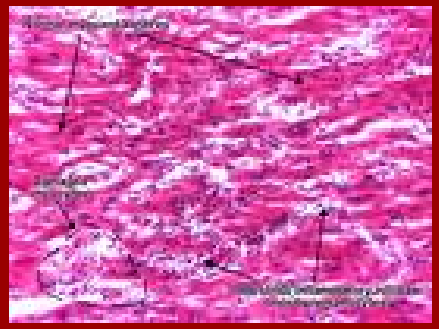
# *Parasympathetic Denervation of the Iris*



# *Microvascular Involvement*

Clinical, pathological and experimental evidence of microvascular abnormalities in Chagas heart disease. Striking myocardial perfusion defects in the presence of normal coronary arteries. Intimal proliferation in intramyocardial arterioles, capillary basement membrane thickening, and occlusive platelet thrombi in intramural coronary arteries.

# *Is There Parasite-dependent Myocardial Damage?*



Myocardial lesions are usually devoid of parasites.

Poor correlation between the level of parasitemia and disease severity.

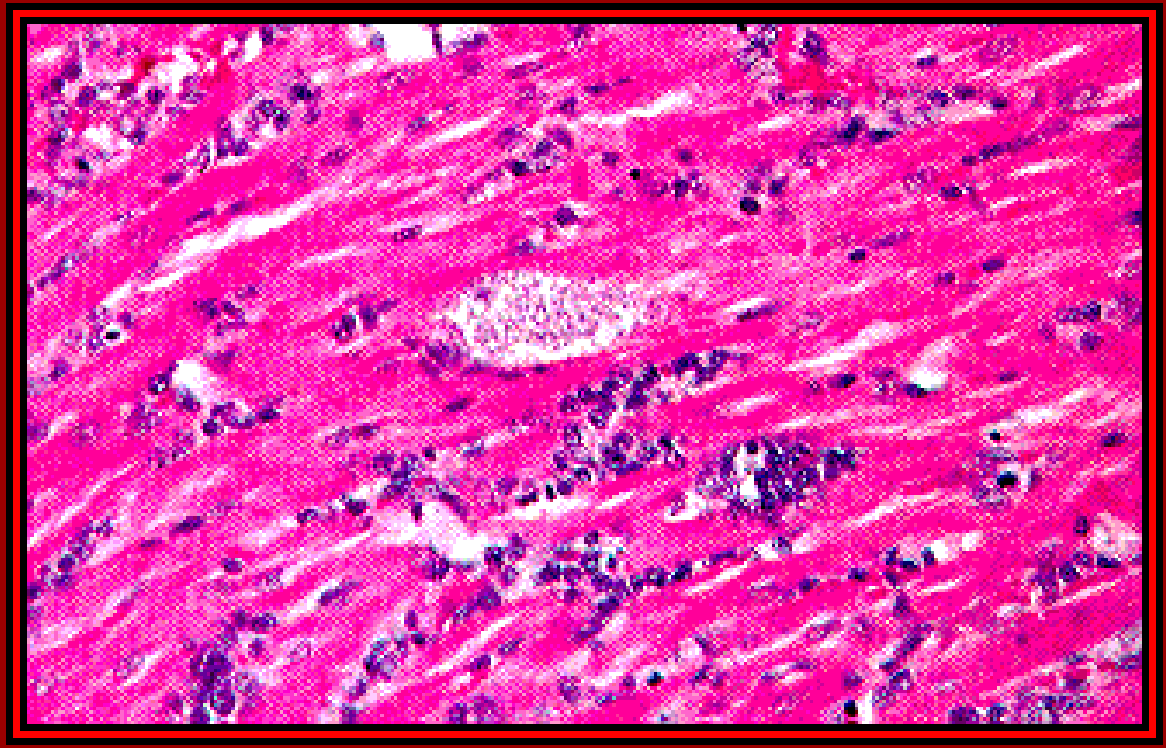
Seropositivity for T cruzi antigens is far more frequent than the incidence of cardiac involvement.

# *Immune Mediated Myocardial Injury*

Chronic Chagas heart disease has the hallmarks of delayed hypersensitivity reaction, namely, mononuclear inflammatory infiltrates with immunoglobulin and complement deposition in myocardial tissue.

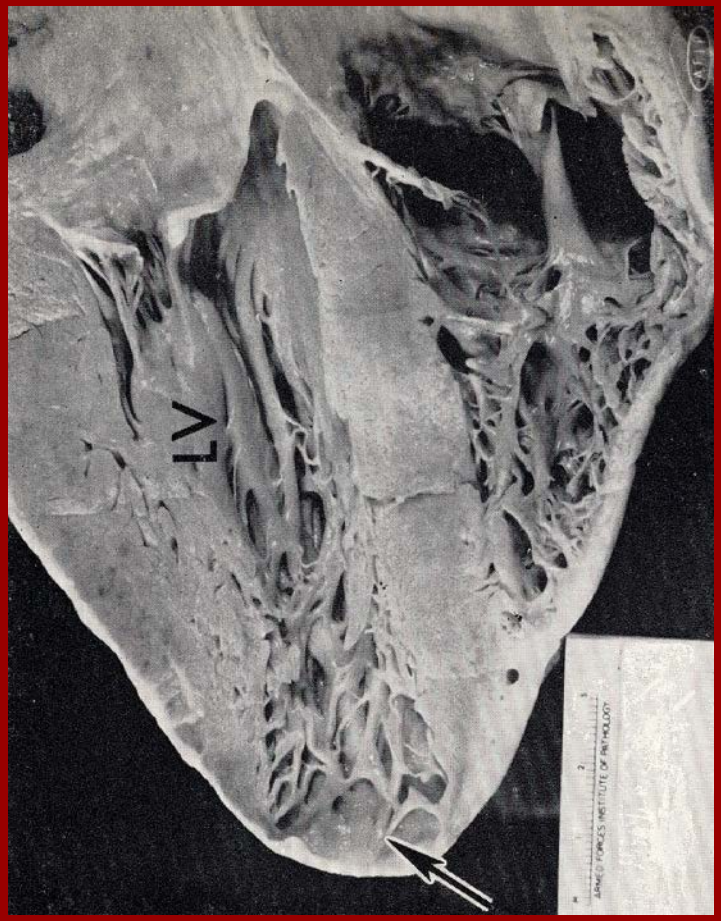
*Eosinophilia*

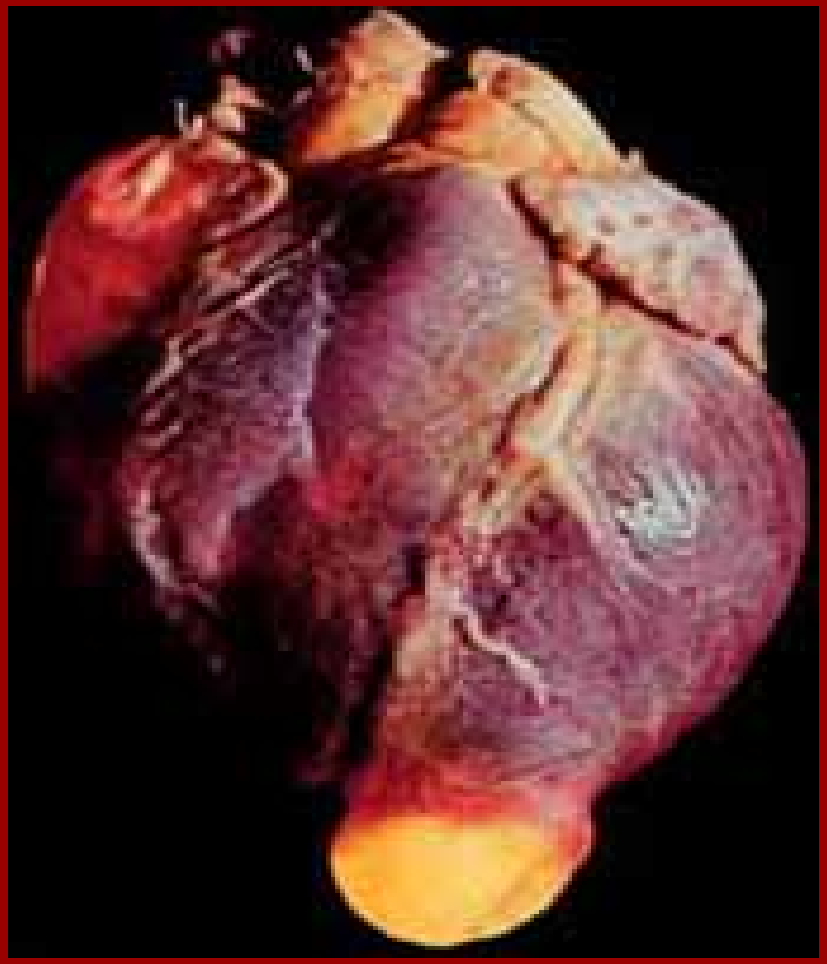
# *Acute Chagasic Myocarditis*



Tissue parasitism elicits a strong cellular and humeral immune response against *T cruzi* but does not eliminate the parasite.

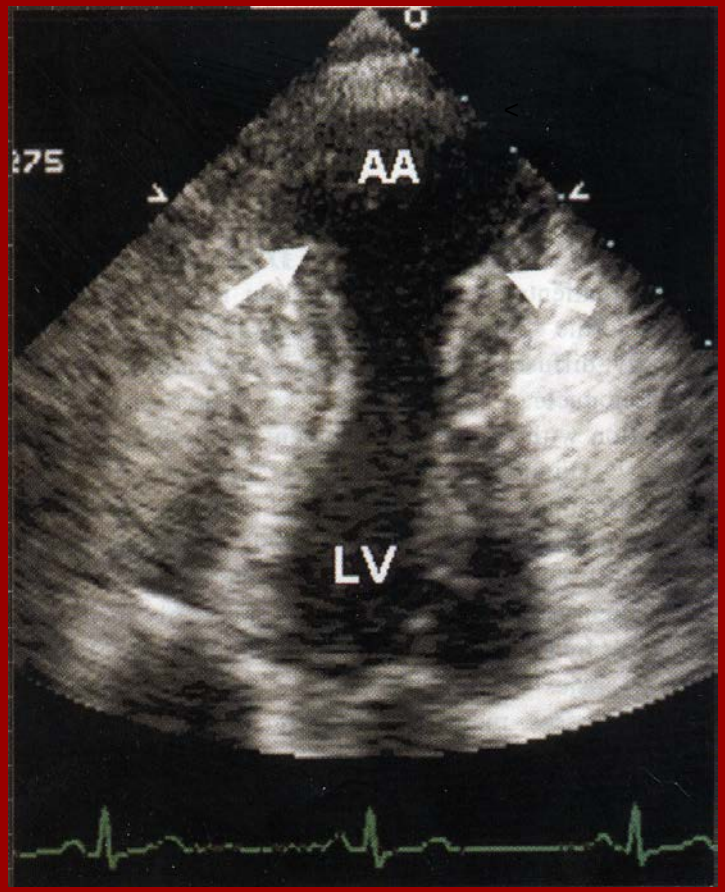
# *Chronic Chagasic Cardiomyopathy Left ventricular Apical Aneurysm.*



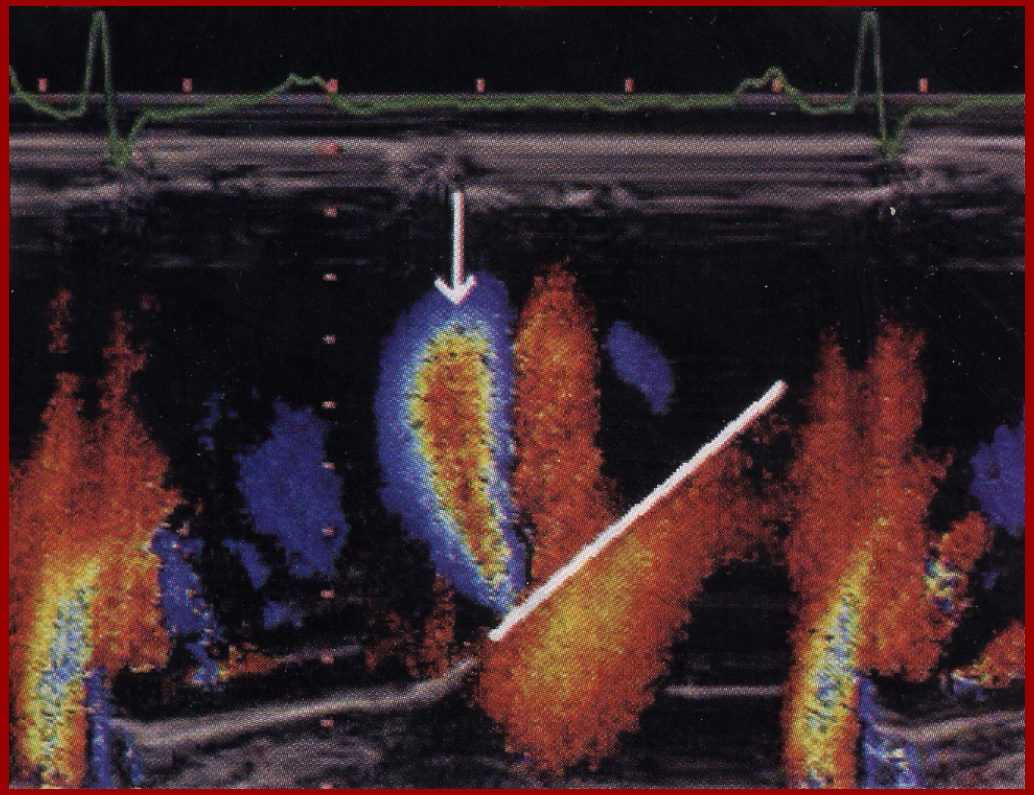



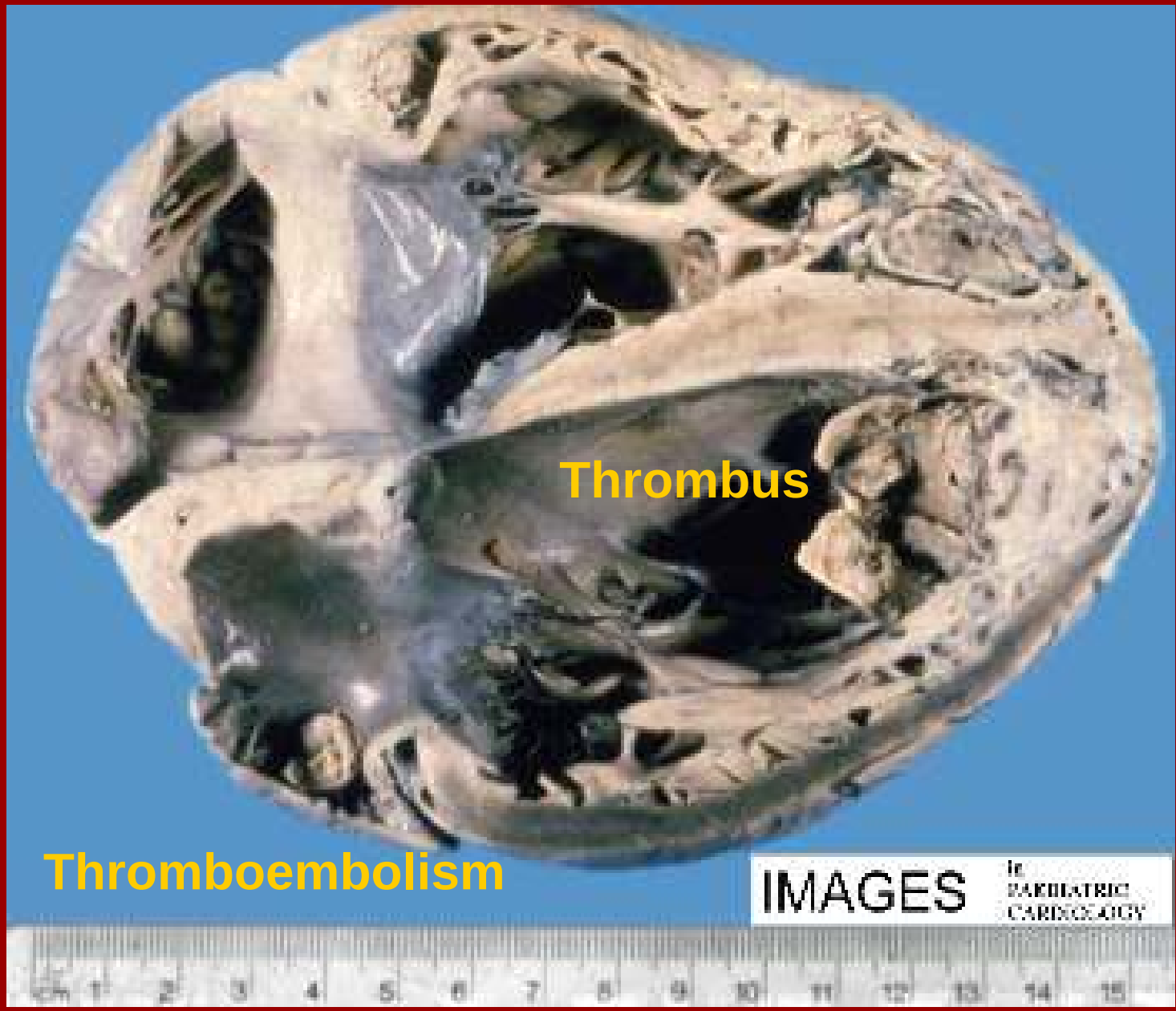
# *Left Ventricular Apical Aneurysm*

Twenty year old Argentine male with asymptomatic bifascicular block.



Color Doppler M-mode velocity propagation of LV inflow tract (vertical arrow). Diminished slope of color edge in early diastole (white line) represents lower blood flow velocity toward the aneurysmal apex.




Thrombus
Thromboembolism
IMAGES
PAEDIATRIC
CARDIOLOGY

# *Electrocardiocardiographic Abnormalities*

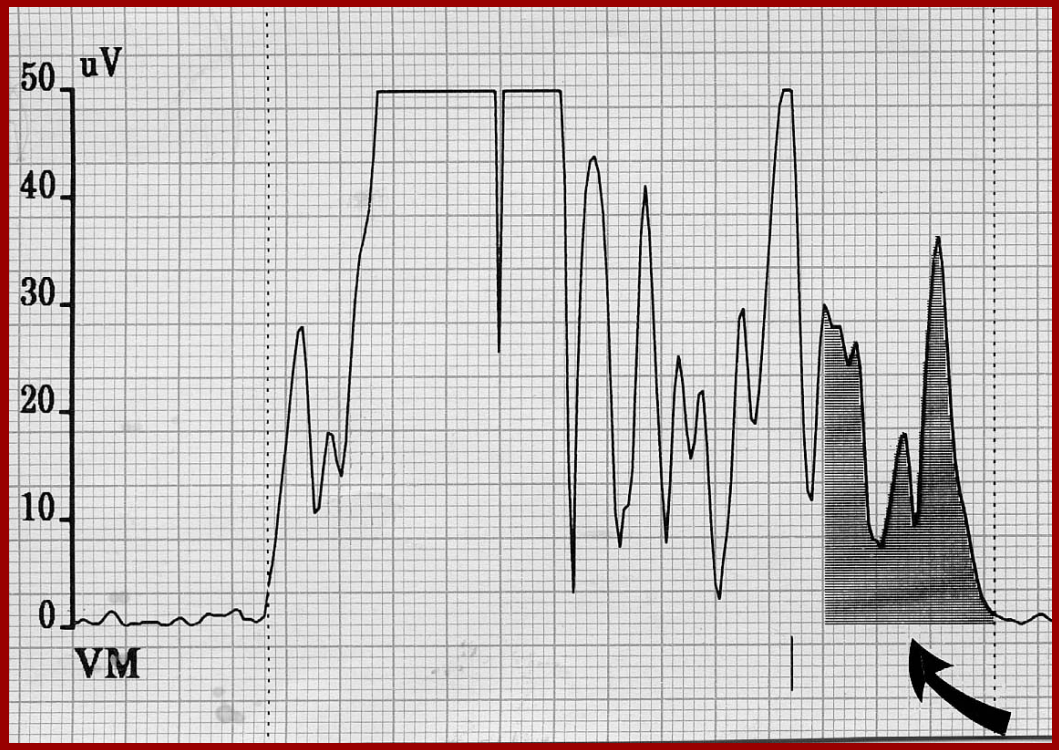
Sinus bradycardia
Atrioventricular block
Right bundle branch block
Left anterior fascicular block
Bifascicular block
Complete heart block
Multiform PVC’s
Abnormal ST-T segments
Abnormal T waves
Abnormal Q waves

# *Sudden Cardiac Death*

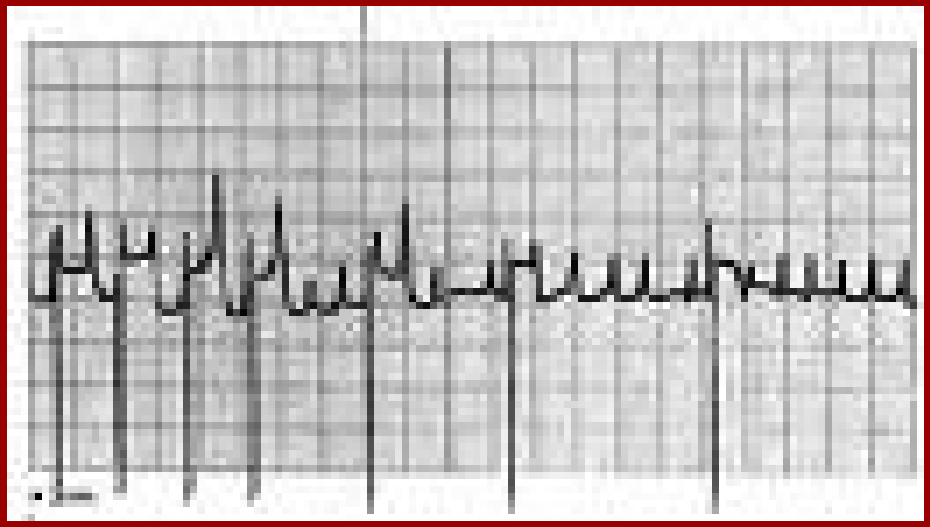
Third degree heart block

Ventricular tachycardia/fibrillation

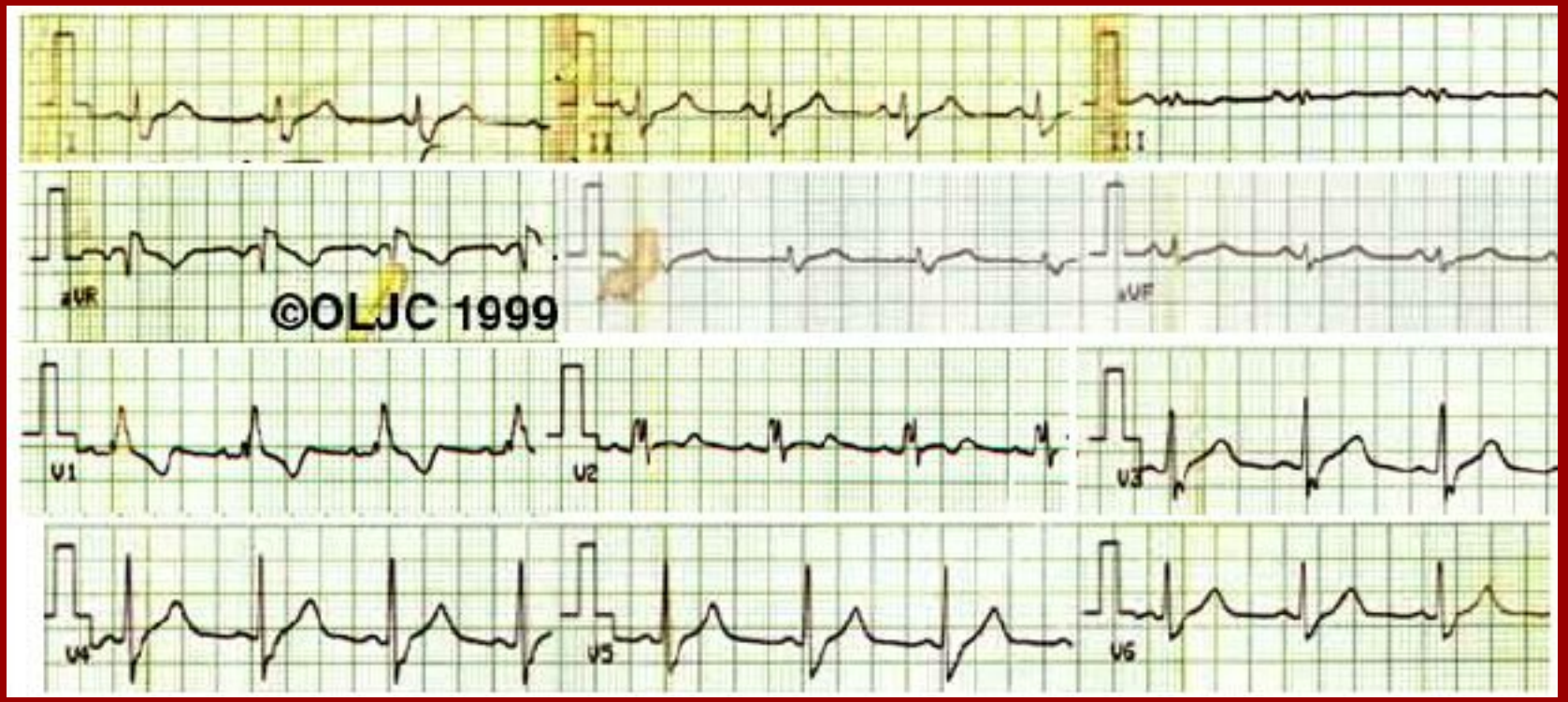
# *SAECG With Late Potentials*



# *AV Conduction Defects*

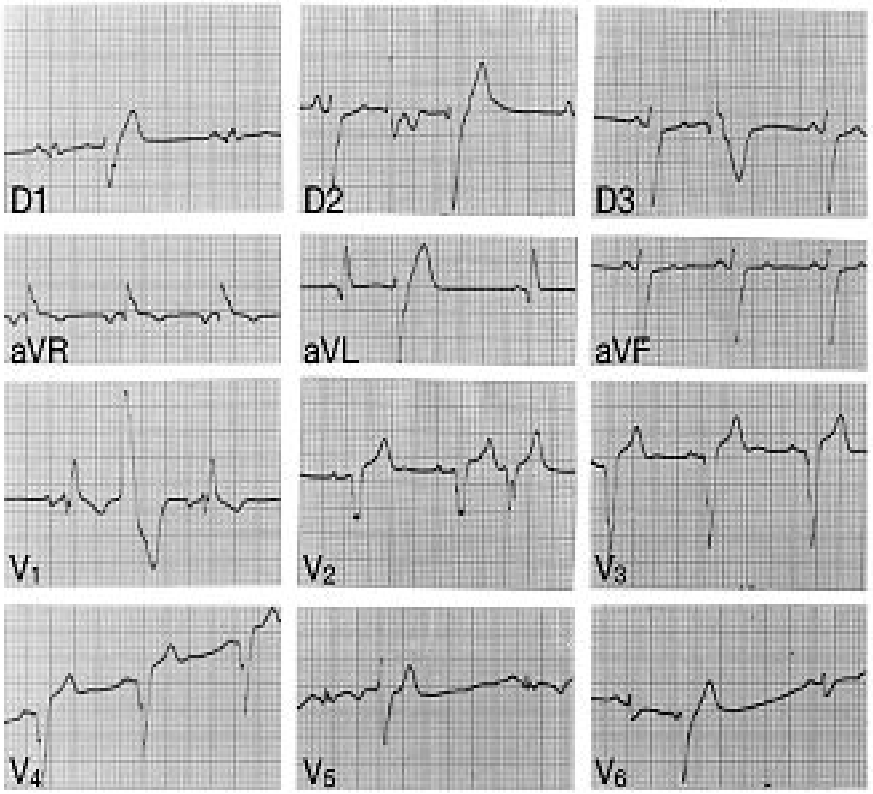


# *Right Bundle Branch Block*



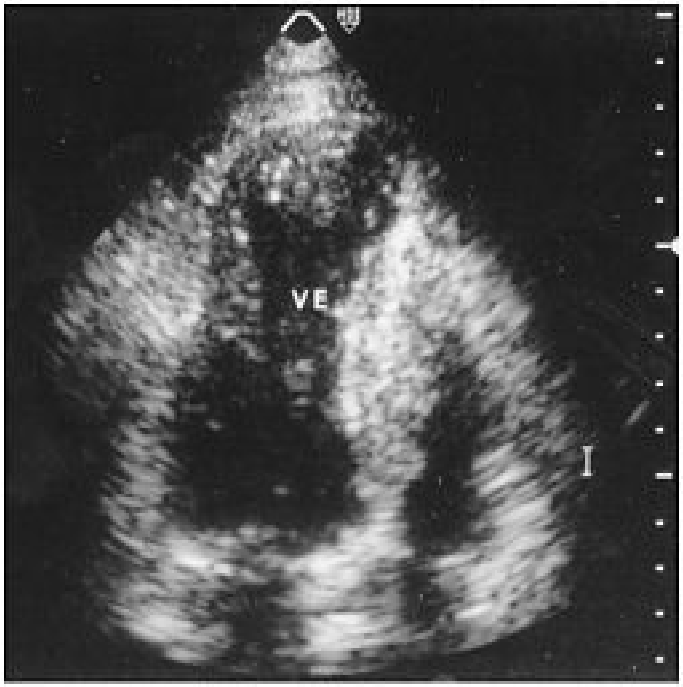
# Bifascicular Block

# Apical Aneurysm




(A)

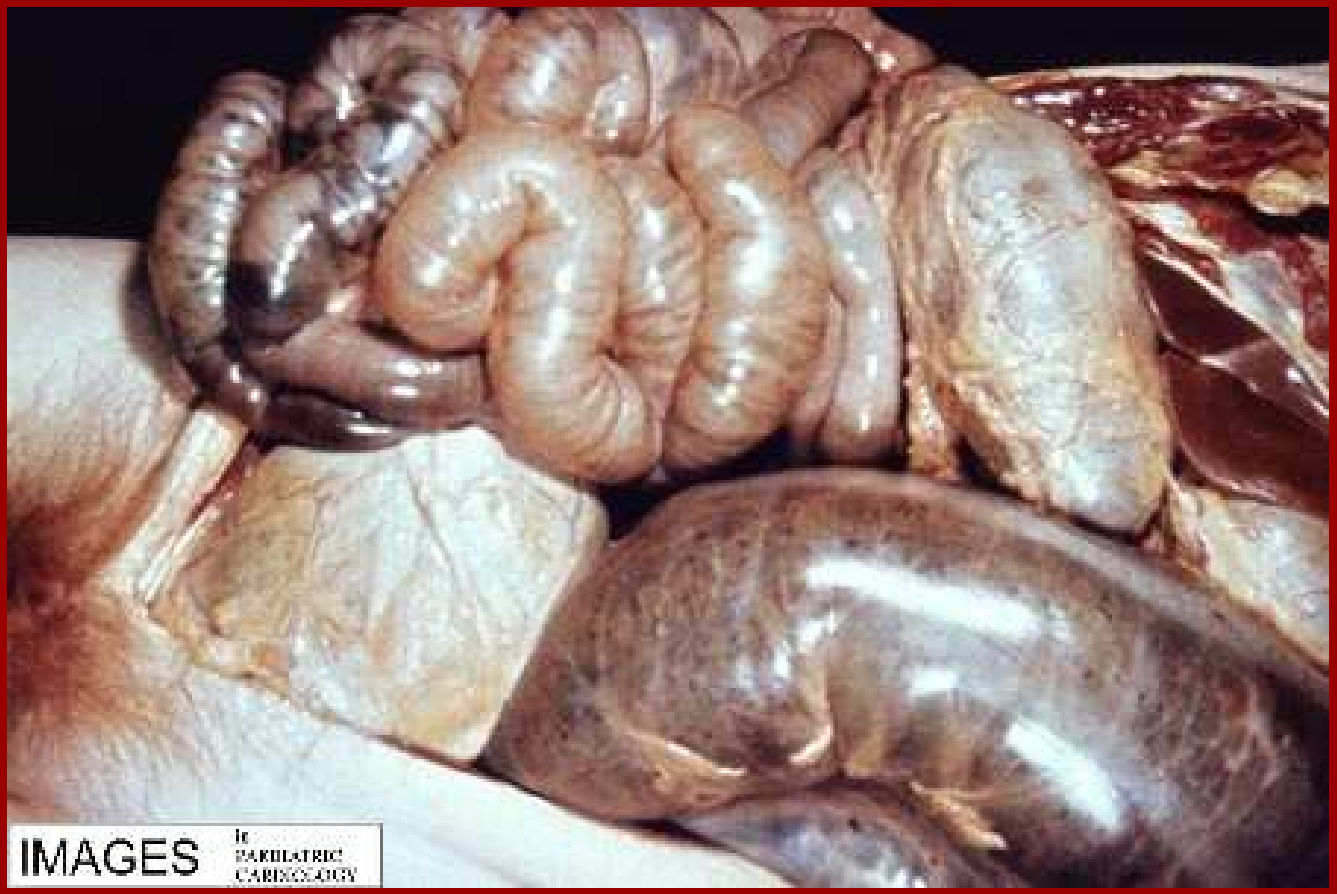
(B)



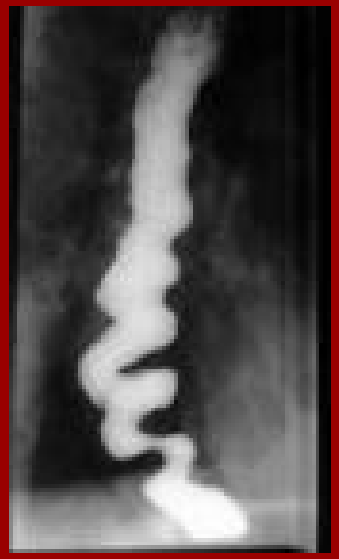
# *Hollow Organ Involvement*

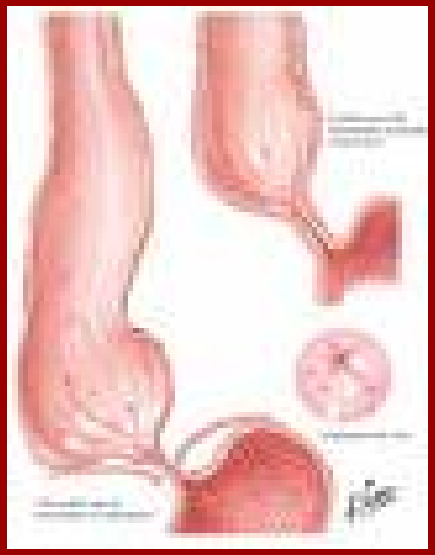
Gastrointestinal symptoms with chronic *T.cruzi* infection result from denervation of hollow viscera, especially esophagus and colon, rarely stomach, bladder and ureter.

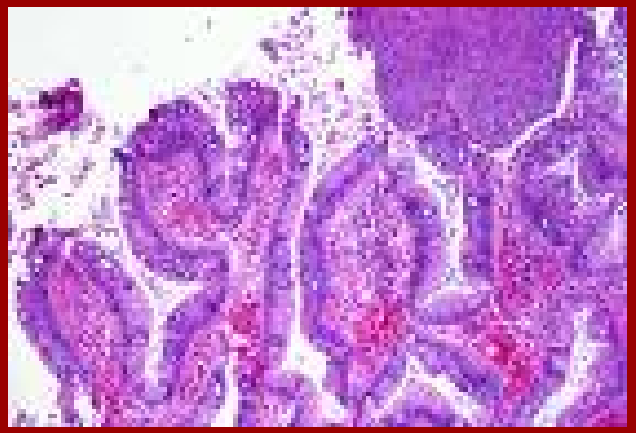
# *Megacolon*



# *Mega Esophagus*







# *Chagasic Pancreatitis*

Acute Chagasic pancreatitis results from local parasitism. Necrosis is caused by release of pancreatic enzymes from ruptured parasitized cells and pseudocysts.

# *Treatment of American Trypanosomiasis*

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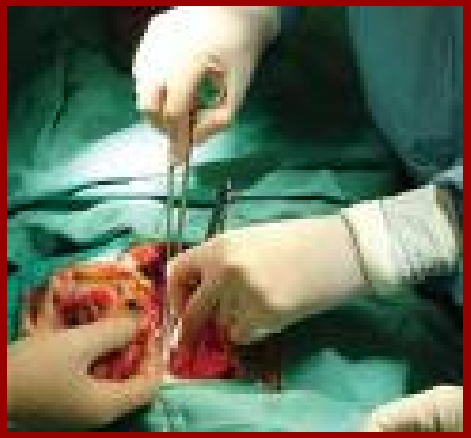
Bed Net

There is no preventive vaccine.

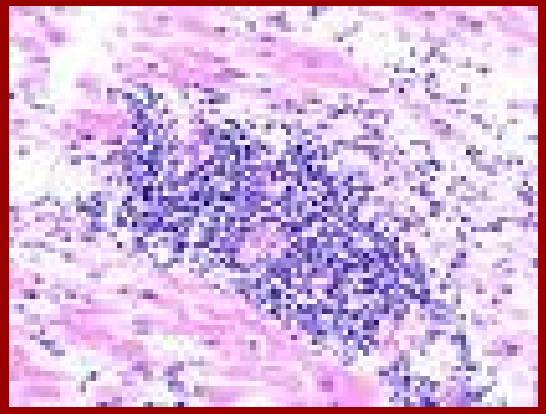
, Anti-trypanosomal medications achieve only a 50% rate of parasitologic cure even in the early acute stage, and are accompanied by signifcant toxitity.

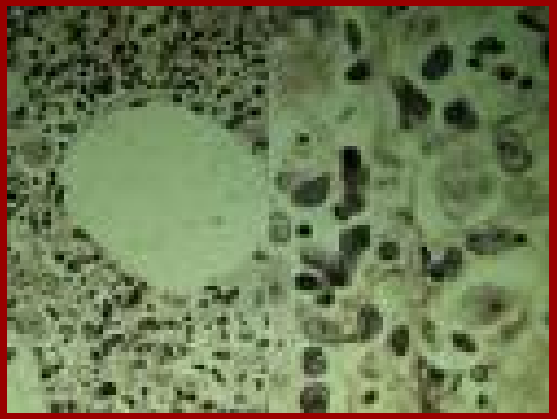
Chronic stage--- No effective treatment .

# *Heart Transplantation*



Transplantation is problematic for chronic Chagas heart disease.





Heart transplantation in patients with with Chagas' cardiomyopathy is accompanied by high rates of acute reactivation. A new acute phase is experienced, with fever, skin lesions, and myocarditis. Trypanosoma cruzi can be recovered in myocardial biopsies and in skin lesions.

Marta Del Carmen Sandoval (391-28-13)

The pathology report (read by Dr. Fishbein) from 2/7/2009 (labeled "MEDIASTINAL HEM") is the explanted heart which shows intracellular parasites and amastigotes. There is also diffuse myocarditis with eosinophils

# *Chagas Disease*
# *Heart Transplantation*
# UCLA

In December 2005, a 64 year old man with idiopathic cardiomyopathy underwent heart transplantion. In January 2006, he was treated with enhanced immunosuppression for organ rejection. In February, he was admitted to hospital with anorexia and fever. A peripheral blood smear revealed T Cruzi. Blood cultures were positive, and endomyocardial biopsy contained the parasite.

# *National Reference Centers for the Chagas Disease*

The *Chagas Disease Laboratory of Argentina* serves as a National Reference Center.

*Health Ministry* initiatives have been established in Brazil, Bolivia, Chile, Paragray and Uruguay.

# Summary

## *Ancient, Exotic, Endemic, Deadly*

Chagas disease began millions of years ago as an disease of wild animals. DNA evidence of Trypanosoma cruzi has been found in 4000 year old South American mummies. In 1909, Carlos Chagas of Brazil described the clinical picture of a new disease and identified the causative agent as a blood-sucking triatomine reduvid parasite.

Chagas disease is the commonest cause of heart failure and sudden cardiac death in Mexico, Central and South America.

# *What Next?*
# *Where Next ?*

Never make predictions, especially about the future,

BUT

Latin American immigration to the United States is likely to spread this ancient, exotic and deadly disease.

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# *Emergence of Chagas disease in the United States and Canada*

Transfusion-Associated Chagas' Disease in the United States.

Increasing Chagas seroprevalence among blood donors in
Los Angeles County.