AUTOIMMUNITY AS A RESULT OF CHAGAS DISEASE

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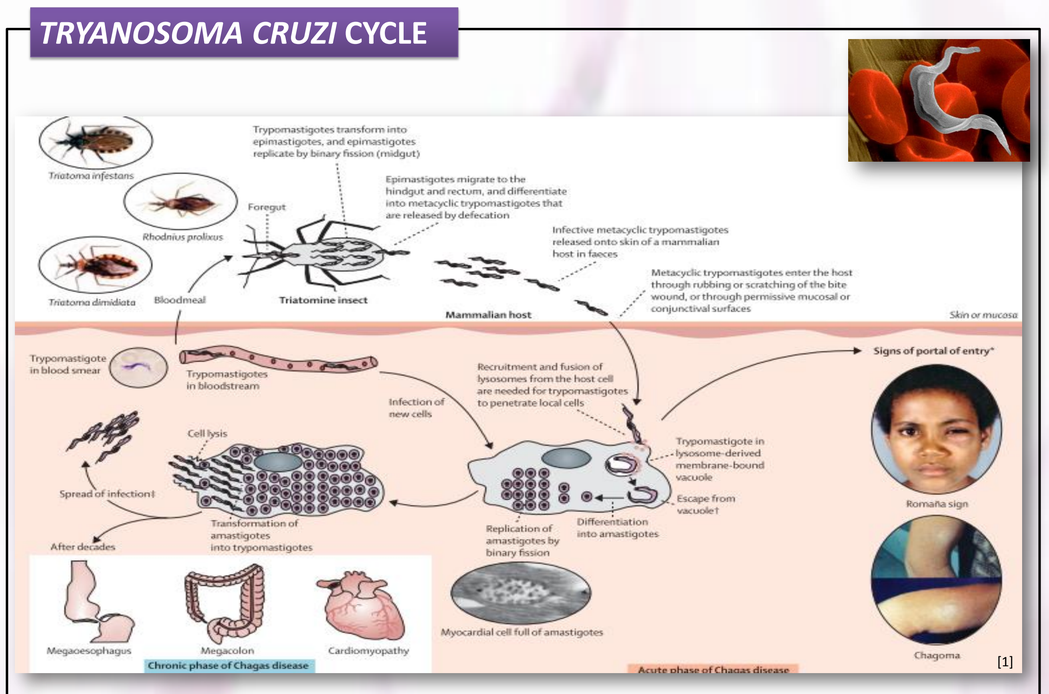
INTRODUCTION: Since Chagas disease was discovered in 1909, the development of the disease has caused large uncertainty: the pathology, the autoimmunity, which has been recently confirmed, and the damage induced in humans. Because of this many studies have been done in order to understand the disease process. The autoimmunity caused by *Trypanosoma cruzi* has aroused great interest in the scientific community and great controversy because the scientists are positioned against or in favor of the autoimmunity in this pathology.

There are 7-8 millions people infected and 25 millions in risk of infection (in rural areas without health access).

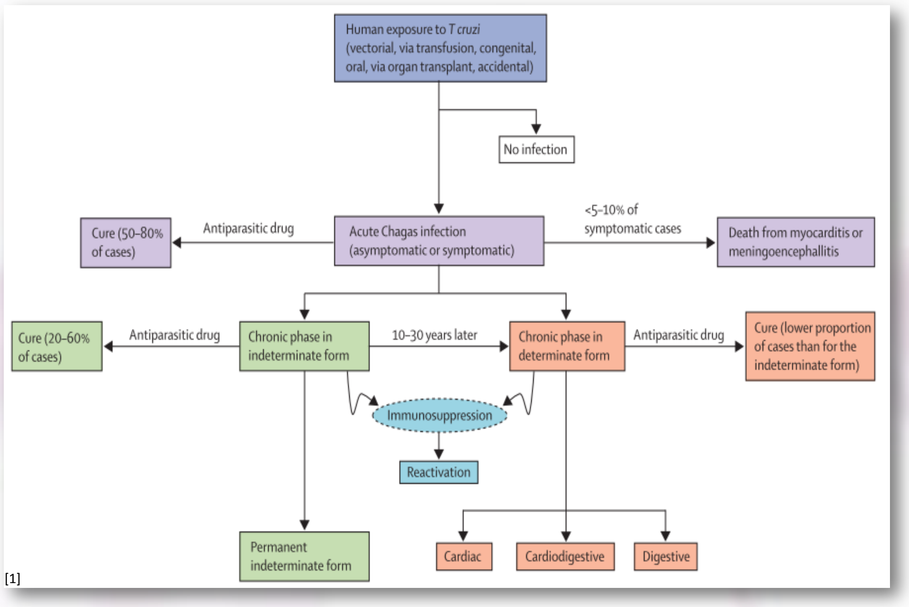
WHO dates 2013

TRYANOSOMA CRUZI CYCLE



[1]

NATURAL HISTORY OF *T.CRUZI* IN HUMAN



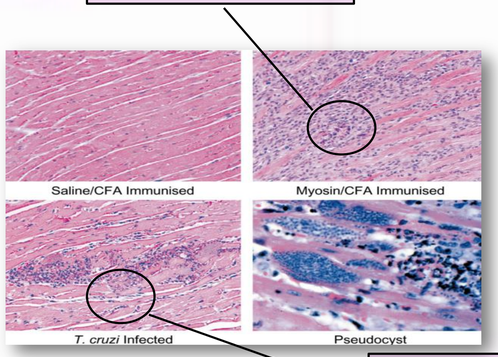
[1]

Heterogeneity of Chagas disease:
-Variability of the immune response [2]
-Host and parasite genetic differences [3]
-Each infected person can be infected with many *T.cruzi* strains [4]

AUTOIMMUNITY

IN FAVOR: AUTOREACTIVITY

Mononuclear cell infiltration, myocyte swelling and fibrosis



Intracellular infiltration, necrosis, swelling and parasite pseudocyst.

A/J strain 21 days after of the immunisation/infection. [3]

Myosin

Proliferation of chronical infected mice CD4 T cells in contact with myosin [5]

Mice myocarditis is developed when myosin/ *T cruzi* immunization occurs. **So myosin has an important paper in the pathology**. [6]

Other cardiac injures produce antimyosin antibodies and healthy people have it too. [7]

Cha Antigen

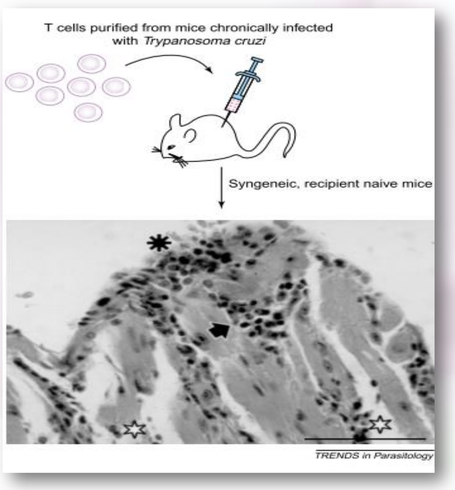
Human infected serum react with Cha antigen [7]

P protein

Introduction a lysate or P protein in mice induce functional damage in heart and autoantibodies in front the cardiac tissue. [5]

There are **molecular mimicry** [5]

IN FAVOR: AUTOANTIBODIES



Black arrow: lynphocits; black star lmyocarditis limit and white star general edema [8]

The introduction of immune cells for a infected mice to a non infected produce myocarditis in it, without the parasite [9]

There are autoantibodies a few weeks after the infection but unless pass years this don't cause the chronic phase. [7]

There are autoantibodies but what role they do in the pathology?

Induction of autoantibodies with autoantigens induce cardiac damage [4]

Passive transfer of autoantibodies failed in the induction of myocarditis[9]

The parasite presence isn't be necessary for the pathology, but the auto-reactive cells needs to be activated previously by the parasite [10]

AGAINST: PARASITE PERSISTECE

The level of myocarditis and autoimmunity in the chronic phase depend on the parasitemia in the acute phase: susceptibility and treatment. [9]

Vaccination will decrease the symptoms in the chronic phase [9]

The immunosuppression increase the infection and the severity of the disease [2]

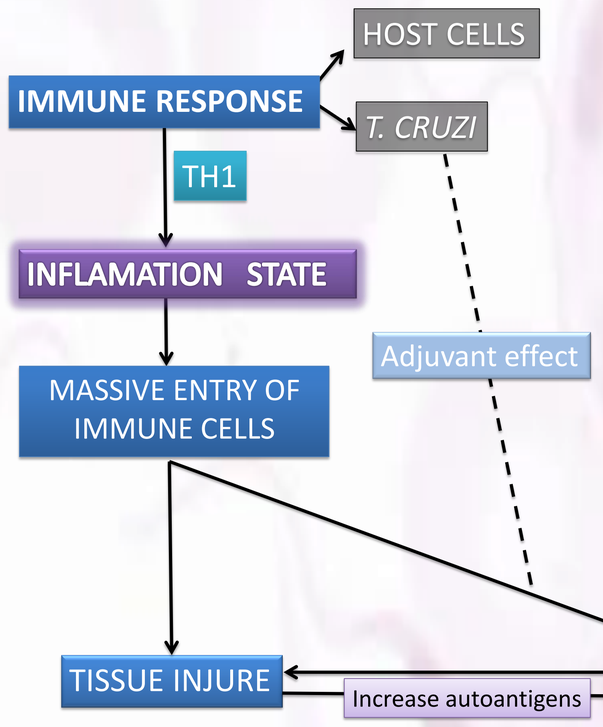
Chagasic patients	Anti-Cha antibodies	Anti-*T. cruzi* antibodies	Myocarditis
Symptomatic	+++	+++	+++
Asymptomatic untreated	++	++	-
Asymptomatic treated	+	+	-

The presence or absence of myocarditis was given by clinical histories of patients.Antibody response was quantitated as reported elsewhere (127): +, OD 450 nm<0.3; ++, OD 450 nm 0.3-1.0; +++, OD 450 nm<1.0.

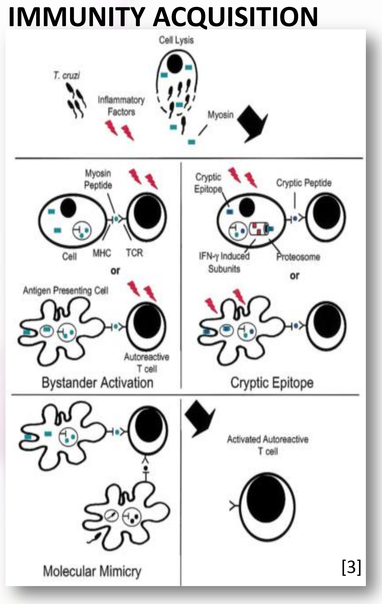
[9]

But there aren't be relation between the major parasitemia and the severity of the pathology [8]

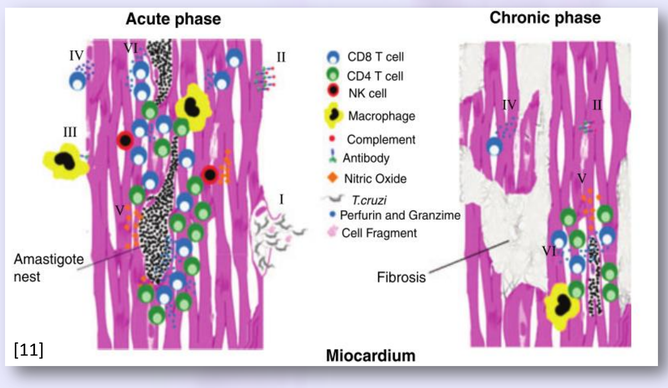
BOTH: PARASITE PERSISTENCE AND AUTOIMMUNITY



POSSIBLE MECHANISMS FOR IMMUNITY ACQUISITION



[3]



[11]

The multiplication of *T.cruzi* produce a cardiomyocyte destruction and consequently a immune response in front *T.cruzi* but also the expose of intracellular components active an immune response in front them. And molecular mimicry too. This increase the injury because the autoantibodies and the autoreactive T cells. [11]

T. cruzi is the trigger but the autoimmune is that produces the damage in the chronic phase [9]

kDNA

T.Cruzi introduce it genome in the host cell and change the phenotype of the host cells causing the autoimmunity [12]

CONCLUSIONS

-There is large controversy of the results of the autoimmunity because of the different experimental conditions
-The scientists are positioning for or against of the autoimmunity to be cause of the pathology, but neither demonstrates that the other theory is incorrect [2]. It's thought that the two theories not are esculent themselves in the development of the pathology.
-The contribution of the parasite and the immune system in the pathology isn't clear yet. It's very difficult to separate the immune response front autoantigens that front *T.cruzi*

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