REVISÃO

# IMPLICATIONS OF SUDDEN DEATH IN CHAGAS DISEASE

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## ABSTRACT

American Trypanosomiasis or Chagas disease is an important problem of public health affecting 20 million people in Latin America. It is caused by the flagellate parasite *Trypanosoma cruzi*. Chronic progressive heart disease develops in approximately 20 to 40% of infected persons. Chagas heart disease is one of the leading causes of sudden death after coronary heart disease. Approximately, half of the patients with Chagas heart disease died suddenly. The mechanism of sudden death in Chagas disease include ventricular fibrillation or tachycardia, severe bradyarrhythmia, embolic complication and spontaneous ventricular rupture. Proarrhythmia is common due to the coexistence of heart failure and multiple electrophysiologic abnormalities including sinus node dysfunction, intraventricular and atrioventricular conduction abnormalities, severe multiform ventricular arrhythmia, abnormal Q waves and altered ST segment and T wave abnormalities. Thus the ventricular arrhythmias of Chagas heart disease are one of the most demanding models on which an antiarrhythmic drug can be tested. Chagas heart disease is now a widen problem as a result of immigration. The transmission of Chagas disease via blood transfusion is not confined to countries where the disease is endemic. The migration of persons infected by *Trypanosoma cruzi* poses a public health problem even for countries where the disease is not transmitted by vector. Most of the Latin American immigrant with Chagas heart disease living in United States and Europe are either undiagnosed or misdiagnosed as having either idiopathic cardiomiopathy or coronary artery disease.

KEYWORDS: Chagas disease. Sudden death. American Trypanosomiasis

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## CHAGAS DISEASE AS AN IMPORTANT PROBLEM OF PUBLIC HEALTH

American trypanosomiasis or Chagas disease, first described in 1909 by the Brazilian physician Carlos Chagas who also discovered its etiological agent and mode of transmission, is a disabling and potentially lethal disease (3). It is caused by the flagellate parasite *Trypanosoma cruzi*, a protozoan harbored by a variety of domestic and wild animals (3). The insect vectors of the disease are present throughout most South and Central America, and their zone of distribution extend across the southern United States, where at least some of these vectors are infected with Trypanosoma (13,19). In Latin America, 20 million people are thought to have Chagas disease and 90 million are considered to be at risk of infection (19). It is the most common cause of dilated cardiomiophaty in countries where the disease is endemic and is responsible for over 30 percent of deaths from any cause and nearly all deaths from cardiovascular causes in areas where the disease is endemic (2,16) Chagas disease commonly presents with symptomatic ventricular arrhythmias, symptomatic bradiarrhythmias, sudden death, heart failure, embolic events, chest pain and high susceptibility to proarrhythmia (2). The clinical picture mimics that of coronary artery disease as well as idiopathic dilated cardiomyopathy. The prognosis is poor for patients with malignant ventricular arrhythmias, heart failure, left ventricular aneurysm or global systolic dysfunction (6,14).

The infection is characterized by an acute symptomatic phase with high parasitemia and is followed by a lifelong intermediate phase in which low numbers of parasites are sequestered in tissues; however the acute phase often is clinically silent (2). Chronic progressive Chagas heart disease develops in approximately 20 to 40 percent of infected persons (6,14). This chronic phase is usually manifested by a cardiomyophathy due to progressive multifocal damage in both the myocardium and the conduction system (6,14). It has long been observed that loss of cardiac innervation is frequently found pathologically in Chagas disease. This abnormality often precedes other evidence of cardiac involvement and is associated with clinically detectable abnormalities of autonomic function. Such a strong propensity for autonomic dysfunction is a unique feature of Chagas disease that distinguishes it from other cardiomyopathic disorders and has led some to hypothesize that it may contribute to the pathogenesis of cardiac damage (15).

Within the group of patients with Chagas disease, atypical chest pain occurred in 53 percent. Whether the ischemic like syndrome of the chagasic patients was due to coronary vasospasm because an autonomic imbalance or because of abnormalities of endothelium - derived relaxing factors has to be determined. In a group of chagasic patients with left ventricular apical aneurysm, the intracoronary infusion of acetylcholine or adenosine elicited a



paradoxical coronary vasoconstrictive response, suggesting that an abnormality of the endothelium-dependent coronary vasomotion may have a role in both the chest pain and the development of segmental-wall-motion abnormalities (17).

The pathogenesis of the cardiomyopathy in chronic Chagas disease is incompletely understood. A dynamic hyphotesis begins with direct parasite-related tissue damage, followed by progressive damage perpetuated by autoimmune and microvascular abnormalities. Studies in animals suggest involvement of cellular mechanisms particularly CD4 + T lymphocytes, along with macrophage activation and inflammatory cytokine mediators. Autonomic dysfunction probably has a secondary role, and the contribution of persistent occult infection remains unclear. Further understanding of the pathogenetic mechanisms is paramount to devising potential strategies for treatment and vaccination (12).

In its usual mode of transmission, the disease is spread by the insect vectors, usually members of the reduviidee family (Kissing bug). These insects puncture the skin of the host to suck blood. They carry *Trypanosoma cruzi* in their gastrointestinal tract; they defecate as they suck blood, and the excreted *Trypanosoma cruzi* then penetrates into the host through the punctured skin. Blood transfusion is the second most frequent mode of transmission of Chagas disease. The congenital form, transmitted through the placenta, is also relatively frequent. The risk of infection is directly related to socio-economic factors, since the triatomine bugs preferred habitat is in crevices in the wall of poor-quality houses in rural areas and periurban slums.

## DIAGNOSIS OF CHAGAS DISEASE

When *Trypanosoma cruzi* infection of the heart is demonstrated by pathologic examination of cardiac tissues or by xenodiagnosis, the diagnosis is certain. However the pathologic verification is rare. Therefore, diagnosis of cardiac involvement in Chagas disease is usually made when a combination of epidemiologic, serologic, and clinical criteria are present (2,3,6,16,19). It is particularly important to use such a strict case definition in populations in which Chagas disease is uncommon, such as United States and Europe. Case definition criteria for diagnosis required a combination of epidemiologic, serologic and clinical criteria to be met (6). These included (3) a history of residence in an area where Chagas disease was endemic (19) an unequivocally positive serologic test for *Trypanosoma cruzi* (13) a clinical syndrome compatible with Chagas heart disease, and (16) no evidence of another cardiac disorder to which the findings could be attributed.

## SUDDEN DEATH IN CHAGAS DISEASE

Chagas heart disease is one of the leading causes of sudden death after coronary artery disease. The cause of death in Chagas heart disease is sudden cardiac death in 50% of cases, congestive heart failure in approximately 40%, and cerebral embolism in 10% (2,6,8,10). Sudden death has been mentioned as the most frequent terminal event observed in any stage of Chagas disease. Patients dying suddenly have less extensive structural abnormalities than those dying of congestive heart failure and also have more complex and sustained ventricular arrhythmia on ambulatory ECG (6,8,4). The frequency of sudden death due to Chagas disease is most likely overlooked in many cases. This is supported by autopsy studies of fatal traffic accidents and sudden unexplained death where the disease is endemic, which reveal that chagasic heart disease is frequently the sole finding (7).

The mechanism of sudden death in Chagas disease include (10): 1) ventricular fibrillation or tachycardia, 2) severe bradyarrhythmia, 3) severe embolic complication, 4) exceptionally spontaneous ventricular rupture.

Approximately half of sudden death patients due to Chagas disease are asymptomatic before death and this is the first manifestation of the disease in such patients and nearly all have significant ventricular abnormalities and conduction system disease (10). In few cases, constituting less than 6%, only minimal myocardial involvement is found (10,12).

Proarrhythmia may occur in-patients with Chagas disease (10,7,9). Conventional antiarrhythmic agents, except amiodarone, may increase the risk of ventricular fibrillation, or aggravate a preexistent cardiac failure (10,9). The high susceptibility to proarrhythmia is probably due to heart failure and multiple electrophysiologic abnormalities including:

1) Frequent sinus node dysfunction
2) High rate of involvement of the conduction system that produces the characteristic ECG abnormalities of right bundle branch block or left anterior hemiblock or both, found in 10 to 80% of patients with overt cardiac disease (8,9). It is uncommon to encounter a patient who has overt Chagas disease without an abnormal ECG. It is believed that ECG conduction abnormalities develop approximately 10 to 20 years after infection (16,6).
3) High rate of severe multiform ventricular arrhythmia.
4) High frequency of atrioventricular block.
5) Abnormal Q waves
6) Abnormal ST segment and T-wave abnormalities
7) Autonomic dysfunction.



Thus the ventricular arrhythmias of Chagas heart disease are one of the most demanding models on which an antiarrhythmic drug can be tested (17,4). This is emphasized by our report of 10 Chagas heart disease patients who died during ambulatory electrocardiographic monitoring (10). In 6 of our 10 patients, the terminal event was *torsade des pointes*, as a result of type IA antiarrhythmic drugs. In 3 cases the arrhythmia was sustained ventricular tachycardia, and AV block was the cause of death in one.

Several studies suggested that amiodarone should be tried empirically first, and if the drug fails, electric stimulation-guided therapy should be performed (4,9). The implantable cardioverter-defibrillator has been used successfully in small numbers of patients with Chagas heart disease (18). Aneurismectomy, chemical ablation of ventricular arrhythmias and catheter ablation of ventricular tachycardia also has been reported, but present experience is inadequate to determine their long-term effects on survival and arrhythmia recurrence.

## CHAGAS DISEASE IN EUROPE AND UNITED STATES

Chagas disease is of interest to the medical community both inside and outside Latin America. Its unique pathologic characteristics and pathogenesis are useful models for the study of cardiac innervation, the cardiac conduction system, and mechanism of heart damage in cardiomyophaties states.

Also important, cases of Chagas heart disease are likely to be encountered by clinicians wherever infected persons reside, not solely where it is endemic. As a result of modern transportation and immigration, Chagas heart disease is now a widen problem, especially in the United States, where there are estimated to be 500.000 infected persons (13,6).

The prevalence of chagasic infection in immigrants from Latin America settled in Europe has not been assessed. The overall 7.4% incidence of Chagas disease in Latin America will serve to calculate the number of persons infected with *Trypanosoma cruzi* living in Europe. Most of these individuals probably are either undiagnosed or misdiagnosed as having either idiopathic (dilated) cardiomiopathy or coronary artery disease, since Chagas disease is largely unrecognized and blood screening is rarely performed.

The two most important public health questions relating to the presence of *Trypanosoma cruzi* infected immigrants in Europe, the United States and Canada are:

1) The prevention of transmission of the parasite by transfusion of blood. The transmission of Chagas disease via blood transfusion is not confined to countries where the disease is endemic (13,19). The migration of

persons infected by *Trypanosoma cruzi* poses a public health problem even for countries where the disease is not transmitted by vector.

2) The detection and medical care of patients with chronic Chagas heart disease.


## RESUMO

Conseqüências da morte súbita em doença de Chagas

A Tripanosomíase Americana ou doença de Chagas é um importante problema de Saúde Pública que acomete 20 milhões de pessoas na América Latina. Causado pelo parasita flagelado *Trypanosoma cruzi*, leva a doença cardíaca crônica e progressiva em aproximadamente 20 a 40% dos indivíduos infectados. A cardiopatia chagásica é estatisticamente uma das principais causas de morte súbita, vindo logo após da doença cardíaca coronária. Aproximadamente metade dos pacientes com cardiopatía chagásica morre subitamente. Os mecanismos de morte súbita na doença de Chagas incluem fibrilação ventricular ou taquicardia, bradiarritmias severas, complicações embólicas e ruptura espontânea ventricular. A proarritmia é freqüentemente observada como coexistência de insuficiência cardíaca e múltiplas anomalias eletrofisiológicas, que incluem disfunção do nodo sinusal, anormalidades da condução intraventricular e atrioventricular, arritmias ventriculares severas e multiformes, ondas Q anormais e alterações do segmento ST e anormalidades da onda T. As arritmias ventriculares da cardiopatía chagásica constituem-se, portanto, um dos modelos preferidos para testar uma droga antiarrítmica. A cardiopatia chagásica é atualmente um problema mundial, em função da imigração. A transmissão da doença de Chagas pela transfusão de sangue não se encontra apenas restrita àqueles países onde a doença é endêmica. A migração de pessoas infectadas pelo *Trypanosoma cruzi* leva a um problema de saúde pública, mesmo em países onde não há transmissão vetorial. A maioria dos imigrantes da América Latina com cardiopatia chagásica que residem nos Estados Unidos e na Europa não são diagnosticados ou são equivocadamente diagnosticados como portadores de cardiomiopatia idiopática ou de doença coronária.



UNITERMOS: Doença de Chagas. Morte súbita. Tripanosomíase Americana.


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