

GHH Seminars – Chagas Disease – WHO, Geneva, Oct. 2009

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Slide 1

Good afternoon. I would like to thank the Wellcome Centre for the History of Medicine and the World Health Organisation, specially Dr. Sanjoy Bathacharya and Mr. Thomson Prentice, for the invitation to participate in this seminar. It is a great honour to be here to speak about a disease that acquires a special visibility this year, in the centennial of its discovery by the Brazilian physician Carlos Chagas. Chagas' disease has been an example of the close relations between scientific knowledge, sociopolitical intervention, and health problems associated to poverty, critical issues on the contemporary International Health agenda.

Slide 2 – Main issues

The history of Chagas disease in Brazil should be viewed as a long and collective process by which an infirmity has been framed simultaneously as a medical-scientific object and as a social object. I argue that it was considered as 'the disease of Brazil': it became the symbol of a 'diseased nation' that could not achieve civilization because of the endemic diseases that affected its rural laborers; and it also became emblematic of the science that was then revealing this situation and indicating ways to overcome it. This is a case that shows to what extent Brazilian scientists produced innovative knowledge within the

international universe of tropical medicine, which, at the same time, was deeply influenced by contemporary political, social and economic trends of the time.

Slide 3: The beginning of a “new century”

In the early years of the 20th century, the world experienced great optimism regarding science as a key element to progress. In Brazil, which had recently abolished slavery and instituted the republican regime, there was also great enthusiasm. The new century began with a large urban renewal of the Brazilian capital. The city of Rio de Janeiro was the country's main port, through which the agricultural production was exported and many immigrants arrived. The young physician Oswaldo Cruz, trained at the Pasteur Institute in Paris, and director of the recently created bacteriological Institute of Manguinhos, was commissioned to sanitise the city and to turn it into the “showcase” of a tropical country that aspired to become modern. It was in this context that Carlos Chagas, born on a farm in the state of Minas Gerais, studied at the Medical School of Rio de Janeiro. His graduation thesis for the medical degree, defended in 1903, was about malaria and was developed at the Manguinhos Institute.

Slide 4: The training in malaria

Malaria jeopardised some of the important modernisation works of the country. Having already combated two epidemics of the disease, in 1907 Chagas was designated to conduct a third campaign against it in the northern Minas Gerais, where an epidemic paralysed the extension works of the railway Estrada de Ferro Central do Brasil. This railway was the main means of transportation for the Brazilian agricultural production and an important vehicle to populate the country's hinterlands. It was during this campaign that, unexpectedly, Chagas made the discovery that would consecrate him.

Slide 5 - The Trypanosoma cruzi discovery:

In the settlement of Lassance, while coordinating the campaign against malaria, Chagas examined species of Brazilian fauna, motivated by his interest in entomology and protozoology, important areas of research at the Manguinhos Institute. In 1908, he heard about a hematophagous insect that proliferated in the wood-and-mud huts typical of rural areas. It was popularly known as 'barbeiro' [barber] since it tends to bite peoples' faces while they are sleeping. Aware of the importance of bloodsuckers as transmitters of parasitic diseases, Chagas examined some bugs and found flagellate protozoan forms that could be a natural parasite of the bug or else a trypanosome in vertebrates. It could even be an evolutionary stage of *Trypanosoma minasense* he had previously described in marmosets in that same region. Since he did not have laboratory facilities in Lassance to elucidate the matter, he sent a few insects to Oswaldo Cruz in Rio de Janeiro, for some experiences. Chagas then established that it was not the *Trypanosoma minasense* but rather a new species of trypanosome, which he named *Trypanosoma cruzi* in honor of Oswaldo Cruz. At the time, studies about diseases caused by trypanosomes (especially African trypanosomiasis) were on the agenda of European tropical medicine, and Chagas was aware of them, especially because of his interchanges with German protozoologists.

Slide 6 - The discovery of a new tropical disease at Lassance

Suspecting that *Trypanosoma cruzi* could be pathogenic to humans, Chagas returned to Lassance and, in April 1909, identified the new parasite in the blood of a feverish two-year old girl. Berenice was the first case of what would be from then on considered a new human disease. The discovery was celebrated by the medical community as a great 'feat' of Brazilian science: **one researcher, during a short period of time, identified a new disease, its transmitter and its pathogen.** Chagas achieved high scientific prestige in Brazil and abroad, being twice nominated for the Nobel Prize for Medicine.

Slide 7 - The first studies

The study of the new trypanosomiasis, initiated in 1910, became the main topic in the research agenda at the Oswaldo Cruz Institute. Together with other researchers, Chagas engaged himself in the investigation of the various aspects of the disease: the vector, the parasite, its reservoirs, the clinical picture, the diagnosis methods, and possible means of treatment. He divided the infection into two forms - acute and chronic -, pointing out that in the chronic phase, trypanosomiasis produced neurological, cardiological and endocrinological disorders (particularly thyroid complications). Chagas considered that in regions where the infection by *T. cruzi* occurred, endemic goiter (very common in the interior of Brazil) was not the same as in Europe, but rather a consequence of the *T. cruzi* on the thyroid. Endemic goiter was thus seen as the main clinical sign of the new disease, and an important element for its social framing as an infirmity that damaged the physical and mental development of rural population.

Slide 8 - The discovery of an unknown and poor country

The new trypanosomiasis was framed as a new nosological entity as well as a public health issue. Chagas advocated that it was a terrible scourge over a vast zone of the country, thereby rendering a sizeable population worthless to the progressive evolution of the nation. At a time when progress was being celebrated, Chagas denounced that this was a disease that revealed an unknown Brazil: the one of the hinterlands. The wood-and-mud hut was the major symbol of that ailment so intimately associated to poverty, in an essentially rural country. This idea of the social importance of rural endemic diseases was largely propagated by the Brazilian sanitarian movement, which between 1916 and 1920 united physicians, intellectuals and politicians who defended that the country's backwardness was due not to the tropical climate or to the racial composition of its population, but to the diseases that affected the hinterlands. **This idea conferred specific frames to tropical medicine in Brazil. Mentioning the Europeans engaged in combating sleeping sickness in Africa for colonialist interests, Chagas stressed that in Brazil the study of the tropical nosology should be made in the benefit of the nation itself.**

Slide 9 – Controversies

Nevertheless, in the mid 1910's, the disease became the object of intense queries. Studies made in Argentina confronted Chagas' formulations about the chronic clinical forms, particularly the correlation with endemic goiter. According to some researchers, trypanosomiasis and goiter were totally different diseases, overlapped in the regions studied by Chagas. Thus, there could be certainty only about the acute cases of trypanosomiasis, and, as they pointed out, the recorded ones were restricted to few dozens in Minas Gerais. In 1916 Chagas reaffirmed that the disease was not limited to few acute cases neither to Brazil. Although he continued to believe in the association with goiter, he affirmed that the issue was open to further discussions; he began to minimise the importance of the endocrinological aspects and to highlight the cardiological ones.

In 1919, some Brazilian physicians added a strong political content to the controversy. They argued that the extension and the importance of Chagas disease were exaggerated, because the criteria for its estimate – the association with goitre – was mistaken. They also argued that the notion of a diseased country was anti-patriotic and would frighten immigrants and investments. The controversy further intensified in a strong debate at the prestigious National Academy of Medicine. With great repercussion in the press, the polemic was related to doubts that really surrounded clinical and epidemiological pictures of the disease, but also to the intense nationalistic debate that took place at that moment; many physicians opposed to the idea of tropical medicine because they considered it to reinforce ancient determinisms and stereotypes about the

country. The dispute was also nurtured by rivalries with Chagas, related to his work as Director of the Oswaldo Cruz Institute and of the National Department of Public Health. From then on, Chagas carried on with his work. But the polemics had set a mood of uncertainty towards the disease.

Slide 10 – Research in Argentina

Ironically, the fundamental stimulus to overcome this uncertainty came from Argentina, with studies conducted since 1926 by the physician Salvador Mazza in the hinterlands of the country. In 1935, one year after Chagas's death, the physician Cecílio Romãna, a member of Mazza's group, described a clinical sign that allowed the identification of acute cases of the infection: a swelling of the eyelid as a result of the contamination of the conjunctive by the infected faeces of the bug. The so-called "Romãna sign" led to the diagnosis of hundreds of acute cases in Argentina and some other countries in Latin America, indicating the continental dimension of the disease.

Slide 11 - Disciples in Brazil

In Brazil, Chagas' followers engaged in the continuity of the research on the American trypanosomiasis. Evandro Chagas (Chagas' eldest son) initiated an important investigation work and specially the propagation of information on the disease among rural physicians, which resulted in finding an important focus in the west of Minas Gerais, in a small town named Bambuí, where, in 1943, was created a research post of the Oswaldo Cruz Institute, whose direction was assigned to Emmanuel Dias, a disciple of Carlos Chagas. The contribution of the Bambuí group to the scientific and social acknowledgment of Chagas disease would be decisive.

Slide 12 – The work of Bambuí group

By applying the modern electrocardiograph techniques of the time, the group deepened the study of the chronic cardiac form. **The assumption regarding the endemic goitre was put aside and, by the end of the 1940's, the chronic chagasic cardiomyopathy was defined as the essential clinical manifestation of American trypanosomiasis.** At a moment when the world – and Brazil included – was living the “development dream” in the aftermath of the Second World War, and in which the health issue gained visibility with the debates on the “vicious circle of disease and poverty”, the Bambuí scientists propagated the idea that this cardiac disease was a serious public health problem because it incapacitated individuals for work in their productive age.

Within a context of great enthusiasm about the “magic bullets” to win the battle against tropical diseases, such as DDT, Dias and his collaborators tested several insecticides against the triatomines and, in 1948, they established the efficacy of the gamexane. The Argentineans Romaña and Abalos reached the same conclusion at the same time. **In 1950, the first campaign held in Brazil to combat Chagas disease was initiated, using gamexane in dwellings. Established as a medical fact, Chagas disease became a sanitary issue to be tackled by the Brazilian State.**

The work of Dias and his collaborators should be understood in a historic context particularly favourable to projects directed to the development of the hinterlands. Even though Brazil was living an industrialization and urbanization process,

especially since the thirties, the topic of settling and developing the interior took on a new meaning; it would be a way of guaranteeing supply to a national consumer market and thereby sustaining the new economic model of substituting imports. In Minas Gerais and other rural areas of the country, the concern over economic development fueled interests in programs meant to modernize the agricultural production and to halt the rural exodus towards urban centers.

Slide 13 – The mobilisation of the physicians of the hinterlands

The recognition of Chagas disease as a medical and social issue was also achieved because of the intense social and political mobilisation undertaken by Emmanuel Dias to convince society about the importance of American trypanosomiasis. The information on the disease was spread particularly among the physicians in the hinterlands, who were called to be allies of the scientists by providing them with new data about the disease. Those physicians started to see the disease as a symbol of their own identity, as “doctors of Central Brazil”, as they called themselves. From the 1950’s on, the theme was studied at medical schools created in regions where the disease was endemic, such as in Goiás, the state where the new capital, Brasília, was built as the symbol of the Brazilian development project. The hinterland physicians had a fundamental role also by their own contribution to knowledge. In 1956, a physician from Goiás, Joffre Rezende, published the first work on a new form of the chronic disease: the digestive form.

Slide 14 – The mobilisation of the international agencies

Emmanuel Dias also engaged in mobilizing the international agencies – particularly the Panamerican Sanitarian Bureau – and his Latin-American colleagues. He claimed for a campaign for the eradication of the main vectors of the disease in the Americas, similarly to the WHO campaign for the eradication of malaria. In 1960, one year after the 1st International Congress on Chagas Disease, held in Rio de Janeiro, the WHO organised a meeting of experts in Washington to evaluate strategies for the study and the combat of Chagas disease. That same year, the Brazilian Ministry of Health also held an important meeting to discuss the subject. In 1962, one year after the researcher Zigman Brener had established the possibility of cure for experimental Chagas disease, a meeting was promoted in Rio de Janeiro by Eaton Laboratory of US to discuss the perspectives for therapeutics. **Those events marked the broad recognition of the relevance of the disease.** Nevertheless, in that year of 1962 *nineteen sixty two*, Dias' work was suddenly interrupted by his death.

Slide 15 - New paths for fighting the disease

In the subsequent decades, news trails would be followed for the combat of the disease. The expectations of a campaign co-ordinated by WHO against the infirmity in the American continent did not materialise. In Brazil, the National Programme for the Control of Chagas Disease was implemented during the 1980's, after the first National Serological Survey. In 1991, the governments of Argentina, Bolivia, Brazil, Chile, Paraguay and Uruguay established the important Southern Cone Initiative, aimed at interrupting vectorial and transfusional transmission in the region. After Uruguay and Chile, Brazil achieved this goal in 2006.

Slide 16 – New paths for studying the disease

From the seventies on, new interests for the disease increased in the field of basic research, motivated by the new molecular biology approaches. This process, supported by the scientific and technological development policy fomented in Brazil in the 1970's, attracted new generations of researchers and led to the institutionalization of an academic community on the American trypanosomiasis. Besides the Annual Meetings of Basic Research on Chagas Disease, initiated in 1974, an important mark of this expansion was the creation, in the following year, of the WHO/TDR, in which Chagas disease had and continues to have a special relevance. The genetic sequencing of the *T. cruzi*, as part of the Trypanosomatids genome project initiated in the 1990s by the TDR and other scientific institutions in many countries, including in Brazil, was an example of the ability of some developing countries to undertake scientific innovation aimed at providing solutions to health problems.

Slide 17 – Some challenges of the 21st century

Chagas disease is still an important problem to be faced. In a globalized world, with intense migration, it has become 'urbanized' and the issue of transfusional transmission has gained prominence (particularly in non-endemic countries that receive migrants from endemic areas). In countries where vector transmission is controlled, the challenge is to maintain political priority and epidemiological surveillance. Chagas disease in the Amazon region – where transmission patterns assume peculiarities that do not exist in other places – is an emerging public health problem that needs to be faced, in which the environmental issue assumes special relevance. **Furthermore, in a broader context, the search for new and more efficient ways of treatment is one of the most important issues to be solved.**

I would like to finish this presentation pointing out to some connections between past, present and future.

Slide 18 – Eyes to the future

This year, I spoke about Chagas disease to children at Lassance, where it was discovered a hundred years ago. As I told them about the past, their past, I asked myself: what can we tell them about the future?

Slide 19 – Some lessons from history

I think one of the “lessons” from history has to do with a science with a double aim: to produce innovative knowledge and to find solutions for the concrete social problems. Furthermore, in a globalised world, in which science presupposes extensive networks, it is interesting to observe that, since 1909, the production of knowledge about Chagas disease was a collective process, in which scientists acted not only in the laboratories but also in the broader social life, searching for alliances in order to convince various social groups that this was an important public health problem. It is now for us to think how to articulate science and society to face the challenges posed today by this and other neglected diseases. Although reality has changed in certain aspects, some permanencies continue.

Slide 20 – Past and present

I took this photograph few months ago. If this house has no more vectors of Chagas disease, it continues to be one of the images of poverty and iniquity in developing countries. Our commitment must be to face this situation.

Slide 21: Thank you

If we advance in this direction, those children – and many others – will certainly be very grateful. Thank you very much.