The Rise and Fall of Chagas Disease

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American Trypanosomiasis, known as Chagas disease, was discovered in 1909 under peculiar circumstances: its discoverer, Carlos Chagas, was sent to a small village of Central Brazil to carry out an anti-malaria campaign when he came across a blood sucking insect—the vector for the parasite infection. He had been alerted to the coincidence of peculiar symptoms and the presence of this insect in the wood and earth dwellings of the region. He was deeply involved in theoretical controversies in international protozoology; he was engaged in the consolidation of a scientific role and corresponding institutional conditions in Brazil, and equally immersed in the nationalist sanitary struggles of his days. In these contexts, Chagas assembled a remarkable discovery discourse, regarding the biology of the parasite, its life cycle and mode of transmission. Furthermore, he provided the clinical description of a new disease. Despite immediate international recognition, however, the unstable institutional arrangements surrounding his work damaged its local legitimacy for decades. His authority was widely recognized abroad, but rejected at home.

Introduction

In a railway wagon, young Carlos Chagas, a Brazilian physician, improvised his clinic and laboratory in the Winter of 1907. He was in Lassance, a Brazilian hinterland far away from Rio de Janeiro, the capital of the country, where Chagas worked for the Instituto Soroterapico de

This investigation has been supported by the Program of Small Grants for Research in Social and Economic aspects of Tropical Diseases of the Laboratorio de Ciencias Sociales—Universidad Central de Venezuela, with financial support from the Special Program for Research and Training in Tropical Diseases (TDR)—UNDP/World Bank/WHO. The authors are greatly indebted to Vassiliki B. Smocovitis and to Marcos Cueto for their reading and comments.

Perspectives on Science 1999, vol. 7, no. 4

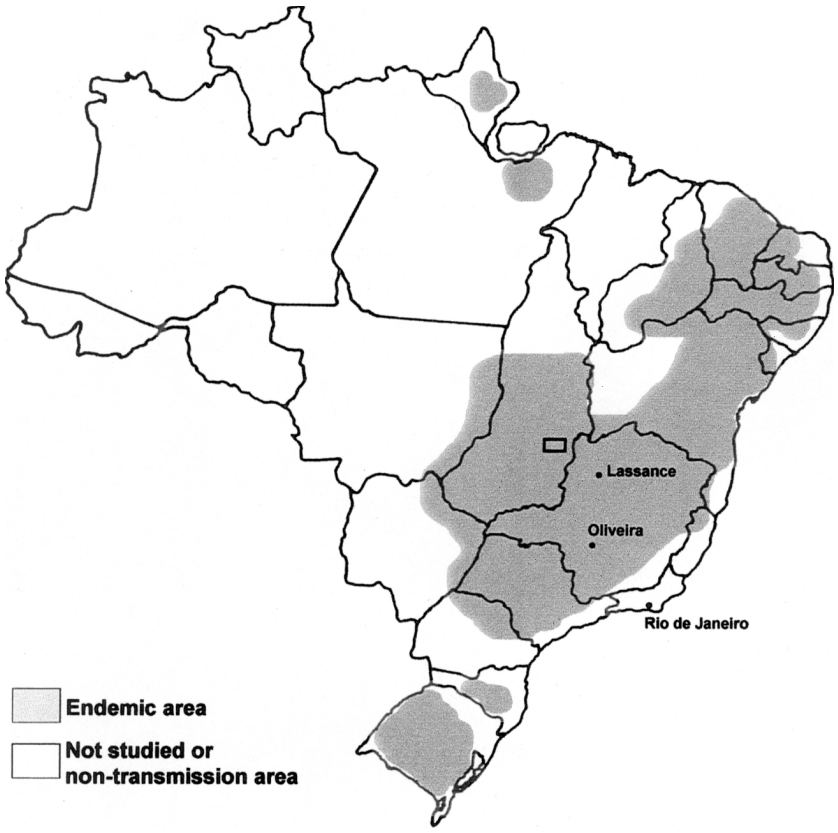

Figure 1. Geographic distribution of Chagas disease in Brazil and main locations in the history of Chagas disease; the cities of Lassance, Oliveira, and Rio de Janeiro. Modified from D.P. Neves, *Parasitologia Humana.* Rio de Janeiro: Livraria Atheneu, 1987: 84.

Manguinhos (*Manguinhos Serum Therapy Institute;* see figure 1). He strained night and day with his colleague Belizario Penna against the scourge of malaria. The construction of the Central do Brazil railroad had been interrupted due to a malaria epidemic.[1] Among the acquaintances that Chagas made in Lassance was Cantarino Motta, chief-engineer of the construction, who had requested health care intervention on his malaria stricken workers. In 1908, Cantarino intruduced Chagas to a blood sucking insect that preyed at night on the people of that region. Chagas was quiet and

1. See Chagas' first report about Lassance (Chagas 1907*a*).

thoughtful that night while he listened to Cantarino as the engineer described the strange symptoms that affected those people.[2]

Months later, in February 1909, Chagas published the first of a series of articles on what later became known as Chagas disease.[3] He described a trypanosome, a protozoan that invaded human cells. He described the insect that transmitted it to humans and he described a complicated set of symptoms that characterized the parasitic infection. He had discovered a new tropical disease.[4] In 1910 he was named member of the National Academy of Medicine in Brazil. In 1912 he received the Schaudinn prize in Hamburg, the most important award in parasitology at the time. Nationally and internationally acclaimed for his discovery, Chagas became a hero.

A decade after the German award, however, the existence of the disease itself was challenged in the highest forum of Brazilian medicine, the same National Academy of Medicine that had acclaimed him earlier. Chagas defended himself against an angry group of physicians who claimed the trypanosome was not really pathogenic, that the symptoms which Chagas had described were doubtful, and that the discovery was not even his own work.[5]

Finally, in 1933, E. Villela realized that thousands were dying of Chagas disease in Belo Horizonte, close to Lassance, without even being diagnosed. The disease had disappeared from the minds of Brazilian doctors.[6]

How could a disease be so successfully "invented"[7] from scratch, immediately receive accolades at home and abroad, and yet soon after be so easily disqualified? In this paper, we explore the strange circumstances sur-

2. See Carneiro (1963), pp. 7–10; Carlos Chagas Filho (1974).

3. The first article mentioning what later became *Trypanosoma cruzi* was "Neue Trypanosomen." *Archiv für Schiffs-und Tropenhygiene* 13 (1909), 120.

4. Chagas disease is, even now, an important tropical disease. It is caused by the parasite *Trypanosoma cruzi,* a flagellate of the Kinetoplastida Order, Family Trypanosomatidae. It is transmitted by triatomine blood-sucking insects. According to the World Health Organization, it now affects 16 to 18 million people in South America. In spite of the successful control programs developed recently, 25% of the Latin American population is presently considered at risk. See WHO, http://www.who.int/ctd/html/chagcsstrat.html. The infection is complex. After the short acute phase, it develops into a chronic stage in which different syndromes might emerge. After several years, 27% of those infected develop cardiac problems which may lead to sudden death, 6% develop digestive damage, and 3% present peripheral nervous involvement. At present, Chagas disease has no cure. See World Health Organization—Division of Control of Tropical Diseases "Chagas Disease Elimination." See http://www.who.ch/ctd/.

5. See Carlos Chagas Filho (1974), O. Fonseca Filho (1974).

6. See E. Villela (1930).

7. The term "invention" is used by Chagas himself to describe his discovery. See Chagas (1928).

rounding the discovery, the initial acceptance and subsequent rejection of Chagas disease. We examine the peculiar sequence of events leading to the "invention" of the disease. The vector and the etiologic agent, for instance, were discovered before the actual symptoms. We also examine the wider context for the recognition of Chagas' work. The discovery satisfied the demands of an international audience focused on understanding the etiology of tropical diseases, promoting the specificity of these infections, and articulating the insect-vector theory. Finally, we contrast the conditions for international acceptance with those that determined its rejection at home. Chagas' agenda was to carve a niche for experimental medical science in Brazil. This cause did not have a great number of supporters and never achieved consensus in the country.

In order to put together the pieces of this puzzle, we shall begin our journey far from where the dramatic construction and de-construction of Chagas disease took place. We will start in turn-of-the-century Europe, where tropical medicine was emerging and growing in importance.

Microbes and national imperatives

The history of Chagas disease cannot be understood outside of the history of early twentieth-century tropical medicine. A radical change in the perception of disease had taken place with late nineteenth-century germ theory. It produced a new scientific and optimistic perspective on the diseases associated with the tropics. Michael Worboys places the emergence of tropical medicine in the crossing of germ theory and the new requirements of "constructive imperialism," in the turn of the century (Worboys 1976, 1993).

In 1899, P. Manson, a British army physician, defined tropical diseases as those caused by protozoan or more complex organisms (Worboys 1993, p. 518). Such tropical diseases were, for him, necessarily parasitic in nature and depended on a geographically limited factor for transmission. This definition separated the "cosmopolitan" bacterial diseases from the ecologically limited parasitic diseases. The definition was coupled to the "insect vector theory," according to which, in parasitic diseases, the etiologic agent developed one or more stages of its life cycle within an insect vector. This form of transmission would be typical of protozoa or helminths. Bacterial diseases, instead, would be transmitted by direct contagion. The critical support for this theory was the discovery, between 1898 and 1899, that malaria parasites were transmitted by the mosquito (Harden 1985; Worboys 1993, p. 514).

Thus, whenever a parasite was involved in a disease, especially a protozoan one, an arthropod vector was also expected. Parasite hunting became the sport of the season.

Although separated from bacteriology,[8] parasitology was emerging and growing through the emphasis placed on protozoa and worms by the rise of tropical medicine (Worboys 1983, pp. 10–11). By the late nineteenth century, the enthusiasm for parasites led to the search for and discovery of many causative agents and biological cycles of "tropical" diseases. Among these were the identification of the malaria *Plasmodium* parasites, by A. Laveran in 1880; the identification of the malaria insect vector and life cycle by R. Ross and G. B. Grassi in 1897; the discovery of the causative agent of Kala azar, *Leishmania donovani,* by W. B. Leishman and C. Donovan in 1900; the identification of the life cycle of *Schistosoma* worms, that caused bilharzia, by R. Leiper in 1915; the elucidation of filariasis transmission by mosquitoes by P. Manson in 1879; and the discovery of African trypanosomiasis by Bruce, between 1896 and 1902 (Worboys 1983; Curtin 1989, p. 136; Farley 1991, pp. 45–71; Desowitz 1993, p. 44).[9]

Causative agents of "tropical diseases" were varied in their taxonomy as well as their ecology. The first to be studied were parasitic worms. Then came the malaria family of related human and animal diseases. Trypanosomes came last, with the first human pathogenic species identified only in 1903 (Worboys 1993). The first trypanosome was found in 1841 in the blood of a trout, but the first identification of a disease caused by this group of organisms in mammals was conceived only in 1880, when Evans observed a tripanosomiasis in equines (Laveran & Mesnil 1904, p. 2). Laveran and Mesnil argue that it was only in 1897, with Bruce's study of Nagana, a disease affecting equines and other mammals, that a first model of the interaction of these organisms and their hosts was established. In 1899, Rabinowitsch and Kempner did the first cytological study of a trypanosome and in 1903 Novy and McNeal established a method to develop pure trypanosome cultures in blood-gelatin media.[10]

8. Institutional aspects of this separation include the disputes between Manson and his emerging London School and King's College bacteriologists, who would be willing to bite into the new and promising tropical medicine field. The convenient compromise was to consider bacteriology dispensable to a specialty whose objects comprised chiefly protozoa and worms (Farley 1991, pp. 25–28).

9. There were also important discoveries involving bacterial and viral infections, such as leprosy, cholera and yellow fever. About them see Worboys (1993, 1983). The obvious prestige of parasitological tropical medicine and the importance attributed to the discoveries related to it is also reflected in the Nobel awards. Among the first ten laureates in medicine and physiology, two were awarded the prize for contributions in tropical medicine: R. Ross in 1902, and A. Laveran in 1907. Besides these, R. Koch, an important player in the tropical medicine scene, received the 1905 Nobel prize for his work on tuberculosis. See the Nobel Foundation Web Site, http://www.nobel.se, last accessed April 27, 1999.

10. This is an important path since the ability to isolate, cultivate in vitro and then produce an experimental infection was a decisive sequence in the demonstration of the involvement of "germs" in specific diseases (Laveran & Mesnil 1904, p. 3).

Trypanosomiases were considered to be always tropical. In the beginning of the century an animal disease had been identified in South America, at the Chaco region (which includes a part of Brazil). A. Laveran and F. Mesnil, in their 1904 work, named this the *great decade of trypanosome studies* (Laveran & Mesnil 1904).

The late nineteenth and early twentieth century witnessed the establishment and rapid growth of an international institutional network for tropical medicine. Schools, departments, and institutes of tropical medicine were founded by the major colonial powers. In 1899, the first such institutions were established in England: the London School of Tropical Medicine and the Liverpool School of Tropical Medicine. Following that, in 1900, The first American tropical medicine institution was founded at Harvard University; in 1901 the Institut für Schiffs- und Tropenkrankheiten was founded in Hamburg, Germany, and in the same year Paris had its Institut de Médecine Coloniale. More chairs, schools, and institutes were subsequently created in the United States, Germany, Brussels, and the Netherlands (Worboys 1993, p. 520).

While the inevitable rivalries between competing colonial powers took place, there was also sharing of a common intellectual background. International meetings and awards were opportunities for such exchanges, including the International Sleeping Sickness Conference in London in 1907 (Worboys 1994, p. 98), the International Conferences in Hygiene and the Schaudinn prize, awarded by the Institut für Schiffs- und Tropenkrankheiten in Hamburg for important contributions in protozoology every four years.

Tropical medicine became a leading specialty in the medical sciences.[11]

Several discoveries in Tropical Medicine were made by army doctors or in imperial colonial medical services (Despowitz 1993, pp. 40–59, 165–167; Worboys 1993). Schools of tropical medicine were imperial business, justified by the necessity to care for the health of white settlers or to control urban epidemics that threatened colonial affairs. Tropical medicine and public health were largely military issues. Farley describes, for example, the invasive health care measures adopted by the United States during the cholera and plague epidemics in the Philippines in the beginning of the century as strictly a war action, with the isolation of infected people in "detention pavilions" and strong repression (Farley 1991, p. 37).[12] Thus, some understand tropical medicine as scientific and technological expressions of early twentieth century European and American imperialism (Farley 1991, pp. 13–156; Mac Leod 1988; Arnold 1988).

11. See Worboys (1993).
12. See also Arnold (1988, pp. 12–13).

From this perspective, tropical diseases are historically studied as an European, particularly British (and, to a lesser extent, American) concern. Worboys suggests that the problems of other regions were overlooked because metropolitan interests were not directly implicated (Worboys 1993).

In the gradient of medical interest diseases that affected white settlers, soldiers and indigenous people alike topped the list. Urban epidemics, such as cholera or plague, required the most stringent sanitary/military intervention. They affected the safety of white settlers and, therefore, of the empire. They could affect trade. Rural endemic diseases elicited a lesser reaction since they affected only poor indigenous people. However, they could impair colonization projects, such as railroad construction, agriculture, etc. Subsequent historical interest reflects this gradient.[13]

An atypical discovery

Given these determinants of historical interest, Chagas disease never received much attention. It was not important during the period when most historical writings were celebrations of heroic metropolitan deeds. It wasn't highlighted in the following, more critical periods in medical historiography either, because Brazil was not a colony by the end of the nineteenth century.

The history of Chagas disease is undeniably a part of the early history of tropical medicine-parasitology, sharing determinants, intellectual milieu, and theoretical assumptions with most other episodes. It is, however, historically atypical. Whereas most diseases discovered in the period affected European colonies, Brazil was an ex-colony.[14] Unlike other colonial powers, Brazil's former metropolis, Portugal, was scientifically backward.

The war against tropical diseases was part of the agenda of imperialism. However, in Brazil, tropical medicine was associated with interests of nationalist elites struggling to fulfill the requirements of economic development and meeting the cultural standards of the "civilized world" through the establishment of scientific and higher education institutions.[15]

Another discrepancy between the history of Chagas disease and that of other tropical diseases concerns its discoverer. Chagas disease was discovered by a Brazilian physician, with no training abroad and no connection with military institutions.

13. See, for example, Farley (1991, pp. 3–4).

14. African colonies dealt with Bilharzia, Asian and African colonies with malaria, Indian and other Asian colonies with Kala azar. See Farley (1991, p. 6) and Desowitz (1993, p. 34).

15. About the interests related to the early establishment of scientific and higher education institutions in Brazil, see Schwartzman (1991, pp. 50–59).

The discovery itself was unlike other such discoveries: usually, diseases were recognized as morbid entities, an etiologic agent was discovered (sometimes followed by some years of controversy about its life cycle), and then the arduous task of searching for the vector began. Sometimes this took decades.[16] By contrast, the discovery of the causative agent of Chagas disease, *Trypanosoma cruzi,* of its vector, a blood sucking insect, and the clinical description of the disease were all done in the same year: 1909.

Previous accounts of the discovery and early research on Chagas disease are largely "heroic" re-constructions made by early twentieth-century Brazilian parasitologists. Other commentators follow a similar line[17]: Chagas was depicted as favored by chance because he was a "genius," a prepared researcher or a competent protozoologist; his reasoning took him from the insect to the disease through a series of sequential inferences.

Later, historians attempted to provide different, and more critical, interpretations. N. Sepan's analysis of the institutional context of early century Brazilian biomedical sciences includes comments on Chagas' discovery. She describes it as an example of biological research resulting in a discovery of practical importance, where most of the concepts involved were already elaborated by European scientists. According to her account, Brazilian researchers only have followed established lines and Chagas reasoned by analogy with the malaria model as to the role of the blood sucking insect in the transmission of a disease (Stepan 1976, pp. 118–20).

More recently, F. Delaporte presented another reconstruction. His claims are as follows: (1) In Lassance, Chagas was actually trying to elucidate the cycle of a non-pathogenic parasite that affected monkeys—*Trypanosoma minasense*—when he accidentally came across *T. cruzi.* Since

16. The etiological agent of Bilharzia, caused by worms of the genus *Schistosoma,* was discovered between 1851 and 1852 by Theodor Bilharz, who identified the worms and their eggs. The life cycle and species were not correctly identified until 1915. See Farley (1991, p. 70). The parasite that causes Kala azar, the scourge that tormented Asia in the late nineteenth century, was discovered in 1900 by Leishman and Donovan. It took additional years to correctly identify it as a protozoan of the genus *Leishmania.* Twenty six years later the sandfly *Phlebotomus argentipes* was recognized as its vector and the transmission mechanism became known only in 1940 (Desowitz 1993, p. 58). Malaria was known as a disease from ancient times. The causative agent for malaria was first observed in 1880 by Laveran, but the transmission by the mosquito was only established in 1897 by Ross.

17. See for example Dias (1994), Carneiro (1963), Chagas Filho (1974), Fonseca Filho (1974, pp. 43–66). Emanuel Dias was a Manguinhos physician and researcher, active from the 1930s on. Emanuel Dias was a key figure in the restoration of the interest in Chagas disease with his research on chagasic cardiopathy and his public health initiatives. Carneiro was an observer during the Academy debate. Chagas Filho is Chagas' son and Fonseca Filho was part of the Manguinhos team and a defender of Chagas during the "Academy debate." English language accounts with a celebratory tone include: Kean (1977), Lewinsohn (1979), Lewinson (1981).

T. minasense would have been his real "research line," he had ignored the hematophagous (blood-sucking) fauna of the region; (2) When he dissected the insects and observed parasites in their guts, he believed them to be developmental forms of *T. minasense;* (3) He sent the infected insects to O. Cruz, director of the Serum Therapy Institute of Manguinhos in Rio de Janeiro, looking for confirmation of his beliefs; (4) Cruz tested the insects and rejected Chagas' hypothesis. Chagas realized he was mistaken and that Cruz had the opportunity to make a discovery. He made changes in the reported periods of observation of blood forms in laboratory animals so as to make the observation coincide with his presence in Rio and grant him the discovery; (5) Since the new parasite was pathogenic, Chagas produced a hurried description of symptoms in analogy with sleeping sickness (Delaporte 1994/95).

M. Perleth has studied the influence of the German Schaudinn school of protozoology on Chagas' work and suggested that

> Chagas' description of American trypanosomiasis of 1909 is a reflection of the Schaudinn School of protozoology (Perleth 1997, p. 92).

Stepan, Delaporte and Perleth describe and interpret the discovery of Chagas disease according to one or another version of the "diffusion model."[18] According to it, "non-scientific societies" are seeded with Western science and gradually grow autonomous, until they can finally break loose of the colonial umbilical cord. They grow from total reliance upon "central" (European or American) institutions and ideas to an ideal stage of independence and self-reliance (Basalla 1967). The problem with this model is that it does not fit reality. First, "non-scientific societies" are not passive recipients of "western science"—there is a great deal of manipulation and originality from early stages.[19] Second, science does not "natu-

18. The version sketched and criticized here is taken from the most cited work about this model, G. Basalla's (1967) "The Spread of Western Science." Stepan comments on this model (Stepan, 1976, pp. 14–20) and "employs" it throughout her book (p. 36 and p. 79, for example). She remarks, however, that the increasing inter-dependence of scientists in later stages does not fit Basalla's model, with which she otherwise agrees. Perleth explicitly adopts Basalla's model. See Perleth (1997, p. 60).

19. About colonial science and early attempts to make original contributions in Spanish America, see J. Canizares Esguerra "Spanish America" (n.d.) and Canizares Esguerra (1999). About yellow fever in Brazil and the theories around it, see Chalhoub (1993). Original and pioneering contributions in Tropical Medicine from Brazilian physicians in the XIXth century were actively disregarded by Europeans. J. Peard (1997) describes them and claims: "One of the most interesting critiques leveled at traditional medical historians is that they concentrated only on the outward movement of Western medicine from its metropolitan centers; they failed to ask how medicine practiced in faraway places subtly al-

rally" evolve to a stage of autonomy and isolation.[20] In consequence, we are left with only one disconcerting alternative describing everything that is done by non-central scientists as imitation of their central colleagues (since independence never happens).

Diffusion takes for granted that everything in the "non-scientific" society's science must have been passively fertilized by someone "central." The only question is: who is the father? I. Löwy, for example, claimed that the Pasteur Mission working in Rio de Janeiro from 1901 to 1905 was the father of the Brazilian Tropical Medicine baby.[21] Extended to the level of the individual scientific accomplishment, the result is "imitation," "analogy," and "reflection." In the discovery of Chagas disease, Stepan saw an analogy with the malaria model, Delaporte saw an analogy with the sleeping sickness model and Perleth saw the reflection (imitation) of a German school. No space is left for active participation and originality.

All practitioners of Tropical Medicine were working under a common conceptual framework that included the insect-vector model. Chagas was as much an imitator as were Leishman, Donovan or Bruce.[22] Nevertheless, no one has ever felt the need to explain away their discoveries.

In this paper, we offer a more detailed description and a different interpretation of Chagas' discovery. We depict him as an active participant, although an atypical one, in the enterprise of Tropical Medicine. We claim that only a proper understanding of this participation can account for his unusual sequence of hypothesis, as well as his moves.

Chagas and Manguinhos

Chagas was born in 1879 in the city of Oliveira, Minas Gerais. He studied medicine in Rio de Janeiro—then the national capital—from 1896 to 1901. His graduating hematology thesis was developed in the

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tered and adapted Western medicine to local milieux and, in turn, often influenced medical thinking in the metropolitan centers." See J.G. Peard (1996, 1997).

20. Actually, this condition requires active measures at the economic and political level. And when this happens, the picture is not one of a blooming local scientific culture, but one of decadence and mediocrity. About Venezuela, see H. Vessuri (1991) and T. Glick (1984); about Brazil, see Schwartzman, (1991, pp. 237–247).

21. Regarding the Pasteur Mission, I. Löwy claims that "The temporary transfer of a "model" European laboratory to a developing country may be related to the fact, unusual in a peripheral country, that a Brazilian scientific institution, the Instituto Soroterapico de Manguinhos (later, Instituto Oswaldo Cruz), was able to attain an international reputation as an important centre of research in tropical medicine between 1910 and 1930." Löwy is not able to provide evidence, however, for the actual training of the Manguinhos scientists by the French mission. The French mission did not transfer its laboratory equipment to Manguinhos, nor did it employ Manguinhos personnel. See I. Löwy (1990).

22. M. Worboys, who is not concerned with diffusion, mentions Chagas' discovery in his work about tropical diseases and suggests that "In this case, the parasite-vector model

Manguinhos Serum Therapy Institute and was about malaria. He did not remain in Manguinhos on that occasion and worked for some time in private practice (Chagas Filho 1993, pp. 3–48). His relationship with the Serum Therapy Institute, however, was soon re-established through its malaria control programs.

Chagas was committed to academic work very early. His first interest was obviously malaria (Chagas 1905, 1906). In 1907 he identified new species of mosquitoes, the vectors in malaria transmission (Chagas 1907*b,* 1907*c,* 1907*d*). In 1908 he published his first paper in an international journal (Chagas 1908*a*). He emerged as the highest Brazilian authority on malaria and was a pioneer of its control.[23]

Chagas was part of the team at Manguinhos Serum Therapy Institute, which was considered to be the first reference center in Brazilian experimental medicine. This Institute was created to produce anti-plague serum when the country was threatened by an epidemic. It was inaugurated in 1900 and in 1902 Oswaldo Cruz was named director of the Institute.[24]

Manguinhos had a controversial as well as spectacular impact in the area of urban sanitation. The calamitous sanitary situation drove president Rodrigues Alves to centralize the sanitary services in a Federal Department of Public Health. Its immediate task was to control urban epidemics, like yellow fever and smallpox, and to prevent the emergence or aggravation of other diseases, like plague. Oswaldo Cruz, already in charge of the Serum Therapy Institute, was named director of the Federal Department in March 1903. He proposed a bold plan to control yellow fever, smallpox, and plague. It included an incisive intervention in Rio and important new actions at the Federal level. The program was presented by Rodrigues Alves as a new sanitary law and elicited strong opposition from different political segments, as well as from the population, whose daily life was affected. It included the unification of sanitary services, the adoption of a unified sanitary code and compulsory vaccination. The reaction against Cruz's program was so strong that force was required to prevent conflict. In 1905 Cruz announced that the yellow fever epidemic had been controlled. By the end of 1906, Cruz, an obscure scientist in 1903, was ac-

identified a pathogen and its mode of transmission before the disease syndrome was described clinically" (Worboys 1993, p. 528).

23. See Fonseca Filho (1974, p. 19).

24. Other enterprises involving a scientific approach to public health emerged in the state of São Paulo during the last years of the nineteenth century, also related to the control of endemic diseases such as smallpox, cholera and malaria. See Schwartzman (1991, pp. 83–91). Similar experiences were being developed in other parts of Latin America, with the emergence of their first science pioneers and the articulation of basic research with applied activities. See M. Cueto (1989*a*).

claimed as a national hero and internationally recognized as the man responsible for the improvement of Brazil's public image. Meanwhile, as a result of Cruz's new powers, the internal conditions in Manguinhos improved dramatically. The team of researchers increased in number, new installations were built and the general infrastructure was enhanced. The deeds of the Institute received national and international recognition (figure 2).[25]

Following that, original contributions in microbiology and protozoology in Manguinhos received attention from renowned researchers in central scientific institutions.[26] Stanislaus Von Prowazek, G. Giemsa and Max Hartmann came to Brazil between 1908 and 1909. Prowazek and Giemsa were professors at the Hamburg Institute of Tropical Medicine (*Institut für Schiffs—u. Tropenkrankheiten,* Hamburg). Hartmann came from the Berlin Institute of Infectious Diseases (*Intitut für Infektionskrankheiten).*[27]

Prowazek and Hartmann had been interested in flagellates in general and trypanosomes in particular for a long time. Their early work on trypanosomes had been published in 1905 and 1907 (Prowazek 1905; Hartmann & Prowazek 1907). In the 1907 paper they discussed the roles of certain cellular organelles. Their main theses, insisted upon by Hartmann in 1907 (Hartmann 1907) and by Hartmann and Chagas in 1910 (Hartmann & Chagas 1910), was the presence of two nuclei in protozoa. In their view, protozoa carried a nuclear structure responsible for locomotion and another structure—a "trophic" or "generative" nucleus—which would be the main nucleus.

To articulate their theses, Hartmann and von Prowazeck were hunting for parasites, much like everybody else in tropical medicine. Manguinhos

25. Brazil was invited to participate in the XII International Conference in Hygiene which took place in Berlin, in 1907. Manguinhos reported new species of mosquitoes (vectors in many tropical diseases such as yellow fever and malaria), by A. Neiva, the discovery of the exo-erythocitic cycle of *Haemoproteus columbae,* by Aragão and anti-malaria campaigns, by Carlos Chagas. Because of all its deeds, Manguinhos received the gold medal conferred by the judges in Berlin. See Stepan (1976, pp. 98–99).

26. One remarkable example of such contributions is the identification of the exo-erythocitic cycle of *Haemoproteus columbae.* This protozoan parasite was known to infect pigeon red blood cells and its sexual reproduction had been identified years before. Nevertheless, nothing was known about the asexual reproduction in the vertebrate host. H. B. Aragão, a Manguinhos researcher, showed that it took place at the pulmonary endothelium by a process called "schizogony." See Henrique de Beaurepaire Aragão (1907). This work had obvious repercussion as to the understanding of malaria and Aragão's discovery was acclaimed worldwide. At the same time, yellow fever was being studied by other researchers. See Fonseca Filho (1974, pp. 42–43 and pp. 32–33).

27. See Jaime L. Benchimol (1990, pp. 45–6).

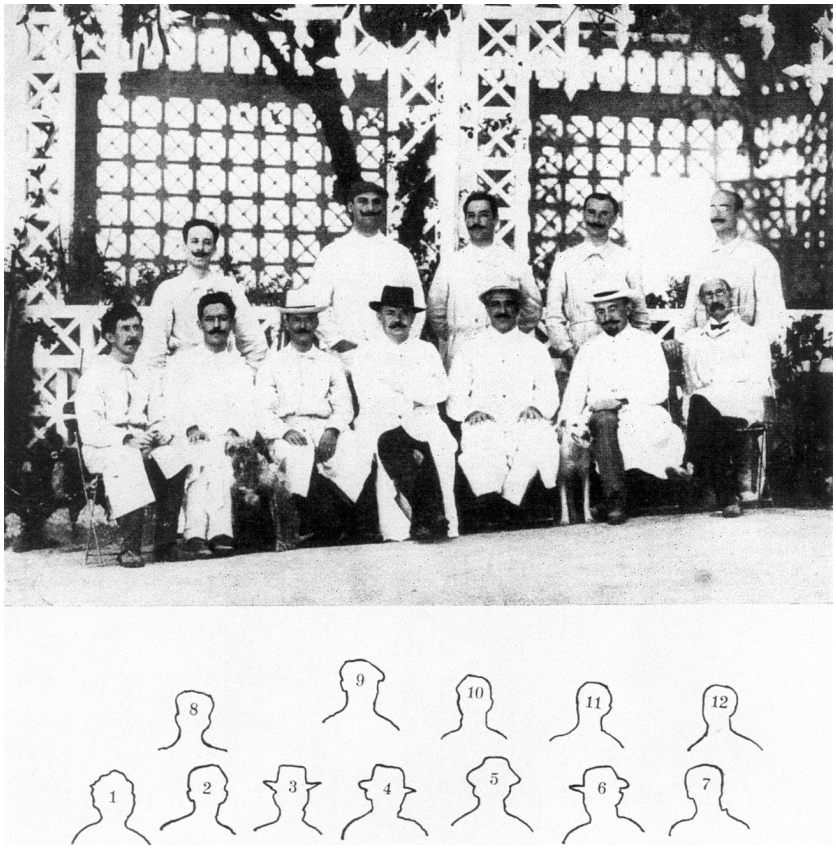

Figure 2. Manguinhos in 1908. 1. Alcides Godoy; 2. José Gomes de Faria; 3. Antonio Cardoso Fontes; 4. Max Hartman; 5. Oswaldo Cruz; 6. Stanislas von Prowazek; 7. Adolpho Lutz; 8. Carlos Chagas; 9. Henrique da Rocha-Lima; 10. Henrique Figueiredo de Vasconcelos; 11. Henrique Beaupaire Aragão; 12. Arthur Neiva. From O. da Fonseca Fo. *A Escola de Manguinhos.* São Paulo: Fundação Oswaldo Cruz, 1974, p. 23.

was as good a place to be: it was in the tropics, it had become an important center for urban sanitation and it was becoming prominent for its scientific endeavor in experimental medicine.

Around the middle of the decade, Manguinhos opened the era of rural endemic diseases. The new focus responded to demands from governmental and private companies whose activities in rural Brazil were being hampered by the unsanitary condition of their workers (Fonseca Filho 1974, p. 19). The main problem was malaria. Around 1906 the con-

struction of a hydro-electric plant in Itatinga (state of São Paulo) was suspended due to a malaria epidemic among the workers. The company in charge—Companhia Docas de Santos—resorted to Carlos Chagas. He carried out the first anti-malaria campaign in Brazil. Soon after, Chagas engaged in a similar job in the state of Rio, where the water supply was being increased. With the experience and authority achieved by two successful campaigns, Chagas was assigned yet another task. Malaria was obstructing the construction of an important railroad that was to extend the access to the hinterland by train. The company in charge—Estrada de Ferro Central do Brazil—again requested the help of Manguinhos professionals and Chagas was sent to Lassance, in the state of Minas Gerais. In the beginning of the century, its inhabitants were affected by malnutrition, syphilis, ancylostomiasis (hookworm infection), endemic goiter and—of course—malaria and American Trypanosomiasis.[28]

A journey to the middle of nowhere

Chagas arrived at Lassance early in June of 1907 with Belizario Penna, who also worked in Manguinhos. He described his findings and first steps in a report addressed to the sub-director of the sixth division of the Estrada de Ferro Central do Brazil, in January 25, 1908.[29] He found that most workers were infected with malaria and many of them had severe symptoms. Chagas and Belizario set up their operations in a wagon that moved along the railroad.[30] Most of the time, they were very busy with their anti-malaria affairs. Nevertheless, in that same year, as a good parasite hunter, Chagas identified a trypanosomatid parasite in the blood of a monkey he called *Hapalle penicillata.*[31] He named the parasite *Trypanosoma minasense* and wrote a small note on it December 15, 1908. In this 1908 note, however, Chagas mentioned not one, but two trypanosomes. He felt confident about the taxonomic identification of one of them, but not about the other:

> We are currently studying two trypanosome species, both from the *Hapalle penicillata.* The first one is a habitual parasite of the *Hapalle,* being found in almost all the animals in certain regions. [...] Of

28. See Chagas Filho (1993). The general epidemiological condition was also described by J.C. Dias (1995).

29. This report is reproduced as "'Adenda: Lassance,' 1907, Carlos Chagas" (Chagas 1907*a*).

30. See Carneiro (1963, p. 8).

31. And, afterwards, *Callitrix penicillata.*

the other trypanosome species, whose life cycle presents great interest, we will later give description.[32]

Chagas was led to his famous discovery through his introduction to the vector, a triatomine insect (figure 3A). He was first shown one in a visit to Cantarino Motta, engineer in charge of the construction team of the railroad works in Pirapora in 1908, one year after his arrival in Lassance. The second tripanosome mentioned in the *Brazil Medico* note on *T. minasense* was already *T. cruzi:* two days after the Brazil Medico note, Chagas sent another note to the *Archiv für Schiff und Tropenhygiene* (dated December 17, 1908). This time, it contained a brief account of *T. minasense* and a rich and speculative description of *Trypanosoma cruzi* (Chagas 1909*a*). Therefore, Chagas became acquainted with *T. cruzi* between June and November 1908. By early December, he knew that his parasites did not belong to the same species. But little is known about the circumstances of the *minasense* discovery. Both notes are brief and nothing can be inferred from such documents.

Cantarino Motta was a key factor in the story. The engineer, more familiar with the habits of the local population (he had been there since 1902), showed a blood sucking hemipteran insect to Chagas. Local people called this insect *barbeiro*—the "barber." The insect apparently was nicknamed after barbers, who, in the hinterland, performed bleedings and applied leeches with therapeutic purposes.[33] In an interview to a newspaper of the state of Paraná, in 1955, Motta claimed that he also suggested a relation between the insects and "some disease." He claimed to have told Chagas about a coincidence of goiter and idiocy in people and the occurrence of the insect in the house. The insect dwelt in the interstices of wood and earth walls (figure 3B). Chagas reportedly remained silent and thoughtful after the engineer's remarks (Carneiro 1963, pp. 8–10). The exact content of that conversation is probably lost forever, but we do know that Chagas promptly dissected the insect and examined the contents of salivary glands and digestive tract (Chagas 1922). Moreover, he never abandoned his belief in the relation between trypanosome infection and goiter, although he never succeeded in gathering conclusive evidence for it.

He tentatively identified the insect as an hemipteran of the family *Reduviidae* and of the genus *Conorhinus.* In the dissected digestive system of the insect, Chagas found protozoa of *crithidia* form in the posterior in-

32. Chagas published two short notes on *Trypanosoma minasense.* See: Chagas (1908*b*), and Chagas (1909*a*). The first note is dated December 15, 1908. The second is dated December 17 and was published in February 1909.

33. See Chagas (1910).

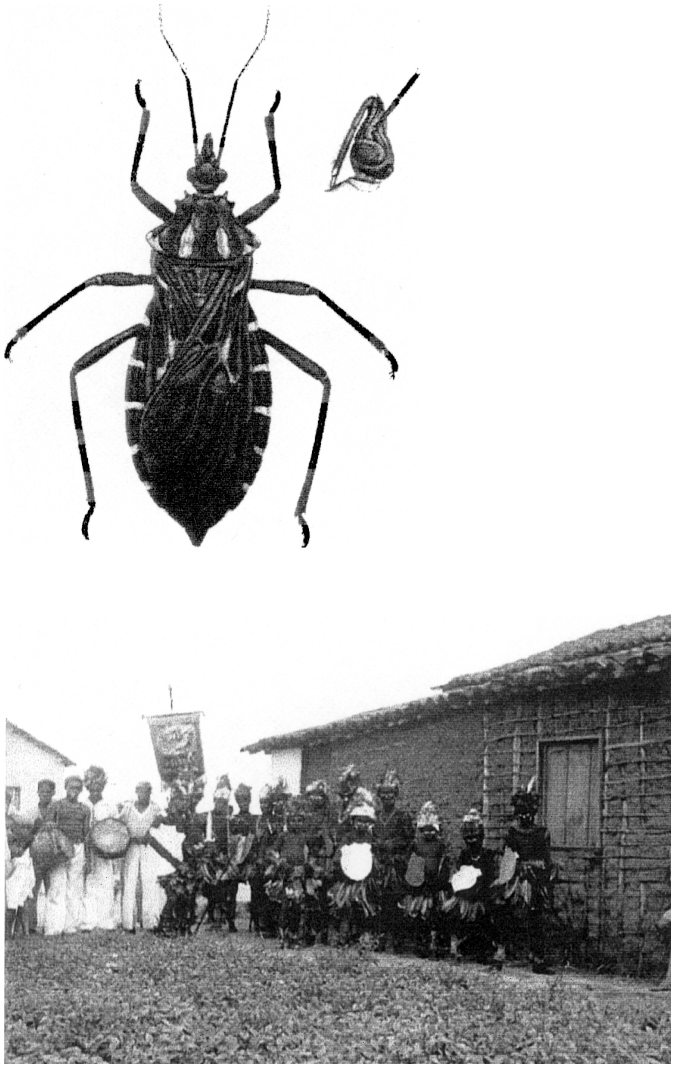

Figure 3. A. The "barbeiro" (the insect vector of Chagas disease).
B. Wood and earth houses where the barbeiro feeds on human blood. From C. Chagas, E. Villela & H. da Rocha Lima, Amerikanische Trypanosomenkrankheit. Chagas-Krankheit. In: C. Mense, ed., *Sonderabdruck aus Handbuch der Tropenkrankheiten.* Leipzig: Verlag Von Johann Ambrosius Barth, 1929: 673–728, p. 675 and p. 676.

testine of the insect (Chagas 1922). Chagas reasoned that either these were normal parasites of the insect or intermediary forms of a parasite with a complex life cycle, a vertebrate hemoflagellate (Chagas 1922). On the one hand, he suspected that the crithidia could be intermediate forms of his *T. minasense,* which he already knew to be an endemic vertebrate hemoflagellate in that region (Chagas 1911; 1922, p. 68). On the other hand, Chagas frequently stressed the association between man and insect, which strongly suggested that man was the vertebrate host (Chagas 1909*b,* 1909*c,*[34] 1910). At any rate, he sent the insects to Manguinhos to be tested. They were used by Cruz in experimental infection in many animals. Blood forms were detected in those animals after a period that ranged from 20 to 30 days. The experiments showed not only that the morphology of the blood forms of the parasite was very different from the previously identified *T. minasense* but also that the laboratory animals developed certain specific symptoms associated with a disease. The whole experimental procedure lasted "some months" and was concluded in April 1909 (Chagas 1910).

Chagas, who had followed his insects to Manguinhos, in Rio de Janeiro, soon after sending them, returned to Lassance. He had a disease in hand—hopefully, a human disease. He assumed that the insect was domiciliary and proceeded to search for infected domestic mammals in the region.[35] He obviously searched for infected humans as well. First he found the parasite in domestic animals—cats and dogs—but finally he came across a sick child in fever with free trypanosomes in the blood. The first paper reporting the human blood forms of this specific patient is dated April 15, 1909. In this paper, Chagas made a tentative clinical picture of the disease. Its symptoms included acute anemia, marked organic decay, subpalpebral edema, frequently general edemas and considerable ganglion swelling with large ganglions in peripheral pleads. He observed atrophy in development in certain children and reported acute cases with fever and other morbid manifestations.

In a more detailed paper, Chagas described the pathogenic trypanosome. He examined the parasites in human patients and laboratory animals, monkeys and guinea pigs. The parasites thus found are called

34. This paper was published in Portuguese and German, side by side in different columns.

35. Chagas was convinced that the insects were exclusively domiciliary. Actually, they were not. The hemipteran he found in Lassance was later identified as *Panstrongylus megistus,* one of the possible vectors in the transmission of American tripanosomiasis. Unlike *Triatoma infestans,* another triatomine vector, *megistus* is not exclusively domiciliary nor are its domiciliary populations large. Chagas (1909*c,* 1910, 1922). About the vectors, see, for example, H. Lent & Wygodzinsky (1979).

"blood forms." He observed the parasites in naturally infected and laboratory infected triatomine insects. These parasites are called "insect forms." He conducted experiments on infection—both blood forms and insect trypanosome infection in various laboratory animals—and he cultured the parasites in the laboratory. After that, Chagas described the morphology and biology of his parasites. To describe the morphology, he reported *in vivo* observations and other microscopic studies in fixed preparations using more than one technique (Chagas 1909*c*).

What Chagas' experiments showed him was a parasite with two different developmental paths inside the vertebrate host and inside the insect. Figure 4 depicts Chagas' model for T. cruzi's development. In the vertebrate host, it had a malaria-type cycle inside blood cells, as well as schizogonic reproduction. It also had a development path leading to the fusiform infective forms. In the insect, the parasite could either adopt a "culture"-like reproduction behavior that apparently had no relation to infection, or it could follow the path leading to infective forms.

Chagas made sure that the insects were parasite free before feeding on infected blood. He also tried to show that there was no mechanical transfer of parasites, but a true parasite-vector biological relationship, since insects which had been fed infected blood for less than three days were not infective. On the other hand, they would remain infective for a very long time (more than twenty days) after being fed infected blood.

Chagas was also successful in culturing his trypanosomes and in showing the controversial blepharoplast to be a "real" nucleus: it stained like nucleus and it acted like nucleus in cell division.[36]

Finally, Chagas claimed that a new taxonomic genus should be created to harbor his parasite because of the peculiarities of the trypanosome's life cycle, where schizogony and intra-globular life are combined with free flagellates in blood plasma. He called the genus '*Schizotrypanum*' and the parasite '*Schizotrypanum cruzi.*'

Chagas claimed that his work supported the "Schaudinn school" of protozoology as to the straight taxonomic proximity between trypanosomes and hematic protozoa such as malaria plasmodia (hemosporidians at

36. The blepharoplast was, for Chagas and Hartmann, the "second" nucleus. It corresponds to the structure we presently call kinetoplast. The kinetoplast is a DNA-containing structure located at the trypanosome's single mitochondrion. The size and form of the kinetoplast varies according to the developmental stage of the parasite. See Z. Brener (1992).

the time[37]), and, specifically, "Hartmann's theory" of the structure of the protozoan cell.[38]

The new trypanosome and its transmission became the central research focus in Manguinhos.[39]

The discovery had great impact. Chagas was immediately acclaimed a great discoverer at home and abroad. In October 26, 1910, Chagas was named full member of the National Academy of Medicine.[40] Between 1911 and 1912 Chagas was invited to speak and to receive honors in Minas Gerais and São Paulo, and his prestige was acknowledged in the whole country.[41] In 1912, the international competition sponsored by the Institute for Tropical Diseases of Hamburg took place. Every four years, it granted the "Schaudinn Prize" (in memory of the pioneer of protozoology) to the most important contribution in protozoology. Chagas won the award. The competition included eminent researchers and pioneers, such as Laveran, Leishman, Roux and others.[42] In a short time, American tripanosomiasis was incorporated in protozoology textbooks.[43]

37. Malaria parasites belonged to the group of hemosporidians in the beginning of the century. Presently they belong to Sporozoa and Trypanosomes to Mastigophora.

38. The following year Chagas co-authored a paper with Hartmann reinforcing Hartmann and Prowazek's thesis of the binuclear nature of protozoa and in 1911 Chagas published another paper on the structure of protozoa, along the same line. See M. Hartmannn & Carlos Chagas (1910), and Chagas (1911).

39. Other physicians and researchers concerned with tropical medicine in Brazil joined the effort as well: in 1910, Antonio Carini, at the Pasteur Institute in São Paulo, found the lung forms that Chagas claimed to be "schizogonic" forms of the parasite in uninfected animals. This was further studied by H. Aragão, from Manguinhos, who, in 1911, confirmed they were not developmental forms of Chagas' parasite. They were later identified as another organism, *Pneumocystis carinii.* Gaspar Vianna, another Manguinhos researcher, studied the small, round forms ("leishmania" forms) he found in almost all the tissues of infected animals and showed their role in the reproduction of the parasite in the vertebrate host (Vianna 1911). See also acknowledgment by Chagas of Carini's findings, as well as of the contributions of other researchers who studied the new parasite in Chagas (1913).

40. This was done as an exceptional procedure: for someone to be named member of the National Academy of Medicine, a vacancy had to appear, usually by the death of another member. See description of Chagas' nomination in Chagas Filho (1993 pp. 90–91); Carneiro (1963. p. 24); Carlos Chagas Filho (1974).

41. Chagas spoke at the founding of the Belo Horizonte Medical School, in Minas Gerais, and in the major medical institutions in São Paulo. The press devoted much attention to him. See Chagas Filho (1993, pp. 97–98).

42. The other candidates were Ehrlich, E. Roux, E. Metchnikoff, A. Laveran, C. Nicolle and W.B. Leishman. See Carneiro (1963, pp. 28–30); Carlos Chagas Filho (1974).

43. See, for example, M. Hartmannn & C. Schilling (1917) and R.W. Hegner & W.H. Taliaferro (1925).

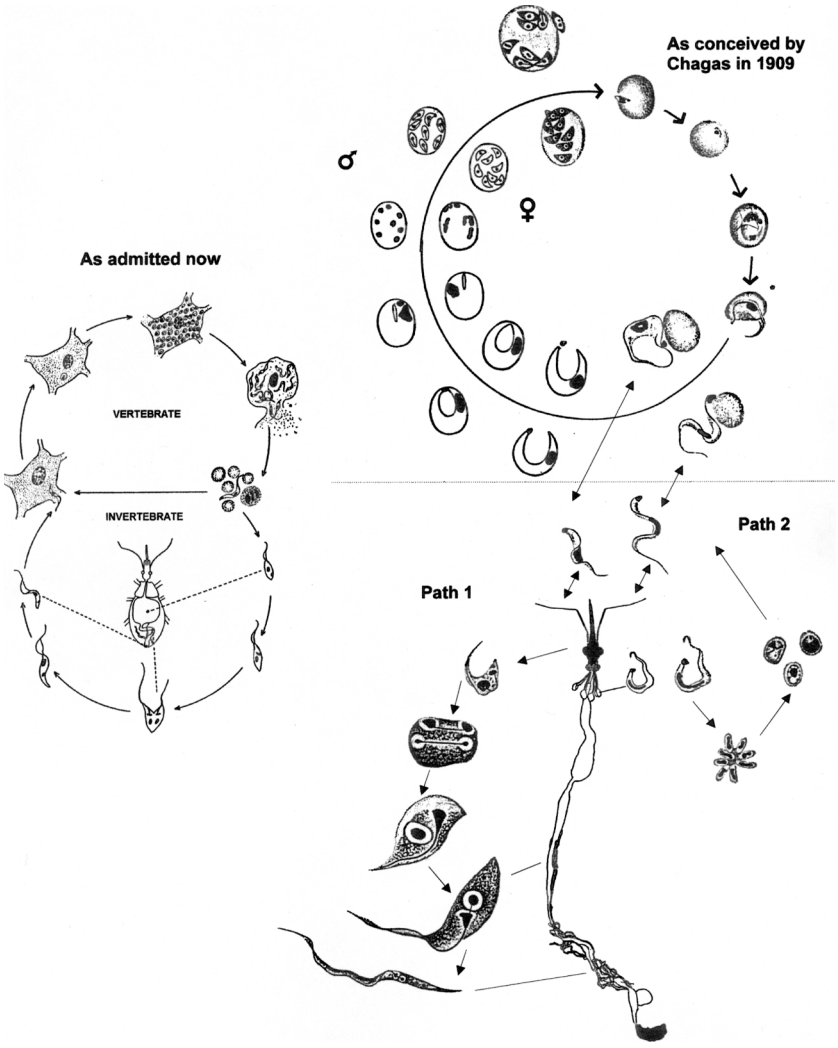

Figure 4. The cycle as proposed by Chagas in 1909. The infective forms of the parasite would be inoculated into the blood of a vertebrate where they would quickly reach the lungs. There, a complex set of transformations and the type of multiplication known as "schizogony" (where the nucleus divides before the rest of the cell becomes segmented) would take place. Chagas believed the different forms exhibited by the parasite in all stages were male and female forms. They would undergo different transformations. The product of schizogony would be small claviform organisms that would be able to invade red blood cells. There they would develop into mature parasites swimming in the plasma. These would either undergo schizogony in the lungs again, or be ingested by the blood sucking insect.

In the insect, the parasite would present two types of development: the first one (PATH 1) would be merely "culture" growth, with no significance as to the infection of the vertebrate host. Here, ingested parasites would lose their flagella and would become increasingly rounded. They would then undergo successive binary divisions. From this stage they would transform into crithidia-like forms which would also be able to divide. PATH 2 is inferred by Chagas from the rounded forms he interprets as products of sexual activity: ingested parasites would mate, an activity not actually observed by Chagas. As a result, these rounded forms (interpreted as "ookinets," the name for a product of fecundation) would be formed. They would then undergo schizogony. All this would take place at the insects' mid-gut. Following that, the small resultant parasites would develop into fully infective forms, which would then migrate to the salivary glands, passing through the general cavity. Infection would take place as parasites were inoculated into the vertebrate by the sting.

The cycle figure is a reconstruction made by the authors. Cell drawings were cut from Chagas' original papers and re-arranged.

The modern cycle is depicted on the left side of the page. On the vertebrate host, infective forms (either blood or insect forms) invade cells and become rounded. Such "leishmania" forms multiply by binary division and mature into infective blood forms. The cell eventually breaks open and the free parasites either infect more vertebrate cells or are ingested by a "barbeiro." In the insect's digestive tract they develop into critidia forms, which undergo successive binary divisions. These mature into infective forms in the insect's rectum. Modified from Silva, L.H.P & Camargo, E.P. "Ciclo evolutivo do *Trypanosoma cruzi.*" In J.R. Cançado, ed., *Doença de Chagas.* Belo Horizonte: Imprensa Oficial do Estado de Minas Gerais, 1968: 86–99.

The most obscure aspect of Chagas' recognition remains the nominations he received for the Nobel Prize. Manoel A. Pirajá da Silva, a Brazilian physician, was the first to nominate him in 1913. Pirajá da Silva was working in Europe when he was requested by the Nobel Committee to nominate a candidate for the Prize. Hilário de Gouvêa, also a Brazilian physician, made the second nomination, in 1921. Chagas never received the Nobel Prize. In 1913, the Prize was conferred to Charles R. Richet for his work on anaphylaxis. No one received the 1921 Prize.[44]

The invention of Chagas disease

In a period of less than ten months Chagas was introduced to a domiciliary blood sucking hemipteran insect; he examined the contents of salivary glands and guts; he found a trypanosome; he sent it to Manguinhos to infect laboratory mammals; it turned out to be morphologically different from *T. minasense* and pathogenic. Chagas searched for infected individuals and found domestic animals and a sick child; finally, Chagas reported his findings in local and international scientific journals.

There is no doubt that Chagas developed the human disease hypothesis as soon as he came across the insect. This is not surprising: any good "parasite hunter" would be suspicious about the peculiar combination between blood sucking insects and the health condition he encountered in Lassance. It was natural for him to suppose that this insect might be a vector of some disease. Given the assumptions of the insect-vector theory, it would probably be a protozoan or a helminth.

We can reconstruct the path taken by Chagas from the moment he met the insect to the completion of his discovery as a sequence of adjusted hypotheses. His first hypothesis comprised four components, which required corresponding observations: (1) a vector, requiring the domiciliarity of the insect; (2) an hematozoarian parasite, requiring vertebrate blood forms; (3) man as the (or at least a) vertebrate host, requiring human blood forms; and finally, (4) a disease, requiring symptoms.

COMPONENTS	REQUIREMENTS
1. A vector	Domiciliarity of the insect
2. An hematozoarian parasite	Vertebrate blood forms
3. Man as the vertebrate host	Human blood forms
4. A disease	Symptoms

44. See M. Coutinho (1999); M. Coutinho, O. Freire Jr. & J.C.P. Dias (1999).

Each requirement was met in accordance with its difficulty. Evidence for this hypothesis construction model abounds. The first is his insistence on the domiciliarity of the insect. Locals claimed that the *barbeiro* was wild and came indoors just to feed. Today we know that they were right. Yet, at that time, Chagas believed the insects were exclusively domiciliary.

The requirement of vertebrate blood forms was met through a routine laboratory procedure, although time of residence in blood and patterns of cell invasion were utterly unknown. Human blood forms were more difficult because they required an acute patient, which was rare. The worst requirement was symptomatic consistency.

Given the first component—the vector—Chagas proceeded to dissect the insect. There he found the protozoa he was looking for. They had the morphology of crithidia, which indicated they could either be natural parasites of the insect or intermediary forms of hemoflagellate—he opted for the latter.[45] The health condition of the locals made the insect-vector model a strong bet. The updated hypothesis could be stated as: *if the crithidia are intermediate forms of a vertebrate hemoflagellate, then there should be one or more vertebrate hosts* (and a complex life cycle); *one of the vertebrate hosts might be the Callitrix and the hemoflagellate might be the T. minasense.* The updated hypothesis does not conflict with the early one: rather, it strengthens its agenda. The experimental infection was now required not only to obtain blood forms and proceed through the early hypothesis, but also to check the updated one. The experiments confirmed the complex cycle involving a vertebrate, revealed the difference between the candidate trypanosomes, and gave indications as to an acute stage of the disease, in which blood forms could be detected. He arrived at his final hypothesis: *if the trypanosome is a parasite with a complex life cycle, an intermediate insect host, and a vertebrate host (preferably human[46]), then it displays a cycle in the insect and it should be transmitted through the sting, upon feeding; if it is transmitted through the sting, then infective forms should be preferentially found in salivary glands; if the parasite's morphology and behavior bear similarities both with hemosporidians and trypanosomes, then its blepharoplast is a nucleus and the parasite can reproduce by schizogony; the disease caused by this insect should display an*

45. The question of whether parasites of crithidia appearance observed in blood sucking insects were developmental forms of complex cycle flagellates (demanding a vertebrate host as well) or natural parasites of the insect was an important one in those years. W. S. Patton reviewed the literature on the current controversy concerning the possible relation between insect intestinal crithidia and vertebrate hemoflagellates in Patton (1909).

46. In his first paper, Chagas suggested that the development in humans and *Callitrix* showed important life cycle differences in relation to other mammals. That should indicate that man and the monkey were probably the natural hosts (Chagas 1909*c*).

acute form, relative to the bursts of flagellates in the blood, and a chronic form, associated to the damage caused to the tissues.

At this point, Chagas' observations and interpretations could be outlined as:

Observation	TANSITION	Interpretation
A. A prtozoan.	(unproblematic)	A parasite
B. An insect host for the parasite	(unproblematic)	A parasite cycle A part of a complex parasite cycle involving another host
C. A complex cycle involving a vertebrate host	(problematic)	A disease A human disease

Put together as a whole, the package constituted a novel and a highly interesting, central, and prestigious object in the intellectual contexts of the time.

Science and Medical learning for development

Chagas' discovery provided reinforcements to others besides the insect-vector model, or Prowazek and Hartmann. There was a political agenda that received much support from the recognition of Chagas' work. Chagas believed that science was a crucial endeavor for Brazil. His understanding of the role of science in the national culture and society was two-pronged: on the one hand he argued that tropical medicine was a special enterprise for Brazil and that substantial public effort should be allocated to its development. He defined tropical medicine in a broader way than European pioneers at the beginning of the century, in that it comprised all those diseases transmitted in an "indirect" manner, where the etiologic agent spends part of its life outside the human host. Thus, he included more diseases that affected the health of Brazilians in tropical medicine than the earlier definition did. Eradication and prevention would be among the most important tasks for development. From this perspective, tropical medicine was both noble and patriotic (Chagas 1926).

On the other hand, Chagas understood that the microscope was medicine's basic tool. To prevent and eradicate, it was necessary to study and identify. Germany and the United States were good examples. The tropi-

cal medicine arena promised Brazilian scientists vast possibilities and prominent scientific deeds. Within the theoretical and methodological frameworks offered by bacteriology, protozoology, and biology, among others, Brazilian scientists should grasp the opportunities provided by their "privileged" location with the country's unique medical/scientific objects. Chagas longed for this "nationalization of Brazilian medicine" (Chagas 1928, pp. 184–5).

He warned his audience that although the preferential research objects should be pathogenic organisms, scientists and doctors should be free to carry out their sophisticated esoteric tasks:

> Let no one argue, to exclude research from medical schools, that the researcher frequently sidetracks towards the domains of pure science, and that the evolution of medicine will profit little from it. In fact, I don't know the limits between the pure and applied sciences. Science is one only, and what today represents an abstract scientific achievement, with no use, tomorrow will be an applied notion and, sometimes, of the highest practical range.[47]

Tropical medicine thus had a double function: it was a militant fight against disease, to "improve the Brazilian race" and provide conditions for development, and it was the "biological study of pathogenic parasites," inseparable from experimental medicine. Hygiene, sanitation, and high quality (understood as international quality) medicine and science were wrapped together.[48]

This was part of the "Manguinhos culture," where the role of science was heroic and concerned with national development. The sophisticated basic research in the labs went hand-in-hand with the brave expeditions

47. "*Nunca se allegue, para excluir a pesquiza do ensino medico, que não raro o pesquizador se desvia para os dominios da sciencia pura, e pouco aproveitará, dahi por deante, á evolução da medicina. Eu não sei, em verdade, onde os limites entre as sciencias puras e as de applicação. A sciencia é uma unica, e o que hoje representa uma conquista scientifica abstracta, sem qualquer fundo utilitario, será amanhã uma noção applicada e, as vezes do mais alto alcance pratico*" (Chagas 1928, p. 881).

48. He wrote: "The history of tropical disease is, primarily, the biological study of pathogenic parasites. Those who study and practice medicine in warm countries cannot do without the microscope because it is from its handling that result essential indications for the purpose of our venture—that is, the treatment and prognostic of disease" (*A historia da doença tropical é, primacialmente, o estudo biologico dos parasitos pathogenicos. Do microscopio não podem, agora prescindir os que estudam e praticam a medicina nos paizes quentes, porque é de seu manejo que resultam indicações essenciaes á finalidade do nosso mistér, isto é, ao tratamento e ao prognostico da doença*). See Chagas (1926, p. 858).

that took Cruz's small army to the most distant and poor areas of Brazil. To "learn and cure" could have been their motto.[49]

Despite Chagas' international recognition, few besides his close collaborators at Manguinhos shared his belief in the need to carry out high quality, international level, research. Few attributed a special role in development to research.

In 1920, Chagas became the first director of the National Department of Public Health. He was named by President Epitácio Pessoa himself. Chagas produced a deep public health reform for the country, centralizing guidelines which should be based on solid knowledge. He was harshly criticized for this plan, being frequently accused of surrendering to the American model of public health (Chagas Filho 1993, p. 163, p. 171). Like Cruz before him, Chagas faced reaction against vaccination and against other urban modernization measures. He remained in the position until 1926 (Chagas Filho 1993, pp. 168–9).

Forming the new generations of physicians and health professionals was one of Chagas' main concerns. He created the first Special Hygiene and Public Health course in Brazil in 1925. In 1926, the first Tropical medicine course started at the School of Medicine in Rio de Janeiro. He received support from the Rockefeller Foundation, enabling many young Brazilian sanitation professionals to study at Johns Hopkins University School of Public Health. Chagas believed that medical students should be exposed to research early in their academic lives and that the best brains should be attracted to it. He harshly contested "backward" contenders that defended a more academic learning in medical schools and claimed that every advance observed in Brazil in his time could be accounted for by the introduction of science and experimental medicine in Manguinhos. The Serum Institute and the medical school should be one, together in the heroic scientific adventure (Chagas 1928).

Fact or Artifact

Chagas' academic boldness was not immune to the corrosive effects of controversy. The celebrated scientific fact became vulnerable to the deconstructive processes capable of bringing it back to a condition of doubt and skepticism.

49. Answering requests from governmental or private corporations, Manguinhos sent its teams of doctors and researchers to the inhospitable places where occupation was taking place. The mode of transportation was frequently horseback. These expeditions had a powerful political appeal, in a time when the Republic sought consolidation. Manguinhos' doctors expressed a strong commitment towards the people and the nation. Accounts of these expeditions can be found in Fonseca Filho (1974, pp. 18–19).

There is evidence of some opposition to Chagas as early as 1910, one year after his discovery. At this early stage, hostility apparently emanated from the opening of the position of "head of service in Manguinhos." Rocha Lima, an important Brazilian researcher and head of service in Manguinhos, left with Prowazeck to work at the Hamburg Institute of Tropical Medicine. Oswaldo Cruz was upset with this.[50] The position was filled through a meritocratic procedure that left no doubt as to who would be the winner. Chagas' contributions scored the highest in the system established by Cruz to rank the candidates.[51] Among these candidates were Chagas' close collaborators, such as Ezequiel Dias and Henrique Aragão. Antagonism towards Chagas began to brood there.[52]

The first public contentions came from R. Kraus in the 1916 Pan-American Medical Congress in Argentina. Kraus was an eminent German microbiologist at Argentina's Bacteriological Institute. Chagas was told that Kraus was going to contest his findings in the congress and headed for Buenos Aires, where the two had an intense argument. Kraus found many infected triatomines in human dwellings in certain regions of Argentina, but no cases of human infection. He claimed that the parasite itself could be of small virulence and Chagas' claims could be overestimated or ungrounded. Chagas answered that the trypanosomes in that region were still not adapted to man.[53] Most accounts do not go over details about the Buenos Aires episode. In Chagas Fo's book about his father, the author states that Chagas was disturbed by finding material from Manguinhos in Kraus' laboratory. He was in-

50. A detailed analysis of this episode, along with the connections with Aragão and the relationship between Afrânio Peixoto and R. Kraus can be found in J. L. Benchimol & L. A. Teixeira (1993).

51. Published work that contained "important discoveries" or the introduction of new methods were scored 7 to 9; theses, original or experimental contributions and studies in systematics scored 4 to 6; finally, preliminary notes and simple descriptions scored 1 to 3. Letter from Oswaldo Cruz, see "Um documento Histórico"(1979) and also Chagas Filho (1993, pp. 94–96).

52. See Chagas Filho (1993, p. 96).

53. C. Chagas Filho (1974). Other Latin-American researchers disputed Chagas' statements as to many different issues at the time. One example is A. Reina Guerra, who, like others, contested the etiologic role of T. cruzi in chronic cardiopathy, as stated by Chagas (1916). See A. Reina Guerra (1939). It was only much later, by the late forties, that the "Bambuí group," led by Emmanuel Dias, could provide evidence for Chagas' statements about heart disease, and thus restore the legitimacy of his discovery discourse. They not only showed Chagas' early clinical interpretation to be correct about chronic cardiopathy, but they also supported his claims as to "allergic" mechanisms that could sustain inflammatory and other pathogenic processes in the chronic phase, in the presence of few parasites. See Francisco S. Laranja, Emmanuel Dias, G.C. Nóbrega and A. Miranda (1956).

vited there by Kraus himself, but noticed the stamps from his institution in several slides. He did not recall having received any request from Kraus. It was clear that people from Manguinhos had been feeding Kraus' arguments against Chagas (Chagas Filho 1993, p. 105).

When Chagas arrived from his trip to Buenos Aires, he found Oswaldo Cruz's health rapidly declining. He feared the consequences of Cruz's death to Manguinhos. Chagas' children knew that their father was conscious of the opposition he faced at the institution. Cruz died in February 11, 1917 and Chagas was named director of the Institute three days later. Figueiredo de Vasconcellos, who had been in charge of the Institute during Cruz's leave, became Chagas' enemy forever. He had hoped to take Cruz' place. As soon as Chagas assumed the new position, he announced his understanding of the experimental medicine mission of the institution and his intention of emphasizing research activities. He sent researchers to study abroad, especially in the United States (Chagas Filho 1993, pp. 115–19).

Another important source of opposition was the prominent, although controversial role Chagas was playing in Brazilian public health. When Chagas was named director of the Department of Public Health in 1920, Afrânio Peixoto, a powerful man in the Brazilian medical establishment, was upset. He wanted the job and he did not share the meritocratic values underlying Chagas' recognition abroad. There is evidence that Peixoto had great influence over the National Academy of Medicine (Chagas Filho 1993, pp. 188–9, p. 192).

The twenties were the period when Chagas consolidated his prestige in European and American Institutions and, paradoxically, faced the worst and most effective attacks from Brazilian physicians. In 1921 he received an honorary doctorate from Harvard and in 1925 he became member of the Hygiene Committee of the League of Nations.[54] In Brazil, the challenges to Chagas' discovery climaxed in the "Academy debate" that happened between 1922 and 1924, in which H.B. Aragão, Afrânio Peixoto, and Figueiredo de Vasconcelos were important players. In November 30, 1922, Afrânio Peixoto spoke to the National Academy of Medicine at the reception of Figueiredo de Vasconcellos, former Manguinhos researcher. He said:

> You could have found some mosquitoes, you could have invented a rare and unknown disease, about which much was said, but whose

54. He was the first Brazilian doctor *honoris causa* in Harvard. He was invited to many other countries, such as Portugal, Spain, Germany, and Belgium, where he interacted with medical researchers. He also visited Latin American medical institutions. About his travels abroad in the twenties, see Chagas Filho (1993, pp. 122–27).

> victims almost no one knew, hidden in a countryside dwelling of your province, a disease that you could magnanimously distribute among your fellow countrymen, accused of being cretins.[55]

Chagas sent Miguel Couto, then president of the Academy, two letters of protest, which were read at the December 14, 1922 session. He demanded the appointment of a commission of academics to judge his discovery and he offered to resign from that Academy in case the commission did not validate his claims. He demanded that the commission judge whether the disease was a new morbid entity, with well defined etiopathogeny, characteristic symptoms, and defined clinical syndromes and also judge his ethical procedure, the credits of his findings, and its scientific and social relevance.[56] This was a wide range of demands, resulting from the fact that, during the challenge, all aspects of his discovery were at stake, including his own participation. Kraus questioned the epidemiological distribution of the disease and the virulence of the parasite. Peixoto suggested that it was rare and unknown and its symptoms were questionable. Opponents called it "the Lassance disease" instead of Chagas' disease,[57] thus discussing both Chagas' claims about its wide distribution and the authorship of the discovery. Figueiredo de Vasconcelos and Henrique Aragão, both from the original Manguinhos team, claimed that the discovery should be attributed to Oswaldo Cruz, not to Carlos Chagas (Carneiro 1963, p. 65).

It was a strained and difficult process. Almost one year later, Chagas contested the approach adopted by the commission saying he wouldn't accept a judgment that wasn't based on a real epidemiological assessment made through local examination—he wanted the commission members to take a journey through the country. The commission threatened to resign (Carneiro 1963). Another participant, O. da Fonseca Filho gave his account of the discussion that took place in the Academy between November 8 and December 6, 1923: Afrânio Peixoto abandoned the site and left Figueiredo de Vasconcelos and Parreiras Horta to defend him against Clementino Fraga, who represented Chagas. Fraga presented accounts

55. Peixoto was using irony, a privileged weapon for this physician. He was praising Vasconcellos for not having done as Chagas. Peixoto was a powerful man in medical institutions, both in Rio and in Bahia, where he came from. He was also comfortable among the local elite. Afrânio Peixoto 1922, in Fonseca Filho (1974, p. 65). See also Chagas Filho (1993, p. 225).

56. See Carneiro (1963, pp. 64–75).

57. See the account given by Carneiro (1963, pp. 64–75), about the debate to which he attended as member of the Academy and follower of Chagas' contenders. The expression "Chagas disease" was coined years before by the president of the National Academy of Medicine, Miguel Couto.

given by other doctors and researchers concerning the extent of the distribution of human infection by the parasite and that matter was decided in Chagas' favor.[58] In the November 16 session, Bento Cruz, Oswaldo Cruz's son, argued in favor of Chagas priority in the discovery.[59] Finally, on December 6, 1923, the conflict seemed to be over. However, at least up to the middle thirties, the disease was ignored in medical curricula and hospital diagnosis as well.[60] It took time and effort to restore the legitimacy of Chagas disease.[61]

The majority of the participants in the Academy debate did not share Chagas' affiliation to international scientific communities. They ignored the disciplinary context that rendered Chagas' protozoological findings so relevant. Since all the aspects of his discovery were neatly bound together, the legitimacy of his protozoological assertions was checked by epidemiological and clinical arguments.

Chagas' familiarity with the international scientific styles of his time was not enough to protect his statements. His recognition by the correspondent communities was equally insufficient. The correctness of his hypotheses and his errors had little to do with the de-constructive process. Discovery construction is complex and social to a large extent. However, it cannot be reduced to institutional sanctioning: Chagas achieved a formal victory and a functional defeat. Although the commission's conclusions favored him, the disease lost its capacity to mobilize scientific production. It only became undisputed and was studied again after Chagas' death.

Concluding remarks

This is a story about obvious scientific success and also about defeat. On the one hand, no one would dispute Chagas' success in the early days of the discovery: he was rapidly recognized and received all the accolades a

58. Fonseca Filho (1974, pp. 64–66). Clementino Fraga's account was very detailed and especially careful, scientifically updated and precise in the protozoology section. Fraga's letters containing Olympio da Fonseca's and Magarino Torre's findings and opinions are reproduced in Chagas Filho (1993, pp. 205–215).

59. See Chagas Filho (1993), reproduced in pages 199–200.

60. See E. Villela (1930). The positions of Chagas' enemies (like Afrânio Peixoto) as professors at the medical schools of the time, with recognized leadership in faculty environments can largely explain the exclusion of the disease as a study topic.

61. There are reasons to believe that the anti-Chagas group might be responsible for Chagas' failure to be awarded the Nobel Prize. Other early century tropical disease discoverers were awarded the Prize: Ronald Ross in 1902 and Charles Louis Alphonse Laveran in 1907. Four out of six of Chagas' contenders in the Schaudinn Prize competition were awarded the Noble Prize as well: Laveran, in 1907; Paul Ehrlich and Elie Metchnikoff, in 1908; and Charles Jules Henri Nicolle, in 1928. Chagas seems to have been in the "Nobel track." In Brazil, however, The Nobel Commission inquiries met an atmosphere of skepti-

good scientist might desire. On the other hand, by now, no one would doubt that the de-construction was extremely effective. It was a scientific defeat, since there was very little advancement of knowledge about any aspect of Chagas disease until his death in 1934. It was also a public health disaster, since the disease was not studied, students were not trained to diagnose it and sanitation measures for its prevention were not undertaken. Considering the recent success of various prevention campaigns using simple methods, it is reasonable to assume that millions of Latin Americans died prematurely as a consequence of the de-construction of Chagas disease.[62]

To understand such a paradoxical chapter of the history of science, we might profit from a drama metaphor. In the Chagas disease play, there is something weird with the sequence from the first to the second act. The characters are different, the setting is differently arranged and the effects are not the same. They are so different that they cannot be acts of the same performance. We realize that we are, in fact, watching different plays.

In the first play, Chagas was the hero. The supporting actors were the good guys, sharing with him meritocratic values, modernizing perspectives, and an understanding of the international nature of science and its role in development. Facing local health problems with this perspective was a priority. These values comprised the prevailing version of nationalism in the first play.[63] Cruz, Chagas' enthusiastic protector, was alive and strong, enjoying the climax of his political prestige in the Federal Government. The central object, *Trypanosoma cruzi,* was reasonably well behaved in the laboratory. The international medical community praised parasitological tropical medicine above all and was clamorous and supportive with the new discovery.

When Cruz died, the second play took the stage. An incomplete troupe kept on the old performance, but with no success on Brazilian ground. In the second play, nationalism assumed different colors: any modernizing

cism surrounding the disease. Research on this matter is in progress. See M. Coutinho (1999*a*); M. Coutinho, O. Freire Jr. & J.C.P. Dias (1999); Nobel Foundation Web Site (2000). About the restoration of Chagas disease's legitimacy, see M. Coutinho (1999*b*).

62. The South Cone Initiative of the WHO, involving Argentina, Brazil, Chile, Paraguay and Uruguay, is one such case. The infection reduction in Brazil and Uruguay in the period from 1985–1996 for the age group of 0–14 years is 96%. For all the countries in the program, the reduction has been of 83%. See World Health Organization (2000).

63. Other examples of a nationalistic motivation for the study of local health problems are the Andean biology tradition in Peru initiated in the 1930's, studied by M. Cueto, the *Escola Tropicalista Bahiana* of the 1860's-1890's in Brazil, studied by J. Peard, and the leprosy control in Colombia in the 1920's, studied by D. Obregón. In the first two cases, pioneers confronted the still prevalent beliefs about tropical degeneration and inferiority with science. See M. Cueto, (1989*b*); J. Peard (1996, 1997); D. Obregón (1996).

initiative was seen with suspicion. Revealing to the world a consumptive disease such as the American Trypanosomiasis was considered anti-patriotic.[64] The supporting actors had no idea what science was all about and could not care less about Chagas' international prestige. However, we must never forget that they were the ones in charge, in spite of Chagas' administrative positions and in spite of his formal victory in the Academy. They opposed and sabotaged Chagas in every instance;[65] they denied better salaries and full time employment for his researchers,[66] which gradually led to Manguinhos' decline; they controlled medical education in Brazil and prevented the students from learning about Chagas' disease. The parasite, well behaved in the laboratory, proved to be a very difficult pathogen to study. It was not easily detectable in the bloodstream in the chronic stage of the disease and there was no definite diagnostic procedure to detect the acute cases, where the parasites could be found. *T. cruzi* remained elusive for years. Across the ocean, tropical medicine had changed and was no longer oriented to parasites and vectors.

The change of tide simply destroyed the whole edifice of scientific excellence that Cruz and Chagas had erected. To explain why this scientific enterprise in particular and many others in Latin America suffer from such instability, we must understand the interplay of factors determining the fate of scientific initiatives in each case. H. Vessuri's account of the development of science in Argentina shows it to be punctuated by promising initiatives and their rapid failure. The early development of plant genetics, abruptly aborted when the pioneers were forced to emigrate in 1947; the attempts to stimulate the study of physics, astronomy, mathematics, and chemistry in the 1930s and 1940s by Enrique Gaviola, which met an "unresponsive, short-sighted milieu"; the electronic components research halted by the military coup of 1966, among others, are sad examples of this trend. Vessuri points out that talented Argentine scientists faced unfavorable socio-political conditions as soon as they were seen as a threat to the *status quo*—whatever that was at the moment.[67]

64. Afrânio was the champion of this nationalistic discourse. He claimed that Chagas had made his reputation over the tragedy of Brazilian country folk who suffered from goiter and idiocy. See Carneiro (1963, pp. 70–75); Pedro de Toledo claimed that Chagas jeopardized Brazil's chances of competing with other nations for the immigrants that were pouring out of Europe. Parreiras Horta suggested that Chagas had broadcast to the world an image of Brazil as a country of weak and sickly people, incapable of productive work. Chagas Filho (1993, pp. 203–3).

65. About the political difficulties faced by Chagas in the government, see Chagas Filho (1993, p. 142).

66. See Chagas Filho (1993, p. 173).

67. See Vessuri (1996*a*).

The confluence of independent interests involved in granting support and recognition for the activities undertaken by Manguinhos (Brazilian authorities', the medical community's, the international tropical medicine community's, etc.) help to account for the early recognition that Chagas received. Nevertheless, their very independence may also account for the later de-construction. As soon as the contingently favorable factors were gone, traditional interests and petty politics took over and quenched the embryonic scientific enterprise.

To understand the interplay of factors we must consider both the local and the wider international contexts for science. The discovery of Chagas disease and the subsequent research it engendered cannot be described solely in terms of the local demands and health conditions. Manguinhos was meeting the political interests of important local social segments with sanitation initiatives much like those found all over the world. Manguinhos' scientists were enjoying support for their scientific endeavors in the country because of the products they rendered in sanitation and hygiene at the local level. However, although "science," broadly understood as an enterprise that produced useful knowledge, was incorporated as something vaguely valuable, Brazilian scientists never succeeded in convincing society that their activity was socially relevant. The idea that a *space for science* was unsatisfactorily established in Brazil has been explored by Schwartzman (1991). In other countries, such as Argentina, political instability and government brutality against the scientific community have been major explanations for scientific failure (Vessuri 1996*a*). The abortion of promising scientific initiatives in Latin America, however, cannot be blamed on military coups *per se.* A public consensus about the role of scientific investigation beyond immediate practical results has never been achieved. This has been exemplified by Vessuri, in Argentine physics, astronomy, mathematics, and chemistry in the 1930's and 1940's (Vessuri 1996*a*). The pitfalls of consensus building with respect to the role of science are not exclusively the responsibility of the traditional elites, either. T. Glick discussed the consequences of leftist *dependentista* theories when, in the 1970's their advocates took over Venezuela's science and technology agency, the CONICIT. Believing that "imported" science "was a means of cultural domination," they questioned the utility of basic science. As a consequence, there was a divorce between basic and applied scientists, which hampered research development.[68] This condition of disagreement differed from that enjoyed by the European scientists, who worked in countries where science was a traditionally established enterprise.

68. See Glick (1984).

Chagas' discovery cannot be described as a simple application or mimicry of European tropical medicine either. When Chagas met the blood-sucking insect in Lassance, he did not come to the human disease hypothesis by simple substitutions on the malaria puzzle, as Stepan claims (Stepan 1976, pp. 118–20). The analogy with malaria appears as a secondary addition to Chagas' early model. It was inserted there to provide support for M. Hartmann's theory. This is when the Schaudinn school comes in, and it stops there. Accordingly, Chagas was not yet committed to the Schaudinn school of protozoology in 1907, when he first went to Lassance, as Perleth's explanation would require.[69] Chagas generated his human disease hypothesis because he was a legitimate practitioner of tropical medicine and, as such, he shared the community's emphasis on the insect-vector theory, with all its examples. He mobilized the concepts he was familiar with as soon as he met the *barbeiro* and, in his own words, he *invented a disease* (Chagas 1928). After that, back in Rio de Janeiro, he profited much from his interaction with the German researchers. They helped with the interpretation of cytological experiments and he followed their theoretical perspective. The *binucleata model* was never pursued in Trypanosomiasis research again. Finally, Delaporte's claims about the analogy with sleeping sickness to explain Chagas' early model of the disease are not supported by the historical evidence.

The establishment of a stable scientific tradition from a successful episode, its strengthening and diversification, the extension of its relations to other social actors, and the reproduction of its patterns have never taken place in Brazil. The country had a scattering of successful episodes, but their effects on the scientific establishment dwindled quickly. In this respect, other Latin American countries are similar, as seen. They lacked the institutional and political conditions to support the internationalization sought by isolated groups of scientists.[70]

International factors played a role in the success of Chagas' discovery, and also in its subsequent decline. The same can be said about local factors. This is certainly true about any scientific endeavor. What is relevant here is the independence of the factors and the resulting isolation of Chagas and his institution. Internationalization might not be the key to success, but isolation seems to be a certain road to ruin.

69. In order for the discovery to be a "reflection of the Schaudinn school of protozoology," Chagas would have to be committed to it *before* he elaborated his hypothesis. Therefore, before he went to Lassance. See M. Perleth (1997, p. 92).

70. In his history of Brazilian science, S. Schwartzman (1991) details the rise and decline of each successful initiative. About other Latin American countries and Latin America in general, see Vessuri (1991, 1996*b*). See also the "success stories" reported by T. F. Glick (1994), and Cueto (1989*a*).

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