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Review

When a misperception favors a tragedy: Carlos Chagas and the Nobel Prize of 1921

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ABSTRACT

Carlos Chagas, the discoverer of Chagas' disease was nominated to the Nobel Prize in 1921, but none did win the prize in that year. As a leader of a young scientist team, he discovered all aspects of the new disease from 1909 to 1920. It is still obscure why he did not win the Nobel Prize in 1921.
Chagas was discarded by Gunnar Hedrèn on April 16, 1921. Hedrèn should have made a written report about the details of his evaluation to the Nobel Committee. However, such a document has not been found in the Nobel Committee Archives. No evidence of detractions made by Brazilian scientists on Chagas was found. Since Chagas nomination was consistent with the Nobel Committee requirements, as seen in the presentation letter by until now unknown Cypriano de Freitas, it become clear that Chagas did not win the Nobel Prize exclusively because the Nobel Committee did not perceive the importance of his discovery.
Thus, it would be fair a posthumous Nobel Prize of 1921 to Carlos Chagas. A diploma of the Nobel Prize, as precedent with Dogmack in 1947, would recognize the merit of the scientist who made the most complete medical discovery of all times.

Chagas disease is still a plague for people living in Latin America, where it affects about 10 million people, 25 million are at risk of acquiring the disease, and about 10,000 persons are expected to die yearly. Nevertheless, Chagas' disease is no longer confined to Latin America, but has become global in view of international immigration [1]. Because of cardiac involvement [2,3], the global annual economic burden of Chagas' disease is high not only for Latin America countries, but also to non-endemic countries. For example, the annual costs of Chagas disease are estimated to be US$ 129 million for Brazil and US$ 118 million and US$ 9 million for the USA and Spain, respectively. The global annual economic burden of Chagas' disease is US$ 7.2 billion, only lower than that of pulmonary or breast cancer, and higher than that of cholera and rotavirus [4].

Carlos Chagas, the discoverer of Chagas' disease, was officially nominated to the Nobel Prize in 1913 and 1921, but he never won the prize. Working in the Brazilian hinterland as a leader of a young scientist team, he was able to discover, among others, the etiology (1909), the vector (1909), the life cycle of *Trypanosoma cruzi* (1909), the differentiation between the acute and the chronic stage of the new disease (1910), the possibility of autoimmunity involvement in the pathogenesis of the disease (1911), the cause of sudden cardiac death in young persons (1912), the incurability of the disease (1916), the natural reservoir (1918), and the importance of the heart disease as the principal clinical manifestation of the disease (1920) [5].

By 1920, Chagas' disease had been found in other countries of Latin America, thus heralding what a scourge the disease could be. It is still obscure why such a discovery was not recognized by the Karolinska Institute, particularly in 1921, when none received the Nobel Prize. It has been suggested that detractions on Chagas' work and on its personal character in Brazil and abroad could have disfavored Chagas' candidacy for the Nobel Prize [6,7]. To clarify this matter further, we report herein the results of an "in loco" visit to the Archives of Nobel Committee by one of the authors (RBB) on April 23, 2013.

1. Background

1.1. Alfred Nobel and the benefit to the mankind

Alfred Nobel was born in Stockholm in 1833. In 1863 he found a way to use nitroglycerine safely and in a practical manner, got a patent for what he called dynamite, which made him very wealthy over time [8]. Although he was a chemist, Nobel had a profound personal interest in medical sciences in general, and in experimental medicine in particular. In 1890, for example, he was assisted by Johan Johansson, a physiologist from the Karolinska Institute, for five months on experimental blood transfusion work in his laboratory in Paris. Afterwards, Johansson kept close contact with Nobel until his death [9].

In 1895, Nobel worked out the final version of his will; surprisingly, 64% of his fortune should be used to make a fund at the Royal Swedish Academy of Sciences to yearly laureate, among other areas, the most

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important scientific research in Physiology and Medicine. The reason was to allow the awardee to work in his research field with no economic concerns within the next 20 years [10]. The prize should go annually to "those who, during the preceding year, shall have conferred the greatest benefit to mankind". In the field of Medicine and Physiology, the prize should go to the "person who shall have made the most important discovery" [9].

The Royal Swedish Academy of Sciences was entrusted by Nobel to select the winners, but their members were hesitant to take responsibility for the awards. A private foundation (the Nobel Foundation) was created in 1900, which since that time manages the fund and coordinates, manages, and supports the awards of the Nobel Prize of Physiology and Medicine [11].

1.2. The Nobel Committee (1918 to 1926) and prize selection

The mechanism of prize selection of that time was, essentially, similar to that used currently. From the beginning, members of the Karolinska Institute asked for scientists from around the world to nominate candidates for the Nobel Prize in Physiology and Medicine, and they evaluated the nominations for prize-worthy. In 1918, however, a Nobel Committee was created to handle the nominations for the Nobel Prize. According to the Nobel Archives, the Nobel Committee of 1921 was composed by J.E. Johansson (Professor of Physiology, Chairman), G. Hedrén (Professor of Pathological Anatomy, Vice-chairman), J. Akerman (Professor of Chemical Medicine), S. Jöqvist (Professor of Surgery), and F. Lennmalm (Professor of Neurology). The secretary, who remained in office until 1960, was Göran Liljestrand [12].

Nominations for the prize were made only by duly qualified persons: members of the Karolinska Institute, members of the medical section of the Royal Swedish Academy of Sciences, members of the Universities of Uppsala, Lund, Oslo, Copenhagen, and Helsinki, and previous prize winners. Nominations had to be accompanied by "the description of the discovery recommended and a detailed argument for an award, supported by publications and other relevant documents". Nominations received after January 31, those made by unduly persons, personal nominations, nominations with no clear reasoning for awarding, and nominations concerning discoveries considered too late were discarded by February 1. This represented about 17% of all nominations at that time. However, nominations that arrived later at the Nobel Committee with no culprit by the sender were considered in the next year [9].

About 70 to 80% of nominations were not new and had already been evaluated by the Nobel Committee previously. Those who had already been disregarded remained so unless new facts indicated the need of reconsideration. Then, the candidate could be reevaluated. Other nominations might previously been considered prize-worthy by the Nobel Committee, but for unknown reasons the prize had not been awarded. If the discovery was not considered too old, the candidate might be reevaluated. The nominators not discarded were submitted to a detailed evaluation, and a written report for each nominee should be discussed in a Committee meeting (s) by April. Theoretically, new nominations should follow the same way [9]. However, such new candidates were, with a few exceptions, not further evaluated, being "a priori" discarded [10].

By April, the Nobel Committee decided which candidates deserved further evaluation, which occurred until August, and was usually carried out by experts, the majority of them are from the Karolinska Institute, although outside reviewers could also be used. The results of such additional investigation carried out on the candidates selected by the Nobel Committee should be written and sent before September 1. During that month, the members of the Nobel Committee discussed the reports received and suggested a name to receive the prize, which was finally voted in October by members of the Karolinska Institute [9]. Written protocols of the Nobel Committee evaluation meetings could be found in April, when every evaluator exposed the reasons for either discarding or presenting the reasons for the selection of a nominee, and in September, when the name for the prize was suggested.

1.3. Johan Johansson's chairmanship (1918–1926)

Because Johansson took part personally in the discussions with Nobel about the prize, he became very influential on the way the laurel should be given. In 1919, he was decisive by imposing the necessity of a new discovery for a candidate to be awarded. He also played a role in the modification of the statutory rules, when the words "in the preceding year" came to be understood as "the most recent achievements", and older works were considered only if "their significance has not become apparent until recently" [9].

Johansson's chairmanship was characterized by mistakes and irregularities. In 1920, for example, he took part in all the process of evaluation of his close friend Krogh, who won the Nobel Prize that year [11]. In 1922, the Nobel Committee decided that no nominee deserved to receive the prize, and recommended that the money was allocated to a fund. In 1923, however, the committee retroactively recommended the award for 1922 [11] so that Hill and Meyerhof, without being nominated for the prize that year, *a sine qua non* condition according to the statutory rules to win the prize, awarded the Nobel Prize. Finally, in 1923, Banting and Macleod won the Nobel Prize because the discovery of insulin. Nevertheless, there was an ample evidence at that time that insulin had been discovered by Paulesco one year BEFORE [13]. Macleod, who did not author the paper with Banting, was indicated by Krogh, the old friend of Johansson, because Macleod allowed him to get a license to manufacture insulin in Scandinavia [11].

Johansson created a fund to save money for the building of a Nobel Institute, which would have the task of checking the experiments carried out by the nominees for the Nobel Prize. In 1921 and 1923, the Nobel Prize was not awarded probably because of this [12]. In fact, the Nobel Assembly decided not to give a prize in 1921 "to use the money for investments in science at the institute" [11].

Another member of the Nobel Committee of 1921 was Frithiof Lennmalm, who was an important supporter of the eugenics movement in Sweden, which had close relationships with eugenicists in German at that time. To achieve their objectives, which lead to 65,000 forced sterilization procedures in Sweden, the eugenicists wanted the creation of a racial institute to institutionalize eugenics [14]. Lennmalm proposed the creation of a Eugenic Nobel Institute in 1919, and was supported by all members of the Nobel Committee, but the members of the Karolinska Institute rejected the proposition. Gösta Häggvist (a member of the Nobel Committee who evaluated two nominees for the Nobel Prize) ultimately supported the Nazi regime [14].

In summary, of the 9 prizes available during the Johansson's chairmanship (the period of Chagas' nomination), 3 (30%) of the them were not given and allocated to a fund, 1 prize was given to Fibiger in 1926 for the erroneous discovery that cancer is induced by a metazoan [15], 1 prize was given to scientists that indeed had not made the discovery, 1 prize was given to scientists who were not nominated for the prize in the year that they won the prize, and 1 was given to a very close friend. However, Johansson was the principal evaluator of the time (Table 1). Three laureates had been evaluated by Johansson (Krogh in 1920, Hill and Meyerhof in 1922, and Eithoven in 1924), other by Hedrén (Jules Bordet in 1919) and others by Sjöqvist (Banting and Macleod in 1923). In 1918, 1921, and 1923 the Nobel Committee did not suggest a prize.

2. Chagas' nominations for the Nobel Prize of 1921

Chagas was nominated for the Nobel Prize two times in 1921. The nomination by Hilário de Gouvêa has previously been published [6], and its details have been discussed elsewhere [5]. Now, we have found a new nomination at the Archives of the Nobel Committee, whose details were unknown by the scientific community until now.