

The railroad worker's Disease

Teaching Notes

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Carlos Ribeiro Chagas is sent to the small town of Lassance, in the interior of Brazil, to deal with what was understood as malaria and which was so afflicting the workers that it was preventing the construction of the railroad, which was part of a development plan of the country. In 1909, the scientist and physician ended up describing a new disease (Chagas disease), its vector (kissing bug) and its causative agent (the protozoan *Trypanosoma cruzi*). Its inclusion in the international scientific context of diseases caused by protozoa is due to the unprecedented triple discovery. Chagas disease, also known as American trypanosomiasis, is endemic in 21 Latin American countries and the southern United States. It is now also spreading through international migrations into Europe, Canada, New Zealand, and Australia. It affects 6-7 million people, causing 10,000 deaths per year, and puts 75 million people at risk of infection.

NOS features include

- A. The role of political and economic factors in supporting scientific research [the work of scientists]
- B. The role of personal background, motivations and skills
- C. The role of analogy (e.g., comparisons between a new disease and those already described)
- D. The role of local or anecdotal knowledge versus systematic investigation
- E. The role of chance or contingency
- J. The role of patience and persistence
- F. The role of collaboration
- G. The relationship between laboratory studies and field studies
- H. The application of research knowledge to public health
- I. Incentives and rewards

THINK Exercises

The current material includes some considerations that aim to assist teachers in using Carlos Chagas' historical narrative in the classroom. The primary purpose of these questions is for students to develop scientific thinking skills and to reflect on the Nature of Science (NOS) explicitly. To that purpose, questions were offered that tried to guide the narrative while also addressing some elements of the nature of science indirectly and overtly.

It is up to the instructor to explicitly convey and lead the discussion of the issues offered in each section for the students' better comprehension. The questions serve as key stopping points since they allow for hypothesis development, debate, and communication. It is proposed that the "think questions" be addressed individually or in small groups and then shared with the classroom group. To avoid spoilers in the narrative and hinder part of the experience of engaging with the narrative investigation, this work should be done without consulting the internet or printed sources.

The questions are open-ended, and the notes here complement the narrative and serve only to guide the possible diversity of responses. The teacher should avoid overt clues or "fishing" for answers, implying that a particular response is expected or considered "more right." The case study should illustrate the blind, uncertain process of science in the making. To help promote Thinking skills, the teacher should encourage (and reward) thoughtful responses, well-articulated reasoning, and respectful dialogue among students with different ideas or perspectives. We offer broad comments for each of the 13 "think questions" in this material, indicating the components of the nature of science mobilized and the scientific content developed and pushed at each point.

[Think Question 1] As president of the railroad, what would be your response regarding the workers? What are your concerns, and what actions are available to you?

The students are expected to point out that as the railway director, Aarão Reis should hire and send a private medical team to solve the issue or use his political influence to demand that the state/government send a medical team. This would be only the first layer of expected responses. It is up to the teacher to ask for a deeper analysis of what the concerns and motivations for this action would be. Carlos was not sent to Lassance out of government or director generosity, much less out of personal affinity with the region or the local population. Economic factors, such as the fact that the expansion of the railroad was at risk, motivated and encouraged the sending of Carlos to the place (Lassance). This shows how political and economic interests can influence the construction of knowledge. The teacher must pay attention to this factor. Some students may bring up a possible concern from the railway director or the government for the workers and local people, and this should be respected but

can be used to provoke debates. A possible push to foster the debate would be to ask why specifically that region and at that time.

[Think Question 2] Given the list of symptoms, how would you determine if the railroad workers' disease in Lassance is a variant form of malaria or a different disease entirely? What additional information would you like to collect? What criteria would you apply before seeking an alternative treatment or remedy?

Despite the story leading to the understanding that it was another disease and not a local variation of malaria, it is enriching when different hypotheses appear, which must be respected. Disagreement can be used to promote debates, always with a mediation that avoids the institution of winners and losers. Students should be encouraged to present not only the conclusions of their arguments but the data and justifications that led them to these conclusions.

The second issue at this first stopping point is the one in which creativity is most expressed. There are many possibilities for ways in which Carlos could seek to increase the reliability of his conclusion. Among the criteria for deciding whether it is another disease or not, it is important that students not only consider the similarities and differences between the symptoms but raise the importance of investigating whether the causative agent is the same and the possibility of having another vector.

It is feasible to investigate the idea that illnesses may be diagnosed by semiology or by examining patterns of recognized symptoms. However, it is clear that only disorders that have already been characterized may be evaluated, which is unfortunate when a condition has not yet been identified. Therefore, comparing existing disorders to emerging ones in order to characterize them is essential. The comparison to malaria in the story was made because both illnesses are spread by insects and are caused by protozoa. Furthermore, both are prevalent tropical illnesses that are linked to underprivileged socioeconomic groups.

The fact that some of the symptoms attributed to the illness under investigation were in reality connected to population malnutrition or other diseases is another problem that may be addressed. This creates opportunities to talk about the challenges of determining whether symptoms are caused by a certain disease. How can one tell the new illness' symptoms from those of other diseases? How can one connect a symptom to a specific disease? Such thoughts provide a forum for discussion on scientific study approaches and the importance of creativity in obtaining good results.

[Think Questions 3] Should Carlos take Cornélio's suggestion seriously? Give at least one reason for heeding his advice and at least one reason for doubting it. What could you do to investigate Cornélio's information further?

The testimony of Cornélio Homem Cantarino Motta, based on what he heard from residents of the region, was fundamental. But it was necessary to verify the information and look for probable links between the bug and the victims. Many people helped Carlos in his efforts at Lassance. Carlos' discoveries were aided by local people, doctors and engineers working in the battle against malaria. This is because, during the conversations, other sources of information appeared, allowing Carlos to decide whether to continue or change the course of his investigation.

The chance may have led Carlos to the residence of engineer Cornélio Homem Cantarino Motta, who knows that may have changed the course of investigations into the illness of railroad workers. Carlos had the option of ignoring the engineer's statement about the bedbug, but the attention he paid to the information was fundamental, as was the respect for what he heard. Carlos, studious and a holder of what is meant by academic knowledge, could have made fun of the engineer or discredited the locals, but he chose not to.

This is an opportunity to discuss the importance of serendipity in the construction of scientific knowledge. The concept of serendipity is closely related to the observer's repertoire, who may encounter unexpected results and events throughout a scientific investigation that will lead them to an important discovery.

Science can be understood as a way of building knowledge that differs from other forms of construction, such as religious, philosophical or popular. This is an opportunity to explore the differences between ways of building knowledge. The objective is not to make an in-depth analysis of the subject but rather to dispel the myth that information not related to science is not important. The objective is not to equate various forms of information but rather to value the common knowledge that exists outside academia. Along the same lines, it is not intended to build a single and closed scientific approach but to recognize that scientific knowledge has qualities that distinguish it from other types of information, such as popular knowledge.

There are many possible answers to this second question at this stopping point. The teacher must consider all the possibilities without giving greater value to those that turned out to be the way Carlos proceeded. He must also analyze the feasibility and anachronisms of the proposals.

[Think Questions 4] How might you determine if the trypanosome forms observed in the kissing bug and the marmoset are different species or variants of the same species? What expertise and resources do you need for this investigation? How will you secure them?

Again there are many possible answers to this first question at this stopping point. A protozoan can inhabit different hosts for different stages of its life cycle, and each one presents different forms. To solve this question, Carlos would then need to conduct experiments that his precarious facilities in Lassance did not allow. It is up to the teacher to give vent to proposals for ways to investigate this issue, but always consider the impossibility of developing these investigations without the proper conditions.

The process by which knowledge is created and the fact that scientific discoveries are impacted by the research and knowledge environments of the time are both essential aspects. As examples, (i) the identification of microorganisms as pathogens in contrast to the impalpable miasmas, (ii) Finlay's recognition, at the historical time when the story takes place, that insects could be disease transmitters; and (iii) the discovery of various protozoa with the boom in research in tropical diseases all contributed to the understanding of the factors that were associated with a new tropical disease (particularly in Germany).

The thought that follows is appropriate in this situation: Would it be feasible to characterize Chagas without Finlay's demonstration of the link between tropical illnesses and insect-borne disease transmission? We have a situation with significant potential to dispel the myth of a scientist as a solitary genius who, in a burst of creativity, diagnoses a new illness on their own, given that protozoa were popular in the scientific setting of the time. Carlos was a committed researcher who kept up with developments in his field, and this directly affected the information he created. It is also worth noting that the Manguinhos Institute's renown allowed Carlos to have contact with up-to-date scientific information from other research centers and with great names in the field, demonstrating the importance of internationalization over isolation of a country and its research centers.

[Think Question 5] How can you confirm that the disease in the marmoset is the same as that in the Lassance group after ruling out one of the trypanosomes as pathogenic?

Among the different possible answers to the question of this stopping point, students are expected to point out the importance of trying to look for *T.cruzi* in the blood of sick people in Lassance. If this appears, it is important for the teacher to say that this type of analysis was possible. Students can make proposals, such as infecting humans with *T.cruzi*, which should be debated about the ethics of using humans.

[Think Question 6] Should the blood investigations be abandoned or continued? If so, for how long? What factors guide your decision?

There is no correct answer to the questions at this stopping point. One possibility to enhance the debate is to ask students to answer how many patients would they investigate the blood? Another possible provocation is to ask when persistence in this strategy is perseverance and when it becomes stubbornness? An important point is to reinforce that collecting blood samples presupposes going on foot to people's homes, conducting a consultation, and returning to the laboratory. Another point is to encourage students to establish criteria for this sampling.

In order for the students to understand how establishing such criteria can be arbitrary and result in different practical outcomes for the researcher's life as well as for the discoveries themselves, it is interesting to discuss with the class what strategies they would adopt to make this difficult decision. There is a need for examples that debunk the myth that scientific discoveries are the result of flashes of brilliance, which include the intensive work done to find kissing bugs and examine any connections that they could have to the emerging illness – while still battling malaria in the region. Thus, these reflections aim to link scientific findings to the effort and study of the people involved. At numerous stages in the narrative, it is mentioned that Carlos' diligent effort and thorough training were major contributing aspects, and it was this that led to the triple discovery of Chagas disease.

[Think Question 7] In what ways does this unexpected finding change the course of the investigation? How might such events affect how you plan and conduct scientific investigations?

The episode in which Carlos Chagas is called back to attend to the patient and, this time, finds *Trypanosoma cruzi* in her blood after having previously examined many people, including the girl Berenice, and not having discovered protozoa in her blood, provides another opportunity to consider the role of chance in the story. Even the fact that Carlos Chagas was sent to Lassance (and not someone else) might be viewed as a fact based on chance. Other instances of how chance played a part in the story might be used by the students. Depending on how this conversation turns out, it would be good to use this part of the nature of science to investigate the importance of resiliency and tenacity for scientific studies.

[Think Question 8] Is the presence of *T. cruzi* in the patient's blood in this one case sufficient to show that it causes the disease? If not, why not? How else might you link together the relevant evidence about the protozoa in kissing bugs, patients' blood, and other animals?

It is important to consider that having found the protozoan in the blood of a single sick child is not evidence that guarantees that this is the cause of the disease. It could be a coincidence, and this possibility can be explored. Including because the blood of many people was investigated. For your final questions at this stopping point, it is interesting that the teacher allows the students to express

their creativity, including encouraging the design of experimental proposals. However, proposals involving using human beings as experimental subjects may arise, which must be ethically debated. Feasibility and anachronisms must also be considered.

[Think Question 9] What do you conclude from these experiments in the context of all the other evidence gathered through Carlos's work?

The combination of evidence, such as the existence of trypanosomes in other patients with comparable symptoms, the effects of inoculations, and the presence of trypanosomes life forms found within Kissing bedbugs, coupled with their life behaviours, allowed Carlos to grasp the life cycle of *T. cruzi* and the sickness linked with this protozoan. With this proof and thanks to Carlos' efforts, the new condition was termed Chagas disease (Carlos' surname) at the suggestion of physician Miguel Couto (1865-1934). The finding was notable since it was the first time that a single individual had identified a novel illness, its causal agent (*T. cruzi*), and its vector (the kissing bug). Although they can be understood as rhetorical questions, it seems interesting to ask the students: Do you believe the findings regarding Chagas disease could have been achieved without the field research? And without experiments in the lab? The teacher can then ask the students to develop their answers, encouraging them to bring the contributions that each type of study had in the construction of knowledge about Chagas disease. Also, asking for limitations of each study.

[THINK Question 10] What types of scientific work were needed to generate this evidence, and how was each important?

Students must recognize that the world of science is often quite competitive, but that cooperative relationships also occur and are very important. The relationship between Carlos Chagas and Oswaldo Cruz was the most representative information in history linked to this element of the nature of science. Oswaldo Cruz's assistance during the laboratory experiments was critical because he was working with previously unknown species and had only primitive facilities in a train compartment in Lassance. As a result, field observations might be supplemented by information from laboratory experiments. This was only feasible because Carlos Chagas' investigations could utilize the facilities that the Manguinhos Institute had to provide.

[Think Question 11] Imagine the impact of Chagas's investigations and conclusions on the science of studying diseases. How might understanding the history of this one case shape public policy on funding science and using its results?

Firstly, students can be encouraged to discuss the importance of discovering a new disease. What are the implications of this? Implications for railroad workers, implications for the population of Lassance, Brazil, and the world? And what are the implications for Carlos Chagas? And for the Manguinhos Institute? And for the Brazilian and worldwide scientific community? It is expected that students will say that this discovery should shape actions and public policies in order to combat the spread of Chagas disease effectively. The teacher can then give a spoiler, or present the data provided in the classroom presentation material, that this disease remains a global public health problem, affecting millions of people, and then return to the question. Another avenue for discussion could be to ask the students to examine the likely causes of this lack of dialogue across different areas of society and what the consequences are for the treatment of infectious diseases. This way, the narrative can highlight the disparity between medical and scientific knowledge and public health initiatives.

[Think Question 12] Why and how are awards important (and from whom)? What level of recognition does a discovery like this deserve?

Its importance in the international scientific context of protozoal diseases is due to the unprecedented triple discovery associated with this disease. Awards are granted to researchers who make significant discoveries or contributions in their fields of expertise and are seen as a form of validation and legitimization of their work. Awards can bring visibility and prestige, helping to attract funding for future research, collaborations, and partnerships with other institutions and researchers.

To give materiality to the discussion and promote engagement, the teacher can ask, "Why didn't Carlos Chagas win the Nobel? Did he deserve it?" The great engagement throughout the narrative commonly makes students feel as if they were the ones overlooked. It can also be asked if it would have been different if the same work had been done in the US or Europe.

[Think Question 13] Discuss how the case of Carlos Chagas & the Railroad Workers' Disease illustrates various features of science and how it works:

Based on the discussion of the previous thinking questions, look at the aspects associated with knowledge production listed below and give examples of the moments in the "triple discovery" story where you could reflect on them. It is important that the teacher emphasizes the nature of science and urge students to find sections in the narrative that demonstrate these elements (table below). Recalling the passages assists students in comprehending the aspects, recalling the story, and participating in this stage of formalization. When formalizing these characteristics, reminding the class that several reasons might obstruct scientific labour and discoveries is appropriate. Scientists do not operate in solitude

since their job requires collaboration, perseverance, devotion, funding, and so on, which goes beyond a misinformed picture of science in which scientists are solitary geniuses.

Relation between aspects of nature of science and the think questions

NOS aspects	Points where it is possible to reflect on
How political and economic considerations affect scientists' work	1, 10,11
The role of personal motivations and skills	3, 10
The role of the analogy between a new disease and others previously described	2, 4, 8, 9, 10
The role of local knowledge as opposed to systematic research	3
The role of chance/serendipity in scientific work	3, 7, 8, 10
The role of contact amongst scientists in validating a finding vs personality clashes	8, 10, 12
The role of complementation between laboratory and field studies	2, 4, 5, 6, 8, 9, 10
The gap between medical/scientific knowledge and public health actions	11
The importance of having access to scientific information and being updated on current scientific knowledge	1, 4, 5, 6
The role of resilience/perseverance in scientific research	6, 7, 10