

The Case of a Tropical Disease and Its Treatment: Science, Society, and Economics



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Part I—A Mysterious Ailment

Although he was afraid to take off from work and risk losing his job at the banana plantation, Adrian Mora decided he was much too weak to continue his ten hour shift. He had already spent most of the morning applying pesticides and covering clusters of bananas on the trees with plastic bags in order to protect them from wind, birds, and insects. He informed his boss, Don Jose, he must go home and rest, but he would work extra hours later in the week to make up the lost time.

He walked through the farm, set against the edge of remnant fragments of lowland tropical rainforest. This part of southwestern Costa Rica used to be continuous forests and mangrove swamps, but as the land was developed for fruit plantations, cattle ranches, and other types of agriculture, the forests were cleared. Small wooden houses set on low stilts now lined cleared strips of land between the bananas and the forest edge. Palm trees were left standing to provide some scant shade and so that the workers could make use of the palm fronds for roof thatch. Tangled scrubby, secondary growth vegetation stretched out to the houses from the forest edge, years after the clear-cutting. Many workers lived here to be near the plantation rather than commute from the town of Quepos 65 km away.



Map based on public domain material from *CIA World Factbook*.

Adrian was an illegal immigrant from Nicaragua. He had fled south with his brother, Alejandro, to Costa Rica in search of a better economic future about seven years ago. He and his brother did not want to risk the chance that they might be deported, so they had never applied for official permission to live in Costa Rica. Another Nicaraguan immigrant had helped him and Alejandro get jobs at the banana plantation as temporary workers. The brothers worked whenever the plantation needed some extra help, especially during harvest time. They moved around from one farm or plantation to the next as unskilled laborers. At the plantation Adrian made 110,000 colones (about US\$200) per month. This was less than Costa Rican minimum wage, but since he and his brother were not legal workers, they were not listed on official employee records. As an *indocumentado*, Adrian had to take whatever work was available, and often for less than what a *Tico* would be paid

and without other benefits.* The brothers continued to send money to their mother and younger siblings back in Nicaragua. At least the plantation owner allowed him and his brother to live in one of the plantation houses for free.

Adrian arrived back at the three-room house that he and Alejandro shared. They had trouble keeping the house clean because they rarely took a day off while working at the plantation. Since their jobs were not secure, they worked as much as possible when the plantation needed them. Cracks between the slats of the wooden walls and floor allowed dirt and insects to enter the house. Adrian looked up at a few, small open spaces in the thatched roof, and realized they needed to collect more palm fronds to patch it.

As he lay in his hammock into the evening hours, he wondered why he was not feeling well. “Maybe I’ve just been in the sun too long. Or maybe I am sick from the chemicals sprayed on the fruit trees,” he thought. “I have heard of Ticos who have gotten cancers from their prolonged exposure to the pesticides. Could the pesticide that we use on the bananas cause me to feel so poorly?” Adrian rubbed absent-mindedly at his eyelid, which was becoming swollen. “I am so tired, and should eat something to keep my strength. But I am not hungry at all.”

Adrian was worried enough he considered visiting a doctor at a local clinic. “Despite my low wages, I could probably still afford to visit a doctor.” Costa Rica had a national health care system with affordable services and treatments, and healthcare was extended to illegal immigrants as well as citizens and legal refugees. “But I do not want to take the chance that if I go to a doctor, someone might find out that I am here illegally and report me.”

His heart seemed to beat oddly and he felt flushed. Adrian hoped that this was simply a result of his anxiety. He blankly stared at the insects swarming around the electric lamp on the porch, lit each night to keep away nocturnal animals. Adrian swatted at a bug alighting on his forehead as he drifted off to a restless sleep.

**Indocumentado* literally means “undocumented” or without identity papers; the term is commonly applied to illegal immigrants. *Tico* is a nickname for Costa Ricans; the formal Spanish name for a person from Costa Rica is Costarricense.

Background

In order to become familiar with diseases endemic to Costa Rica, read the following webpages on health concerns in Mexico and Central America from the U.S. Centers for Disease Control and Prevention:

- <http://wwwn.cdc.gov/travel/regionCentralAmerica.aspx>
- <http://wwwn.cdc.gov/travel/destinationCostaRica.aspx>

Make sure to investigate the links to additional information on diseases listed for this region, or other internet sites which include information on these diseases and their symptoms.

Questions

1. What are some important infectious human diseases that are endemic to Costa Rica and Central America, based on information from the Centers for Disease Control?
2. What types of symptoms characterize these diseases?
3. What are some similarities in the symptoms of these diseases that might complicate diagnosis of a specific condition?
4. What are some peculiar or specific symptoms to each disease that might aid in diagnosis?
5. How might a patient’s environment (e.g., living conditions, socioeconomic situation) relate to accurate diagnosis?

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Part II—The Diagnostic Dilemma

Adrian's condition had deteriorated by the next day. His left eyelid was extremely swollen and he had developed a high fever. There was no way that Adrian could work. Alejandro was worried and decided that his brother needed to see a doctor. If Adrian could not work, their boss at the plantation might simply fire him. Alejandro helped Adrian walk to the highway where he could flag down a bus to Quepos, while Alejandro returned to the plantation.

After waiting for a few hours at a small clinic on the outskirts of Quepos, Adrian was seen by Dr. Rodriguez. The doctor was immediately suspicious that Adrian might have Chagas disease due to his swollen eyelid, a characteristic symptom known as Romaña's sign (see Figure 1), and given that he lived in an area in which the disease vector was prevalent. Dr. Rodriguez took a blood sample from Adrian. Visual inspection of the blood with a thin blood film under a microscope confirmed the doctor's initial guess. There were characteristic forms of the unicellular protozoan *Trypanosoma cruzi* in his bloodstream. These forms of the protozoan, known as trypomastigotes (see Figure 2), are present in the bloodstream of individuals in an acute stage of Chagas disease.

Dr. Rodriguez explained to Adrian that he had Chagas disease, caused by a type of trypanosome, which is a microscopic protozoan. While the disease can be transmitted through blood transfusion from an infected individual or from mother to child during pregnancy the most common form of transmission is through the bite of an insect vector, a type of triatomine insect, which is also known as the *vinchuca* or "kissing bug" (see Figure 3). Given that Adrian lived near the forest, the triatomine that infected him was likely *Triatoma dimidiata*. The doctor further explained that the bug serves as a host for the protozoan. When these bloodsucking bugs bite a human, the protozoan enters the human's blood from the infected bug feces deposited at or near the bite. The *vinchuca* likes to bite people around the mouth or eyes because the skin is thinner there. If the bug is infected with *T. cruzi* and the bug feces get into the bite, another open cut, or into the eye, there is a good chance the person will become infected.

"Adrian, it is estimated that 17 million people throughout Central and South America are infected with this disease and that 50,000 will die annually. You have symptoms characterizing the acute stage of Chagas disease, and there is a small chance you could eventually die if your symptoms become severe enough. If instead you seem to get better, even without treatment, after years or even decades of being infected with the parasite you could develop serious problems in your heart or other internal organs from long-term infection. The protozoa will settle into your muscles, heart tissue, or intestines and you could eventually die from complications and damage to the organs. Once the parasites become established in your body, which is considered the chronic stage of the disease, it is nearly impossible to treat. We need to attempt to destroy all of the parasites in your body now."

Dr. Rodriguez wanted Adrian admitted to a hospital for treatment, but Adrian was adamant that he would not go. "I do not want to be stuck in a hospital in Quepos, away from my brother." Adrian did not speak out loud his other fears—that he would be fired from his job at the plantation and someone at the hospital might suspect he was in Costa Rica illegally. Dr. Rodriguez gave up trying to convince Adrian to admit himself to a hospital, and instead told Adrian that he must start medical treatment to destroy the protozoa. The doctor provided Adrian with a prescription for benznidazole, which is one of the only two drugs presently available to treat Chagas disease. The doctor warned Adrian about the need to take the medication on the prescribed schedule, as well as potential medication side effects, including sleeplessness, nausea,

diarrhea, and skin rashes. The doctor also warned him that it was important to complete the full course of medication, or he was less likely to be cured.

“You will have to visit me for an additional serological blood test after you finish taking the medications to determine if there are any remaining protozoa in your body. Approximately 30 to 40% of individuals treated in the acute stage of Chagas disease may not be completely rid of the parasite following the initial course of medication.” Dr. Rodriguez continued, “If side effects of the drugs become very strong, you need to see me as soon as possible. The drugs are very potent, and could make you ill.”

The doctor knew about the condition of the houses around the fruit farms, and told Adrian, “Your house may be harboring more *vinchucas*, or new bugs may enter your house from the nearby forest and reinfect you. You will need to take measures to prevent additional bites from these insects.”

Adrian asked whether he could treat the disease with some pills he had remaining from a previous prescription for a skin infection. He also wondered if there was some kind of injection that could make him immune to the disease in the future. Dr. Rodriguez responded that the pills were probably a general bacterial antibiotic, which were not any use in treating the parasite. An injection wouldn't have helped either. “Currently, there is no vaccine to prevent Chagas disease, and it is unlikely a vaccine will soon be developed. Your best option to prevent future infections is to not be bitten by any more *vinchucas*.” Dr. Rodriguez was himself frustrated at the lack of prevention and treatment options available for this disease, but could do nothing more than send Adrian on his way.



Figure 1. Romaña's sign is a swelling of the area around the eye indicative of a bite wound or due to rubbing the bug feces into the eye. Photo courtesy of WHO/TDR.

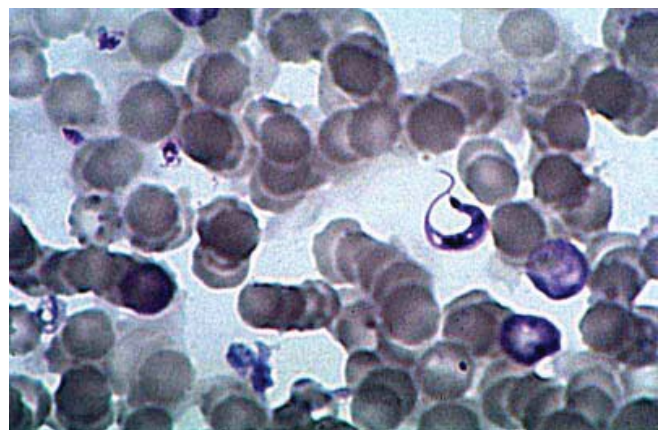


Figure 2. *Trypanosoma cruzi* seen in a human blood smear. Flagellated trypomastigote is in mid-right portion of the smear. Photo courtesy of WHO/TDR/Stammers.



Figure 3. The vinchuca or kissing bug is found in Costa Rica as well as other countries of Central America. *Triatoma dimidiata* adults, nymphs and eggs. Authors: María Carlota Monroy Escobar and Dulce María Bustamante Zamora, Laboratory of Applied Entomology and Parasitology, Department of Biology, San Carlos University, of Guatemala. This work is licensed under the Creative Commons Attribution-ShareAlike 2.5 License.

Background

Read the following references, which provide background information on Chagas disease, triatomines (kissing bugs), and medications for treatment.

- Information provided by the World Health Organization regarding Chagas disease at <http://www.who.int/tdr/diseases/chagas/>.
- Information on *Triatoma dimidiata* and control mechanisms by Ramsey and Schofield (2003).
- Information sheets from PharmGKB about the two standard medications for treating Chagas disease, benznidazole and nifurtimox:
 - <http://www.pharmgkb.org/do/serve?objId=803&objCls=DrugProperties>
 - <http://www.pharmgkb.org/do/serve?objId=845&objCls=DrugProperties>

Questions

1. How does the kissing bug (e.g., *Rhodnius sp.*, *Triatoma dimidiata*) locate its human prey?
2. What type of environment does the kissing bug inhabit?
3. Given the behavior and ecology of this insect, what are some factors that could cause the incidence of Chagas disease to increase in Central and South America in areas like the banana plantation, and why?
4. What are some of the steps that can be taken to reduce the likelihood of infection by Chagas disease through insect vectors like kissing bugs?
5. Which of these approaches might be easiest, or most useful, for Adrian, given his circumstances?

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Part III— The Search for an Alternative Treatment

Adrian considered purchasing the medication prescribed by Dr. Rodriguez. He wondered how much the medication would cost and how long he would have to wait for the prescription to be filled. He considered the possible side effects of the medication, how long he would have to take the pills, and how often he would need to take them each day. How was he to work outside at the plantation if sunlight reacted with the medication to cause skin rashes? Where could he store the medication to keep it cool and retain its effectiveness? And he still might not be cured after weeks of treatment! As he stood outside the clinic in Quepos, he looked down the road in the direction of the nearest pharmacy, with no idea what to do.

Then Adrian recalled that his brother knew someone who had lived in this area before it was converted to plantations. His brother's friend, Carlos, had spent time with several groups of indigenous Costa Rican peoples in the south of the country, including the Bribri and the Guaymi. Carlos had learned how the *curanderos* (healers) among the Bribri and Guaymi used different plants to treat many ailments, including arthritis, infertility, and other diseases. Adrian had hope that there was a more natural and less expensive way to treat the “kissing bug” disease. Adrian decided that he would have his brother arrange a meeting with Carlos to get advice on alternative treatments for Chagas disease.

The following day Carlos met with Adrian at his house at the plantation and Adrian explained the diagnosis of Chagas disease. Adrian's left eyelid was almost swollen shut and he still had a high fever. Carlos nodded



Figure 4. *Neurolaena lobata*, used to combat fevers, stomach aches, intestinal parasites. Photo provided by Daniel Atha, The New York Botanical Garden. Used with permission.

his head, “Chagas disease is very uncommon among indigenous Central Americans—but people do become infected occasionally. What you should do is brew a tea from a plant called *gavilana*. Drink a cup of this tea every day until the eye is no longer swollen and there is no more fever. It may take a few weeks for the symptoms to go away, but if you keep drinking the tea you will eventually feel better.” Carlos told Adrian the story of a young girl with Chagas disease who seemed on the verge of death. “She was given *gavilana* tea for four weeks every day without fail, and her eye got better and all of her other symptoms disappeared. She is now a grown young woman, with her own family—and she has had no problems with her eye since then.”

Carlos continued, “I will show you how to find the *gavilana*. It is a relatively common plant in grasslands, bordering forests, and cleared areas near forests” (see Figure 4).

Adrian was very hopeful that this remedy would work. Then he would not have to use an expensive, unnatural medication, and if he was feeling better in a few weeks, he wouldn't even visit Dr. Rodriguez again. If one cup of tea each day might cure him in a few weeks, maybe drinking more tea more often would cure him even sooner

Questions

1. What might be some general advantages and disadvantages of using ethnobotanical products to combat diseases?
2. More specifically, from Adrian's perspective, why would use of *gavilana* tea be preferred to the medications prescribed by the doctor?
3. What would be some potential consequences for Adrian if he opted for this type of self-treatment?
4. Based on the information provided, what kinds of evidence did Carlos have that *gavilana* is effective in treating Chagas disease?
5. What kinds of evidence would be necessary to reliably demonstrate that an ethnobotanical treatment is effective in treating Chagas disease?

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Part IV—Quest for a New Treatment*

The indigenous peoples of Costa Rica were no longer the only ones who were knowledgeable about the potentially useful properties of *gavilana*, or *Neurolaena lobata*, in treating Chagas disease. As it so happened, an ethnobotanical anthropologist who had been working with one group of Guaymi in Costa Rica for the last several years had collected detailed data on this group's use of medicinal plants. Dr. Allison Woodrow's data included interviews with Guaymi *curanderos* indicating that *N. lobata* and several other local plants were used to treat a variety of illnesses that induce fever. In particular, *N. lobata* was used to treat a condition that sounded similar to Chagas disease, including the symptom of eyelid inflammation.

A multinational pharmaceutical company based in the United States, Alpha Pharmaceuticals, continuously monitored ethnobotanical research. They were aware that approximately 25% of pharmaceuticals developed are based on natural products, primarily plants. A research and development employee discovered one of Dr. Woodrow's publications listing medicinal uses of plants by the Guaymi. The company decided to pursue research on the pharmacological properties of this and other plants used by the Guaymi.

The pharmaceutical company had a standing agreement with the National Biodiversity Institute (INBio) in Costa Rica, such that INBio researchers and scientists could collect samples of natural materials (mainly from plants) in Costa Rica and provide these samples to Alpha Pharmaceuticals. Although INBio was a private organization, it could collect materials from public lands, including some forest reserves. Alpha Pharmaceuticals had arranged to pay INBio a set amount for thousands of plant samples, including specimens of *N. lobata*; however, any financial gains made from the development of useful products would belong only to Alpha Pharmaceuticals. The company planned to invest millions of dollars to test hundreds of plant species against many ailments, from influenza to cancer, to see if there were pharmacologically active properties in the plants that could be developed into marketable medications. If *N. lobata* could be developed into a treatment for Chagas disease, the company would market it throughout Central and South America at prices competitive with benznidazole and nifurtimox. With millions of infected individuals in this region, the company could make a good deal of money.

Background

Read Berger et al. (2001) regarding scientific studies of *Neurolaena lobata* (*gavilana*) and its effects on protozoan diseases like Chagas disease.

Questions

1. How does research on the potential effectiveness of *N. lobata* to treat Chagas disease follow the scientific method?
2. Based on this reading, compare what is known regarding the effectiveness of treatment of Chagas disease with *N. lobata* and what is known regarding the effectiveness of nifurtimox or benznidazole.
3. What additional research would be necessary to develop a marketable treatment for Chagas disease based on *N. lobata*? (See study by Cavin et al., 1987 for a possible model.)

*Note: This part of the case asks students to explore the ramifications of a fictional agreement between INBio and the fictional company Alpha Pharmaceuticals using the actual Merck-INBio agreement as a model. Also, although the Guaymi and Bribri are indigenous peoples of Costa Rica and there has been ethnographic research on the Guaymi and Bribri and their use of plants, the specific information and use of plants attributed to these indigenous peoples described herein is completely fictitious.

4. If a drug based on *N. lobata* becomes popularly recognized as the drug of choice in the treatment of Chagas disease, what are some of the potential consequences to the status of this plant in natural environments?
5. Specifically, who will be harvesting the plant?
6. What are the possible effects of intensive harvesting of the plant on the environments in which it exists?

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