Case Teaching Notes

for

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

by

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Introduction / Background

This case study was originally designed for a Costa Rican study abroad course, but is also appropriate for traditional science courses. The protagonist of the case, Adrian, is a banana plantation worker who develops a mysterious illness. The storyline of the case follows his eventual diagnosis and dilemma over treatment options. In working through the case, students must examine the complex and multidisciplinary issues associated with the epidemiology of a disease including biological, socioeconomic, cultural, environmental, and ethical issues. In particular, students become acquainted with infectious diseases, pathogens, and vectors endemic to this area of Central America as they are asked to diagnose Adrian's condition. They also examine alternate approaches to treating an illness that plagues thousands of Central and South American citizens. Additional topics include disease symptoms and health effects in infected individuals; environmental, cultural, and socioeconomic variables affecting disease transmission, prevalence, and treatment; research and development of new therapies; and rights to knowledge and products for treating diseases.

The case was constructed to be broad enough for use in general education courses for non-specialized students; however, it may be especially useful for courses with a component on health care, pharmacology, microbiology, medical anthropology, ethnobotany, or epidemiology. Instructors could choose to focus more on the biological components of the case, or could choose to focus more on the socioeconomic and ethical components, depending on course goals and subject area.

The case is set in southwestern Costa Rica in order to link with travel-study opportunities in this country, a common location for travel study of U.S. institutions. For those who are able to use the case study on-site in Costa Rica, optional instructional "field" activities for Costa Rican forest habitats and local communities are described in these teaching notes. The case can be used in a classroom setting anywhere without the "field" activities; however, using the case in Costa Rica has the advantage of helping students contextualize the case.

Objectives

In working through this case study, students will:

General

- Analyze the complex relationships among disease epidemiology, socioeconomic and cultural variables, and environmental factors.
- Apply reasoning and external resources (research publications, government fact sheets, etc.) toward problem solving (e.g., diagnosis of disease, development of a treatment plan).
- Acquire an understanding of the following key terms: benznidazole, biopiracy, bioprospecting, Bribri, Chagas disease, endemic, epimastigotes, ethnobotany, Guaymi, *Neurolaena lobata*, nifurtimox, pathogen, protozoan, Rhodnius, Romaña's sign, serological, *Triatoma dimidiata*, tripomastigotes, *Trypanosoma cruzi*, and vector.

Part I

- Compare and contrast some of the important endemic diseases of Central America, and particularly of Costa Rica, many of which are not common or present in the U.S.
- Identify and consider different variables (symptoms, living conditions, environment) that are useful in accurate diagnosis of a disease.

Part II

- Explain the importance of intermediate hosts in disease transmission and alternative mechanisms for disease control and prevention, addressing not just the pathogen, but also disease vectors.
- Develop an understanding of the relationship between specific environmental factors, socioeconomic factors, and a disease.
- Investigate political and socioeconomic factors that affect development of, access to, and utilization of, prevention and treatments.

Part III

- Formulate reasons why non-standard medical treatments, such as traditional medicinal plants, are used, and conceptualize some of the potential consequences of their use.
- Critically evaluate the types of evidence that are needed to demonstrate that medical treatments function as intended. This should be put in the framework of the scientific method, and emphasize the scientific method as a process for gaining knowledge.

Part IV

- Debate the complex ethical, sociopolitical, and environmental issues associated with the use and ownership of biodiversity, genetic materials, cultural knowledge, and national heritage, specifically with regards to the development of health treatments.
- Discuss the environmental, political, and socioeconomic impacts of forest resource utilization—i.e., harvesting of plants from a natural environment, including potential contributions to national economies, international trade opportunities, habitat change and degradation, and effects on animal and plant populations.

Blocks of Analysis

Chagas disease is a systemic illness caused by trypanosomal protozoan parasite *(Trypanosoma cruzi),* infecting humans via the bloodstream (Barrett et al., 2003). Chagas disease, also known as American trypanosomiasis (Centers for Disease Control and Prevention), is a New World disease. It is related to African sleeping sickness, which is caused by another trypanosomal parasite, *T. brucei* (Barrett et al., 2003). In the Americas, 16–18 million people are estimated to be infected with the Chagas disease pathogen (WHO, 2005).

There are characteristic symptoms of initial infection of the disease (lasting up to approximately 60 days), which may manifest to varying degrees. Children are typically most severely affected by initial infection. During this “acute stage” of the disease, symptoms include swelling at the site of the infection, nausea, vomiting, diarrhea, periodic high fevers, or more severe heart arrhythmia and encephalitis (Umezawa et al., 2001; WHO). Death during the acute stage is rare; however, the cure rate with treatment is only about 60% (Luguetti, 1997). If the individual retains the parasites in the body through lack of treatment or treatment that is not completely effective, the protozoa settle into body tissues (primarily skeletal muscle, the heart, and intestinal organs). Severe and permanent damage may occur to these organs over decades, in part perhaps as a result of the body’s own autoimmune response to the parasites (Tarleton and Zhang, 1999).

Health complications and sudden death associated with heart damage may occur many years after initial infection. It is estimated that 25–30% of infected individuals will suffer permanent damage of organs, and that Chagas disease results in approximately 50,000 deaths annually (Centers for Disease Control and Prevention; Umezawa et al., 2001; WHO).

Chagas disease may be transmitted in three ways: 1) congenitally from mother to infant; 2) through blood transfusions from an infected individual to another person; and 3) through bites of an insect vector, which serves as an intermediate host (Kollien & Schaub, 2000; Umezawa et al., 2001). The latter is the most common form of transmission. Chagas disease is a zoonotic disease, and opossums, rodents, and armadillos may be primary source hosts for the disease (Ramsey and Schofield, 2003; Zeledón et al., 2001). The primary vectors for transmission are bloodsucking bugs of the subfamily Triatominae, commonly known as "assassin bugs" or "kissing bugs" (Barrett et al., 2003; Kollien & Schaub, 2000). These insects are known as kissing bugs for their tendency to bite at the thinner-skinned parts of the face around the mouth or eyes—thus leading to one of the characteristics symptoms of the disease, Romaña's sign (Centers for Disease Control and Prevention). Different triatomine species are the primary vectors in different regions of the Americas. In Costa Rica, *Triatoma dimidiata* is the primary non-domiciliated vector, and species of Rhodnius are the primary vector insects that are "domesticated" (Barrett et al., 2003; Ramsey and Schofield, 2003; Schofield and Dujardin, 1997).

The complete elimination of Chagas disease is unlikely, but there have been large-scale regional and national campaigns to combat the disease, primarily directed at eliminating the insects that act as disease vectors (Kollien & Schaub, 2000; Ramsey and Schofield, 2003; Schofield and Dujardin, 1997; WHO 2004a). Some of these campaigns, such as the Southern Cone Initiative instituted in 1991 in the countries of Argentina, Bolivia, Brazil, Chile, Paraguay, and Uruguay, have been extremely successful (Ramsey & Schofield, 2003; Schofield & Dujardin, 1997; WHO 2004b). Transmission of the disease has been extensively curtailed, or even stopped altogether in some regions (Moncayo, 2003; Ramsey & Schofield, 2003; WHO 2004b). These programs focus on vector control through pesticide application in human habitations to kill the bugs and screening of donated blood (for transfusions). The programs have been well-funded and have included commitments to long-term approaches with surveillance and treatment of vector populations over years (Dias et al., 2002; Moncayo, 2003; Ramsey & Schofield, 2003). One other reason for the success of these programs is that triatomine bug vectors in many parts of Latin America are primarily domiciliated. In the Southern Cone of South America, the particular triatomine vector species is not well adapted to the natural habitats (likely having been brought to the region inadvertently by humans), and its survival seems to depend on occupation of human dwellings. This makes complete eradication of the vectors in certain areas a real possibility (Dias et al., 2002; Ramsey & Schofield, 2003). Given that sylvatic triatomine species act as carriers of Chagas disease in many other parts of Central and South America, reinfestation of human dwellings and transmission of the disease will always be a possibility, although control of domiciliated insects may drastically reduce disease prevalence (Ramsey & Schofield, 2003).

We focused on Chagas disease in this case study (although similar complex epidemiological issues surround many diseases) for several reasons. The disease is uncommon and little-known in the United States, but is very prevalent in parts of Central and South America where it mainly afflicts rural populations or people in poor living conditions. Spread and prevalence of the disease is tied to socioeconomic conditions as well as increasing deforestation and development of natural habitats (Barrett et al., 2003; Grijalva et al., 2005; Ramsey and Schofield, 2003; Zeledón et al., 2001). Thus, the case study allows students to learn about a disease outside their own typical sphere of concern and to consider epidemiologically related social and environmental issues. There is no certain cure for the disease, and development of a vaccine is highly unlikely due to the autoimmune response caused by the disease (Tartleton and Zhang, 1999). Thus, most health efforts directed toward Chagas disease focus on vector control and early treatment in the acute stage. Also, since Chagas cases have now been reported as far north as Texas, Oklahoma, and California (Moorhouse, 2006), this disease is also a potential threat in the United States. The distribution of this disease thus serves as a reminder of the geographical and environmental continuity of the Americas.

Studies indicate that a minimum of about 25% of pharmaceuticals are derived from "natural products," primarily of plant origin, accounting for approximately $75 billion in this market (see Kate & Laird, 2000). Recent pharmacological research on Neotropical plants has included work on the antihelminthic, antiprotozoal, and antimicrobrial compounds of herbaceous and woody species. In this study, one plant species common and native to Costa Rica, *Neurolaena lobata* (jackass bitters, *gavilana*), is used as an example of a plant that might be developed into a drug to treat Chagas disease. Selection of this species is based on recent research of this plant for treatment of Chagas disease (Berger et al., 1998, 2001). Part IV of the case study was developed to explore issues associated with "bioprospecting," resulting effects on natural habitats, and conflicts over rights to information and genetic resources used to develop marketable treatments. In particular, the case study elaborates on a fictional scenario in which *N. lobata* would be developed into a medication used to treat Chagas disease. 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 (Joly et al., 1990; García-Serrano and Del Monte, 2004). However, the specific information and use of plants attributed to these indigenous peoples in the case study is completely fictitious.

Classroom Management

This case study is intended to be taught in an interrupted format using a series of interrelated stages; however, components of the case may also be used independently with as much or as little background information as desired. When "field tested" in a second-year medical microbiology course in the School of Pharmacy at Southern Illinois University—Edwardsville, students were assigned Part I and given a week to write their answers to the corresponding questions. The major emphasis was not on students coming up with a correct diagnosis. Rather, the students were expected to follow a rubric that emphasized research, application, synthesis, and professional writing. We had previously covered world-wide vector-borne diseases so the students' working knowledge of the potential disorders was pretty advanced. Approximately 75% of the students diagnosed Adrian correctly while the rest predicted other disorders such as malaria or typhoid fever. Students were then given the subsequent parts of the case and time to research and report their answers the following week. We were then able to focus on treatment and preventative measures. Throughout the case, time was made in class for students to discuss their answers; they also discussed the case on the discussion board of the Blackboard site for the course.

Part I—A Mysterious Ailment

For students with less background in biology or epidemiology or restricted access to reference materials, instructors might consider limiting students' search for the correct disease diagnosis with a set of readings or handouts (such as Centers for Disease Control and Prevention or WHO fact sheets) to a subset of diseases endemic to Central America. In this way, students do not have to search through all possible ailments that might afflict someone with Adrian's symptoms. Suggested readings include:

- http://wwwn.cdc.gov/travel/contentDiseases.aspx
- http://wwwn.cdc.gov/travel/default.aspx
- selected diseases from http://www.who.int/topics/en/

Instructors might help direct students with general questions about the "clues" provided in the case study. For example, instructors could have students list in separate columns Adrian's symptoms and those of different potential diseases, and then compare the columns. This exercise could be done by students individually, in subgroups, or in open-class discussion (e.g., on a whiteboard or chalkboard).

For more advanced students with stronger medical backgrounds who are able to diagnose Adrian's condition quickly, the instructor may have students compare and contrast Chagas disease with similar disorders that are endemic to this region of Central America, placing special emphasis on vector and pathogen taxonomy. The following advanced questions could also be added to those in Part I (see Answer Key for suggested answers to these additional, advanced questions):

6. What are Adrian's symptoms?
7. What are features of his environment that could help in diagnosing Adrian's ailment?
8. What diagnosis would you make based on Adrian's symptoms and his environment?

Part II—The Diagnostic Dilemma

Like many human diseases involving a pathogen with various stages in its life cycle, a primary host, and a vector, understanding Chagas disease can initially seem overwhelming. We suggest arranging the students into groups that will lead the whole class in the following instructional discussions:

- Triatomines (insect vectors)—how *Triatoma dimidiate* and other kissing bugs locate their prey, transmit pathogens, etc.
- Protozoans (pathogen)—how the life cycle of *Trypanosoma cruzi* has evolved with human and other vertebrate hosts and the various stages of its life cycle.
- Human (host) immune responses and clinical signs of Chagas, as well as other hosts (intermediate or definitive) plagued by infection of this pathogen.

We recommend use of additional visuals on the structure and life cycle of the pathogen, *T. cruzi,* as well as the biology and behavior of the vector, *T. dimidiate* (or other related triatomine bugs). Images having liberal terms of use for non-commercial purposes can be found at http://www.who.int/tdr/tropical_diseases/databases/imagelib.pl.

An actual specimen of a reduviid bug can also be acquired for classroom examination. While kissing bugs (subfamily Triatominae) can be found in the southwestern part of the United States, other types of assassin bugs, a reduviid of a distinct subfamily, Reduviinae, may be collected in other regions. A good insect guide can provide guidance on the local distribution of reduviid bugs and their preferred habitats. (Be careful when attempting to handle live bugs as they can give a painful bite.) Detailed information on how to collect and preserve insects can be found at the following USDA website: http://www.ars.usda.gov/Main/site_main.htm?docid=10141&page=1&pf=1&cg_id=0.

Additionally, a PBS *Nature* program, "Bloody Suckers," contains a segment on triatomine bugs. For more information on this video, visit the PBS website: http://www.pbs.org/wnet/nature/bloodysuckers/. The video can be purchased online through a link on this site.

For more advanced students with clinical backgrounds, questions 6 and 7 could be added; question 8 could be used for those interested in socioeconomic aspects (see Answer Key for suggested answers to these additional, advanced questions).

6. What are some features of the standard treatments for Chagas disease, e.g., benznidazole (dosage and duration of treatment, cost, side effects, storing requirements, etc.)?
7. Which of these features might make following treatment protocol difficult for Adrian, and why?

8. Adrian is fearful that his illegal status will be discovered. He is Nicaraguan and has left his country for a better life in Costa Rica. Describe living conditions (health care, unemployment rates, etc.) in Costa Rica and compare them to neighboring Central American countries.

This part of the case also provides an opportunity for debate for instructors favoring such an approach. The following question set has been used in this way for students to further explore the ramifications of this case (see Answer Key).

- Chagas disease is occasionally transmitted in the United States, mainly as a result of occasional bites of "wild" (non-domiciliated) kissing bugs found in the southern part of the country. If Chagas disease was more common in the United States or other industrialized countries, do you think prevention and treatment programs would receive more notice or be approached differently? Do the same issues or problems with treatment of Chagas disease by standard medications that may affect Adrian in Costa Rica also exist in the United States? Why or why not? Should this disease be upgraded in its worldwide epidemiological importance? Why or why not?

Part III—The Search for an Alternative Treatment

In Part III students are asked to reflect on the use of ethnobotanical treatments. It might be useful for instructors to compare Adrian's use of *gavilana* tea with herbal remedies available in the U.S. at health food stores for a variety of purposes. Instructors might emphasize that the disappearance of symptoms (as in the story of the young Guaymi girl with Chagas disease) may not necessarily be due to the treatment (e.g., *gavilana* tea). This would be a good example of a spurious correlation. In particular, for Chagas disease, the disappearance of acute stage symptoms should occur approximately six to eight weeks after initial infection, which is during the time frame in which the girl improved. For example, possible factors important to identifying function of a treatment would include reduction in, or elimination of the parasite load, observed effects on the parasite in response to the treatment substance, and negative serological tests for antigens. Instructors might also want to emphasize the importance of controlled experiments to determine the effect of a specific independent variable (plant compound) on the dependent variable (parasites).

Part IV—Quest for a New Treatment

This section lends itself well to a debate on the sustainable use of "natural" ecosystem resources versus biopiracy. Suggested readings that can lead to a pro/con debate on the use and misuse of medicinal plants include:

Biswal, M. and D. Biswal. 2003. Issues relating to traditional knowledge systems and intellectual property rights (IPRS). XII World Forestry Congress, Quebec City, Canada. http://www.fao.org/DOCREP/ARTICLE/WFC/XII/0911-A3.HTM. Accessed on Oct. 17, 2006.

Coughlin, M.D. 1993. Using the Merck-INBio agreement to clarify the Convention on Biological Diversity. *Columbia Journal of Transnational Law* 31(2):337–375. http://www.ciesin.columbia.edu/docs/008-129/008-129.html

Mongabay.com. Tropical rainforests: Saving what remains. http://rainforests.mongabay.com/1007.htm

Schippman, U., D.J. Leaman, and A.B. Cunningham. 2002. *Impact of Cultivation and Gathering of Medicinal Plants on Biodiversity: Global Trends and Issues.* FAO, Biodiversity and the Ecosystem Approach in Agriculture, Forestry and Fisheries, Interdepartmental working group on biological diversity for food and agriculture, Rome. http://www.fao.org/DOCREP/005/AA010E/AA010E00.HTM

For more advanced students, the following additional questions could be assigned (see Answer Key for suggested answers to these additional, advanced questions). For background, students should read Rodríguez (2002) and use the Merck-INBio agreement described in this article as a model for this case's fictional agreement between INBio and Alpha Pharmaceuticals.

7. If *N. lobata* is in high enough demand to produce a treatment for Chagas disease, Costa Rica may be able to sell the plant to pharmaceutical companies sufficiently to make this a profitable activity. As *N. lobata* grows primarily in grasslands or cleared areas that were previously forest, what are the possible implications to the maintenance of forest areas?
8. How could the Costa Rican government address potentially conflicting needs to protect forest habitats, preserve healthy populations of *N. lobata* , and provide pharmaceutical companies with the plants to produce treatments developed from this plant?
9. How will benefits of the successful development of a Chagas disease treatment (access to the drugs, drug patents, financial profits) be allocated to the indigenous peoples, the Costa Rican citizens, the Costa Rican national government, INBio, and the pharmaceutical company?
10. Do you think this distribution of benefits is fair or unfair? Why? More generally, who should have the rights to cultural knowledge, environmental resources, and the products developed from them?
11. What is the difference between "biopiracy" and "bioprospecting"?

Optional Debate

This part of the case lends itself well to a debate format. After discussing questions 7–11, split the class into three subgroups representing 1) the Guaymi, and other indigenous peoples with cultural knowledge of the use of the plants; 2) the Costa Rican government that is controlling access to national lands and resources; and 3) the pharmaceutical company that is conducting the research. Each subgroup should make a case why the party represented should receive some benefit from the drug development, and the nature of that benefit. See Answer Key for representative positions that may be taken by each group.

Optional On-Site Activities

Part I

Visit a banana plantation and view the working situation and setting. Discuss whether this particular setting seems similar to that described in the case study. What are the housing conditions near the plantation? What types of habitats surround the farm? What are some characteristics of the plantation that you observe that might affect disease prevalence and transmission?

An alternative activity would be to talk to local residents about their knowledge of Chagas disease. Do they know anything about the disease, and if so, what? Would they recognize the triatomine vectors? What would be their response to a diagnosis of Chagas disease? That is, would they seek treatment from a medical doctor, and why or why not?

Part II

Collect or survey insects, either using a white sheet strung up near lights at night or via foliage nets (Zeledón, 2001a). Attempt to find and identify triatomine (or reduviid) bugs, including *T. dimidiate*. This may also be done by surveying for insects in a stratified sample of different habitats (primary forest, secondary forest, near human-inhabited structures). Based on the insects collected or surveyed, calculate what proportion of the sample are triatomine bugs.

Part III

Attempt to identify *Neurolaena lobata* plants in Costa Rican habitats. Identify the types of habitats in which this plant species is found. Alternately, students can conduct a botanical transect to estimate population size and density of *N. lobata*.

Part IV

Visit the Museo Nacional in San Jose and learn more about the indigenous peoples that lived in Costa Rica before the Spanish conquest, and what has happened during and after the conquest. Discuss how modern-day bioprospecting based on the knowledge from indigenous cultures compares to colonial treatment of indigenous peoples.

Answer Key

Answers to the questions posed in the case study are provided in a separate answer key to the case. Those answers are password-protected. To access the answers for this case, go to the key. You will be prompted for a username and password. If you have not yet registered with us, you can see whether you are eligible for an account by reviewing our password policy and then apply online or write to answerkey@sciencecases.org.

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