NATIONAL CENTER FOR CASE STUDY TEACHING IN SCIENCE

African Illness: A Case of Parasites?

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Part I – Sub-Saharan Safari

A 51-year-old man named Robert Bragg reported to a hospital in the United Kingdom complaining of general malaise (discomfort), myalgia (muscle pain), fevers, headache, vomiting, and diarrhea. He complained that during the day he felt weak and tired; he was unsure if this was because his symptoms kept him awake at night, or if something else was causing his fatigue.

Robert had recently returned from a two-week safari in central Africa. He said that he felt fine during the entire trip, but reported that he had received numerous bug bites while on safari. He also said that while he was in Africa he routinely ate unfamiliar foods, including meats, which may have been prepared and stored under conditions that would not be considered sanitary practices in the United Kingdom.

Doctors suspected Robert's symptoms were caused by an infection he developed while on safari.

Questions

1. Make a list of human pathogens that are endemic to sub-Saharan Africa and can be transmitted through bug bites or consumption of contaminated foods. Looking over your list, what do you think is the most likely cause(s) of Robert's illness?
2. What tests should doctors conduct to confirm this diagnosis?

Part II – Diagnosis

Because Robert had spent much of his time outdoors in an area of the world where the Anopheles mosquitoes that transmit malaria are common, the doctors immediately suspected he had contracted malaria. His symptoms matched those generally expected of people with malaria, but to confirm the diagnosis doctors collected a blood sample from Robert to analyze for the presence of the *Plasmodium falciparum* parasites that cause the disease.

When doctors looked at Robert's blood smear under a light microscope, they did not see any malaria parasites. However, they did make a startling discovery.

"I found *Trypanosoma brucei* parasites in the patient's blood," one of the doctors remarked.

"What is *Trypanosoma brucei?*" asked a nurse. "Is it a type of malaria?"

"*Trypanosoma brucei* is a protozoan parasite. It is not closely related to *Plasmodium falciparum* genetically, but there are many similarities in the way it infects people and in the symptoms it causes. The disease caused by *Trypanosoma brucei*, called African trypanosomiasis, is also known as African sleeping sickness. All of the patient's symptoms are explained by this diagnosis."

Figure 1. T. brucei trypomastigotes (blood stage form) in a blood smear.

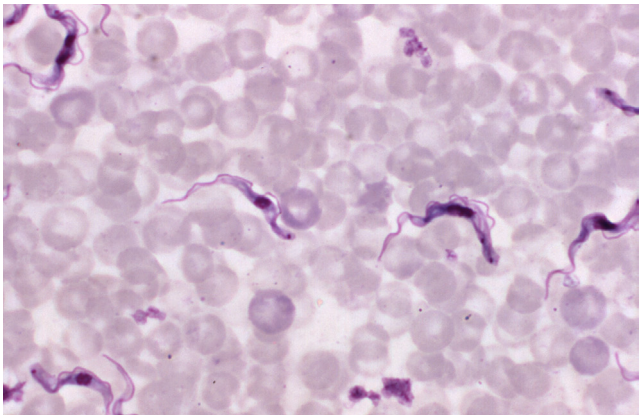


Image courtesy of Centers for Disease Control and Prevention/ Dr. Mae Melvin, ID# 10167 in CDC Public Health Image Library (PHIL). Public domain.

Use the sources below to learn more about African trypanosomiasis.

- "Parasites—African Trypanosomiasis," Centers for Disease Control and Prevention http://www.cdc.gov/parasites/sleepingsickness/
- "Trypanosomiasis, African," World Health Organization (WHO) http://www.who.int/topics/trypanosomiasis_african/en/

After thoroughly investigating these and other relevant sources, answer the questions below.

Questions

1. What is a protozoan? How is a protozoan parasite different from bacteria and multi-celled parasites such as intestinal worms? How does *T. brucei* differ from the closely related American trypanosome *T. cruzi*, the causative agent of Chagas disease, and from the *P. falciparum* parasite that causes malaria? Describe notable differences in morphology, life cycle, infectivity, transmission, geographical range, disease presentation, and treatment.
2. How do people become infected with *T. brucei?* What are the risk factors as far as behavior, lifestyle, and geographic location?
3. What are the clinical manifestations and symptoms of African trypanosomiasis? Compare and contrast these with the symptoms of malaria.
4. Why does *T. brucei* infection cause the symptoms that led to the term "African Sleeping Sickness"?
5. How is *T. brucei* infection diagnosed? What factors often make diagnosis difficult?

Part III – Symptoms and Treatment

The doctors informed Robert of the diagnosis. After they explained the cause of his illness, Robert asked "Will I be ok? Do you have a medication to kill *Trypanosoma brucei?"*

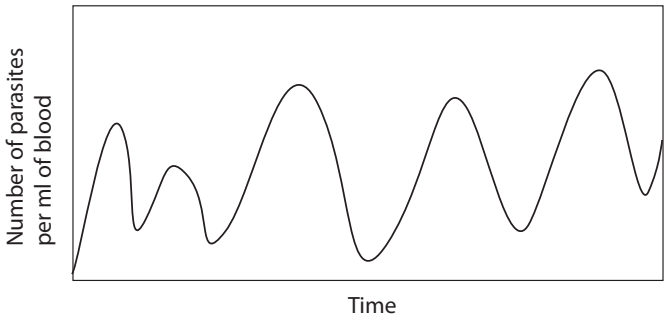
"There is medication to treat this disease, Mr. Bragg," said the doctor. "It's called suramin. It is very effective at killing *Trypanosoma brucei* when given early enough in the disease process, but it can also cause severe side effects, including joint pain, severe weakness, light sensitivity and even loss of consciousness. We need to start your treatment at once despite these side effects because the disease has a high fatality rate if left untreated. Fortunately, you are not exhibiting signs of severe damage to your central nervous system, such as violent behavior, convulsions, or coma, so I think that we have caught the disease at an early enough stage for treatment to be successful. However, we will first examine your central nervous system (CNS) fluid for the presence of parasites to confirm that the disease has not progressed."

"All right, doctor. Do what you have to… but is there any chance that I can recover from this parasite on my own, without risking the side effects of that medication?"

A second doctor interjected: "Actually, the human immune system is somewhat capable of killing *Trypanosoma brucei* and lowering the parasitemia (number of parasites in the blood); however, the parasite has adapted a way to continually evade the immune system so that it can continue replicating."

"If we were to count the number of parasites in your blood every day," explained the doctor, "we would likely notice that the parasitemia level would steadily increase for a period of time, perhaps one week, then the parasitemia level would fall drastically over one or two days as large numbers of parasites were killed by your immune system, only to rise again the following week. This trend would continue until you were given medication to clear the parasites, and would look like this if graphed." The doctor then pointed to a graph in a paper he was holding (Figure 2).

Figure 2. Parasitemia level vs. time



"I don't understand," said Robert. "If my immune system is capable of killing the parasites, why would the number of parasites in my blood repeatedly rebound in that way?"

The doctor explained that in order for African trypanosomes to become successful extracellular parasites and survive in the bloodstream of their human hosts, they had evolved a mechanism to evade the host's immune response.

"African trypanosomes are covered by a protective coat containing proteins called variant surface glycoprotein (VSG). Although VSG helps protect the parasite, it's also an antigen, which means it triggers the immune system to respond by making antibodies against it, which can lead to the destruction of the parasite. The genome of African trypanosomes contains many variations, or alleles, of the gene that encodes VSG. Only one allele is expressed at a time, but the parasite can vary which allele is expressed, allowing it to change its VSG coating as soon as the host's immune system becomes effective at recognizing one particular variant of VSG."

The doctor continued: "Every spike in parasitemia levels in the graph represents a switch in VSG expression. It takes time for the immune system to adapt to each new VSG. Once it does, parasites are rapidly killed and parasitemia levels drop sharply, only to increase again after another round of VSG switching."

Questions

1. Investigate the different parts of the human immune system and explain which cells/products of innate and adaptive immunity are responsible for recognizing antigens on the surface of *T. brucei* and clearing the parasite.
2. What would happen if *T. brucei* suddenly loss the ability to undergo antigenic variation?
3. If researchers developed a drug that could prevent *T. brucei* from undergoing antigenic variation, do you think it could be successful in eradicating African Sleeping Sickness? Would the drug have to be administered at a certain point before or after infection in order to be helpful?
4. Based on the similarities and differences you identified earlier between *T. brucei, P. falciparum,* and *T. cruzi,* do you predict that *P. falciparum* and *T. cruzi* undergo similar antigenic variation? Why or why not?

Part IV – Public Health Campaign

In addition to the extensive toll on human life, African trypanosomes also cause a widespread and devastating disease in livestock cattle called Nagana. Nagana causes three million cattle deaths per year, which amount to a loss of $4 billion a year to struggling African economies. Because there is no effective vaccine against African trypanosomes, the most effective way to prevent the spread of the disease is through multi-faceted public health campaigns directed at eliminating parasite contact through other means.

Design a public health campaign to dramatically reduce or eradicate African trypanosomiasis in both humans and cattle from a community in Africa. In your plan, include strategies to stop the spread of African trypanosomes, as well as ways to educate the public and local governmental and health agencies so that this information can be disseminated and implemented.

References

Internet Sites

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Image of *T. brucei* trypomastigotes, image ID #10167, from Centers for Disease Control and Prevention (CDC). http://phil.cdc.gov/PHIL_Images/10167/10167_lores.jpg

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