Case Teaching Notes

for

"Hunting the Ebola Reservoir Host"

by

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Introduction / Background

Filoviruses, to which Ebola virus belongs, cause severe hemorrhagic illness in humans and non-human primates, with case fatality rates ranging from 50–90% (Pourrut et al., 2005). Due to the high pathogenicity of filoviral infections in humans, continued re-emergence of filoviral outbreaks in endemic areas, and the potential for filoviral introduction into non-endemic areas, continuing research focus has been placed on understanding the natural history of filoviruses (Feldmann et al., 2004). Despite the greater than 40 years that have passed since the initial emergence of filoviral zoonoses, the natural reservoir host has still not been conclusively identified. However, bats have been implicated in some zoonotic transmission events due to substantial evidence of potential contact with bats during outbreaks (Feldmann et al., 2004; Leroy et al., 2005; Leroy et al., 2009; Pourrut et al., 2007; Pourrut et al., 2009; Hayman et al., 2010). This case uses the research on the Ebola reservoir host to motivate students to consider the characteristics of a viral host species and how it can be identified. It is presented in the form of an interrupted case. The storyline is inspired by a compilation of the research conducted on several Ebola outbreaks and does not reflect a specific event.

This case was developed for an introductory level, biology-majors course in infectious diseases. It could also be used in a class on epidemiology, microbiology, virology, or medical laboratory. With some guidance, it could also be adapted for use in a senior high school biology course. The case was given to students on the first day of class as a way to introduce them to infectious disease and epidemiological investigations. Students do not need a background in epidemiology or disease biology, but some foundation in molecular biology (particularly knowing what an antibody is) would be helpful. The case takes approximately one hour to complete, but an instructor wishing to explore certain aspects in more depth (e.g., immunohistochemistry) may wish to set aside two hours.

Objectives

Upon completion of this case study, students should be able to:

- Explain some of the factors that can lead to disease spread in a population.
- Describe what makes an organism suitable as a reservoir species for a virus.
- Extract potentially relevant information from a context-rich situation or laboratory data.
- Analyze how social, biological, and environmental settings can influence disease spread.
- Understand concepts of group-specific risk to infection.

Classroom Management

Overview

Students should begin by breaking into groups of three or four students. These will be their groups for the rest of the case study; however, whole class discussions will follow each small team period to share and compare the groups' predictions and interpretations. Using an overhead projector or white or black board may be helpful during group discussions.

For each part of the case study, hand out one copy of the case to each team of students to begin working on together. The time allotments given for each part allocate half of the time to individual group discussion and half of the time for the groups to come together for a class-based discussion of their findings.

Part I – The Cycle Starts Again (20 min)

Part I introduces students to the social setting where the Ebola epidemics are occurring. The context-rich description of the setting contains information about viral infection symptoms, specific infection risk groups, and behaviors that may contribute to infection and disease transmission. Students are asked to assess how behaviors can allow disease transmission and how this can create specific risk groups. Students are also asked about the kinds of factors that might affect disease emergence, leading to occasional re-emergence of a disease.

Students may experience some difficulty answering Question 4 (understanding what may allow for occasional re-emergence of a disease in a population). Instructors may wish to prompt them to think about the fact that most microorganisms cannot survive outside of a host. How is it that the human population is not constantly infected? How is the virus surviving during these interim times? Once students have worked out the concept of a host species, ask them to reconsider the question: Why is human infection periodic? If students are focusing on environmental determinants such as floods due to rainy seasons, etc., ask them to think again about what is necessary for a microorganism to subsist. If the microorganism is still around when a flood allows an outbreak to occur, why is that? How has that microorganism survived during the time since the last emergence?

Part II – Consulting the Disease Detectives (20 mins)

Part II allows students to verify that they answered the questions to Part I correctly, and then prompts them to incorporate all that they have learned in order to shape how their investigation should move forward.

If students experience difficulty creating a set of criteria for reservoir hosts, direct them to re-read the section where Joe talks about why humans cannot be the reservoir host for Ebola. Ask them why Joe rules out humans as the natural reservoir host and base their criteria around what Joe thinks allows for a successful reservoir host.

It is especially important that students understand that the virus must be able to live in the reservoir animal without causing the animal to develop the infection and die. This concept is crucial for the proper understanding of other sections of the case study, and therefore should be stressed during the group discussion.

The idea that the women's involvement in the funeral rites serves as a basis for disease transmission in the population is inspired by the work of Hewlett & Amola (2003).

Part III – News Spreads Quickly (15 mins)

Part III asks students to use the framework that they created in Part II of the case to evaluate the suitability of great apes as Ebola reservoir hosts given information regarding how great apes respond to Ebola infections. The intent of this section is to solidify the characteristics of both good and poor reservoir hosts candidates, stressing that animals that succumb to the infection are very poor candidates for reservoir hosts, since viral replication and spread cannot continue once the animal has died.

If students have difficulty answering the question for this section, ask them to go back to Part II and look at why Joe doesn't think that humans can act as the natural reservoir hosts for the virus. Then ask them to compare human infections with great ape infections, which should prompt the students that the large great ape die-offs likely show that apes cannot act as the reservoir species.

During the group discussion portion of this section, the instructor may wish to reiterate for students that while great apes are probably not the reservoir species for Ebola, humans may well become infected by these species when hunting them. Solidifying this distinction should help to clarify the difference to be made between reservoir species and species that can transmit the disease.

Part IV – Help From The Lab (30 mins)

In this section students are provided with lab-based data adapted from Swanepoel et al. (1996). Immunohistochemistry is used in this paper to quantify the amount of virus found in tissue samples from animals collected in Africa near sites of Ebola outbreak following inoculation with Ebola virus. Immunhistochemistry is described in this section of the case. Instructors may wish to spend a bit of time to ensure that students understand the technique used to investigate the ability of the virus to replicate in the tissues of each species. This would be a nice springboard for discussing other methods that could be used to detect virus in a tissue. PCR is an obvious method (qRT-PCR in particular). If students are familiar with the ELISA technique, instructors may wish to draw parallels between the two methods. In this section, students must analyze and interpret data to identify the species that has many of the characteristics of a reservoir species for Ebola. In order to fully understand this, it would be helpful to allow students access to their computers to research qRT-PCR and ELISA tests.

Part V – Further Discoveries (30 mins)

In this section students are presented with a scenario for which bats are a likely source of infection for the initial case in the Ebola outbreak (the idea for this story was inspired by Leroy et al., 2009). In this section students should demonstrate their assimilation of knowledge regarding how Ebola can be spread and what we need to know about a species to determine conclusively whether it can act as the reservoir species or not. Students should not have difficulty with this section given that it reviews concepts already discussed throughout the case; however, if students have difficulty understanding how to create a schematic diagram, instructors should suggest to students to use arrows to draw to whom the infection has been passed and how this passage may have been enabled.

It may be worthwhile pointing out to students at the end of the case that while fruit bats are currently a highly suspected reservoir species for Ebola in Africa, there are still unanswered questions about this hypothesis and it has not yet been confirmed. Arthropods have also been suggested as a possible reservoir species, although the evidence for this is not as strong as for the bats (Pourrut et al., 2005).

Follow-up/Extension Activities

The activities listed below may be used to supplement the case study. Students could be asked to:

- Research and write a paper on all the evidence that points to fruit bats as the reservoir host for Ebola.
- Research and write a paper showing support for a reservoir species other than bats.
- Perform further research on the role of burial practices in the spread of disease, and/or describe another instance where social or cultural practices can lead to the spread of infection or the creation of specific risk groups. These findings could either be written as a paper or presented to the class orally or in a poster presentation.
- Report on a recent Ebola outbreak. The CDC maintains a website of all known epidemics (CDC, 2012).
- For a slightly more entertaining and attention grabbing extension, have students read the article *Crisis in the Hot Zone* (Preston, 1992) or the book *The Hot Zone*, which is based on the article (Preston, 1994) or watch the disaster film *Outbreak* (Petersen, 1995) about viral hemorrhagic fevers and hold a class discussion about the possibilities of an outbreak in North America and what could be done to prevent or control them.

Suggestions for Shortening the Case

This case has two somewhat distinct angles: Parts I and II, which ask students to think globally about disease spread and the different factors that can affect an epidemic, and Parts III through V, which focus on principles of reservoir hosts and how we can identify them. To shorten the case study, the instructor could choose which perspective is the most important for their students and do either the first or second angle.

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**.

Suggested Readings for Instructors

Feldmann, H., Wahl-Jensen, V., Jones, S.M., & Stroeher, U. (2004). Ebola virus ecology: A continuing mystery. *Trends in Microbiology* 12(10): 433–437

Pourrut, X., Kumulungui, B.,Wittman, T.,Moussavou, G.,Delicat, A.,Yaba, P., Nkoghe, D., Gonzalez, J.P., & Leroy, E.M. (2005). The natural history of Ebola virus in Africa. *Microbes and Infection* 7: 1005–1014.

BIOL 375 Virology (2010). Infection mechanism of genus Ebolavirus. Microbe Wiki. Kenyon College. Accessed 2 August 2011 from http://microbewiki.kenyon.edu/index.php/Infection_Mechanism_of_Genus_Ebolavirus.

References

Centers for Disease Control & Prevention. (2012). Outbreak Postings. Special Pathogens Branch. Retrieved 10 October 2012 from http://www.cdc.gov/ncidod/dvrd/spb/outbreaks/index.htm.

Hayman, D.T.S., Emmerich, P., Yu, M., Wang, L-F, Suu-Ire, R., Fooks,, A., Cunningham, A., & Wood, J. (2010) Long-term survival of an urban fruit bat seropositive for Ebola and Lagos bat viruses. *PLoS ONE* 5(8): e11978. Accessed 2 August, 2011 from http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0011978 doi:10.1371/journal.pone.0011978.

Hewlett, B., & R. Amola (2003). Cultural contexts of Ebola in northern Uganda. *Emerging Infectious*

Diseases 9(10): 1242–1248.

Feldmann, H., Wahl-Jensen, V., Jones, S.M., &Stroeher, U. (2004). Ebola virus ecology: a continuing mystery. *Trends in Mivrobiology* 12(10): 433–437.

Leroy, E.M., Kumulungui, B., Pourrut, X., Rouquet, P., Hassanin, A., Yaba, P., Délicat, A., Paweska, J.T., Gonzalez, J.P., & Swanepoel, R. (2005). Fruit bats as reservoirs of Ebola virus. *Nature* 438: 575–576.

Leroy, E.M., Epelboin, A., Mondonge, V., Pourrut, X., Gonzalez, J.P., Muyembe-Tamfum, J.J., & Formenty, P. (2009). Human Ebola outbreak resulting from direct exposure to fruit bats in Luebo, Democratic Republic of Congo, 2007. *Vector-borne and Zoonotic Diseases* 9(6): 723–728.

Kopelson A (Producer), Kopelson A (Producer), Katz G (Producer) Petersen W (Director) (1995). *Outbreak* [Motion picture] United States of America: Warner Bros.

Pourrut, X., Kumulungui, B.,Wittman, T., Moussavou, G., Delicat, A., Yaba, P., Nkoghe, D., Gonzalez, J.P., & Leroy, E.M. (2005). The natural history of Ebola virus in Africa. *Microbes and Infection* 7: 1005–1014.

Pourrut, X., Delicat, A., Rollin, P.E., Ksiazek, T.G., Gonzalez, J.P., Leroy, E.M. (2007). Spatial and temporal patterns of *Zaire ebolavirus* antibody prevalence in the possible reservoir bat species. *Journal of Infectious Diseases* 196 (Supplement 2): S176–183.

Pourrut, X, Souris, M., Towner, J. S., Rollin, P. E., Nichol, S. T., Gonzalez, J., & Leroy, E. (2009). Large serological survey showing cocirculation of Ebola and Marburg viruses in Gabonese bat populations, and a high seroprevalence of both viruses in Rousettus aegyptiacus. *BMC Infectious Diseases* 9(1): 159.

Preston R (1992). Crisis in the hot zone. *The New Yorker* (October 26, 1992): 58–80.

Preston R (1994). *The Hot Zone*. New York: Anchor Books.

Swanepoel, R., Leman, P.A., Burt, F.J., Zachariades, N.A., Braack, L.E.O., Ksiazek, T.G., Rollin, P.E., Zaki, S., & Peters, C.J. (1996). Experimental inoculation of plants and animals with Ebola virus. *Emerging Infectious Disease* 2(4): 321–325.

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