EBOLA: FEAR OF THE UNKNOWN

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On the streets of Dar es Salaam people whispered to one another with fear and interest. It was rumored that a person had arrived at the National Hospital (i.e., formerly the Muhimbili Medical Center) with *Ebola*. It was popularly related that, as the person arrived at the medical facility, staff and visitors ran out in terror. One person said that if it is really Ebola we will certainly all die. "Don't shake hands!! Don't touch anyone!!! How can you ride a 'daladala' without touching?" Similar interest immediately followed a report that a woman had arrived by a passenger plane in Canada with a suspected case of *Ebola*. Warnings were issued. Fellow airline passengers were contacted and temporarily quarantined. People were eventually assured that the patient had finally been isolated and tests were being conducted. It was stressed that people should not panic. Popular sentiment, however, is dramatic fear and even panic, recalling images of the 1995 movie "Outbreak." While certainly rational in the midst of this sickness, some of the fear is related to just not knowing very much about this disease. This article is an attempt to assemble and present some existing information on *Ebola* for the larger community. To the general public *Ebola* is another disease like HIV/AIDS or a cousin to it. While having some truth to it, this analogy is not quite accurate as scientific inquiry demonstrates.

History

The *Ebola* virus, named after a river in the Democratic Republic of the Congo (formerly Zaire) in Africa, is a member of the virus family Filoviridae. Analysis has indicated that there are at least four subtypes of Ebola viruses: the original strain isolated from Zaire in 1976 and subsequently reappearing in 1995; a subtype isolated from Sudan in 1976 and again in 1979; *Reston* subtype isolated from monkeys imported into the United States from the Philippines in 1989; and a newly discovered subtype isolated from Côte d'Ivoire in 1994. Genetic analysis has found virtually no difference between the 1976 and 1995 isolates of the *Zaire* subtype, or between the two isolates from Sudan, or the three isolates of *Reston* Subtype. These three subtypes differ between each other considerably, however, and from the newly described isolate from Côte d'Ivoire. Analysis of material obtained during a 1994 outbreak in Gabon indicates that this subtype is genetically virtually indistinguishable from the *Zaire* subtype.[1]

The *Ebola* virus is closely related to the *Marburg* virus in that both cause severe hemorrhagic fevers. The *Marburg* virus was first recognized in laboratory workers in Marburg, Germany, and Belgrade, Yugoslavia, in 1967. These workers had been exposed to tissues and blood from African green monkeys imported from Uganda. There were 25 primary cases and six secondary cases in the outbreak. Seven of the primary cases died. Since then, sporadic, virologically confirmed *Marburg* disease cases have occurred in Zimbabwe, South Africa and Kenya.

The dates mentioned above seem to indicate that *Ebola* is a very new type of disease. However as the following description presents, this may be a very old virus that has been ravishing humanity for millenniums rather than decades.

> "The plague of Athens (430-427/425 B.C.) persists as one of the great medical mysteries of antiquity. . . . In an unprecedented, devastating 3-year appearance, the disease marked the end of the Age of Pericles in Athens and, as much as the war with Sparta, it may have hastened the end of the Golden Age of Greece. Understood by Thucydides to have its origin 'in Ethiopia beyond Egypt, it next descended into Egypt and Libya' and then 'suddenly fell upon' Athens' walled port Piraeus and then the city itself. There it ravaged the densely packed wartime populace of citizens, allies, and refugees. Thucydides, himself a surviving victim, notes that the year had been 'especially free of disease' and describes the following major findings: After its 'abrupt onset, persons in good health were seized first with strong fevers, redness and burning of the eyes, and the inside of the mouth, both the throat and tongue, immediately were bloody-looking and expelled an unusually foul breath. Following these came

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[1] *Encyclopedia of Virology Plus* CD-ROM. (Edited by Robert G. Webster and Allan Granoff.) 1995, Academic Press Ltd. For further reading see also Jahrling, PB (1991) Filoviruses and arenaviruses. In Balows A (ed.) *Manual of Clinical Microbiology*. Washington, DC: American Society for Microbiology. Martini GA and Siegert R (eds) (1971) *Marburg Virus Disease*. New York: Springer Verlag. Pattyn SR (ed.) (1978) *Ebola Virus Hemorrhagic Fever*. Amsterdam: Elsevier/ North-Holland Biomedical Press.

> sneezing, hoarseness, . . a powerful cough . . . and every kind of bilious vomiting. . . . . and in most cases an empty heaving ensued that produced a strong spasm that ended quickly or lasted quite a while.' The flesh, although neither especially hot nor pale, was 'reddish, livid, and budding out in small blisters and ulcers.' Subject to unquenchable thirst, victims suffered such high temperatures as to reject even the lightest coverings. Most perished 'on the ninth or seventh day . . . with some strength still left, or many later died of weakness once the sickness passed down into the bowels, where the ulceration became violent and extreme diarrhea simultaneously laid hold.' Those who survived became immune, but those who vainly attended or even visited the sick fell victim."[2]

By comparison, a modern case definition of *Ebola* virus infection notes sudden onset, fever, headache, and pharyngitis, followed by cough, vomiting, diarrhea, maculopapular rash, and hemorrhagic diathesis, with a case-fatality rate of 50% to 90%, death typically occurring in the second week of the disease. Disease among healthcare providers and care givers has been a prominent feature.

Signs and Symptoms

However, the signs and symptoms of *Ebola* hemorrhagic fevers (EHF) are not the same for all patients. The table below outlines symptoms of the disease, according to the frequency with which they have been reported in known cases.[3]

Clinical symptoms are similar with *Marburg* and *Ebola* virus infections. Following incubation periods of 4-16 days, the onset is sudden, marked by fever, chills, headache, anorexia and myalgia. These signs are soon followed by nausea, vomiting, sore throat, abdominal pain and diarrhea. When first examined, patients are usually overtly ill, dehydrated, apathetic and disoriented. Pharyngeal and conjunctival injections are usual. Most of the patients develop severe hemorrhagic manifestations, usually between days 5 and 7. Bleeding is often from multiple sites, with the gastrointestinal tract, lungs and gingiva the most commonly involved. Bleeding and oropharyngeal lesions usually herald a fatal outcome. Death occurs between days 7 and 16, usually from shock with or without severe blood loss.

Researchers do not understand why some people are able to recover from EHF and others are not. However, it is known that patients who die usually have not developed a significant immune response to the virus at the time of death.

Spread

Infection with *Ebola* virus in humans is incidental. Humans do not "carry" the virus. Because the natural reservoir of the virus is unknown, the manner in which the virus first appears in a human at the start of an outbreak has not been determined. However, researchers have hypothesized that the first patient becomes infected through contact with an infected animal. After the first case-patient in an outbreak setting (often called the index case) is infected, the virus can be transmitted in several ways. People can be exposed to *Ebola* virus from direct contact with the blood and/or secretions of an infected person. This is why the virus has often been spread through the families and friends of infected persons: in the course of feeding, holding, or otherwise caring for them. People can also be exposed to Ebola virus through contact with objects, such as needles, that have been contaminated with infected secretions.[4]

Time Frame	Symptoms that occur in most	Symptoms that occur in some
Within a few days of becoming infected with the virus:	high fever, headaches, muscle aches, stomach pain, fatigue, diarrhea	sore throat, hiccups, rash, red and itchy eyes, vomiting blood, bloody diarrhea
Within one week of becoming infected with the virus:	chest pain, shock, and death	blindness, bleeding

[2] References: Langmuir A. D, Worthen T. D, Solomon J., Ray C. G, Petersen E. The Thucydides syndrome: a new hypothesis for the cause of the plague of Athens. N Engl J Med 1985;313:1027-30. Morens D. M, Littman R. J. Epidemiology of the plague of Athens. Trans Am Philological Assn 1972;122:271-304. Morens D. M, Littman R. J. The Thucydides syndrome reconsidered: new thoughts on the plague of Athens. Am J Epidemiol 1994;140:621-7. Grmek M. D. History of AIDS: emergence and origin of a modern pandemic.Princeton, NJ: Princeton University Press, 1990. Page D. L. "Thucydides" description of the great plague. Classical Quart 1953;47 n.s. 3:97-119. Thucydides. Peloponnesian War. Bk. 2, chs. 47-52. Major R. H. Classical descriptions of disease. 3rd ed. Springfield, IL: Charles C. Thomas, 1945. Benenson AS, editor. Control of communicable diseases manual. 16th ed. Washington, DC: American Public Health Association, 1995. Mandell G.L, Bennett J.E, Dolin R. Mandell, Douglas and Bennett"s principles and practice of infectious diseases. 4th ed. New York: Churchill Livingston, 1995. Centers for Disease Control and Prevention. MMWR 1995;44:25:468-75.

[3] Website of Special Pathogens Branch, Division of Viral and Rickettsial Diseases, National Center for Infectious Diseases, Centers for Disease Control and Prevention, U.S. Department of Health and Human Services.

[4] Center for Disease Control, "Management of patients with suspected viral hemorrhagic fever," in *Morbidity and Mortality Weekly Report.* 1988; 37 (suppl 3): 1-16.

Health facility acquired EHF frequently occurs with outbreaks of EHF. In healthcare facilities, patients are often cared for without the use of a mask, gown, eye goggles, gumboots or gloves, and exposure to the virus has occurred when health care workers treated individuals with EHF without wearing these types of protective clothing. This often happens at early stages of the outbreak, as many *Ebola* symptoms are similar to those of other diseases. In addition, when needles or syringes are used, they may not be of the disposable type, or may not have been sterilized, but only rinsed before reinsertion into multi-use vials of medicine. If needles or syringes become contaminated with virus and are then reused, numbers of people can become infected.

The *Ebola-Reston* virus subtype, which was first recognized in a primate research facility in Virginia, may have been transmitted from monkey to monkey through the air in the facility. While all *Ebola* virus subtypes have displayed the ability to be spread through airborne particles (aerosols) under research conditions, this type of spread has not been documented among humans in a real-world setting, such as a hospital or household.

Clinical Diagnoses

Diagnosing EHF in an individual who has been infected only a few days is difficult because early symptoms, such as red and itchy eyes and a skin rash, are nonspecific to the virus and are seen in other patients with diseases that occur much more frequently. However, the phenomenon of high fever, with itchy eyes, sore throat, hiccups plus the vomiting of blood in a few days is not common to most viral infections. If a person has the constellation of symptoms described in the table above, and infection with *Ebola* virus is suspected, the public should take note and quickly refer the patient to a hospital where several laboratory tests should be done promptly. These include a blood film examination for malaria and a blood culture. If the suspected patient has bloody diarrhea, a stool culture should also be performed.

Antigen-capture enzyme-linked immunosorbent assay (*ELISA*) testing, *IgG ELISA*, polymerase chain reaction (PCR), and virus isolation can be used to diagnose a case of EHF within a few days of the onset of symptoms. Persons tested later in the course of the disease or after recovery can be tested for IgM and IgG antibodies; the disease can also be diagnosed retrospectively in deceased patients by using immunohistochemistry testing, virus isolation, or PCR.[5]

[5] Ibid.

Treatment

There is no standard treatment for EHF. Currently, patients receive supportive therapy. This consists of balancing the patients fluids and electrolytes, maintaining their oxygen status and blood pressure, and treating them for any complicating infections. During a large outbreak of EHF in Kikwit, Democratic Republic of the Congo, in 1995, eight patients were given blood of individuals who had been infected with *Ebola* virus but who had recovered. Seven of the eight patients survived. However, because the study size was small, and because the characteristics of the participants predisposed them toward recovery, the efficacy of the treatment remains unknown.

Humoral immune response to *Marburg* and *Ebola* viruses can be detected as early as 10-14 days after infection. Antibodies are directed primarily against the surface glycoproteins. Owing to the unreliability of neutralization tests, little can be said about their protective effects. Little is known also about cell-mediated immune response to these viruses.

Prevention

The prevention of EHF in Africa presents two main challenges. First is the lack of understanding of the identity and location of the natural reservoir of *Ebola* virus. Second, there are few established primary prevention measures. If cases of the disease do appear, current social and economic conditions favor the spread of an epidemic within healthcare facilities. Therefore, healthcare providers must be able to recognize a case of EHF should one appear. They must also have the capability to perform diagnostic tests and be ready to employ practical viral hemorrhagic fever isolation precautions, or barrier nursing techniques. These techniques include the wearing of protective clothing, such as masks, gloves, gowns, gumboots and goggles; the use of infection-control measures, including complete equipment sterilization; and the isolation of EHF patients from contact with unprotected persons. The aim of all of these techniques is to avoid any contact with the blood or secretions of any patient. If a patient with EHF dies, it is equally important that direct contact with the body of the deceased patient be prevented.

In conjunction with the World Health Organization, CDC has developed practical, hospital-based guidelines, titled *Infection Control for Viral Haemorrhagic Fevers in the African Health Care Setting*. The manual describes how health care facilities can recognize cases of viral hemorrhagic fever, such as EHF, and prevent further hospital-based disease transmission by using locally available materials and low financial resources if a case

of VHF is diagnosed in the facility. A similarly practical diagnostic test that uses tiny samples from patients' skin has been developed to retrospectively diagnose EHF in suspected case-patients who have died. The health workers should make a formal report of any cases to the WHO. All contact people should be followed up and their temperatures read twice daily. Anyone with a registered temperature of 38.5 C should be sent immediately to be hospitalized. Community members should also care to disinfect patients' excreta, sputum, blood and all objects with which the patient had contact. This can be done with a bleaching agent of .5% sodium hypochlorite or simply boiling for sufficient time.

Experimental work on *Marburg* and *Ebola* viruses has been greatly impeded in the past by the high pathogenicity of these agents. With the advent of recombinant DNA technology, however, we are beginning now to understand the molecular structure of these viruses and will soon understand the details of virus replication and virus-host interactions. Use of new strains of lower pathogenicity, such as the Reston virus, will contribute to reach these goals. These new approaches will also allow refinement of the diagnostic tools to permit more accurate virus identification in the field and to better understand frequency, natural reservoirs and transmission modes of these viruses.

Challenges

Scientists and researchers are faced with the challenges of developing additional diagnostic tools to assist in early diagnosis of the disease and ecological investigations of *Ebola* virus and the disease it causes. In addition, one of the research goals is to monitor suspected areas to determine the incidence of the disease. More extensive knowledge of the natural reservoir of *Ebola* virus and how the virus is spread must be acquired to prevent future outbreaks effectively. Finally, a recent news report in March of 2001, indicated that tremendous advances had been made in research on a vaccine. It is hoped that human trials will begin within three years.

References

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3. WHO Recommended Guidelines for Epidemic Preparedness and Response: *Ebola Haemorrhagic Fever (EHF).*

EBOLA HAEMORRHAGIC FEVER OUTBREAK IN UGANDA: THE MWANZA REGION EXPERIENCE

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Background

Ebola virus causes viral haemorrhagic fever and belongs to the family Filoviridae. Sporadic outbreaks of Ebola virus have been reported in Zaire now the Republic of Congo in 1976 and 1995, in Sudan in 1976 and 1979, and in Gabon in 1996. Mortality rates ranging from 50% to 90% were reported during these outbreaks (WHO, 1997).

Most of those who became infected during the outbreaks were individuals who came into contact with an Ebola patient either at home or at health facilities while caring for patients. Infections acquired at health facilities occur through contact with body fluids of an *Ebola* patient or contact with contaminated objects such as needles, syringes, etc or inadequate barrier technique especially during the early stages of the epidemic and unhygienic practices. Also contact with body or body fluids of the dead during traditional preparations for burial is an important route of transmission (WHO, 1997). Because transmission of *Ebola* virus occurs very readily, and the incubation period may take up to 21 days, it is possible that infected individuals could travel to other areas before developing disease. Thus control measures against *Ebola* outbreak should include restriction of movement of people to and from affected areas.

Mwanza Response to the Ugandan Outbreak

Although Mwanza Region does not share a common border with Uganda, it has direct communication links either through water (Lake Victoria) or air travel, which allow easy movement of people from either side. Therefore, the outbreak of *Ebola* in Uganda put Mwanza at great risk of experiencing the outbreak. This called for establishment of control measures urgently.

Regional Task Force

Realizing the threat of Ebola outbreak for the region, a Regional Task Force was formed under the chairmanship of the Regional Administrative Secretary (RAS) to chart out strategies for prevention of Ebola outbreak. Members of the Task Force included: the regional heads of police, immigration, information, health and security, and the Directors of Bugando Medical Centre (BMC) and National Institute for Medical Research (NIMR), Mwanza Centre. Others were a consultant physician from BMC, the Health officer in-charge for the Region, District and ports, the Regional Nursing Officer, the Medical Officer of health, Mwanza City and the Head of Medical Stores Department (MSD), Lake Zone. The Regional Medical Officer was the secretary of the task force.

The Task force adopted the following strategies: provision of health education to the general public, carry out active surveillance of Ebola, restrict movement of people between Mwanza and Uganda and preparation for provision of proper management of Ebola patients if the outbreak occurred in Mwanza.

Provision of Health Education

Health education was provided to the general public informing them on the possibility of the outbreak, and to create awareness among people about symptoms suggestive of ebola especially from visitors. In case the outbreak occurs people must understand what to do especially in informing relevant authorities within their respective areas. More emphasis was put on attendants of guest-houses, fishermen and fishing communities. It was realized that these were the people who were more likely to come into contact with people from Uganda in the course of their activities. The attendants of guest-houses were warned on the possibility of having visitors who might be sick on arrival or fall sick while at their premises. If this happened they were instructed to take all necessary precautions and report immediately to the relevant authorities. Moreover, they were also warned never to hide a sick person in their premises. The health department in the Region in close co-ordination with those in the Districts prepared and distributed fliers containing the health messages and mobilized and sensitized people in collaboration with District Task Forces. Religious leaders also provided health messages in mosques and churches.

Active Surveillance for Ebola

In order to monitor closely people arriving from Uganda, a questionnaire was developed and administered to elicit detailed information on: countries visited in the last 21 days, their health status, detailed contact address while in Mwanza, their contact person or Institution and expected duration of stay. They were also given the address of the Regional Medical Office to contact if any problems developed while in Mwanza. Guest-houses were also visited regularly to check for any visitors especially from Uganda to monitor any possibility of developing *Ebola* disease while in Mwanza. Guest-houses were also checked for likelihood of presence of unreported cases of Ebola. This was done in close co-ordination between the departments of health, police and immigration. The general public was also strongly urged to inform health personnel whenever they suspect an individual to have *Ebola* disease.

Restriction of Movement Between Mwanza and Uganda

Both Tanzania and Uganda own cargo ships plying between Mwanza and Port Bell in Uganda. These ships are very popular with petty business people for transportation of goods from either side. The Task Force realized the risk this informal route poses for possible transmission of *Ebola*. All shipping companies were informed about the consequences of their practice and were asked to stop carrying passengers using cargo vessels. The health and police departments at ports were asked to enforce the order.

Preparations for Managing Ebola Patients

Training of staff in health facilities on how to handle and manage *Ebola* patients was given by trainers from Bugando Medical Centre (BMC). BMC, Sekou Toure and all the other District hospitals in the Region identified staff that will specifically be managing Ebola patients alone and allocate dedicated sites for managing patients. The Regional Medical Office in collaboration with Zonal Office for MSD ensured that all equipment and supplies required for management of patients were available and distributed to all hospitals. As part of the preparations, the Directors for Mwanza City and all Districts were asked to identify sites where individuals who would die from Ebola disease would be buried.

Institutions within Mwanza Region were assigned specific tasks. The Regional Medical office co-coordinated all activities related to health education and procurement of supplies required, and BMC and Sekou Toure hospitals were charged with handling of all suspected cases of *Ebola*. NIMR, Mwanza Centre co-ordinated handling and transportation of specimens from

Mwanza to Muhimbili Medical Centre in Dar es Salaam as well as handling of questionnaires from ports. The information department co-coordinated the media for regular feedback by the Task Force Chairperson.

External Support

Staff from the Emergency Unit of the Ministry of Health visited Mwanza regularly during whole period of outbreak in Uganda and met members of the Task Force. Besides the supervisory role of these visits, they also provided opportunity for exchange of information and assurance of support at national level. Members of the Task Force saw this as very useful.

Problems Encountered

Most of the activities were implemented without any problems, but difficulties were encountered on restricting business persons and pupils studying in Uganda from using cargo ships when coming back for holidays or business trips. Although these people no longer used these ships for travelling from Mwanza to Uganda, they used them on their way back despite formal communications with authorities in Uganda. This was a challenge because most of them were Tanzanians returning home.

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