EBOLA VIRUS DISEASE INFORMATION

FOR NIH CLINICAL CENTER STAFF*

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Executive Summary

Ebola Virus Disease (EVD) is caused by the Ebola Virus, an RNA virus that was first identified in 1976. Ebola virus has been associated with epidemics in Africa and is capable of causing severe disease in humans. The outbreak in 2014 in Guinea, Sierra Leone and Liberia is the largest in history and is by far the most severe Ebola outbreak since its discovery. By the end of September 2014 the number of cases reported in the West African epidemic exceeded the total of all previously reported EVD cases combined.

Ebola virus spreads in humans as a result of direct contact with blood or body fluids from an infected symptomatic person, contact with the body of a person who is recently deceased from EVD, or through exposure to objects that have been contaminated with infected body fluids or secretions. **Individuals who are not symptomatic are not contagious. EVD transmission requires direct contact with a symptomatic patient or their body fluids.** The symptoms of the disease are initially non-specific (and generally progress by about day five of illness to include gastrointestinal symptoms, such as severe watery diarrhea, nausea, vomiting, and abdominal pain. Some patients develop hiccups, chest pain, shortness of breath, headache and/or confusion. **Although the symptoms of EVD are nonspecific, it is symptoms in the context of a relevant exposure and/or travel history that raise suspicion of EVD.**

We have learned a great deal from the experiences of our colleagues who have cared for patients with EVD at Emory University and the University of Nebraska Medical Center. Almost all of their patients have had problems maintaining their intravascular volumes, due to low serum albumin and extensive vascular leak syndrome. Fluid losses in the first two patients at Emory averaged 5 to 10 liters a day. The problem with vascular volume has been compounded by severe electrolyte abnormalities. Nonetheless, both these institutions have conclusively demonstrated that these patients can be cared for both safely and successfully.

This document describes the Clinical Center's high-containment Special Clinical Studies Unit and emphasizes the important role NIH plays in these kinds of public health crises. Finally, the document summarizes procedures to be used for the safe care of patients who have EVD, for the safe performance of laboratory and other diagnostic tests and for the safe management of the patient environment and hospital waste from EVD patients.

The Ebola Virus

The Ebola virus is a member of the *Filoviridae* family that was first discovered in 1976 near the Ebola River in what is now the Democratic Republic of the Congo. Since 1976, outbreaks have appeared sporadically in Africa. Viruses in the *Filoviridae* family form filamentous infectious viral particles. The Ebola genome is encoded in the form of single-stranded negative-sense RNA that is encased in a glycoprotein coat. A closely related virus is the Marburg virus. Historically these agents have been known as "viral hemorrhagic fever" viruses. Both Ebola and Marburg are capable of causing severe disease in humans.

The Current Ebola Outbreak in West Africa

The 2014 Ebola epidemic is the largest in history, affecting multiple countries in West Africa. The outbreak began in Guinea in December 2013 then spread to Liberia and Sierra Leone. A much smaller cluster occurred in Nigeria, and single cases have been imported to Senegal and the United States. As of October 2014, the World Health Organization (WHO), the United States Centers for Disease Control and Prevention (CDC) and local governments had reported a total of 8,399 suspected cases and 4,033 deaths (with 4,633 cases and 2,423 of the deaths having been confirmed with laboratory testing). These documented cases likely far underestimate the extent of the epidemic. The World Health Organization has estimated that as many as 2.5 times the number of reported cases have actually occurred.

The current epidemic of EVD is the most severe outbreak of Ebola since the discovery of Ebola viruses in 1976. In September of 2014 the number of cases reported in the West African epidemic exceeded the total of all previously reported cases. The epidemic has caused significant mortality, with a case fatality rate in West Africa reported to be as high as 71%. Most healthcare facilities treating these patients lack infrastructure and supplies and are substantially understaffed, thereby increasing the chance of staff becoming infected. In August, the WHO estimated that as many as 10% of the dead were health care personnel.

New cases continue to be reported from Guinea, Liberia, and Sierra Leone. Nigeria and Senegal have successfully controlled transmission.

Ebola Virus Transmission

We have limited scientifically documented information about how Ebola is transmitted from animals to man. In Africa, fruit bats are thought to be the natural host of the Ebola virus, while some other animals in the 'bush' are susceptible. Scientists have suggested that animal-to-human transmission may occur as a result of the handling and consumption of 'bushmeat' (i.e., meat from wild animals hunted for food).

Ebola virus spreads in the human population as a result of direct contact with blood or body fluids from an infected symptomatic person, contact with the body of a person who is recently deceased from EVD, or through exposure to objects that have been contaminated with infected body fluids or secretions.

> ***KEY POINT:*** **Individuals who are not symptomatic are not contagious.**

Clinical Manifestations of Ebola Virus Disease

Patients with EVD typically have abrupt onset of fever and other symptoms typically 8 to 12 days after exposure (range 2-21 days; the incubation period for the current outbreak has a mean of approximately 9 to 11 days). Initial signs and symptoms of EVD are nonspecific and may include fever, chills, myalgias, and malaise. Due to these nonspecific symptoms, particularly early in the course, EVD can often be confused with other more common infectious diseases that are endemic to West Africa, such as malaria, typhoid fever, meningococcemia, and pneumonia.

Patients typically progress from these initially non-specific symptoms (usually at about 5 days into the course of the illness) to develop gastrointestinal symptoms, such as severe watery diarrhea, nausea, vomiting and abdominal pain. Some patients develop hiccups, chest pain, shortness of breath, headache and/or confusion. The latter neurological symptoms may be accompanied by seizures, and cerebral edema has been reported. Patients often have conjunctival injection. Despite EVD being known as one of the "viral hemorrhagic fevers", hemorrhage occurs in a minority of cases; in the current outbreak it has been reported in only 18% of patients. When present, bleeding usually manifests itself later in the course of the illness and is often

not severe (e.g., petechiae, easy bruisability, ecchymoses, oozing from needlestick sites, nosebleeds). Major hemorrhage is less common; and frequently manifests as intestinal bleeding.

Patients also may develop a generalized erythematous maculopapular rash by day 5 to 7 (usually involving the neck, trunk, and arms) that can desquamate. Pregnant women may experience spontaneous miscarriages. In the current outbreak in West Africa the most common signs and symptoms reported from the time of symptom-onset to the time the case was detected include: fever (87%), fatigue (76%), vomiting (68%), diarrhea (66%), and loss of appetite (65%).

> ***KEY POINT:*** **Although the symptoms of EVD are nonspecific, it is symptoms in the context of a relevant exposure and/or travel history that raise suspicion of EVD.**

Exposures to EVD Associated with Risk for Transmission

The U.S. Public Health Service considers the following types of exposures to be associated with a "*high risk*" for transmission:

- Percutaneous (e.g., needle stick) or mucous membrane exposure to blood or body fluids of EVD patient;
- Direct skin contact with, or exposure to blood or body fluids of, an EVD patient in the absence of appropriate personal protective equipment (PPE);
- Processing blood or body fluids of a confirmed EVD patient while not wearing appropriate PPE or while not adhering to standard biosafety precautions; and
- Direct contact with the body of a deceased EVD patient while not wearing appropriate PPE in a country where an EVD outbreak is occurring.

The U.S. Public Health Service considers the following types of exposures to be associated with a "*low risk*" for transmission:

- Household contact with an EVD patient
- Other close contact with EVD patients in health care facilities or community settings. Close contact is defined as being within

approximately 3 feet (1 meter) of an EVD patient or within the patient's room or care area for a prolonged period of time (e.g., health care personnel, household members) while not wearing recommended PPE (i.e., standard, droplet, and contact precautions; see Infection Prevention and Control Recommendations below)
- Having direct brief close contact (e.g., shaking hands) with an EVD patient while not wearing recommended PPE (brief interactions, such as walking by a person or moving through a hospital, do not constitute close contact)

KEY POINT: **EVD transmission requires direct contact with a symptomatic patient or their body fluids.**

Clinical Experience Managing EVD in the US

Physicians and nurses at Emory University Medical Center and the University of Nebraska Medical Center have already gained valuable experience caring for a handful of EVD patients. The director of the containment unit at Emory has recently provided the following information about their clinical experiences. He noted that Ebola patients in Africa have only limited clinical evaluations and essentially no laboratory testing due to the lack of any infrastructure to support these kinds of evaluations. The Emory team was able to make the following careful clinical evaluations over time in their patients:

- Despite weight gains of 15-20 kg, the patients at Emory were profoundly hypovolemic, due to their low serum albumins and extensive vascular leak, resulting in substantial third-spacing. Fluid losses in the first two patients averaged 5 to 10 L/day.
- Electrolyte losses were significant and included profound hyponatremia, hypokalemia and hypocalcemia, leading to cardiac arrhythmias.
- Nutritional depletion was evident in both the patients, as well.
- At initial assessment at Emory the first two patients were approximately one week into their illnesses, yet the laboratory studies at Emory were their first laboratory tests apart from their original tests for Ebola virus.
- Ebola virus RNA was detected in blood, urine, vomitus, stool, tracheal aspirate, semen and on the patients' skin.
- Ebola virus RNA was not detected in dialysate.

- Extensive environmental testing, including evaluation of many high touch surfaces, such as bed rails and surfaces in the patients' bathrooms did ***NOT*** detect Ebola virus RNA.
- Intensive 1:1 nursing care was necessary around the clock.
- Patients were monitored continuously and this level of nursing care allowed for rapid response to clinical changes.
- Nursing and other team members provided emotional support, and as the patients improved, help with self care and physical therapy.

The clinical leadership of the Emory containment unit concluded that patients with EVD could be safely cared for in developed countries using appropriate safeguards. Providing care for these patients in such sophisticated locations affords close clinical observation and experience in clinical management that can ultimately be relayed to facilities that have lesser medical infrastructure. Because they could manage their patients with close hemodynamic and laboratory monitoring, they anticipate a much lower mortality rate than is the case in under-resourced countries. They emphasized that communication, both internal and external, is critical to manage the situation surrounding a hospitalized EVD patient.

Providing Clinical Care for Patients Known or Suspected to Have EVD

Provision of clinical care for patients known or suspected to have EVD involves the entire institution, not simply the direct care providers. The individuals directing a patient's care must be able to coordinate and orchestrate a substantial group of hospital service providers to assure the highest quality safe care. These services include (but are not limited to): the team transporting the patient from the airport to the hospital, the direct physician and nursing care providers, (including intensive care physician and nursing support, should it be needed), clinical laboratory, specialty and subspecialty clinical consultative services, radiology, environmental service, facilities management, security and media relations.

Individuals involved in the care of the patient, the processing and assessment of clinical specimens from the patient and those involved in managing the waste stream undergo detailed training and are taught meticulous adherence to recommended infection control precautions.

Personal Protective Equipment

The U.S. Public Health Service recommends a combination of standard, contact, and droplet precautions for use in preventing transmission of EVD during health care. Based on our own experience and the experience at Emory University the Clinical Center has chosen to provide an additional level of safety by include double gloving, disposable Tyvek suits, leg coverings, and the routine use of powered, air purifying respirators in the care of these patients.

Management of the Environment of Care

The role of the environment in Ebola transmission has not been established. Limited laboratory studies under experimental conditions indicate that Ebola virus can remain viable on solid surfaces, with concentrations falling slowly over several days. In the only study to assess contamination of the patient care environment during an outbreak, virus was detected on a blood-stained glove and bloody intravenous insertion site. However, virus was not detected in any of 33 samples collected from sites that were not visibly bloody. To date, no epidemiological evidence incriminates either the environment or fomites that could become contaminated during patient care (e.g., bed rails, door knobs, laundry) in Ebola virus transmission. Nonetheless, out of an abundance of caution, and in light of the apparently low dose of virus required to produce infection and the likelihood that patients who are infected have very high viral titers in their body fluids, higher levels of precaution are warranted to reduce the potential risk posed by contaminated surfaces in the patient care environment. The following recommendations are modified from the U.S. Public Health Services' Interim Guidance for Environmental Infection Control in Hospitals for Ebola Virus.

- Staff providing environmental services must wear recommended PPE (as described above) to protect against direct skin and mucous membrane exposure of cleaning chemicals, contamination, and splashes or spatters during environmental cleaning and disinfection activities. Staff must be trained in the proper use of PPE including safe removal to prevent contaminating themselves or others in the process, and to ensure that contaminated equipment is disposed of appropriately.
- Use a U.S. Environmental Protection Agency (EPA)-registered hospital disinfectant, such as those that are used in the Clinical Center, that is

approved for disinfection of non-enveloped viruses to disinfect environmental surfaces in rooms of patients with suspected or confirmed Ebola virus infection. Although there are no products with specific label claims against the Ebola virus, enveloped viruses such as Ebola are susceptible to a broad range of hospital disinfectants used to disinfect hard, non-porous surfaces. As a precaution, selection of a disinfectant product with a higher potency than what is normally required for an enveloped virus, such as Ebola, is being recommended at this time. Hospital disinfectants with activity against non-enveloped viruses (e.g., norovirus, rotavirus, adenovirus, poliovirus) are broadly antiviral and capable of inactivating both enveloped and non-enveloped viruses.

- Avoid contamination of reusable porous surfaces that cannot be discarded after single patient use. Use only mattresses and pillows that have plastic or other covering that are impermeable to fluids. Do not place patients with suspected or confirmed Ebola virus infection in carpeted rooms and remove all upholstered furniture and decorative curtains from patient rooms before use.
- To reduce potential sources of staff exposure, discard (rather than laundering) all linens, non-fluid-impermeable pillows or mattresses, and textile privacy curtains.
- The Ebola virus is a classified as a Category A infectious substance by and regulated by the U.S. Department of Transportation's (DOT) Hazardous Materials Regulations (HMR, 49 C.F.R., Parts 171-180). Any item transported offsite for disposal that is contaminated or suspected of being contaminated with a Category A infectious substance must be packaged and transported in accordance with the HMR. This includes medical equipment, sharps, linens, and used healthcare products (such as soiled absorbent pads or dressings, kidney-shaped emesis pans, portable toilets, used PPE (gowns, masks, gloves, goggles, face shields, respirators, booties, etc.) or byproducts of cleaning) contaminated or suspected of being contaminated with a Category A infectious substance.

At the Clinical Center, staff working in the Special Clinical Studies Unit (SCSU) carry out these cleaning procedures. All patient excreta are subjected to chemical disinfection before being discarded into the sanitary sewer and all trash and used PPE are autoclaved before being shipped for incineration as medical pathological waste. These latter items are placed in an impermeable

bag inside a second autoclave bag. The inner bag is sealed and then disintegrates in the autoclave.

Patient care areas and equipment that are used in the care of patients with suspected or confirmed EVD are cleaned with approved disinfectants (as described above) and decontaminated thoroughly with hydrogen peroxide vapor.

Conducting Laboratory and Other Diagnostic Studies on Patients Known or Suspected to Have EVD

The Emory team emphasized the importance of doing as much point-of-care testing as is possible. They noted that if a specimen from one of their EVD patients were spilled in the main lab, the laboratory would have to be closed for hours to accomplish decontamination, thereby clearly having an adverse effect on the function of the entire hospital. These considerations prompted the Emory team to set up a point-of-care testing area adjacent to the patient care unit. Lab testing was kept to a minimum. At the Clinical Center, we have established a space for point-of-care testing in the SCSU, but also have a BSL-3 laboratory in our Department of Laboratory Medicine where more sophisticated studies can be conducted safely. Laboratory staff have been trained in appropriate procedures to maintain laboratory and healthcare personnel safety.

For radiologic procedures, the Clinical Center has a dedicated portable X-ray machine that is housed in the SCSU. Any other studies required will be conducted within the SCSU using carefully planned safety precautions.

The NIH and NIH Clinical Center's Roles in Addressing the Epidemic of Ebola Virus Disease

The NIH and the NIH Clinical Center have long and august histories of addressing significant public health emergencies as they have occurred in our society. Medical science has had extremely limited experience with this disease in any setting in which the infected patient's physiology can be carefully and systematically assessed. In that context, managing such a patient in the sophisticated clinical research environment of the Clinical Center makes implicit sense and offers a substantial opportunity for us to learn about the disease's unique pathophysiology, as well as the optimal

management of patients who have this disease.

The US Public Health Service and the US military both have scores of healthcare professionals and support personnel deployed to help contain the epidemic in Western Africa. In addition, several humanitarian organizations (e.g., Médecins Sans Frontières) have volunteer clinical staff from around the world providing clinical care to EVD patients in West Africa. All of these individuals are providing care for EVD patients at Ebola Treatment Units in extremely resource-poor settings. Should any of these individuals sustain exposure or infection, the sites that have high containment facilities in the US (including the NIH Clinical Center) offer both superb healthcare infrastructure and competent and highly trained staff that can provide these individuals the best and safest care possible.

The experiences at Emory and the University of Nebraska have demonstrated that – even in the absence of specific treatments – superb supportive care can make a huge difference in patients' outcomes.

NIH is working hard to contribute to both the understanding of the disease as well as strategies for preventing its spread. For example, NIAID has already begun a Phase 1 study of a new candidate Ebola Virus Vaccine at the NIH Clinical Center; this vaccine was developed by NIAID intramural scientists. A second study began this week evaluating another candidate Ebola vaccine. This second vaccine study is also taking place at the Clinical Center and is in collaboration with colleagues at Water Reed National Military Medical Center.

As additional medical countermeasures are developed, the NIH Clinical Center and the Clinical Center's SCSU provide an ideal venue to test these new compounds.

The Clinical Center's Special Clinical Studies Unit (SCSU)

The Clinical Center's SCSU was specially designed to be able to provide safe care for patients requiring any level of infectious diseases isolation. Few such facilities exist in the US. The SCSU includes a high-quality isolation room that can be transformed for provision of intensive care.

Numerous redundant systems and precautions are in place to maintain isolation of the SCSU from the rest of the Clinical Center and the surrounding

community. These systems and precautions include special air handling systems, cardkey restricted access, separate entrance and exit pathways for staff, including a shower prior to exit, and detailed protocols for clinical care and handling waste.

Staff involved in the direct management of the patient or specimens from EVD patients have received training in the use of PPE and in the special clinical procedures that assure they are able to provide high quality care for EVD patients safely. Staff working in the unit have volunteered to participate in the care of EVD patients.

Need for Additional Volunteers

As the epidemic continues in Western Africa and as more US citizens are deployed to combat this epidemic, the likelihood of additional exposures and infections among these individuals increases. The SCSU staff have developed training procedures for additional volunteers to become proficient in the hands-on care of patients requiring this level of isolation. If we are asked to provide care for EVD patients, having additional staff who have been trained, and are confident and competent in the use of PPE will be highly beneficial.

We have additional need for volunteers to fill several roles. In addition to infectious diseases expertise, critical care and medical/surgical nursing, we need volunteers for the role of WatSan (an individual who is not in direct contact with the patient, but supervises the donning and doffing of PPE and the handling of waste according to a carefully defined script), as well as respiratory therapists and other ancillary staff. If you are interested in volunteering, please contact Dr. JoAnn Mican (301-402-1326; JMICAN@niaid.nih.gov.