What Clinicians Should Know About the 2014 Ebola Outbreak

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Abstract

The ongoing Ebola outbreak that began in Guinea in February 2014 has spread to Liberia, Sierra Leone, Nigeria, Senegal, Spain, and the United States and has become the largest Ebola outbreak in recorded history. It is important for frontline medical providers to understand key aspects of Ebola virus disease (EVD) to quickly recognize an imported case, provide appropriate medical care, and prevent transmission. Furthermore, an understanding of the clinical presentation, clinical course, transmission, and prevention of EVD can help reduce anxiety about the disease and allow health care providers to calmly and confidently provide medical care to patients suspected of having EVD.


The first recorded Ebola outbreak began in September 1976 in Zaire (now the Democratic Republic of the Congo) after the index case received a chloroquine injection for malaria at Yambuku Mission Hospital. Although the patient’s malaria symptoms initially resolved, he then developed an aggressive infection with hemorrhagic sequelae 5 days after the injection. Within a week, several other patients who had received injections at the clinic or who were close household contacts of patients developed a similar illness. During a 2-month period, 318 cases of viral hemorrhagic fever were identified in 55 nearby villages, with 88% mortality.

The virus was found to be related to, but distinct from, the Marburg virus and was named after the Ebola River, which traversed through the affected region. Since that time, there have been approximately 20 identified outbreaks of Ebola virus disease (EVD) that have occurred sporadically in Africa, mostly in central and east Africa (Table). The 2014 outbreak is the first to occur in West Africa.

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As stated by Dr Peter Piot, one of the researchers who first identified Ebola virus in 1976, “In general, it is an infection that causes epidemics only if basic hospital hygiene is not respected, and is really a disease of poverty and neglect of health systems.”

THE 2014 WEST AFRICAN EBOLA OUTBREAK

The ongoing outbreak in West Africa is the largest Ebola outbreak in recorded history. The first cases occurred in Guinea in December 2013. Cases were identified in neighboring Liberia in March 2014, and in April the outbreak spread into Sierra Leone. In July 2014, EVD was introduced in Nigeria by an ill traveler from Liberia, with subsequent transmission to health care workers. In September 2014, Senegal had an EVD case imported from Guinea. On September 30, 2014, the first case of EVD was diagnosed in the United States in a patient who had recently traveled from Liberia to Dallas, Texas. He did not have symptoms when leaving West Africa but developed symptoms approximately 4 days after arriving in the United States. He was hospitalized in Dallas and despite supportive care, mechanical ventilation, and hemodialysis, he died on October 8. Two members of the health care team caring for this patient have subsequently been diagnosed as having EVD. Similar transmission of EVD to a health care worker in Spain has been reported, where a nursing assistant developed EVD after caring for 2 repatriated Spanish missionaries who contracted EVD in West Africa. As of October 21, 2014, the West African Ebola outbreak had resulted in 9216 confirmed or suspected cases, with 4555 deaths (Figure 1). Case counts are likely an underestimate of the true number of cases owing to underdiagnosis and underreporting of cases. A separate outbreak of EVD, unrelated to the West African outbreak, has occurred in Democratic Republic of the Congo.

<table>
<thead>
<tr>
<th>Year(s)</th>
<th>Country(ies)</th>
<th>Ebola subtype</th>
<th>Reported human cases (No.)</th>
<th>Reported deaths among cases (No. [%])</th>
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<tbody>
<tr>
<td>1976</td>
<td>Zaire (currently Democratic Republic of the Congo)</td>
<td>Zaire virus</td>
<td>318</td>
<td>280 (88)</td>
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<td>284</td>
<td>151 (53)</td>
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<tr>
<td>1979</td>
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<td>Sudan virus</td>
<td>34</td>
<td>22 (65)</td>
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<tr>
<td>1994</td>
<td>Gabon</td>
<td>Zaire virus</td>
<td>52</td>
<td>31 (60)</td>
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<tr>
<td>1995</td>
<td>Democratic Republic of the Congo (formerly Zaire)</td>
<td>Zaire virus</td>
<td>315</td>
<td>250 (79)</td>
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<td>January-April 1996</td>
<td>Gabon</td>
<td>Zaire virus</td>
<td>37</td>
<td>21 (57)</td>
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<td>July 1996-January 1997</td>
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<td>Zaire virus</td>
<td>60</td>
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<td>1996</td>
<td>South Africa</td>
<td>Zaire virus</td>
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<td>2000-2001</td>
<td>Uganda</td>
<td>Sudan virus</td>
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<td>224 (53)</td>
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<td>Zaire virus</td>
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<td>Zaire virus</td>
<td>57</td>
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<td>Uganda</td>
<td>Sudan virus</td>
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<td>February 2014-present</td>
<td>Guinea, Liberia, Sierra Leone, Nigeria, Senegal, Spain, United States</td>
<td>Zaire virus</td>
<td>4655a,b</td>
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<td>Zaire virus</td>
<td>68ab</td>
<td>49 (72)ab</td>
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</table>

*Laboratory-confirmed cases only.

As of October 13, 2014.

Adapted from http://www.cdc.gov.
to the outbreak in West Africa, is occurring in the Democratic Republic of the Congo.

Previous Ebola outbreaks have largely occurred in rural, isolated villages with limited access to medical care, resulting in outbreaks with high case fatality but limited transmission. With the industrialization and globalization of commerce, there is now increased travel from previously isolated areas, allowing for spread of the outbreak into densely populated urban areas. Increased access to medical care, with amplification of transmission in health care facilities, has also likely contributed to the larger outbreak.

Cultural and societal practices have contributed to the extent of the outbreak in West Africa. Family members are often taking care of sick relatives at home, putting themselves at high risk for infection through contact with infectious materials: blood, feces, vomit, or other body fluids. Family members are fearful that it is the hospitals themselves that are causing the infections; as a result, EVD cases and their contacts have been hidden from health authorities. This is compounded by the limited availability of sanitation and public health infrastructure. Burial practices in several parts of West Africa include preparation of the body for burial and close contact of family members with the deceased, further contributing to the propagation of the outbreak.

Virology

Ebola is one of several viruses that cause hemorrhagic fever, including Marburg, Lassa, Crimean-Congo, Sin Nombre, yellow fever, and Dengue hemorrhagic fever. The hallmark of viral hemorrhagic fever is severe illness, including multiple organ failure and possible death, even in previously healthy persons. Sepsis is often induced through cytokine storm, and hemorrhagic complications occur through thrombocytopenia, hepatic necrosis (with resultant reduction in synthesis of coagulation factors), disseminated intravascular coagulation, and endothelial damage.

There are 5 species of Ebola virus, each being a single-stranded RNA virus in the filoviridae family. The Bundibugyo, Zaire, and Sudan species have been responsible for all of the known Ebola outbreaks, with the Zaire species causing the current outbreak in West Africa. The other 2 Ebola virus species are the Reston Ebola virus, which is limited to the Philippines and has not caused human disease to date, and the Tai Forest Ebola virus, which caused a single human infection in a scientist performing an autopsy on a chimpanzee.

The natural reservoirs and vectors of Ebola viruses are not completely understood, but Ebola is clearly a zoonotic disease. Fruit bats have been implicated in transmission because Ebola viruses can replicate in bats and have been cultured from bat guano. Monkeys

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**FIGURE 1.** Progression of the 2014 Ebola outbreak in West Africa.
and other nonhuman primates may serve as intermediate hosts. Increased human-animal interface in parts of Africa and the black market bush meat trade have been implicated in bringing this zoonotic disease into human populations.

**CLINICAL COURSE**

Patients with EVD have abrupt onset of symptoms 8 to 10 days after exposure (range, 2-21 days). These symptoms are often nonspecific initially, with fever, chills, myalgia, malaise, and possibly a maculopapular rash. After approximately 5 days, patients will often develop abdominal pain, severe watery diarrhea, nausea, and vomiting. Hemorrhagic sequelae may develop, including hematochezia, petechiae, ecchymosis, and mucosal hemorrhage. Fatal cases develop severe clinical signs and symptoms earlier in their course, and death typically occurs 6 to 16 days after symptom onset. Nonfatal cases typically have resolution of fever between days 6 and 11, followed by a prolonged period of recovery with sustained weakness, fatigue, poor appetite, and failure to regain weight that was lost during the acute illness.

Laboratory abnormalities associated with EVD include thrombocytopenia, hemococoncentration due to increased vascular permeability, and initial lymphopenia followed by neutrophilia with a left shift. There is often elevation in transaminase levels, along with evidence of fibrin degradation products and prolongation of prothrombin time and partial thromboplastin time (evidence of disseminated intravascular coagulation).

Diagnostic tests for Ebola include polymerase chain reaction, viral culture, and IgM and IgG enzyme-linked immunosorbent assay tests. Owing to the need for special biosafety precautions for specimen handling, testing for Ebola in the United States is performed only at the Centers for Disease Control and Prevention (CDC) and some state health department laboratories. Ebola testing should be coordinated through local and regional public health authorities.

**TREATMENT**

Treatment for EVD is largely supportive and includes blood product transfusion, electrolyte replacement, and fluid resuscitation, pressors, and ventilatory support as needed. It is important that patients with suspected EVD are also evaluated for and, if necessary, treated empirically for malaria and typhoid fever. Limited experience with treating EVD in resource-rich settings suggests that the availability of supportive care likely improves patient outcomes substantially. There are no licensed medications available for the treatment of EVD, but there are several investigational agents. ZMapp (Mapp Biopharmaceutical) is a combination of 3 monoclonal antibodies that has been used in a handful of patients during the 2014 West Africa Ebola outbreak. Similarly, brincidofovir (Chimerix Inc) is an antiviral medication developed for the treatment of cytomegalovirus and adenovirus that has been used as an investigational agent in patients with EVD. Although the initial reports of use of these investigational medications are promising, there have not been clinical trials to assess their safety or efficacy in humans, and supply is extremely limited at this time. Blood and serum from persons who have recovered from EVD have been used in several cases of EVD, but the efficacy of this approach remains unproved.

There are currently no licensed vaccines for the prevention of Ebola infection. Two candidate recombinant vaccines, a chimpanzee adenovirus and vesicular stomatitis virus, which express Ebola surface glycoprotein, have shown promising results in nonhuman primates. The National Institutes of Health is expecting to start a phase 1 vaccine trial in human volunteers in Fall 2014.

**TRANSMISSION**

Initial introduction of EVD into human populations likely occurs through contact with an infected animal, such as a bat or monkey. Subsequent human infections, however, occur because of direct contact of mucous membranes or broken skin with blood or body fluids of an infected person. Patients are contagious only when they are ill and do not transmit the infection during the incubation period. During severe illness with Ebola, blood, sweat, feces, and vomit are highly infectious. Health care workers and household care providers who come in close contact with patients with EVD without proper personal protective equipment and are exposed to blood, body fluids, secretions, and excretions are at greatest risk of acquiring the infection.

protective equipment (PPE) are at highest risk for secondary infection.

INFECTION CONTROL IN HEALTH CARE FACILITIES IN THE UNITED STATES
The first case of EVD diagnosed in the United States, and the transmission of EVD to members of his health care team, has raised public awareness of the Ebola outbreak. It has also resulted in fears that the outbreak could spread widely in the United States. For sustained transmission of EVD, there needs to be direct contact with blood or body fluids from an infected person while he or she is ill. Owing to standard infection control practices in health care facilities in the United States, along with robust sanitation and public health infrastructures, it is very unlikely that widespread community transmission of EVD will occur in the United States. It is, however, important for health care facilities to be prepared to see imported cases of EVD in recent travelers from affected countries or in contacts of patients with known EVD and to take immediate steps to limit further transmission.

Early recognition is critical for infection control. Health care providers should be alert for EVD and obtain travel and exposure history in persons presenting with febrile illness (Figure 2). Before transmission of EVD to health care workers in Dallas, the CDC’s position was that patients with EVD could be cared for safely in any hospital in the United States.\(^2\) The fact that 2 health care workers taking reasonable precautions acquired EVD in a US hospital has resulted in a paradigm shift. There is a new realization that although all health care facilities should be prepared to see imported cases of EVD in recent travelers from affected countries or in contacts of patients with known EVD and to take immediate steps to limit further transmission.

All PPE should be single use. Either alcohol-based hand sanitizers or soap and water remain acceptable choices for hand hygiene after PPE removal. The guidelines provide detailed instructions on PPE choices and use. Individual institutions may need to adapt these guidelines based on the physical layout of their facility and on availability of specific PPE (Supplemental PPE Checklist; available online at http://www.mayoclinicproceedings.org).

Given the extensive training needs, hospitals should consider training a core team to care for patients with EVD. Emergency department staff, intensivists (adult and pediatric), infectious diseases physicians, nurses, respiratory therapists, and environmental services and laboratory staff should be considered for inclusion on this core team. The number of health care workers who enter the room and provide direct care to a patient with suspected/confirmed EVD should be minimized. A plan should be formulated by the health care team early on in the patient’s hospital course about invasive procedures and escalation of care.

VISITORS
Visitors should be limited. If a visitor is considered essential for the well-being of a patient with EVD, the visitor should be educated about modes of transmission of EVD and appropriate PPE use. The visitor should use the same PPE as health care workers. Visitors who have had contact with the patient with EVD before and during hospitalization are a potential source of EVD for other patients, visitors, and staff. Their movement within the facility should be restricted, and they should be screened for EVD symptoms before each visit to the facility. Virtual visits by family and friends should be considered instead of in-person visits.

LABORATORY TESTING
To reduce the risk of health care worker exposure, blood collections for laboratory tests should be minimized and laboratory testing limited to tests that are essential for the patient’s medical care. The clinical laboratory should be contacted before any samples are obtained and sent for testing so that the
Travel to affected countries (Sierra Leone, Guinea, Liberia) in past 3 wk?

- Yes
  - Fever >38°C or one of the following: Severe headache, Vomiting, Diarrhea, Unexplained bleeding
  - No

Contact in past 3 wk with a known case of Ebola or an ill person from affected countries?

- Yes
  - Mask the patient immediately, arrange for transfer to the hospital
  - If patient is not actively vomiting, bleeding or incontinent of stool, care for patient using fluid-resistant gown, gloves, face and eye protection
  - If patient is vomiting/bleeding or is incontinent of stool, more extensive PPE is needed for patient contact
  - No

Care for patient as per routine

- Outpatient area:
  - Place in a single room
  - Health care workers entering room should have appropriate PPE, be trained in PPE use, be observed by trained monitors when donning and removing PPE
  - Limit blood draws, collect samples in plastic tubes
  - Notify laboratory before sending any samples
  - Do not use pneumatic tube system to transport samples

  In hospital:
  - Place in a single room
  - Health care workers entering room should have appropriate PPE, be trained in PPE use, be observed by trained monitors when donning and removing PPE
  - Limit blood draws, collect samples in plastic tubes
  - Notify laboratory before sending any samples
  - Do not use pneumatic tube system to transport samples
  - Contact local or state health department for assistance with EVD testing and to facilitate transfer to a regional center

Some or low-risk exposure

- Provides essential care
- Delay non-essential medical tests until 21 days after last exposure
- Provide public health authorities so that arrangements can be made for direct active monitoring patient for symptoms for 21 d after last exposure

Some or high-risk exposure

- Care for patient as per routine
- Monitor patient for symptoms of EVD while in health care facility
- At dismissal, contact public health authorities to arrange for active or active direct monitoring of patient for 21 d after last exposure

High-risk exposure

- Percutaneous (e.g., needlestick) or mucous membrane exposure to body fluids of EVD patient
- Direct care of a patient with EVD or exposure to body fluids without appropriate PPE
- Laboratory worker processing body fluids of confirmed EVD patients without appropriate PPE or biosafety precautions
- Direct exposure to human remains in affected countries without appropriate PPE
- Household contact who provided direct care to a symptomatic EVD patient

Some risk exposure

- Direct contact with a symptomatic EVD person with appropriate PPE

Low-risk exposure

- Travel to affected country but no contact with a sick individual
- Brief direct contact, e.g., shaking hands or being in the same room as an EVD patient who is in early stage of the disease

laboratory staff can take appropriate precautions while handling specimens.

The move to regional centers caring for all patients with EVD would enable these centers to plan for dedicated laboratory instruments to process specimens and also expand the menu of tests available to these patients. Patients with EVD can have profound electrolyte imbalances, and the available point-of-care tests may be inadequate for optimum care.

In the event that the patient dies, handling of the body after death should be minimized. All medical devices should be left in situ, autopsy should be avoided, and burial or cremation needs to occur promptly.

CLEANING, LINEN, AND WASTE MANAGEMENT

The Ebola virus is a nonenveloped virus and as such is susceptible to a broad range of hospital-grade disinfectants. However, as an added precaution, the CDC recommends using disinfectants effective against the more resistant nonenveloped viruses (e.g., norovirus, rotavirus, adenovirus, and poliovirus) to disinfect environmental surfaces in rooms of patients with EVD. The product label’s instructions for wet contact time should be adhered to strictly to ensure inactivation of the virus. Environmental services staff should be provided PPE training. Disposable cleaning cloths, mops, and wipes should be used, and they should be placed in leakproof bags after use. Used cleaning cloths and all linens from the patient room should be handled as regulated medical waste. Sanitary sewers may be used for the safe disposal of patient waste because sewage-handling processes in the United States are designed to inactivate infectious agents.

STOPPING THE EBOLA OUTBREAK

The current EVD outbreak in West Africa has been the largest, most prolonged outbreak to date. In addition to the direct effects of EVD on populations, there has been disruption of standard medical care for common communicable diseases, such as malaria, that are endemic in the region and huge economic losses and social disruption in a region where the infrastructure is already significantly weakened by years of war and civil unrest. The World Health Organization has declared the Ebola epidemic to be a Public Health Emergency of International Concern. The international community, the World Health Organization, and the World Bank have committed to a coordinated international response and funding for the relief efforts.

With the first imported EVD case in the United States and subsequent health care worker transmission, all the health care facilities in the United States are actively planning for EVD recognition and containment. Lessons learned from Dallas are being incorporated into EVD health care facility preparedness.

On October 22, the CDC announced that public health authorities will begin active post-arrival monitoring of travelers whose travel originates in Liberia, Sierra Leone, or Guinea. Travelers identified as arriving from these countries by Customs, Border Protection, and the CDC will receive a CARE (Check And Report Ebola) kit at the airport that includes a pictorial description of symptoms, a thermometer, and instructions on who to contact if they develop symptoms. They will be followed up daily by state and local health departments for 21 days from the date of their departure from West Africa. Any traveler who develops symptoms during this period will be directed to a local hospital that has been trained to receive patients with potential EVD. This should limit the number of patients who arrive unexpectedly at emergency departments and also allay public anxiety about delayed diagnosis and potential community transmission.

CONCLUSION

The 2014 West African Ebola outbreak has increased the awareness of the disease among health care providers and the general public in the United States. It is important that health care workers understand the modes of transmission and the clinical course to recognize a potential EVD case. Preventing transmission in the community setting requires early recognition and isolation of patients with EVD in a health care facility that has adequate capabilities for infection control and supportive care. Contact tracing and quarantine of people who may have been in contact with patients with EVD are essential. Finally, efforts to contain the outbreak in West Africa through funding, ensuring the availability of necessary supplies, training, and education need to be pursued aggressively. The global community has been criticized for a slow and inadequate response to the EVD crisis in West Africa so far, but we still
have the chance to avert a global crisis. Nigeria and Senegal are now officially Ebola free, giving us reassurance that EVD control can be achieved even in resource-limited settings.

**SUPPLEMENTAL ONLINE MATERIAL**

Supplemental material can be found online at http://www.mayoclinicproceedings.org.

**Abbreviations and Acronyms:**

CDC = Centers for Disease Control and Prevention; EVD = Ebola virus disease; PPE = personal protective equipment

**Editor’s Note:** The content of this article was current as of October 23, 2014, the date of acceptance. The journal recognizes that this is a rapidly evolving field, and we will provide updates in the electronic and print versions of the journal as appropriate. — Thomas J. Beckman, MD, Associate Editor for Concise Reviews.

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**REFERENCES**