"Ebola Virus Disease"

July 2015

Did the current/recent Ebola epidemic take us by surprise? Will we be better prepared in the future. Our goal is to take a look at significant epidemiological issues related to the Ebola scare.

Pharmacists will be able to:

1. Describe the timeline associated with the recent Ebola epidemic in West Africa.
2. Discuss the clinical characteristics of Ebola Virus Disease.
3. Review the prevention strategies associated with Ebola Virus Disease.
4. List treatment options for Ebola Virus Disease.

Technicians will be able to:

1. Discuss the clinical characteristics of Ebola Virus Disease.
2. Review the prevention strategies associated with Ebola Virus Disease.

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If you have any comments, suggestions or questions, contact us at the above address, or call 1-847-945-8050. **Please write your name, NABP eProfile (CPE Monitor) ID Number & birthdate (MM/DD) in the indicated space on the quiz page.**

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Introduction

The recent (current) 2014 Ebola virus disease (EVD) epidemic in West Africa (Guinea, Liberia, and Sierra Leone) is the largest in history. The most recent outbreak has brought attention to this fatal viral disease which previously had occurred sporadically in Africa since 1976.[1] The current estimates by the Centers for Disease Control and World Health Organization (WHO) report that over 22,500 cases have been reported, (either suspected, probable or confirmed EVD in West Africa) and over 9,000 deaths.[2]

In addition to the unprecedented number of cases of EVD in West Africa, the epidemic took center stage when two Americans who had been treating patients in Liberia were brought back to the United States for treatment. [3,4] Two healthcare workers were given an experimental treatment, ZMapp, which is a mixture of three humanized monoclonal antibodies against Ebola, before their evacuation from Liberia to Emory University Hospital in Atlanta, Georgia. The administration of an experimental drug to these American patients raised awareness of the epidemic worldwide, as well as raised issues of the equity and access to care worldwide. [3]

The current epidemic mainly affects the countries in West Africa. The epidemic started in December 2013 in Guinea and rapidly spread to neighboring countries Liberia and Sierra Leone. In August 2014, the World Health Organization (WHO) declared the epidemic to be a "public health emergency of international concern." By mid-September, nine months after the first case occurred, the reported incidents had far exceeded the previous 24 EVD epidemics combined. [3,4]

Between December 2013 to September 2014, a total of 4507 EVD cases (both confirmed and probable) were reported to the WHO. [5] Despite multinational efforts to control the epidemic, Guinea, Liberia, and Sierra Leone continue to face challenges in implementing infection control measures required to stop transmission and provide care for persons with the EVD. The Ebola virus is spread by contact with bodily fluids of symptomatic patients. Transmission can be stopped with a combination of early diagnosis, contact tracing, patient isolation and care, proper infection control and safe burial practices. Previous outbreaks of EVD in central Africa have been limited in size and geographic region. It was contained by rigorous application of interventions delivered by local health care systems who had experience with treating and controlling EVD. The current EVD epidemic originated in southeast Guinea and spread to bordering Liberia and Sierra Leone rather quickly.[3] Because Ebola was previously unknown in these regions, surveillance systems were non-existent, and healthcare workers did not recognize or have means to manage the outbreak. The combination of these factors lead to the epidemic in the three countries (Liberia, Sierra Leone and Guinea). [3]

Table 1. Timeline of Ebola events.

Date	Events
March 25th, 2014	The Ministry of Health of Guinea has reported an outbreak of Ebola in four southeastern districts. Reports of suspected cases in neighboring countries of Liberia and Sierra Leone are being investigated. Médecins sans Frontières (MSF/ Doctors without Borders) is helping with establishing Ebola treatment centers. In Guinea, a total of 86 suspected cases, including 59 deaths.

Date	Events
March 31st, 2014	The Ministry of Health of Guinea increased the number of suspected and confirmed cases to 112, including 70 deaths and 24 laboratory confirmed cases of Ebola. In addition to MSF, several other international organizations joined the effort to care for patients and provide awareness campaigns as a preventative strategy.
April 30th, 2014	The ministry of health of Guinea reported 221 suspected and confirmed cases of EVD including 146 deaths. 25 healthcare workers have been affected with 16 deaths. The ministry of health and social welfare of Liberia report 13 cases.
May 28th, 2014	The ministry of health reports spread to the western counties of Guinea. The cumulative total of EVD stands at 281 with 186 deaths. Sierra Leone reports 9 suspected cases with 5 deaths under investigation. No cases have been reported in Liberia since April 2014.
June 24th, 2014	The Ministry of Health of Guinea reports 390 cases, including 270 fatal cases. The Ministry of Health and Sanitation of Sierra Leone reported a cumulative total of 158 cases with 34 fatal cases. The Ministry of Health and Social Welfare of Liberia reported 51 overall clinical cases of EVD with 34 fatal cases.
July 22nd, 2014	The first healthcare worker has suspected symptoms of EVD in Liberia.
July 23rd, 2014	Second American healthcare worker develops suspected symptoms suspicious of EVD in Liberia.
July 31st, 2014	The Ministries of Health for Guinea, Sierra Leone, Liberia and Nigeria report a cumulative total of 1323 suspected and confirmed cases of EVD and 729 deaths. This is the first report of a probable case in Nigeria. ZMapp administered to American healthcare workers.
August 2nd, 2014	An American healthcare worker transferred to Serious Communicable Diseases Unit at Emory University Hospital in Atlanta.
August 5th, 2014	Another American healthcare worker transferred to Serious Communicable Diseases Unit at Emory University Hospital in Atlanta.
August 19th, 2014	The first American healthcare worker is discharged from Emory University Hospital in Atlanta.
August 21st, 2014	The second American healthcare worker is discharged from Emory University Hospital in Atlanta.
August 28th, 2014	The WHO reports 3,069 suspected and confirmed cases of EVD and 1552 deaths in Guinea, Sierra Leone, Liberia and Nigeria.
September 6th, 2014	Senegal's Ministry of Health announced a case of EVD. Health and Human Services contracted with Mapp Biopharmaceuticals Inc to develop and manufacture ZMapp. National Institutes of Health will begin human testing of an investigational vaccine to prevent EVD. U.S. Department of Defense has funded two companies to develop EVD vaccine and drug therapy.

Date	Events
September 22nd, 2014	The Spanish National Reference Laboratory confirmed the first human to human transmission of EVD outside of Africa in a healthcare worker. The healthcare worker was part of team providing care for a person with EVD from Sierra Leone.
September 29th, 2014	No further cases in Senegal or Nigeria have been reported.
September 30th, 2014	The first travel-associated cases of Ebola diagnosed in the United States. Patient is treated at Texas Presbyterian Hospital in Dallas, Texas.
October 6th, 2014	The first human to human transmission occurs outside of Africa in the United States.
October 8th, 2014	The CDC implemented enhanced entry screening at five United States airports that receive over 94% of travelers from Guinea, Liberia and Sierra Leone. A case of Ebola reported in Spain. The patient with first travel-associated case of Ebola passes away. New cases continue to be reported in Guinea, Liberia and Sierra Leone.
October 12th, 2014	CDC confirms healthcare worker from Texas Presbyterian is positive for EVD. Healthcare worker is transferred to National Institutes of Health.
October 14th, 2014	Second healthcare worker at Texas Presbyterian Hospital who provided care tests positive for EVD.
October 15th, 2014	The second healthcare worker received care at Emory University Hospital.
October 23rd, 2014	Mali reports its first confirmed case of Ebola in a child who traveled there from Guinea. The child passes away the next day.
October 25th, 2014	CDC confirms a case of Ebola in a medical aid worker who returned from Guinea. Patient is treated at Bellevue Hospital in New York City. WHO released a report stating that 3792 cases have occurred throughout the epidemic. The first healthcare worker is released from the NIH.
October 28th, 2014	The second Texas healthcare worker is discharged from Emory University Hospital.
November 5th, 2014	The WHO reports a decrease in the number of total cases.
November 12th, 2014	Transmission remains intense in Guinea, Liberia, and Sierra Leone. A total of 4 cases of EVD have been reported in Mali. All Ebola patients in the United States are discharged from the hospital.
December 2nd, 2014	WHO declared Ebola outbreak in Spain has ended.
December 31st, 2014	Sierra Leone now has the highest total number of reported cases of the three intense transmission countries with 7897 cases to date. The first case of Ebola detected in the United Kingdom. The case is a healthcare worker who has returned from Sierra Leone.
January 30th, 2015	Fewer than 100 new cases reported in Guinea, Liberia and Sierra Leone. Mali announced the end of the outbreak.
February 8th, 2015	Total cases: 22,859 with 13,955 laboratory confirmed cases and 9,162 deaths.

Adapted from references 2,6,7

THE EBOLA VIRUS

Ebola is a rare, deadly disease caused by infection with one of the five Ebola virus strains. [8] Four of the five virus strains cause disease in humans; they are Ebola virus (*Zaire ebolavirus*), Sudan virus (*Sudan ebolavirus*), Taï Forest virus (*Taï Forest ebolavirus previously known as Côte d'Ivoire ebolavirus*) and bundibugyo virus (*Bundibugyo ebolavirus*). The Reston virus (*Reston ebolavirus*) has caused disease in non-human primates.

The natural reservoir host is unknown for the Ebola virus, but it is hypothesized to be animal-borne with bats being a likely reservoir.

PATHOGENESIS

The Ebola virus enters through the mucous membranes, breaks in the skin or parenterally.[9] It infects many cell types, including monocytes, macrophages, dendritic cells, hepatocytes, adrenal cortical cells and many more. After entering the circulatory system, the virus travels to the lymphocytes and then to the liver, spleen and adrenal gland. When the virus enters the hepatocytes, it causes hepatocellular necrosis, dysregulation of clotting factors and subsequent coagulopathy. The Ebola virus triggers pro-inflammatory cytokines leading to vascular leak and impairment of clotting, and ultimately to multi-organ failure and shock.

CLINICAL MANIFESTATIONS

The early symptoms of EVD include high fever (temperature of up to 40 degrees C), malaise, fatigue, and body aches. [9,10] Typically by day 3-5 of the illness, the gastrointestinal symptoms begin. The symptoms include epigastric pain, nausea, vomiting and diarrhea. Laboratory PCR (polymerase chain reaction) testing is often positive within 24 hours of symptom onset, but some patients remained negative until 72 hours after symptom onset. Episodes of emesis can be recurrent and limit the ability to tolerate oral intake. The diarrheal symptoms are severe with large volumes of watery diarrhea (greater than 5 L per day), that can persist up to 7 days. Associated signs and symptoms include asthenia, headache, conjunctival infection, chest pain, abdominal pain, arthralgias, myalgias, and hiccups. Respiratory symptoms are rare. Neurologic symptoms include delirium, manifested by confusion, slowed cognition, or agitation. Without adequate fluid intake and electrolyte management, severe lethargy and prostration ensue.

Many patients will develop hypovolemic shock manifested by diminished level of consciousness or coma, rapid thready pulse, oliguria or anuria and tachypnea. [10] Distal extremities may remain cold despite high ambient temperature and peripheral vasoconstriction. Clinical significant hemorrhage from the gastrointestinal tract occurs less frequently. Most deaths occur between days 7 and 12 of the illness.

The mortality rate during this outbreak is 71% (95% Confidence interval 68.6% to 72.8%) among patients with a documented outcome in Guinea, Liberia and Sierra Leone.[5] Hospitalized patients had a lower fatality rate of 64.3% (95% Confidence interval of 61.5% to 67%). Patients aged greater than 45 years old had a higher risk of death compared to patients less than 44 years old. Also patients with greater number of symptoms (i.e. diarrhea, confusion, difficulty breathing, etc.) were more likely to die.

TRANSMISSION

The virus can be transmitted to others by direct contact through broken skin or mucous membranes with blood and body fluids (including but not limited to urine, saliva, sweat, feces, vomit, breast milk and semen) from a person who is sick with Ebola, fomites contaminated with the virus, or infected animals (such as fruit bats, apes, or monkeys).[11] Ebola is not spread through the air, by water or by mosquitos. Ebola may be contracted when handling bushmeat (i.e. wild animals hunted for food) or when handling infected bats. Only humans, bats, monkeys and apes have shown the ability to become infected with and spread the Ebola virus. The disease can be transmitted in semen and vaginal fluids even after recovery from EVD. Therefore, the CDC recommends Ebola survivors should not have sexual relations for several months after recovery and use condoms.

EVD can spread easily in healthcare settings when workers are not wearing personal protective equipment (PPE).[11] Personal protective equipment must provide full body coverage without any skin exposure to reduce the risk of contamination. Virus transmission can occur via medical equipment, such as needles and syringes; therefore, proper cleaning and disposal is required. Without adequate sterilization, medical equipment and the health setting can amplify an outbreak. This served to be challenging both in West Africa as well as the United States. The CDC and WHO have provided guidance documents to prevent transmission in the healthcare setting. Some of the key principles include adequate training and competency of all healthcare workers prior to working with Ebola patients, no skin exposure while working with Ebola patients, and each step of donning and doffing of personal protective equipment must be supervised by trained observers to ensure minimal risk to healthcare workers. The guidance documents can be found at: ***http://www.cdc.gov/vhf/ebola/healthcare-us/ppe/guidance.html.***

As of October 23rd, 2014, four hundred and fifty healthcare workers have been infected with Ebola, of whom 244 died.[11] Several United States healthcare workers became infected after working in West Africa and returned to the U.S. for evaluation and treatment. In addition, there have been two imported cases and two locally acquired cases in healthcare workers.

TREATMENT AND PREVENTION

Currently, there are no FDA-approved vaccines or therapies available for EVD.[5,12] The mainstay of clinical management of EVD remains on supportive care of complications such as hypovolemia, electrolyte abnormalities, hematologic abnormalities, refractory shock, hypoxia, hemorrhage, septic shock, and multi-organ failure. The basic interventions, when given early, can improve survival. These interventions include providing intravenous fluids and maintaining electrolyte balance, oxygen status and blood pressure, and treating other infections if they occur. Patients that recover from EVD develop antibodies that can last for 10 years or longer. It is unknown if these patients will remain immune for a lifetime or if they can become infected with a different strain of Ebola.

EMERGING TREATMENTS

Due to the widespread epidemic, treatment and prevention strategies for EVD are an active area of research.[5,12] Clinical trials are currently ongoing evaluating vaccines and antiviral agents. Serum from patients that have recovered from EVD has been used to treat patients

with EVD, but there are no controlled clinical trials evaluating this method of treatment. Since this is an evolving area of research, providers are encouraged to review information available on the CDC website. The most up to date information can found be at: ***(http://www.cdc.gov/vhf/ebola/healthcare-us/preparing/clinicians.html)***.

TREATMENT AND EVALUATION IN THE UNITED STATES

Hospitals around the nation are preparing for a patient from West Africa who may have potential exposure to EVD because the incubation period is approximately 9-11 days from exposure.[14] The CDC has provided detailed definitions for U.S. clinicians evaluating patients with a potential exposure to the Ebola virus. See table 2 for risk stratification.

Table 2. Risk factors that should be considered when evaluating a person for Ebola virus disease (Ebola).

High risk includes any of the following:
• Percutaneous (e.g., needle stick) or mucous membrane exposure to blood or body fluids of a person with Ebola while the person was symptomatic
• Exposure to the blood or body fluids (including but not limited to feces, saliva, sweat, urine, vomit, and semen) of a person with Ebola while the person was symptomatic without appropriate personal protective equipment (PPE)
• Processing blood or body fluids of a person with Ebola while the person was symptomatic without appropriate PPE or standard biosafety precautions
• Direct contact with a dead body without appropriate PPE in a country with widespread transmission or cases in urban areas with uncertain control measures
• Having lived in the immediate household and provided direct care to a person with Ebola while the person was symptomatic
Some risk includes any of the following:
• In countries with widespread transmission or cases in urban areas with uncertain control measures
• Direct contact while using appropriate PPE with a person with Ebola while the person was symptomatic or with the person's body fluids and direct patient care in other healthcare settings
• Close contact in households, healthcare facilities, or community settings with a person with Ebola while the person was symptomatic
• Close contact is being within 3 feet of a symptomatic person for a prolonged period without PPE
Low (but not zero) risk includes any of the following:
• Having been in a country with widespread transmission or cases in urban areas with uncertain control measures within the past 21 days and having had no known exposures
• Having brief direct contact (e.g., shaking hands) while not wearing appropriate PPE, with a person with Ebola while the person was in the early stage of disease
• Brief proximity, such as being in the same room with a symptomatic person (not an Ebola patient care area) for a brief period of time
• In countries without widespread transmission or cases in urban settings with uncertain control measures: direct contact while using appropriate PPE with a person with Ebola while the person was symptomatic or with the person's body fluids
• Traveled on an aircraft with a person with Ebola while the person was symptomatic

No identifiable risk includes:

- Contact with an asymptomatic person who had contact with person with Ebola
- Contact with a person with Ebola before the person developed symptoms
- Having been more than 21 days previously in a country with widespread transmission or cases in urban areas with uncertain control measures
- Having been in a country with Ebola cases, but without widespread transmission or cases in urban settings with uncertain control measures, and not having any other exposures as defined above
- Having remained on or in the immediate vicinity of an aircraft or ship during the entire time that the conveyance was present in a country with widespread transmission or cases in urban areas with uncertain control measures, and having had no direct contact with anyone from the community.

The CDC has detailed guidelines for acute care facilities, emergency departments, and urgent care clinics to adequately prepare for a patient with a potential exposure to EVD.[14] While it is impossible for every healthcare facility to have the properly trained staff, appropriate personal protective gear and isolation rooms for the treatment of EVD patients, CDC does expect each healthcare facility in the United States to implement policies to identify, isolate and evaluate a patient with an EVD exposure and inform public health authorities. Since each healthcare facility may have different resources, they can serve as one of three roles: 1) a frontline healthcare facility, 2) Ebola assessment hospital or 3) Ebola treatment center. Some centers may fulfill multiple roles. Local and state public health authorities along with healthcare administrators will help identify facilities across the state to serve one of the three suggested roles. The specific guidance can be found on the CDC website.

The 2014 EVD epidemic is the largest in history with over 9,000 deaths in West Africa. In the United States, there were two imported cases, including one death, and two healthcare worker acquired cases. The outbreak has reinforced the need for nations to invest in their health infrastructure and disease surveillance to prevent the spread of contagious diseases.

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LESSON EVALUATION

Please fill out this section as a means of evaluating this lesson. The information will aid us in improving future efforts. Either circle the appropriate evaluation answer, or rate the item from 1 to 7 (1 is the lowest rating; 7 is the highest).

1. Does the program meet the learning objectives?

Describe the timeline of the recent EVD epidemic in West Africa	YES NO
Discuss clinical characteristics of EVD	YES NO
Review prevention strategies for EVD	YES NO
List treatment options for EVD	YES NO

2. Was the program independent & non-commercial YES NO

	Low Relevance						Very Relevant
3. Relevance of topic	1	2	3	4	5	6	7

4. What did you like most about this lesson?_____
5. What did you like least about this lesson?_____

Please Mark the Correct Answer(s)

1. **EVD is transmitted by:**
   A. Respiratory droplets
   B. Semen from an infected
   C. Direct contact thru broken skin or mucous membranes with blood & body fluids
   D. B & C
2. **The 2014 Ebola epidemic was widespread in:**
   A. South Africa B. Guinea
   C. Tanzania D. Uganda E. All of these
3. **Sypmtoms of EVD include:**
   A. Hemorrhage, seizures, difficulty breathing
   B. High fever, hemorrhage, bradycardia
   C. Cough, seizures, malaise
   D. Fever, nausea, vomiting, diarrhea
   E. None of these
4. **Currently there are no FDA-approved vaccines or therapies for EVD.**
   A. True
   B. False
5. **Treatment for EVD includes:**
   A. Supportive care
   B. Aggressive fluid resuscitation
   C. Correct electrolyte abnormalities
   D. Maintain oxygenation
   E. All of these
6. **Randomized, controlled trials have proven convalescent serum to be effective in treating with EVD.**
   A. True
   B. False
7. **The lowest risk factor for acquiring EVD is:**
   A. Body of patient who died of EVD
   B. Travel on aircraft with asymptomatic EVD person
   C. Contact with asymptomatic person who had contact with EVD person
   D. All of these
8. **Patients were most likely to die during the 2014 Ebola epidemic if:**
   A. They were 44 years old or younger
   B. They had multiple symptoms
   C. They were hospitalized
   D. None of these
9. **The CDC expects U.S. healthcare facilities to identify, isolate and evaluate patients with EVD exposure and inform public health authorities.**
   A. True B. False
10. **The reported number of deaths in West Africa from the 2014 EVD outbreak was:**
    A. 5,000
    B. Over 9,000
    C. Approximately 12, 500
    D. Over 18,000

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