Published in final edited form as:

Microbiol Spectr. 2016 June ; 4(3): . doi:10.1128/microbiolspec.EI10-0011-2016.

Preparing for Serious Communicable Diseases in the United States: What the Ebola Virus Epidemic Has Taught Us

Jay B Varkey, MD [Assistant Professor of Medicine] and
Emory University School of Medicine

Bruce S Ribner, MD, M.P.H. [Professor of Medicine]
Emory University School of Medicine

INTRODUCTION

The largest and deadliest outbreak of Ebola virus disease began on December 2, 2013 when a 2 year old child developed an illness characterized by fever, black stools, and vomiting in a town called Meliandou, Guinea—a remote and sparsely populated village of 31 households approximately 20 miles from the borders of Liberia and Sierra Leone.(1) The exact source of infection is unclear but likely involved contact with an infected animal. The child died on the 5th day of his illness.(2)

Over the next three weeks, the child's 3 year old sister, mother and grandmother also died. Two women from a nearby village attended the funeral of the child's grandmother; they died three weeks later. A midwife from the child's village was hospitalized and subsequently died. Two healthcare workers who worked at the hospital where the midwife was admitted also became ill and died. Multiple family members who attended the funerals of the healthcare workers also became ill and died.(2) By then, the illness, initially thought to be cholera, had spread to several surrounding districts as well as the capital of Guinea, Conkary—a city of 2 million people.(1)

By March 2014, cases were identified in neighboring Liberia and the disease was identified as being caused by the Ebola virus. In April 2014, cases of Ebola virus disease (EVD) were identified in Sierra Leone. Guinea, Liberia and Sierra Leone had previously never experienced an outbreak of EVD. All previous EVD outbreaks had occurred in mostly rural villages in the central African nations of the Democratic Republic of Congo, Sudan, Gabon, Uganda and the Republic of the Congo. Prior to 2013, the largest documented EVD outbreak occurred in 2000-2001 in the Gulu District of Uganda and resulted in over 400 cases and over 200 deaths.(3) As of December 2015, the West Africa EVD outbreak has resulted in over 28,000 cases and over 11,000 deaths in Guinea, Liberia and Sierra Leone—more than all previous EVD outbreaks combined.(4)

The 42 day waiting period after the last known case of EVD had recovered ended in Sierra Leone on November 7, 2015 and ended in Guinea on December 28, 2015. In Liberia, as of the time of writing this chapter, the 42 day waiting period will end on January 14, 2016.(4) Ending the West Africa EVD outbreak required an unprecedented international response. For the United States, participation in the international response to the West Africa EVD

outbreak provided an opportunity to learn important lessons in 4 key domains critical to preparing for future outbreaks of EVD and other serious communicable diseases: 1. Safe and Effective Patient Care; 2. The Role of Experimental Therapeutics and Vaccines; 3. Infection Control; 4. Hospital and Community Preparedness.

SAFE AND EFFECTIVE PATIENT CARE

There are no specific therapies approved by the US Food and Drug Administration for the treatment of EVD. Therefore, the primary treatment for EVD is supportive care, specifically fluid replacement and electrolyte management. Prior to the West Africa outbreak, the ability of health care workers to provide aggressive supportive care was often hampered by the resource limitations in many central African Ebola treatment centers.(5) Oral rehydration, though readily available even in resource-limited settings, may have been inadequate given the severe fluid losses (5-10 liters per day) caused by EVD-associated gastroenteritis and the intractable nausea and vomiting that frequently accompanies this illness.(6- 7) Similarly, the ability to safely provide intravenous fluids for rehydration and correction of electrolyte abnormalities was often limited by inadequate staffing, limited supplies of intravenous fluids, and inadequate or unavailable laboratory testing.(5) When laboratory testing was available, as during the 2000 outbreak of *Sudan ebolavirus* in Uganda, it demonstrated that renal failure, liver failure, hypocalcemia, hypoalbuminemia and an elevated D-Dimer were associated with increased mortality.(8)

The historic size of this West Africa EVD outbreak required an international response that resulted in both the construction of new Ebola treatment units in Guinea, Liberia and Sierra Leone, as well as the treatment of 27 individuals in Western Europe and the United States. As a result, the ability of health care workers to provide aggressive supportive care was enhanced. In Conakry, Guinea, aggressive supportive care may have contributed to a reduced case fatality rate compared to other more resource-limited areas of the country and compared to historical cohorts.(6) Among patients evacuated to Western Europe and the United States, the majority of patients had significant electrolyte abnormalities (hyponatremia, hypokalemia, hypocalcemia and hypomagnesemia) diagnosed by laboratory monitoring. The patients received multiple different, sometimes overlapping, interventions including supportive care. The case-fatality proportion of patients treated in Western Europe and the United States was 18.5% which is substantially lower than the mortality seen in West Africa ETUs.(9)

The treatment of EVD patients in resource-enhanced settings like Western Europe and the United States also allowed patients with EVD-associated multiorgan system failure to receive, for the first time, advanced critical care interventions like mechanical ventilation and renal replacement therapy.(10) Multi-organ system failure in EVD historically, and during the West Africa outbreak, has been associated with poor outcomes.(11) However, 11/27 patients treated in Western Europe and the United States required advanced critical care interventions (non-invasive mechanical ventilation, mechanical ventilation, vasopressor or inotropic support, and renal replacement therapy); six of the 11 survived.(9) In addition, the experience of providing critical care support to patients with EVD demonstrated that invasive interventions like mechanical ventilation and renal replacement therapy can be

performed safely if performed by trained health care workers who strictly adhere to infection control practices.(10)

The clinical care of patients with EVD does not end with the resolution of viremia. EVD survivors can develop a diverse array of complications during convalescence. Survivors of the 2007 outbreak of *Bundibugyo ebolavirus* in Uganda developed joint pain, sleep disturbances, and neurological abnormalities including hearing loss, memory loss and confusion. In addition, ocular complaints including retro-orbital pain and blurred vision were common.(12) Ocular complaints including sight-threatening uveitis has also been described in survivors of the 1995 outbreak of *Zaire ebolavirus* in Kikwit, Democratic Republic of Congo.(13) In a small survey of 85 EVD survivors of the West Africa, 40% of participants reported “eye problems.”(14) During the current outbreak, one survivor developed severe uveitis during convalescence and viable Ebola virus was isolated from his anterior eye chamber 9 weeks after clearance of viremia.(15)

The pathogenesis of complications that occur during EVD convalescence is unclear but may be multifactorial. It has been hypothesized that some of the complications may be related to post-viral auto-immune disease.(12) It has also been postulated that complications may be from persistent viral replication in immune-privileged sites.(15) Persistent viable Ebola virus has been isolated from semen and aqueous humor of EVD survivors.(15, 16) In addition, one survivor developed meningoencephalitis 10 months after she had cleared her viremia, and Ebola virus was isolated from her cerebrospinal fluid.(17) It is unclear whether Ebola virus persists in other bodily fluids or tissues that are thought to be immune-privileged (e.g. synovial fluid). Prospective cohort studies are underway in West Africa that will hopefully elucidate the causes of complications that occur to EVD survivors during convalescence.

ROLE OF EXPERIMENTAL THERAPEUTICS

While the key to surviving Ebola virus disease is aggressive supportive care, it is possible that the discovery of effective therapeutic agents may improve patient outcomes. Unfortunately, disproportionate media attention to unproven therapeutics during the recent Ebola outbreak led to unrealistic expectations and the almost universal compassionate use of experimental therapeutics in patients repatriated to resource-rich centers. Of the 27 patients treated in resource-rich centers, 70% received at least two investigational therapeutics (9), despite the fact that none had human efficacy or safety data; patients experienced a wide range of possible adverse effects. These adverse effects included systemic inflammatory response syndrome, hypotension, elevated transaminase levels, and transfusion-associated acute lung injury. It is of interest to note that two of the agents that were felt to be the most promising at the beginning of the outbreak were ultimately found to offer no survival benefits (see below). The use of therapeutics and vaccines in resource-limited environments will face a number of challenges, including supply and distribution uncertainty, administration difficulties with agents that must be given parenterally or intravenously, and the difficulties of utilizing oral agents in patients with intractable nausea and emesis (18). Above all, it is imperative that the search for a “magic bullet” not detract from a focus on supplying aggressive supportive care to all patients presenting with Ebola virus infection.

Therapeutics currently considered the best candidates for efficacy in patients infected with the Ebola virus fall into two categories: boosting of passive immunity and pharmaceutical antivirals. Recovery from Ebola virus disease is associated with the production of antibody against the virus (19, 20). It has therefore been hypothesized that the boosting of passive immunity until the host can produce antibody may be of benefit. In a prior outbreak in 1995, 8 patients with Ebola virus infection were given whole blood from outbreak survivors (21). Seven of the 8 patients survived, for a mortality rate of 12.5%, which compared with a mortality rate of 80% in patients who did not receive such transfusions. However, due to the small numbers and other confounding factors this survival difference was not felt to be definitive evidence of efficacy (22). Studies of convalescent serum in non human primates have been inconclusive. While the administration of convalescent whole blood transfusion to rhesus macaques was not found to be protective (23), infected rhesus macaques who received multiple administrations of purified, polyclonal, species-matched IgG from vaccinated animals did appear to be protected (22). In addition to the use of convalescent antibodies, pooled antibodies produced *in vitro* have been studied. ZMapp, a combination of 3 chimeric human/murine IgG1 monoclonal antibodies produced by a tobacco plant (*Nicotiana benthamiana*) has recently been developed (24). In a non human primate trial, ZMapp was 100% protective against Ebola virus infection even when administered 5 days after the animals were infected. While anecdotal evidence supports the efficacy of this preparation in a few of the patients who survived the current outbreak (25), no randomized controlled studies have been completed to date. A definitive answer as to the role of passive immunity in treating patients with Ebola virus disease will await more robust trials in humans.

Pharmaceutical antivirals directed against the Ebola virus have fallen into two categories: small-molecule inhibitors of virus entry and endosomal escape, and compounds that block viral replication. In the first category is a product called TKM-100802, a small interfering ribonucleic acid that silences RNA replication by enzymatic cleavage of mRNA. TKM-100802 targets the L polymerase, viral protein VP24 and VP35 (26). In both guinea pig and non human primate challenge studies, this agent was found to offer protection (27, 28). Unfortunately, in one of the few randomized controlled trials in humans to be performed during the current outbreak, this agent was not found to offer a survival advantage in humans and the trial was halted (29). Favipiravir, a broad spectrum antiviral that inhibits RNA-dependent RNA polymerase, also showed promise in initial animal studies, but again was not found to offer a survival advantage in a randomized trial involving humans. However, a post hoc analysis did suggest that favipiravir might be of benefit in patients presenting early in disease with lower viral loads (30). Other agents that have shown promise in *in vitro* or animal studies include GS-5734, BCX4430 and AVI7537 (18, 26). As these agents have not been evaluated in randomized human trials, their efficacy in humans is yet to be determined.

VACCINES

The high mortality rate associated with Ebola virus infection has added urgency to the search for effective vaccines. Practical difficulties in performing controlled clinical trials for Ebola vaccines are that Ebola outbreaks tend to be unpredictable and sporadic, and the ethical concerns about using a placebo control in the face of exposure to a highly lethal

disease. In 2002, the FDA promulgated the “animal rule” as an alternative pathway to license products against highly lethal pathogens such as Ebola (31). The animal rule has 4 conditions: 1. animal efficacy data (GLP); 2. immune correlate establishment and protection in animals; 3. human safety and immunogenicity data (GCP); 4. induction of an immune correlate in humans. It is anticipated that an effective vaccine will need to elicit both humoral and cell mediated immunity against the Ebola virus. Vaccines for pre-exposure (no identified exposure to the virus) and post-exposure (identified exposure to the virus) use have slightly different requirements. A vaccine for pre-exposure use would optimally induce protection after one, or at most 2, vaccinations. It should protect against multiple strains of the Ebola virus. It should have minimal adverse effects. A vaccine for post-exposure use should produce rapid induction of immunity. For all vaccines, ability to tolerate suboptimal storage conditions will be important, given the supply chain issues in most parts of the world where the Ebola virus is endemic.

Attenuated and inactivated vaccines have not shown protection in non-human primate studies (32), and there have been safety concerns due to the risk of incomplete inactivation. Genetic and subunit vaccines have resulted in incomplete protection (33, 34). The leading candidate vaccines at the present time are vector-based: a live, recombinant vesicular stomatitis virus (VSV) vaccine, and a replication-incompetent adenoviral vector vaccine. Both of these vaccines promote immunity to the Ebola virus glycoprotein. The Ebola virus glycoprotein is responsible for attachment and fusion between the viral and host membranes and produces inhibition of host immune responses. In non human primate models, an antiglycoprotein antibody level of 1:3700 and above allows the animal to survive subsequent lethal challenges with Ebola virus. The VSV vaccine encodes for the Ebola glycoprotein instead of the VSV glycoprotein. The immunity produced by this vaccine is primarily humoral. In non human primates, one dose of vaccine induces immunity and is 100% protective at 14 months(35). As the vaccine virus is capable of replication, the majority of volunteers exhibit some adverse events: 90% reported systemic symptoms, including fever, chills, myalgia and headache (36). Pre exposure studies with this vaccine are limited. In one post exposure study, 7651 individuals in Guinea who were contacts of patients with laboratory confirmed EVD were vaccinated either immediately or 21 days following exposure. In the immediate vaccination group there were no cases of Ebola virus disease with symptom onset at least 10 days after randomization, whereas in the delayed vaccination group there were 16 cases of Ebola virus disease from seven clusters, showing a vaccine efficacy of 100% (37).

The adenovirus vaccine encodes for the Ebola glycoprotein of two Ebola strains: Zaire and Sudan. Unlike the VSV vaccine, it promotes cellular as well as humoral immunity (38). As preexisting immunity to the adenovirus is more common than immunity to VSV, alternate immunization strategies such as multiple doses must be utilized. In human volunteers, minor adverse reactions were seen in 70% (fever and transient leukopenia) (39). Human trials in endemic areas are planned.

INFECTION CONTROL

Prior to the West Africa EVD outbreak, there were relatively limited data in the medical literature to help guide infection control practices when caring for patients with EVD in the United States. The literature that was available was based on the experience of caring for patients with EVD in central Africa—a setting markedly different to modern hospitals in the United States.(40) As of December 2015, 11 patients with EVD have been treated in the United States; ten of the 11 patients were treated in specialized biocontainment patient care units at Emory University Hospital, the University of Nebraska Medical Center and the National Institutes of Health Clinical Center. The eleventh was cared for in an isolation unit developed in Bellevue Hospital Center. In these settings, key lessons were learned to guide infection control policies and procedures to safely care for patients with EVD and other serious communicable diseases.

Although biocontainment patient care units are not required to treat a patient with EVD (41), specific features in the design of these facilities make them ideal environments to effectively treat patients with serious communicable diseases while minimizing the risk of transmission to healthcare workers, other patients, and the public.(42) In biocontainment patient care units, including the Serious Communicable Diseases Unit (SCDU) at Emory University Hospital (see Figure 1), individual patient care rooms are designed to deliver a level of care equivalent to that of a standard ICU, allowing healthcare workers to provide aggressive supportive care to patients who may be critically ill. To maintain staff safety, the SCDU includes dedicated space for staff changing areas and to store personal protective equipment (PPE). Patient care rooms are constructed with seamless surfaces for walls and floors to facilitate effective surface disinfection. To maintain the safety of other hospitalized patients and healthcare workers, the SCDU is located in a secured area of Emory University Hospital that is separate from other patient care areas. All entrances and exits in the SCDU are continuously monitored and limited only to healthcare workers and other individuals authorized to be in the unit (43).

The SCDU is also designed to safely care for patients with diseases that, unlike Ebola, can be spread through the airborne route. Specifically, air in the patients' rooms is under net negative pressure relative to the surrounding areas. Air in the patient rooms has laminar air flow across the patient bed and all air from the patient rooms undergoes high-efficiency particulate air filtration before being 100% exhausted to the outside. The outside exhaust is geographically separate from any hospital air intake locations and is high enough to allow for dilutional disbursement (43).

Independent of the specific design features of the treatment facility, the West African EVD outbreak clearly demonstrated that establishing a trained, competent, interdisciplinary team of providers and emphasizing a culture of safety are critical to effectively care for patients with EVD.(44-45) To staff the SCDU, a core team of nurses, physicians and other healthcare workers with expertise in infectious diseases, critical care and an expressed interest in caring for patients with serious communicable diseases were identified. In order to be part of the team, all providers were required to demonstrate a commitment to practice and promote a “culture of safety.” In a culture of safety, all team members commit to strictly adhere to safe

and effective practices outlined in standard operating protocols and are empowered to ask questions and voice concerns as they arise. Team members were also required to meet the following criteria: 1. Participate in regularly scheduled drill exercises; 2. Demonstrate competency in infection control practices with specific emphasis on protocols for donning and doffing PPE, specimen handling and waste management.(43) Providers who were unable to demonstrate these competencies were not permitted to provide direct patient care to patients with EVD. Drills, training sessions, and competency verification are performed every 3-6 months.

The selection of appropriate PPE for the clinical care team is a critical step to maintaining staff safety when caring for a patient with EVD. The specific type of PPE used by healthcare workers caring for patients with EVD should include a coverall or surgical gowns with head cover that leave no skin exposed. An apron and shoe covers should be added when there is a high risk of exposure to infectious body fluids. At least two sets of gloves should be worn including an outer glove that has extended cuffs. Although Ebola virus is not transmitted through the air, wearing a powered air purifying respirator or N-95 respirator together with a faceshield protects the face and mucus membranes from exposure to infectious fluids and provides additional protection if aerosol-generating procedures are performed.(46) Regardless of the specific type of PPE selected, it is imperative that PPE provide adequate protection but remain comfortable for healthcare workers. It is especially important that direct care providers receive adequate training and demonstrate competency in donning and doffing PPE. Inappropriate donning and doffing of PPE has been identified as a possible risk factor for EVD acquisition among healthcare workers.(47) Therefore, it is imperative that healthcare workers donning and doffing PPE should always be monitored by partners to ensure strict adherence to proper procedures.

In addition to the core group of nurses and physicians providing direct care to patients with EVD, laboratory technologists are critical members of the interdisciplinary team who need to maintain strict adherence to infection control practices. Patients with EVD have a high viral load that can reach levels of $>10^8$ viral particles/ml of body fluid. Ebola virus is highly infectious with an infectious dose that has been estimated to be as low as 0.001 ml of blood.(48) As a result, it is critical that hospitals that care for patients with EVD develop detailed standard operating protocols to maintain safety during laboratory specimen collection, transport and processing. Guidelines from the Centers for Disease Control and Prevention (CDC) state that hospital clinical laboratories can safely handle specimens from patients with EVD if risk mitigation strategies (engineering controls, administrative and work controls, use of appropriate PPE) are implemented.(49) The American Society for Microbiology has, however, issued guidelines suggesting that specimens from patients with EVD should be limited to point-of-care (POC) testing equipment and performed either in the patient's room or in a biological safety cabinet in an isolated area.(50) The SCDU at Emory University Hospital established a self-contained POC laboratory and processed all specimens within a 4-foot laminar flow biosafety containment hood.(51) All laboratory technologists involved in the transport and processing of specimens containing Ebola virus should receive PPE training and demonstrate competency in donning and doffing.

Hospitals preparing to care for patients with EVD also require a multidisciplinary team to develop standard protocols for the management of regulated medical waste. This team should include environmental services, infection prevention and control, biosafety officers, hospital administration, public health officials, and others with expertise in hazardous waste removal. All waste from patients with EVD is disposed in compliance with local, state, and federal regulations. EVD patient care waste is defined and regulated by the United States Department of Transportation as a Category A infectious substance. Therefore, all solid medical waste generated in the SCDU during the care of patients with EVD was sterilized in an autoclave that allowed the waste to be transported and disposed safely as regular medical waste. For units that do not have access to an autoclave, contractors who transport and dispose of Category A waste have special procedures in place for the packaging of such waste. Although CDC guidelines state that liquid waste may be disposed of without treatment in to sanitary sewers, local waste treatment authorities may have different requirements.(52) In the SCDU, a disinfectant was added to all liquid waste in accordance with manufacturers' directions prior to disposal in the sanitary sewer.

Because of the low infectious dose of Ebola virus, health care workers who care for patients with EVD must develop standard protocols to ensure that environmental surfaces in the direct patient care area, laboratory and in the waste stream receive regular cleaning with an appropriate effective disinfectant. The United States Environmental Protection Agency (EPA) has identified EPA-registered disinfectants with a label claim of potency at least equivalent to that for a non-enveloped virus which meet CDC criteria for use against Ebola virus.(53- 54) All disinfectants should be used by trained health care workers in accordance with manufacturers' instructions. Strict adherence to regular cleaning significantly reduces the risk of Ebola virus transmission from bodily fluids and fomites in the environment.(40) For terminal cleaning of the environment after discharge of a patient with Ebola virus disease, it is essential that meticulous attention be paid to disinfection of all surfaces. Most units have followed this with a supplemental disinfection modality such as vaporized hydrogen peroxide or a UV generator.(55)

HOSPITAL AND COMMUNITY PREPAREDNESS FOR EMERGING INFECTIOUS DISEASES

One of the key lessons that the Ebola outbreak of 2013-2015 has taught us is that the United States and the world were ill prepared to address an outbreak of an emerging infectious disease (56- 57- 58). This lesson was particularly jarring given that outbreaks of SARS (severe acute respiratory syndrome), H1N1 influenza, and MERS (Middle East respiratory syndrome) have marked the last decade. Partially due to this lack of preparation, the Ebola outbreak has dwarfed all other outbreaks of Ebola virus disease in terms of number infected and mortality. On the international front, factors that have been identified as contributing to the unprecedented extent of this outbreak have been identified (Table 1).(58- 59)

In addition to the lack of preparedness for isolating and managing infected patients, the delay in implementing research protocols to evaluate treatment algorithms, therapeutic

agents, and vaccines means that many questions regarding these interventions will not be resolved prior to the next outbreak.

In response to this outbreak, many initiatives, both globally and in the United States, have begun. On the international arena, an independent, multinational Commission on a Global Health Risk Framework for the Future has been established to recommend a more effective global architecture for mitigating the threat of epidemic infectious diseases.(57- 60) The U.S. National Academy of Medicine is the secretariat for this commission. In addition, an independent Panel convened by the World Health Organization has proposed an agenda for change (Table 2) which has been largely accepted by WHO administration.(61)

The United States has also witnessed a marked increase in activities focused on emergency preparedness for emerging infectious diseases. In 2015 Congress appropriated \$5.48 billion to the effort to control Ebola virus infection.(62) These funds will be utilized to address a number of areas that require strengthening in order to improve the U.S. response to emerging infectious diseases. Under the Hospital Preparedness Program of the Assistant Secretary for Preparedness and Response (ASPR), funding was distributed to the states and to other grantees to enhance state, local and healthcare system preparedness. These funds were also designed to create one regional Ebola and other special pathogen treatment center in each of the ten Health and Human Services regions.(63) In addition, the Centers for Disease Control and Prevention has developed a tiered approach to manage patients with possible or confirmed Ebola virus disease or infections caused by other serious communicable pathogens.(41) Under this strategy, acute healthcare facilities can serve one of three roles: frontline healthcare facility; Ebola assessment hospital; or Ebola treatment center. Frontline healthcare facilities should, in coordination with local and state health authorities, be able to rapidly identify and triage patients who are suspected of being infected with the Ebola virus. Ebola assessment hospitals are facilities prepared to receive and isolate suspect patients and care for the patient until a diagnosis of Ebola virus disease can be confirmed or ruled out and until discharge or transfer is completed. Ebola treatment centers are facilities that plan to care for and manage a patient with confirmed Ebola virus disease for the duration of the patient's illness. As the Ebola virus outbreak in West Africa is contained, the focus of this network should gradually shift to other serious communicable diseases, although exactly what these infectious diseases should be is yet to be resolved. ASPR has also funded the National Ebola Training and Education Center (NETEC) to develop a robust educational program to improve infectious disease emergency preparedness in the United States. The NETEC will be using a multipronged approach including: site visits for regional Ebola treatment units; establishment of a web based learning management system; development of exercise templates for entities to test their state of preparedness; and a research agenda to answer some of the fundamental questions regarding the treatment of patients with Ebola virus disease and other serious communicable pathogens. The goal of the site visits and exercises is to demonstrate that an institution-wide approach is essential when it comes to managing patients with serious communicable diseases. Areas of preparedness that will receive targeted attention are listed in (Table 3) . One of the most challenging areas for many facilities is to develop a laboratory that can safely evaluate patients for serious communicable pathogens in a timely manner while at the same time testing for other, more common, rapidly fatal diseases such as malaria and typhoid fever.

CONCLUSIONS

The EVD outbreak that began in Guinea in December 2013 has been the largest and deadliest EVD outbreak in human history. The outbreak cruelly demonstrated the significant degree to which developing nations, like those in West Africa, are vulnerable to serious morbidity and mortality caused by the rapid spread of serious communicable diseases like EVD. Paradoxically, the outbreak has also resulted in the largest number of EVD survivors in history. Therefore, it is critical, that the unprecedented international response that helped end the EVD outbreak be sustained to build the infrastructure of vulnerable developing nations. Building and maintaining adequate healthcare infrastructure will be critical to manage the prevalent and poorly understood complications that can occur in EVD survivors as well as to prevent future outbreaks.

The West African EVD outbreak also demonstrated again that emerging infectious diseases have no borders. As such, it is imperative that developed nations with advanced healthcare systems, like the United States, identify lessons that can be learned from the West African EVD outbreak. Specifically, key lessons learned in 4 domains: 1. Safe and Effective Patient Care; 2. The Role of Experimental Therapeutics and Vaccines; 3. Infection Control; 4. Hospital and Community Preparedness will hopefully help both the United States and the international community more effectively respond to future outbreaks of EVD and other emerging serious communicable diseases in the future.

REFERENCES

1. World Health Organization. Origins of the 2014 Ebola Epidemic: One Year Into the Ebola Epidemic. <http://www.who.int/csr/disease/ebola/one-year-report/virus-origin/en/>
2. Baize S, Pannetier D, Oestereich L, Rieger T, Koivogui L, Magassouba N, Soropogui B, Sow MS, Keita S, De Clerck H, Tiffany A, Dominguez G, Loua M, Traoré A, Kolié M, Malano ER, Heleze E, Bocquin A, Mély S, Raoul H, Caro V, Cadar D, Gabriel M, Pahlmann M, Tappe D, Schmidt-Chanasit J, Impouma B, Diallo AK, Formenty P, Van Herp M, Günther S. Emergence of Zaire Ebola virus disease in Guinea. *N Engl J Med*. 2014; 371(15):1418–25. [PubMed: 24738640]
3. Centers for Disease Control and Prevention. Outbreaks Chronology: Ebola Virus Disease. <http://www.cdc.gov/vhf/ebola/outbreaks/history/chronology.html>
4. World Health Organization. Ebola Situation Report-30 December. 2015. <http://apps.who.int/ebola/current-situation/ebola-situation-report-30-december-2015>
5. Fowler RA, Fletcher T, Fischer WA, Lamontagne F, Jacob S, Brett-Major D, Lawler JV, Jacquerioz FA, Houlihan C, O'Dempsey T, Ferri M, Adachi T, Lamah MC, Bah EI, Mayet T, Schieffelin J, McLellan SL, Senga M, Kato Y, Clement C, Mardel S, Vallenat Bejar De Villar RC, Shindo N, Bausch D. Caring for critically ill patients with Ebola virus disease. Perspectives from West Africa. *Am J Respir Crit Care Med*. 2014; 190(8):733–7. [PubMed: 25166884]
6. Bah EI, Lamah MC, Fletcher T, Jacob ST, Brett-Major DM, Sall AA, Shindo N, Fischer WA 2nd, Lamontagne F, Saliou SM, Bausch DG, Moumié B, Jagatic T, Sprecher A, Lawler JV, Mayet T, Jacquerioz FA, Méndez Baggi MF, Vallenat C, Clement C, Mardel S, Faye O, Faye O, Soropogui B, Magassouba N, Koivogui L, Pinto R, Fowler RA. Clinical presentation of patients with Ebola virus disease in Conakry, Guinea. *N Engl J Med*. 2015; 372(1):40–7. [PubMed: 25372658]
7. Schieffelin JS, Shaffer JG, Goba A, Gbakie M, Gire SK, Colubri A, Sealfon RS, Kanneh L, Moigboi A, Momoh M, Fullah M, Moses LM, Brown BL, Andersen KG, Winnicki S, Schaffner SF, Park DJ, Yozwiak NL, Jiang PP, Kargbo D, Jalloh S, Fonnies M, Sinnah V, French I, Kovoma A, Kamara FK, Tucker V, Konuwa E, Sellu J, Mustapha I, Foday M, Yillah M, Kanneh F, Saffa S, Massally JL, Boisen ML, Branco LM, Vandi MA, Grant DS, Happi C, Gevaio SM, Fletcher TE, Fowler RA, Bausch DG, Sabeti PC, Khan SH, Garry RF. KGH Lassa Fever Program; Viral Hemorrhagic Fever

- Consortium; WHO Clinical Response Team. 2014. Clinical illness and outcomes in patients with Ebola in Sierra Leone. *N Engl J Med*. 371(22):2092–100. [PubMed: 25353969]
8. Rollin PE, Bausch DG, Sanchez A. Blood chemistry measurements and D-Dimer levels associated with fatal and nonfatal outcomes in humans infected with Sudan Ebola virus. *J Infect Dis* 196 Suppl. 2007; 2:S364–71.
 9. Uyeki TM, Mehta AK, Davey RT, Liddell AM, Wolf T, Vetter P, Schmiedel S, Grünewald T, Jacobs M, Arribas JR, Evans L, Hewlett AL, Brantsaeter AB, Ippolito G, Rapp C, Hoepelman AIM, Gutman J, the Working Group of the U.S.-European Clinical Network on Clinical Management of Ebola Virus Disease Patients in the U.S. and Europe. Clinical management of Ebola virus disease patients in the U.S. and Europe. *N Engl J Med*. 2016 in press.
 10. Connor MJ Jr, Kraft C, Mehta AK, Varkey JB, Lyon GM, Crozier I, Ströher U, Ribner BS, Franch HA. Successful delivery of RRT in Ebola virus disease. *J Am Soc Nephrol*. 2015; 26(1):31–7. [PubMed: 25398785]
 11. Sueblinvong V, Johnson DW, Weinstein GL, Connor MJ Jr, Crozier I, Liddell AM, Franch HA, Wall BR, Kalil AC, Feldman M, Lisco SJ, Sevransky JE. Critical Care for Multiple Organ Failure Secondary to Ebola Virus Disease in the United States. *Crit Care Med*. 2015; 43(10):2066–75. [PubMed: 26196353]
 12. Clark DV, Kibuuka H, Millard M, Wakabi S, Lukwago L, Taylor A, Eller MA, Eller LA, Michael NL, Honko AN, Olinger GG Jr, Schoepp RJ, Hepburn MJ, Hensley LE, Robb ML. Long-term sequelae after Ebola virus disease in Bundibugyo, Uganda: a retrospective cohort study. *Lancet Infect Dis*. 2015; 15(8):905–12. [PubMed: 25910637]
 13. Kibadi K, Mupapa K, Kuvula K, Massamba M, Ndaberey D, Muyembe-Tamfum JJ, Bwaka MA, De Roo A, Colebunders R. Late ophthalmologic manifestations in survivors of the 1995 Ebola virus epidemic in Kikwit, Democratic Republic of the Congo. *J Infect Dis*. 1999; 179(Suppl 1):S13–4. [PubMed: 9988158]
 14. Trenchard, T. Survivors cope with new Ebola after-effects. *Al-Jazeera*; 2014. <http://www.aljazeera.com/news/africa/2014/12/survivors-cope-with-new-ebola-after-effects-2014121573521561384.html>
 15. Varkey JB, Shantha JG, Crozier I, Kraft CS, Lyon GM, Mehta AK, Kumar G, Smith JR, Kainulainen MH, Whitmer S, Ströher U, Uyeki TM, Ribner BS, Yeh S. Persistence of Ebola Virus in Ocular Fluid during Convalescence. *N Engl J Med*. 2015; 372(25):2423–7. [PubMed: 25950269]
 16. Mate SE, Kugelman JR, Nyenswah TG, Ladner JT, Wiley MR, Cordier-Lassalle T, Christie A, Schroth GP, Gross SM, Davies-Wayne GJ, Shinde SA, Murugan R, Sieh SB, Badio M, Fakoli L, Taweh F, de Wit E, van Doremalen N, Munster VJ, Pettitt J, Prieto K, Humrighouse BW, Ströher U, DiClaro JW, Hensley LE, Schoepp RJ, Safronetz D, Fair J, Kuhn JH, Blackley DJ, Laney AS, Williams DE, Lo T, Gasasira A, Nichol ST, Formenty P, Kateh FN, De Cock KM, Bolay F, Sanchez-Lockhart M, Palacios G. Molecular Evidence of Sexual Transmission of Ebola Virus. *N Engl J Med*. 2015; 373(25):2448–54. [PubMed: 26465384]
 17. Fink, S. Ebola Survivor From Scotland Is Critically Ill. *New York Times*; 2015. <http://www.nytimes.com/2015/10/15/world/europe/scottish-nurse-who-had-ebola-is-back-in-hospital-and-critically-ill.html>
 18. World Health Organization. Potential Ebola therapies and vaccines: Interim guidance. 2014. <http://www.who.int/csr/resources/publications/ebola/potential-therapies-vaccines/en/>
 19. Kraft CS, Hewlett AL, Koepsell S, Winkler AM, Kratochvil CJ, Larson L, Varkey JB, Mehta AK, Lyon GM 3rd, Friedman-Moraco RJ, Marconi VC, Hill CE, Sullivan JN, Johnson DW, Lisco SJ, Mulligan MJ, Uyeki TM, McElroy AK, Sealy T, Campbell S, Spiropoulou C, Ströher U, Crozier I, Sacra R, Connor MJ Jr, Sueblinvong V, Franch HA, Smith PW, Ribner BS. Nebraska Biocontainment Unit and the Emory Serious Communicable Diseases Unit. *Clin Infect Dis*. 2015; 61(4):496–502. [PubMed: 25904375]
 20. McElroy AK, Akondy RS, Davis CW, Ellebedy AH, Mehta AK, Kraft CS, Lyon GM, Ribner BS, Varkey J, Sidney J, Sette A, Campbell S, Ströher U, Damon I, Nichol ST, Spiropoulou CF, Ahmed R. Human Ebola virus infection results in substantial immune activation. *Proc Natl Acad Sci U S A*. 2015; 112(15):4719–24. [PubMed: 25775592]

21. Mupapa K, Massamba M, Kibadi K, Kuvula K, Bwaka A, Kipasa M, Colebunders R, Muyembe-Tamfum JJ. Treatment of Ebola hemorrhagic fever with blood transfusions from convalescent patients. International Scientific and Technical Committee. J Infect Dis. 1999 179 Suppl. 1999; 1:S18–23.
22. Dye JM, Herbert AS, Kuehne AI, Barth JF, Muhammad MA, Zak SE, Ortiz RA, Prugar LI, Pratt WD. Postexposure antibody prophylaxis protects nonhuman primates from filovirus disease. Proc Natl Acad Sci U S A. 2012; 109(13):5034–9. [PubMed: 22411795]
23. Jahrling PB, Geisbert JB, Swearingen JR, Larsen T, Geisbert TW. Ebola hemorrhagic fever: evaluation of passive immunotherapy in nonhuman primates. J Infect Dis 196 Suppl. 2007; 2:S400–3.
24. Qiu X, Wong G, Audet J, Bello A, Fernando L, Alimonti JB, Fausther-Bovendo H, Wei H, Aviles J, Hiatt E, Johnson A, Morton J, Swope K, Bohorov O, Bohorova N, Goodman C, Kim D, Pauly MH, Velasco J, Pettitt J, Olinger GG, Whaley K, Xu B, Strong JE, Zeitlin L, Kobinger GP. Reversion of advanced Ebola virus disease in nonhuman primates with ZMapp. Nature. 2014; 514(7520):47–53. [PubMed: 25171469]
25. Lyon GM, Mehta AK, Varkey JB, Brantly K, Plyler L, McElroy AK, Kraft CS, Towner JS, Spiropoulou C, Ströher U, Uyeki TM, Ribner BS, Emory Serious Communicable Diseases Unit. Clinical care of two patients with Ebola virus disease in the United States. N Engl J Med. 2014; 371(25):2402–9. [PubMed: 25390460]
26. Wong G, Qiu X. Development of experimental and early investigational drugs for the treatment of Ebola virus infections. Expert Opin Investig Drugs. 2015; 24(8):999–1011.
27. Geisbert TW, Lee AC, Robbins M, Geisbert JB, Honko AN, Sood V, Johnson JC, de Jong S, Tavakoli I, Judge A, Hensley LE, MacLachlan I. Postexposure protection of non-human primates against a lethal Ebola virus challenge with RNA interference: a proof-of-concept study. Lancet. 2010; 375(9729):1896–905. [PubMed: 20511019]
28. Geisbert TW, Hensley LE, Kagan E, Yu EZ, Geisbert JB, Daddario-DiCaprio K, Fritz EA, Jahrling PB, McClintock K, Phelps JR, Lee AC, Judge A, Jeffs LB, MacLachlan I. Postexposure protection of guinea pigs against a lethal ebola virus challenge is conferred by RNA interference. J Infect Dis. 2006; 193(12):1650–7. [PubMed: 16703508]
29. Pollack, A. Clinical trial of experimental ebola drug is halted. New York Times; 2015. http://www.nytimes.com/2015/06/20/health/clinical-trial-of-experimental-ebola-drug-is-halted.html?_r=0
30. Sissoko, D.; Folkesson, E.; Abdoul, M.; Beavogi, AH.; Gunther, S.; Shepherd, S.; Danel, C.; Mentre, F.; Anglaret, X.; Malvy, D. Favipiravir in patients with Ebola virus disease: Early results of the JIKI trial in Guinea.. Conference on Retroviruses and Opportunistic Infections (CROI); Seattle, Washington. 2015. Abstract 103-ALB
31. Sullivan NJ, Martin JE, Graham BS, Nabel GJ. Correlates of protective immunity for Ebola vaccines: implications for regulatory approval by the animal rule. Nat Rev Microbiol. 2009; 7(5): 393–400. [PubMed: 19369954]
32. Geisbert TW, Pushko P, Anderson K, Smith J, Davis KJ, Jahrling PB. Evaluation in nonhuman primates of vaccines against Ebola virus. Emerg Infect Dis. 2002; 8(5):503–7. [PubMed: 11996686]
33. Reynard O, Mokhonov V, Mokhonova E, Leung J, Page A, Mateo M, Pyankova O, Georges-Courbot MC, Raoul H, Khromykh AA, Volchkov VE. Kunjin virus replicon-based vaccines expressing Ebola virus glycoprotein GP protect the guinea pig against lethal Ebola virus infection. J Infect Dis 204 Suppl. 2011; 3:S1060–5.
34. Hoenen T, Groseth A, Feldmann H. Current ebola vaccines. Expert Opin Biol Ther. 2012; 12(7): 859–72. [PubMed: 22559078]
35. Qiu X, Fernando L, Alimonti JB, Melito PL, Feldmann F, Dick D, Ströher U, Feldmann H, Jones SM. Mucosal immunization of cynomolgus macaques with the VSVDeltaG/ZEBOVGP vaccine stimulates strong ebola GP-specific immune response. PLoS One. 2009; 4(5):e5547. [PubMed: 19440245]
36. Agnandji ST, Huttner A, Zinser ME, Njuguna P, Dahlke C, Fernandes JF, Yerly S, Dayer JA, Kraehling V, Kasonta R, Adegnika AA, Altfeld M, Auderset F, Bache EB, Biedenkopf N, Borregaard S, Brosnahan JS, Burrow R, Combescure C, Desmeules J, Eickmann M, Fehling SK,

- Finckh A, Goncalves AR, Grobusch MP, Hooper J, Jambrecina A, Kabwende AL, Kaya G, Kimani D, Lell B, Lemaître B, Lohse AW, Massinga-Loembe M, Matthey A, Mordmüller B, Nolting A, Ogwang C, Ramharter M, Schmidt-Chanasit J, Schmiedel S, Silvera P, Stahl FR, Staines HM, Strecker T, Stubbe HC, Tsofa B, Zaki S, Fast P, Moorthy V, Kaiser L, Krishna S, Becker S, Kieny MP, Bejon P, Kremsner PG, Addo MM, Siegrist CA. Phase 1 Trials of rVSV Ebola Vaccine in Africa and Europe - Preliminary Report. *N Engl J Med*. 2015 Epub ahead of print.
37. Henao-Restrepo AM, Longini IM, Egger M, Dean NE, Edmunds WJ, Camacho A, Carroll MW, Doumbia M, Draguez B, Duraffour S, Enwere G, Grais R, Gunther S, Hossmann S, Kondé MK, Kone S, Kuisma E, Levine MM, Mandal S, Norheim G, Riveros X, Soumah A, Trelle S, Vicari AS, Watson CH, Kéïta S, Kieny MP, Røttingen JA. Efficacy and effectiveness of an rVSV-vectored vaccine expressing Ebola surface glycoprotein: interim results from the Guinea ring vaccination cluster-randomised trial. *Lancet*. 2015; 386(9996):857–66. [PubMed: 26248676]
 38. Sullivan NJ, Hensley L, Asiedu C, Geisbert TW, Stanley D, Johnson J, Honko A, Olinger G, Bailey M, Geisbert JB, Reimann KA, Bao S, Rao S, Roederer M, Jahrling PB, Koup RA, Nabel GJ. CD8⁺ cellular immunity mediates rAd5 vaccine protection against Ebola virus infection of nonhuman primates. *Nat Med*. 2011; 17(9):1128–31. [PubMed: 21857654]
 39. Ledgerwood JE, Costner P, Desai N, Holman L, Enama ME, Yamshchikov G, Mulangu S, Hu Z, Andrews CA, Sheets RA, Koup RA, Roederer M, Bailer R, Mascola JR, Pau MG, Sullivan NJ, Goudsmit J, Nabel GJ, Graham BS, VRC 205 Study Team. A replication defective recombinant Ad5 vaccine expressing Ebola virus GP is safe and immunogenic in healthy adults. *Vaccine*. 2010; 29(2):304–13. [PubMed: 21034824]
 40. Bausch DG, Towner JS, Dowell SF, Kaducu F, Lukwiya M, Sanchez A, Nichol ST, Ksiazek TG, Rollin PE. Assessment of the risk of Ebola virus transmission from bodily fluids and fomites. *J Infect Dis* 196 Suppl. 2007; 2:S142–7.
 41. Centers for Disease Control and Prevention. Hospital preparedness: A tiered approach. 2014. <http://www.cdc.gov/vhf/ebola/healthcare-us/preparing/treatment-centers.html>
 42. Smith PW, Anderson AO, Christopher GW, Cieslak TJ, Devreede GJ, Fosdick GA, Greiner CB, Hauser JM, Hinrichs SH, Huebner KD, Iwen PC, Jourdan DR, Kortepeter MG, Landon VP, Lenaghan PA, Leopold RE, Marklund LA, Martin JW, Medcalf SJ, Mussack RJ, Neal RH, Ribner BS, Richmond JY, Rogge C, Daly LA, Roselle GA, Rupp ME, Sambol AR, Schaefer JE, Sibley J, Streifel AJ, Essen SG, Warfield KL. Designing a biocontainment unit to care for patients with serious communicable diseases: a consensus statement. *Biosecur Bioterror*. 2006; 4(4):351–65. [PubMed: 17238819]
 43. Hewlett AL, Varkey JB, Smith PW, Ribner BS. Ebola virus disease: preparedness and infection control lessons learned from two biocontainment units. *Curr Opin Infect Dis*. 2015; 28(4):343–8. [PubMed: 26098504]
 44. Feistritzer NR, Hill C, Vanairsdale S, Gentry J. Care of patients with Ebola virus disease. *J Contin Educ Nurs*. 2014; 45:479–481. [PubMed: 25365183]
 45. Schwedhelm S, Beam EL, Morris RD, Sebastian JG. Reflections on interprofessional team-based clinical care in the Ebola epidemic: the Nebraska medicine experience. *Nurs Outlook*. 2015; 63:27–29. [PubMed: 25645479]
 46. Centers for Disease Control and Prevention. Guidance on Personal Protective Equipment (PPE) To Be Used By Healthcare Workers during Management of Patients with Confirmed Ebola or Persons under Investigation (PUIs) for Ebola who are Clinically Unstable or Have Bleeding, Vomiting, or Diarrhea in U.S. Hospitals, Including Procedures for Donning and Doffing PPE. 2015. <http://www.cdc.gov/vhf/ebola/healthcare-us/ppe/guidance.html>
 47. MacIntyre CR, Chughtai AA, Seale H, Richards GA, Davidson PM. Uncertainty, risk analysis and change for Ebola personal protective equipment guidelines. *Int J Nurs Stud*. 2015; 52(5):899–903. [PubMed: 25575750]
 48. Iwen PC, Smith PW, Hewlett AL, Kratochvil CJ, Lisco SJ, Sullivan JN, Gibbs SG, Lowe JJ, Fey PD, Herrera VL, Sambol AR, Wisecarver JL, Hinrichs SH. Safety considerations in the laboratory testing of specimens suspected or known to contain Ebola virus. *Am J Clin Pathol*. 2015; 143(1): 4–5. [PubMed: 25511134]

49. Centers for Disease Control and Prevention. Guidance for U.S. Laboratories for Managing and Testing Routine Clinical Specimens When There is a Concern About Ebola Virus Disease. 2015. <http://www.cdc.gov/vhf/ebola/healthcare-us/laboratories/safe-specimen-management.html>
50. American Society for Microbiology. Interim laboratory guidelines for handling/testing specimens from cases or suspected cases of hemorrhagic fever virus (HFV). 2014. <https://www.asm.org/images/PSAB/Ebola9-10-14.pdf>
51. Hill CE, Burd EM, Kraft CS, Ryan EL, Duncan A, Winkler AM, Cardella JC, Ritchie JC, Parslow TG. Laboratory test support for Ebola patients within a high-containment facility. *Lab Med*. 2014; 45(3):e109–11. [PubMed: 25184220]
52. Centers for Disease Control and Prevention. Procedures for safe handling and management of Ebola-associated waste. 2014. <http://www.cdc.gov/vhf/ebola/healthcareus/cleaning/handling-waste.html>
53. Centers for Disease Control and Prevention. Interim guidance for environmental infection control in hospitals for Ebola virus. 2015. <http://www.cdc.gov/vhf/ebola/healthcareus/cleaning/hospitals.html>
54. United States Environmental Protection Agency. List L: Disinfectants for use against the Ebola virus. 2015. <http://www.epa.gov/pesticide-registration/list-l-disinfectants-use-against-ebola-virus>
55. Lowe JJ, Olinger PL, Gibbs SG, Rengarajan K, Beam EL, Boulter KC, Schwedhelm MM, Hayes AK, Kratochvil CJ, Vanairsdale S, Frislie B, Lewis J, Hewlett AL, Smith PW, Gartland B, Ribner BS. Environmental infection control considerations for Ebola. *Am J Infect Control*. 2015; 43(7): 747–9. [PubMed: 25934067]
56. Gates B. The next epidemic--lessons from Ebola. *N Engl J Med*. 2015; 372(15):1381–4. [PubMed: 25853741]
57. Dzau VJ, Rodin J. Creating a Global Health Risk Framework. *N Engl J Med*. 2015; 373(11):991–3. [PubMed: 26244878]
58. World Health Organization. Report of the Ebola interim assessment panel. 2015. <http://www.who.int/csr/resources/publications/ebola/ebola-interim-assessment/en/>
59. World Health Organization. Factors that contributed to undetected spread of the Ebola virus and impeded rapid containment. 2015. <http://www.who.int/csr/disease/ebola/one-year-report/factors/en/>
60. National Academy of Medicine. Global health risk framework. 2016. <http://nam.edu/initiatives/global-health-risk-framework/>
61. World Health Organization. WHO Secretariat response to the report of the Ebola interim assessment panel. 2015. <http://www.who.int/csr/resources/publications/ebola/who-response-to-ebola-report.pdf>
62. Wayne, Alex. Congress nearly grants Obama's Ebola wish list with \$5.4B. *Bloomberg*. 2014. <http://www.bloomberg.com/news/articles/2014-12-10/congress-nearly-grants-obama-s-ebola-wish-list-with-5-4b>
63. U.S. Department of Health & Human Services. HHS invests in enhancing domestic preparedness efforts for Ebola. 2015. <http://www.hhs.gov/about/news/2015/02/20/hhs-invests-in-enhancing-domestic-preparedness-efforts-for-ebola.html>

Figure 1.
Schematic of the Serious Communicable Diseases Unit (SCDU), Emory University Hospital

Table 1

Factors Contributing to 2013-2015 Ebola Outbreak (58- 59)

<ul style="list-style-type: none">• Failure of member States to implement the core capacities called for under the International Health Regulations (2005)• The implementation of travel bans and other measures that interfered with the response to the outbreak• Delays in the declaration of a Public Health Emergency of International Concern (PHEIC) by WHO• Lack of familiarity with Ebola by healthcare providers and public health officials in West Africa• The unique introduction of Ebola into an urban setting for the first time as opposed to rural villages• Poor public health infrastructure due to years of civil war• A severe shortage of healthcare workers exacerbated by the many healthcare workers who became infected with the Ebola virus early in the outbreak• Closure of healthcare facilities and departure of foreign healthcare workers due to perceived danger as the outbreak peaked• High risk funeral and burial practices in West African countries• Community resistance due to suspicion of the government and lack of familiarity with Ebola

Table 2

WHO's Agenda for Change (61)

<ul style="list-style-type: none">• Strengthening of the International Health Regulations• Identifying addition resources to support public health infrastructure in member states• Implementation of objective measures to assess core capacities of member states• Altering the WHO structure and culture to improve emergency preparedness and response capacity• Development of a global health emergency workforce to respond to outbreaks and emergencies with health consequences• Improved integration of health security and humanitarian systems• Development of a unified WHO program for outbreaks and emergencies• Development of an “R and D Blueprint” to accelerate research and development on diagnostics, vaccines and therapeutics during outbreaks and health emergencies• Establishment of a WHO Contingency Fund for Emergencies to establish adequate international financing for pandemics and other health emergencies
--

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Table 3

Emergency Medical Services and Emergency Department preparedness

-
- Patient transport
 - Staffing
 - PPE and donning/doffing procedures
 - HCW Monitoring and management of exposures
 - Lab safety and capacity
 - Environmental infection control
 - Waste management
 - Coordinated communication
 - Management of special populations
-