



Ebola Virus Disease in West Africa — Clinical Manifestations and Management

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In resource-limited areas, isolation of the sick from the population at large has been the cornerstone of control of Ebola virus disease (EVD) since the virus was discovered in 1976.¹ Although this strategy

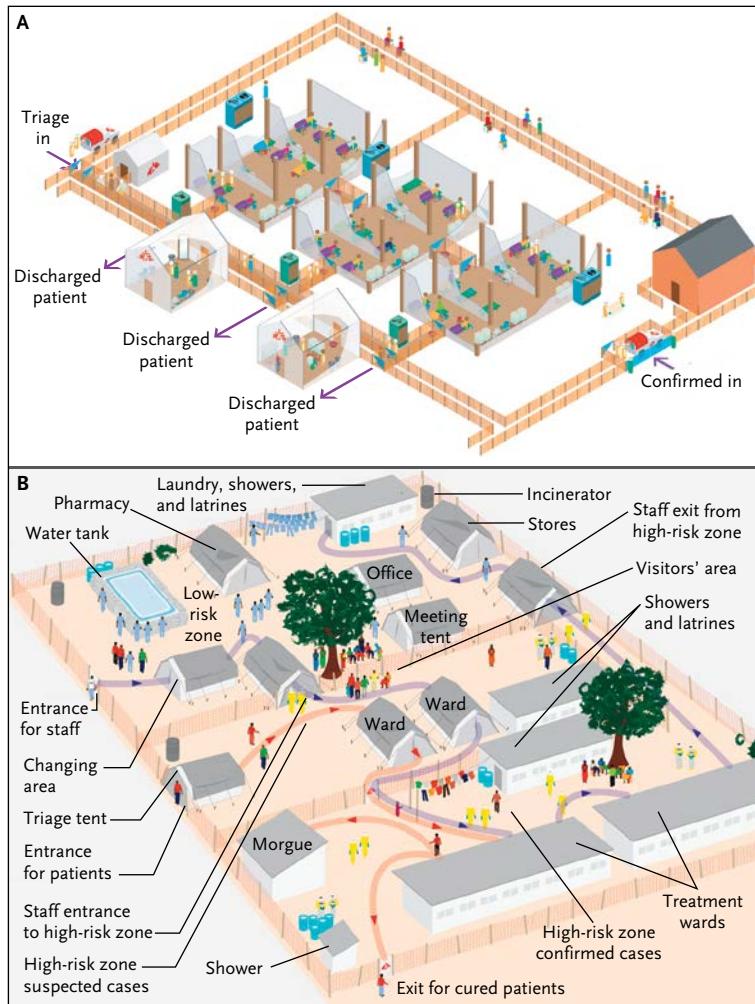
by itself may be effective in controlling small outbreaks in remote settings, it has offered little hope to infected people and their families in the absence of medical care. In the current West African outbreak, infection control and clinical management efforts are necessarily being implemented on a larger scale than in any previous outbreak, and it is therefore appropriate to reassess traditional efforts at disease management. Having cared for more than 700 patients with EVD between August 23 and October 4, 2014, in the largest Ebola treatment unit in Monrovia, Liberia (see diagrams), we believe that

our cumulative clinical observations support a rational approach to EVD management in resource-limited settings.

Early symptoms of EVD include high fever (temperature of up to 40°C), malaise, fatigue, and body aches (see table).^{2,3} The fever persists, and by day 3 to 5 of illness, gastrointestinal symptoms typically begin, with epigastric pain, nausea, vomiting, and diarrhea. Patients routinely presented to our facility after 2 or 3 days of severe vomiting or diarrhea, during which they posed a substantial risk to their communities and had a high probability of testing positive for Ebola virus in blood by

polymerase chain reaction (PCR). Although some patients tested positive on PCR within 24 hours after symptom onset, we found that a negative test result could not be relied on to rule out disease until 72 hours after symptoms began. Of the patients who tested positive for Ebola, none that we were aware of had contracted disease from an infected contact during the early febrile phase of illness. No ancillary testing was available in our facility.

We observed that recurrent episodes of emesis resulted in an inability to tolerate oral intake. Large volumes of watery diarrhea estimated at 5 or more liters per day (a manifestation not unlike that of cholera) presented suddenly, persisted for up to 7 days or (rarely) longer, and gradually tapered off. Associated signs and symptoms included asthenia,



Diagrams of ELWA 3 Ebola Management Center, Monrovia, Liberia.

Panel A shows the high-risk zone, and Panel B shows the complete center. Adapted from Médecins sans Frontières.

headache, conjunctival injection, chest pain, abdominal pain, arthralgias, myalgias, and hiccups. Respiratory symptoms, such as cough, were rare. Commonly observed neurologic symptoms included delirium, both hypoactive and hyperactive, manifested by confusion, slowed cognition, or agitation, and less frequently, seizures. In the absence of adequate fluid and electrolyte replacement, severe lethargy and prostration developed.

In approximately 60% of the

patients we cared for, the development of shock was manifested by diminished level of consciousness or coma, rapid thready pulses, oliguria or anuria, and tachypnea. The distal extremities were cold despite high ambient temperature, and peripheral vasoconstriction was apparent. In aggregate, these clinical findings suggested metabolic acidosis due to severe hypovolemic shock. Evidence of hyperdynamic or distributive shock was infrequently observed and if present was a

late finding. Clinically significant hemorrhage from the upper or lower gastrointestinal tract or both occurred in less than 5% of patients before death. Sudden death occurred in a small fraction of patients who were in the recovery phase of their illness, possibly as the result of fatal arrhythmias. Most deaths occurred between days 7 and 12 of illness.

Symptoms began to improve in approximately 40% of patients around day 10 of illness. We observed the development of oral ulcers and thrush around this time, associated with throat pain and dysphagia. Nearly all patients who survived to day 13 ultimately lived. Our discharge criteria included 3 days without gastrointestinal symptoms and a negative PCR test for Ebola virus in blood. We noted that some patients with initial evidence of clinical improvement developed neck rigidity and diminished levels of consciousness. These symptoms were associated with a slight increase in late mortality. The role of central nervous system involvement by EVD, secondary infection, or aseptic processes could not be assessed.

Particularly vulnerable patient populations included children less than 5 years of age, the elderly, and pregnant women. Of the four women who presented with late second- or third-trimester pregnancies, three died shortly after miscarrying, and none successfully carried a fetus to term. Four Liberian staff members became infected with Ebola virus, and three of them died. According to individual investigations, these infections were not attributable to any known breaches in infection-control procedures in the Ebola treatment unit; instead they are thought to be possibly

Clinical Features of Ebola Virus Disease.		
Phase of Illness	Time since Symptom Onset	Clinical Features
Early febrile	0–3 days	Fever, malaise, fatigue, body aches
Gastrointestinal	3–10 days	Primary: epigastric pain, nausea, vomiting, diarrhea Associated: persistent fever, asthenia, headache, conjunctival injection, chest pain, abdominal pain, arthralgias, myalgias, hiccups, delirium
Shock or recovery	7–12 days	Shock: diminished consciousness or coma, rapid thready pulse, oliguria, anuria, tachypnea Recovery: resolution of gastrointestinal symptoms, increased oral intake, increased energy
Late complications	≥10 days	Gastrointestinal hemorrhage, secondary infections, meningoencephalitis, persistent neurocognitive abnormalities*

* Secondary infections are presumptive diagnoses based on clinical features of distributive shock, oral or esophageal candidiasis, and oral ulcers; meningoencephalitis is a presumptive diagnosis based on clinical features of unconsciousness and stiff neck.

related to transmission in the community where the outbreak was active.

Health care workers in West Africa remain overwhelmed and challenged by the scarcity of resources that would be available in developed countries for improving the care of patients with EVD.⁴ When patients arrived at our facility, they were moderately to severely ill, and each physician was responsible for the care of 30 to 50 patients. Direct patient contact in the Ebola treatment center was typically limited to intervals of 45 to 60 minutes two to three times a day, owing to substantial heat exposure and fluid losses that providers experienced while wearing full personal protective equipment (PPE). Under these conditions, physicians had 1 to 2 minutes per patient to evaluate needs and establish a care plan.

Rapid clinical assessment required triage of patients into one of three categories: those who were clinically hypovolemic, not in shock, and able to provide self-care; those who were hypovolemic, not in shock, but unable to provide self-care; and those in shock with evidence of organ failure whose outcome would not

be altered by any available medical intervention. The majority of patients we cared for were in the first category. We believe that this group had the highest likelihood of having a response to our limited available interventions.

We observed that patients who were hypovolemic, not in shock, and able to care for themselves had potential for recovery with oral antiemetics, antidiarrheal therapy, and adequate rehydration with oral electrolyte solutions. Given the massive fluid losses observed with EVD, oral antiemetics and antidiarrheal therapy appear to be important early interventions that may limit life-threatening dehydration and shock. In our experience, these regimens were successful at controlling symptoms, facilitated oral intake, reduced gastrointestinal fluid losses, and helped to reduce environmental contamination by body fluids. Health care workers with limited time in PPE were then able to direct their efforts toward encouraging and facilitating oral intake.

It was our impression that the cohort of patients who were hypovolemic and not in shock but unable to provide self-care would benefit the most from short-term

intravenous fluid therapy and electrolyte replacement. Establishing intravenous access, delivering an adequate volume of fluid, and ensuring safe management of needles and devices required intensive individual-level patient care. Routine use of intravenous fluid therapy in our facility was prohibited by massive caseloads, limited number of health care workers, and limited time in PPE.

The central purpose of Ebola treatment units has historically been to isolate infected persons early in the course of disease — often soon after fever onset — in order to break the chain of disease transmission in the community. However, all efforts must be made to optimize the level of medical care provided within these facilities. Resistance by infected people to voluntary admission will persist unless the treatment facilities are seen as a place to go for treatment and recovery and not as a place to die isolated from loved ones and the community. Our observations support aggressive use of antiemetics, antidiarrheal medications, and rehydration solution to reduce massive gastrointestinal losses and the consequences of hypovolemic shock. Selective use of intrave-

nous fluid therapy in the population that is most likely to benefit is a rational approach under the current circumstances. When possible, broader use of intravenous fluid therapy and electrolyte replacement, guided by point-of-service laboratory testing, is likely to significantly improve outcomes.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

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