
Ebola virus disease Information for Clinicians in U.S. Healthcare Settings

The Centers for Disease Control and Prevention is working closely with the World Health Organization, state and local health departments, clinicians, and other partners to better understand and manage the public health risks posed by Ebola virus disease (EVD). As of October 30, 2014, five EVD patients have been evacuated from West Africa for further medical care, and two imported cases and two secondary cases of Ebola virus disease have been identified in the United States. The purpose of this document is to provide updated information about EVD to clinicians working in U.S. hospitals and health clinics.

Clinical Presentation and Clinical Course

Patients with EVD generally have abrupt onset of fever and symptoms typically 8 to 12 days after exposure (incubation period for current outbreak has a mean of approximately 9 to 11 days). Initial signs and symptoms are nonspecific and may include elevated body temperature or subjective fever, chills, myalgias, and malaise. Due to these nonspecific symptoms, particularly early in the course, EVD can often be confused with other more common infectious diseases such as malaria, typhoid fever, meningococemia, and other bacterial infections (e.g., pneumonia).

Patients can progress from the initial non-specific symptoms after about 5 days to develop gastrointestinal symptoms such as severe watery diarrhea, nausea, vomiting and abdominal pain. Other symptoms such as chest pain, shortness of breath, headache or confusion, may also develop. Patients often have conjunctival injection. Hiccups have been reported. Seizures may occur, and cerebral edema has been reported. Bleeding is not universally present but can manifest later in the course as petechiae, ecchymosis/bruising, or oozing from venipuncture sites and mucosal hemorrhage. Frank hemorrhage is less common; in the current outbreak unexplained bleeding has been reported from only 18% of patients, most often blood in the stool (about 6%). Patients may develop a diffuse erythematous maculopapular rash by day 5 to 7 (usually involving the neck, trunk, and arms) that can desquamate. Pregnant women may experience spontaneous miscarriages. The most common signs and symptoms reported from West Africa during the current outbreak from symptom-onset to the time the case was detected include: fever (87%), fatigue (76%), vomiting (68%), diarrhea (66%), and loss of appetite (65%).

Patients with fatal disease usually develop more severe clinical signs early during infection and die typically between days 6 and 16 of complications including multi-organ failure and septic shock (mean of 7.5 days from symptom-onset to death during the current outbreak in West Africa). In non-fatal cases, patients may

have fever for several days and improve, typically around day 6. Patients that survive can have a prolonged convalescence. The case fatality proportion among patients in West Africa with a known outcome is about 71% (ranges from 46% in Nigeria to 69-72% in Guinea, Sierra Leone and Liberia). Risk factors significantly associated with a fatal outcome in the affected countries in West Africa include, age >45 years old, unexplained bleeding, and a number of other signs and symptoms (diarrhea, chest pain, cough, difficulty breathing, difficulty swallowing, conjunctivitis, sore throat, confusion, hiccups, and coma or unconsciousness).

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Pathogenesis

Ebola virus enters the patient through mucous membranes, breaks in the skin, or parenterally and infects many cell types, including monocytes, macrophages, dendritic cells, endothelial cells, fibroblasts, hepatocytes, adrenal cortical cells and epithelial cells. The incubation period may be related to the infection route (e.g., 6 days for injection versus 10 days for contact). Ebola virus migrates from the initial infection site to regional lymph nodes and subsequently to the liver, spleen and adrenal gland. Although not infected by Ebola virus, lymphocytes undergo apoptosis resulting in decreased lymphocyte counts. Hepatocellular necrosis occurs and is associated with dysregulation of clotting factors and subsequent coagulopathy. Adrenocortical necrosis also can be found and is associated with hypotension and impaired steroid synthesis. Ebola virus appears to trigger a release of pro-inflammatory cytokines with subsequent vascular leak and impairment of clotting ultimately resulting in multi-organ failure and shock.

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Laboratory Findings

Laboratory findings at admission may include leukopenia frequently with lymphopenia followed later by elevated neutrophils and a left shift. Platelet counts are often decreased in the 50,000 to 100,000 range. Amylase may be elevated, reflecting pancreatic involvement (inflammation/infection). Hepatic transaminases are elevated with aspartate aminotransferase (AST) exceeding alanine aminotransferase (ALT); these values may peak at more than 1,000 IU/L. Proteinuria may be present. Prothrombin (PT) and partial thromboplastin times (PTT) are prolonged and fibrin degradation products are elevated, consistent with disseminated intravascular coagulation (DIC).

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Initial evaluation of patients known or suspected to have EVD

Patients known or suspected to have EVD presenting to healthcare settings should be placed in appropriate precautions as soon as possible to prevent transmission of Ebola virus to others. CDC infection control guidance is available at: <http://www.cdc.gov/vhf/ebola/hcp/infection-prevention-and-control-recommendations.html> (<http://www.cdc.gov/vhf/ebola/hcp/infection-prevention-and-control-recommendations.html>).

A Checklist for Patients Being Evaluated for EVD in the United States is available at:

<http://www.cdc.gov/vhf/ebola/pdf/checklist-patients-evaluated-us-evd.pdf>

(<http://www.cdc.gov/vhf/ebola/pdf/checklist-patients-evaluated-us-evd.pdf>)

An Algorithm for Evaluation of the Returned Traveler is available at:

<http://www.cdc.gov/vhf/ebola/pdf/ebola-algorithm.pdf> ([http://www.cdc.gov/vhf/ebola/pdf/ebola-](http://www.cdc.gov/vhf/ebola/pdf/ebola-algorithm.pdf)

[algorithm.pdf](http://www.cdc.gov/vhf/ebola/pdf/ebola-algorithm.pdf))

Additional information on evaluating patients for possible EVD is available at:

<http://emergency.cdc.gov/han/han00371.asp> (<http://emergency.cdc.gov/han/han00371.asp>)

Interim Guidance for Emergency Medical Services is available at:

<http://www.cdc.gov/vhf/ebola/hcp/interim-guidance-emergency-medical-services-systems-911-public-safety-answering-points-management-patients-known-suspected-united-states.html>

(<http://www.cdc.gov/vhf/ebola/hcp/interim-guidance-emergency-medical-services-systems-911-public-safety-answering-points-management-patients-known-suspected-united-states.html>)

Interim Guidance for Environmental Infection Control in Hospitals for Ebola Virus is available at:

<http://www.cdc.gov/vhf/ebola/hcp/environmental-infection-control-in-hospitals.html>

(<http://www.cdc.gov/vhf/ebola/hcp/environmental-infection-control-in-hospitals.html>)

Patients from countries currently affected by the Ebola outbreak who present with fever could have other potentially fatal infectious diseases that should be considered in the differential diagnosis, including but not limited to malaria, typhoid fever, and bacterial infections such as pneumonia. . Evaluation of febrile illness in a recent traveler should include a thorough travel and exposure history.

Additional information about fever in travelers returning from affected countries is available here:

<http://wwwnc.cdc.gov/travel/yellowbook/2014/chapter-5-post-travel-evaluation/fever-in-returned-travelers> (<http://wwwnc.cdc.gov/travel/yellowbook/2014/chapter-5-post-travel-evaluation/fever-in-returned-travelers>)

For information about malaria please see: http://www.cdc.gov/malaria/diagnosis_treatment/index.html

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Health care providers needing assistance with diagnosis or management of suspected cases of malaria should call the CDC Malaria Hotline:

770-488-7788 or 855-856-4713 toll-free (M-F, 9am-5pm, eastern time).

Emergency consultation after hours, call: 770-488-7100 and request to speak with a CDC Malaria Branch clinician.

Non-urgent questions can be emailed to: malaria@cdc.gov (<mailto:malaria@cdc.gov>)

Travelers from Ebola-affected countries are advised to self-monitor their health for 21 days after departure and to seek healthcare if fever and symptoms develop. Travelers with possible exposure to Ebola virus, for example in a healthcare setting, may need additional public health monitoring and movement controls depending on the risk of exposure and clinical presentation. Clinicians should contact the local or state health department to determine whether these measures are needed.

Additional information is available at:

<http://www.cdc.gov/vhf/ebola/hcp/monitoring-and-movement-of-persons-with-exposure.html>

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The current CDC definition for a person under investigation is available at [Case Definition for Ebola Virus Disease \(EVD\)](http://www.cdc.gov/vhf/ebola/hcp/case-definition.html) (<http://www.cdc.gov/vhf/ebola/hcp/case-definition.html>).

Currently a person under investigation for EVD is defined as illness in a person who has both consistent symptoms and risk factors as follows: 1) Clinical criteria, which includes elevated body temperature or subjective fever, and additional symptoms such as severe headache, muscle pain, vomiting, diarrhea, abdominal pain, or unexplained hemorrhage; AND 2) Epidemiologic risk factors within the past 3 weeks before the onset of symptoms, such as contact with blood or other body fluids of a patient known to have or suspected to have EVD; residence in—or travel to—an area where EVD transmission is active; participation in funeral and burial rituals, or direct handling of bats, rodents, or primates from disease-endemic areas.

Facilities evaluating a person under investigation should contact local or state health department for testing. Health departments should contact CDC EOC (770-488-7100) for testing and consultation.

All laboratory testing should be performed using appropriate laboratory safety guidance. For information regarding guidance of specimen collection, transport, testing and submission for patients with suspected infection with Ebola virus, please see: <http://www.cdc.gov/vhf/ebola/hcp/interim-guidance-specimen-collection-submission-patients-suspected-infection-ebola.html>

(<http://www.cdc.gov/vhf/ebola/hcp/interim-guidance-specimen-collection-submission-patients-suspected-infection-ebola.html>), and: <http://www.cdc.gov/vhf/ebola/pdf/ebola-lab-guidance.pdf>

(<http://www.cdc.gov/vhf/ebola/pdf/ebola-lab-guidance.pdf>) In general, laboratory testing should be kept

to the minimum as required for patient care.

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Treatment

There are no approved treatments available for EVD. Clinical management should focus on supportive care of complications, such as hypovolemia, electrolyte abnormalities, hematologic abnormalities, refractory shock, hypoxia, hemorrhage, septic shock, multi-organ failure, and DIC.

Recommended care includes volume repletion, maintenance of blood pressure (with vasopressors if needed), and maintenance of oxygenation, pain control, nutritional support, as well as treating secondary bacterial infections and pre-existing comorbidities. Among patients medically evacuated from West Africa with EVD, large volumes of intravenous fluids have often been required to correct dehydration due to diarrhea and vomiting. Some patients may develop profound third-spacing of fluids due to vascular leak. Some organizations have suggested the addition of broad-spectrum antimicrobials, particularly in patients with evidence of septic shock. Infection prevention and control measures are a critical part of clinical management – all bodily fluids and clinical specimens should be considered potentially infectious.

Several investigational therapeutics for Ebola virus disease are in development. For information about availability and access to investigational therapeutics, the manufacturers or the [Food and Drug Administration](http://www.fda.gov/CenterforDrugEvaluation/CDER/CDERHome.htm) (<http://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/ucm410308.htm>) should be contacted.

Some information on the clinical features and clinical management for patients with Ebola virus disease in the U.S. at the University of Nebraska Medical Center and Emory University Hospital is available from a COCA call on [October 20, 2014](http://emergency.cdc.gov/coca/calls/2014/callinfo_102014.asp) (http://emergency.cdc.gov/coca/calls/2014/callinfo_102014.asp).

In addition, information on Ebola management is available from [The University of Nebraska Medical Center](http://www.nebraskamed.com/biocontainment-unit/ebola) (<http://www.nebraskamed.com/biocontainment-unit/ebola>) and [Emory University Hospital](http://www.emoryhealthcare.org/ebola-protocol/ehc-message.html) (<http://www.emoryhealthcare.org/ebola-protocol/ehc-message.html>). Canadian guidance on clinical management of Ebola virus disease patients is available from the [Canadian Critical Care Society](http://cccsnew.businesscatalyst.com/website/Guidelines/Ebola%20Clinical%20Care%20Guidelines-2014-10-28.pdf) (<http://cccsnew.businesscatalyst.com/website/Guidelines/Ebola%20Clinical%20Care%20Guidelines-2014-10-28.pdf>).

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Vaccines

There are no approved vaccines available for EVD. Several investigational Ebola vaccines are in development, and Phase I trials are underway for some vaccine candidates.

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(<http://www.cdc.gov/Other/plugins/#pdf>)

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Viral Special Pathogens Branch (VSPB) (</ncezid/dhcpp/vspb/index.html>)