

## Clinical Providers Guide to Ebola Virus Disease

**Purpose:** Information for medical providers regarding the Ebola virus outbreak.

### Clinical Presentation and Clinical Course

- Patients with EVD generally have abrupt onset of symptoms typically 8-10 days after exposure (range 2-21 days). Initial signs and symptoms are nonspecific and may include fever, chills, myalgias, and malaise. Fever, anorexia, asthenia/weakness are the most common signs and symptoms. Patients may develop a diffuse erythematous maculopapular rash by day 5 to 7 (usually involving the face, neck, trunk, and arms) that can desquamate.
- Due to nonspecific nature of these symptoms, particularly early in the course, EVD can often be confused with other more common infectious diseases such as influenza, malaria, typhoid fever, meningococemia, and other bacterial infections (e.g., pneumonia).
- After about 5 days of non-specific symptoms patients can develop gastrointestinal signs such as severe watery diarrhea, nausea, vomiting and abdominal pain. Chest pain, shortness of breath, and headache or confusion may also develop. Conjunctival injection is often present. Seizures may occur, and cerebral edema has been reported. Bleeding is not universally present but can manifest later in the course as petechiae, ecchymoses, oozing from venipuncture sites and mucosal hemorrhage. Frank hemorrhage is less common. Pregnant women may experience spontaneous miscarriages.
- Patients with fatal disease usually develop more severe clinical signs early during infection and die typically between days 6 and 16, usually of multi-organ failure and septic shock. In non-fatal cases, patients may have fever for several days before improving, typically around days 6-11. Survivors can require prolonged convalescence. The World Health Organization has estimated the mortality of the current outbreak of EVD in West Africa to be approximately 55%, but appears to be as high as 75% in Guinea, likely related to the limitations in supportive care due to an inadequate or immature healthcare infrastructure.

### Pathogenesis

- Ebola virus can enter 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 (i.e., 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 can occur and is associated with dysregulation of clotting factors and a subsequent coagulopathy. Adrenocortical necrosis also can also be found and is associated with hypotension and impaired steroid synthesis.

- Ebola virus appears to trigger a release of pro-inflammatory cytokines, and it is the subsequent vascular leak and impairment of clotting which are ultimately felt to be responsible for multi-organ failure and shock.

### 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 into the 50,000 to 100,000 range.
- Amylase may be elevated, reflecting pancreatic involvement (inflammation/infection). Hepatic transaminases are often elevated, with aspartate aminotransferase (AST) exceeding alanine aminotransferase (ALT). Proteinuria may be present. Disseminated intravascular coagulation (DIC) is suggested by elevated Prothrombin (PT) and partial thromboplastin times (PTT) and the presence of fibrin degradation products.

### Initial evaluation of patients known or suspected to have EVD

- Patients known or suspected to have EVD should be placed in appropriate precautions as soon as possible in order to prevent transmission of Ebola virus to others. Refer to <http://www.cdc.gov/vhf/ebola/hcp/infection-prevention-and-control-recommendations.html> for guidance.
- Patients from countries currently affected by the Ebola outbreak who present with fever should have other potentially fatal infectious diseases 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.
- 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. Movement controls depending on the risk of exposure and clinical presentation.
- **Case Definition:** Illness in a person who has both:
  - 1) Clinical criteria, which includes
    - fever of greater than 38.6 degrees Celsius or 101.5 degrees Fahrenheit, and
    - additional symptoms such as severe headache, muscle pain, vomiting, diarrhea, abdominal pain, or unexplained hemorrhage; AND
  - 2) Epidemiologic risk factors within the 3 weeks prior to 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 for EVD infected persons;
    - direct handling of bats, rodents, or primates from disease-endemic areas.

- All laboratory testing should be performed using appropriate laboratory safety guidance. For information regarding proper 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>. In general, laboratory testing should be kept to the minimum required for patient care.

## Treatment

- There are no approved treatments available for EVD. Clinical management should focus on supportive care of complications, such as hypovolemia, electrolyte 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), maintenance of oxygenation, pain control, nutritional support, and treatment of secondary bacterial infections and pre-existing comorbidities.
- 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 and vaccines for Ebola are in development. For information about availability and access to investigational therapeutics, the manufacturers or the Food and Drug Administration should be contacted.

## Web Resources:

- Ebola Hemorrhagic Fever - <http://www.cdc.gov/vhf/ebola/index.html>
- Personal Protective Equipment – <http://www.cdc.gov/vhf/ebola/pdf/ppe-poster.pdf>
- Air Medical Transport Guidance – <http://www.cdc.gov/vhf/ebola/hcp/guidance-air-medical-transport-patients.html>
- Infographics & Illustrations – <http://www.cdc.gov/vhf/ebola/outbreaks/guinea/print-resources-illustrations.html>
- Outbreak Map - <http://www.cdc.gov/vhf/ebola/resources/distribution-map-guinea-outbreak.html>
- Case Definition - <http://www.cdc.gov/vhf/ebola/hcp/case-definition.html>
- World Health Organization - <http://www.afro.who.int/>