November 2014 Ebola Virus Disease

Pan American Health Organization

World Health Organization Regional Office for the Americas

Information for Healthcare Providers
Ebola Virus Disease (EVD)

Background

Ebola virus disease (EVD), formerly known as Ebola hemorrhagic fever, is a severe, often fatal illness. There are no proven effective treatment options, other than supportive care. EVD has the potential for human-to-human transmission. Human-to-human transmission of the Ebola virus is primarily associated with direct or indirect contact with blood and body fluids.

Clinical manifestations

Presentation and acute disease

Recognizing EVD from the early nonspecific symptoms is challenging. It is essential to obtain a careful epidemiological history. The incubation period typically lasts 8 to 10 days, although it can be as short as 2 days and as long as 21 days. While there is distinction between early and late clinical signs of EVD, it is important to remember that patients may present at different times in the course of their illness. Severity of illness may depend on a number of factors including the body's natural immune response, mode of transmission, duration of exposure, infecting dose, phase of illness of the case, and possibly even the virus strain. Thus, front-line health workers should have a high level of suspicion for EVD in patients who follow the case definitions, even when their clinical presentation is mild.

EVD usually begins with fever and profound weakness, often accompanied by myalgia, headache, anorexia, chills, and hiccups. These are usually followed by signs and symptoms that indicate multisystem involvement and include systemic (prostration), gastrointestinal (anorexia, nausea, vomiting, abdominal pain, diarrhea), respiratory (chest pain, shortness of breath, cough, nasal discharge), vascular (conjunctival injection, postural hypotension, edema), and neurological (headache, confusion, coma) manifestations. Hemorrhagic manifestations can arise during the peak of the illness and include petechiae, ecchymosis, and uncontrolled oozing from venipuncture (See Figure). Despite a common belief that hemorrhage is a defining feature of EVD, visible bleeding is not universal. Abdominal pain is sometimes associated with hyperamylasemia and pancreatitis. In later stages, shock, convulsions, severe metabolic disturbances, and, in more than half the cases, diffuse coagulopathy supervene.

Figure – Clinical features in EVD

Note: There is often an overlap of early and late symptoms. Patients often do not develop all the signs and symptoms. Adapted from Chertow et al (9) Note that some patients can be afebrile (up to 13%) (5)

Outcome

The cumulative case fatality rate of the current outbreak is 37%. A documented fever (temperature, >38°C [100.4°F]), weakness, dizziness, and diarrhea on presentation were associated with a fatal outcome. Lethality is higher in adults older than 45 years old (OR 2.47 CI 1.79-3.46) (5).

Considering that the Introduction of EVD in the Americas is possible, the management of viral hemorrhagic fever patients poses a range of unique challenges due to the severity of the diseases, the risks to health staff, and the often negative reactions of the local communities. Specific treatment is not available, and there is no vaccine. This publication comprises the experience of experts as published in a number of WHO and PAHO/WHO guidelines

Initial evaluation: identify, isolate and inform

The diagnosis of EVD is based on 3 components:

1. **History of exposure**

Any acutely ill person presenting with the history of visiting transmission areas or exposure to EVD in the previous 21 days should be considered a suspect case. Unfortunately an exposure history is not always clear (e.g. poor recollection of interpersonal contacts, reluctance to discuss travel history).

2. **Compatible clinical presentation**

3. **Laboratory testing** (refer to Table)

Symptomatic individuals known or suspected to have EVD presenting to healthcare settings should be placed in appropriate isolation as soon as possible to prevent transmission of Ebola virus.

Local and national health authorities should be informed about suspect or confirmed EVD cases

Differential diagnosis

The non-specific signs and symptoms early in the course of EVD render it difficult to differentiate it from other infectious diseases on clinical grounds alone. Differential diagnosis depends on area of acquisition of infection and epidemiological history, and may include:

(1) **Malaria**
(2) **Leptospirosis**
(3) **Typhoid fever**
(4) **Meningococcal sepsis**
(5) **Rickettsial diseases**
(6) **Shigellosis**
(7) **Other viral hemorrhagic fevers**: Hantavirus hemorrhagic fever, yellow fever, dengue hemorrhagic fever.

EVDs may also mimic intra abdominal surgical emergencies.

Laboratory diagnosis

In the absence of effective intervention strategies, diagnosis becomes a key element in our response to Ebola virus infection. Ebola viruses are classified as Risk Group 4 Pathogens, requiring Laboratory Biosafety Level 4-equivalent containment for viral isolation and manipulation. Therefore, laboratory diagnosis for EVD should be done in international reference centers. Laboratory diagnosis of Ebola virus is achieved in two ways: specific detection of nucleic acids by RT-PCR and serologic measurement of immune responses by IgM/IgG detection. The confirmation of EVD is through any of the tests mentioned in the Table). If a negative PCR is obtained early in the clinical course, a second test should be done at least 48h later. Isolation measures should be maintained while waiting for the final result.

General laboratory test results are unspecific, such as leucopenia, thrombocytopenia and transaminase elevation. Electrolytes and pH could be monitored for clinical management maintaining all biosafety measures.

Table - Laboratory tests for EVD

Test	Timing after illness
• **RT-PCR**	Day 3- 16
• **IgM antibody assay**	Day 5 - 1 month
• **IgG or neutralizing antibody assay showing rising titers**	Day 10 – years Two samples separated by 14 days, where first sample is collected after day 7

Clinical management

As until the diagnosis of EVD is ruled out, no microbiology diagnostic test can be performed, therefore, empiric treatment of the most probable infections (such as malaria) should be started as can be lifesaving. Present treatment strategies are mainly symptomatic and supportive. These strategies should include **aggressive fluid and electrolyte replacement**, malaria treatment, broad spectrum antibiotics, and antipyretics before diagnosis. Fluid substitution, preferentially intravenous administration, and analgesics should be provided as needed. In health-care systems with appropriate isolation units, proper intensive care treatment might be advised and should be directed towards maintenance of effective blood volume and electrolyte balance. Shock, cerebral edema, renal failure, coagulation disorders, and secondary bacterial infection have to be managed and can be life-saving. Organ failure should be addressed appropriately—. At present, no strategy has proved successful in specific pre-exposure and post-exposure treatment of Ebola virus infections in man.

There is no specific antiviral drug against EVD, although there is ongoing research on bricidofovir, faviparix or use of convalescent serum. Human convalescent blood or serum has been used as passive immunization to treat patients.

Principles for clinical management

• Case management is based on supportive and IPC measures.
• Supportive treatment should be instituted in all suspect cases without waiting for serological or viral confirmation. Treatment should alleviate the following symptoms:

- Fever
- Bleeding, severe pallor circulatory shock
- Pain
- Difficulty breathing/respiratory distress
- Vomiting, diarrhea, dehydration
- Dyspepsia
- Convulsions
- Signs of hypoglycemia
- Anxiety
- Confusion

In general, treatment should include:

1) Aggressive fluid and electrolyte replacement. Ensure adequate hydration and electrolytic reposition, including glucose 5%. In case that using an i.v. line cannot be possible, two subcutaneous lines can be used with a maximum perfusion rate of 14 drops/ min.
2) Empiric treatment against malaria, typhoid fever or other probable infectious diseases until diagnostic.
3) Analgesics, avoid non-steroidal anti-inflammatory drugs.

Special considerations in pregnancy and for breastfeeding women

EVD has a direct impact on pregnancy with high frequency of spontaneous abortions and higher frequency of severe bleeding than general population

Breastfeeding can transmit EVD from lactating mothers to their babies, therefore must be avoided.

Special considerations for children

Observations in this Ebola epidemic regarding children and adolescents are in agreement with previous findings that the pediatric population is relatively spared. Less than 10% of laboratory confirmed cases were in children and adolescents under 18 years of age. Clinical manifestations were similar to previous Ebola epidemics. Children under the age of five were at an increased risk of contact with sick and dying Ebola parents.

Infection prevention and control

The isolation of patients and use of strict barrier nursing procedures, such as personal protective equipment have been sufficient to rapidly interrupt transmission in hospital settings in rural Africa.

Transmission to health-care workers has been reported when appropriate infection control measures have not been observed. Health care workers must comply rigorously with the IPC measures. In separate documents issues such as PPE and IPC measures will be addressed in detail (7). Availability of adequate PPE should be granted to ensure the clinical management of the patient.

References

1. World Health Organization. Clinical Management of Patients with Viral Hemorrhagic Fever: A Pocket Guide for the Front-line Health Worker. Geneva, 2014. http://www.who.int/entity/csr/resources/publications/clinical-management-patients/en/index.html
2. Pan American Health Organization / World Health Organization. Preparedness and Response for introduction of Ebola virus disease (EVD) in the Americas. Washington, D.C.: PAHO/WHO, 2014. http://www.paho.org/hq/index.php?option=com_docman&task=doc_download&Itemid=&gid=27454&lang=en
3. Feldmann, H and G, Eisbert TW. Ebola Hemorrhagic Fever. Lancet vol 377, pp 849 – 862, 2011.
4. CDC. Information for Clinicians. http://www.cdc.gov/vhf/ebola/index.html
5. Schieffelin JS, Shaffer JG, Goba A, et al. Clinical illness and outcomes in patients with Ebola in Sierra Leone. N Engl J Med. DOI: 10.1056/NEJMoa1411680
6. World Health Organization. Interim Infection Prevention and Control Guidance for Care of Patients with Suspected or Confirmed Filovirus Haemorrhagic Fever in Health-Care Settings, with Focus on Ebola. Geneva, 2014. http://apps.who.int/iris/bitstream/10665/130596/1/WHO_HIS_SDS_2014.4_eng.pdf?ua=1&ua=1&ua=1
7. World Health Organization. Personal Protective Equipment in the Context of Filovirus Disease Outbreak Response. Rapid advice guideline. October 2014. http://apps.who.int/iris/bitstream/10665/137410/1/WHO_EVD_Guidance_PPE_14.1_eng.pdf
8. WHO response team. Ebola virus disease in West Africa--the first 9 months of the epidemic and forward projections N Engl J Med., 2014 Oct 16;371(16):1481-95.
9. Chertow D S, Kleine C, Edwards J K , M.D, et al. Virus Disease in West Africa — Clinical Manifestations and Management. NEJM, DOI: 10.1056/NEJMp1413084