Ebola Haemorrhagic Fever*

Created Dates

Case Definition	March 2015
Reporting Requirements	December 2014
Remainder of the Guideline (i.e., Etiology to References sections inclusive)	December 2014

Case Definition

Confirmed Case[1]

Laboratory confirmation of Ebola virus infection using at least one of the methods below:

- Isolation and identification of virus from an appropriate clinical specimen (e.g., blood, serum, tissue, urine specimens or throat secretions) (performed at the National Microbiology Laboratory);

OR

- Detection of virus-specific RNA by reverse-transcriptase PCR from an appropriate clinical specimen (e.g., blood, serum, tissue) using two independent targets or two independent samples and confirmed by the National Microbiology Laboratory by nucleic acid testing or serology;

OR

- Demonstration of virus antigen in tissue (e.g., skin, liver or spleen) by immunohistochemical or immunofluorescent techniques AND another test e.g., PCR;

OR

- Demonstration of specific IgM AND IgG antibody by EIA, immunofluorescent assay or Western Blot by the National Microbiology Laboratory or an approved WHO collaboration centre;

OR

- Demonstration of seroconversion or a fourfold rise in IgG serum antibody by EIA, immunofluorescent assay or Western Blot from an acute vs a convalescent serum sample (performed at the National Microbiology Laboratory).

Probable Case[2]

Any suspect case evaluated by a clinician, or any deceased suspect case with:

- an epidemiologic link to a confirmed case of EVD

AND

- where it is not possible to collect specimens for laboratory confirmation.

***Denotes potential bioterrorism agent.**

Suspect Case (Person Under Investigation)(1)

A person with clinical illness [1] AND at least one of the following epidemiologic risk factors within the 21 days before the onset of symptoms in whom EVD has not been ruled out:

- Residence in or travel to an area where EVD transmission is active,
- Sexual contact with a probable or confirmed EVD case,
- Health care worker[2] and/or household carer[2], who directly or indirectly cared for a probable or confirmed case of EVD (e.g., direct patient care or contact with environment or fomites of a case),
- Household member of a probable or confirmed case of EVD,
- Close contact in a community setting with a probable or confirmed case of EVD while the person was symptomatic, (Close contact is defined as being for a prolonged period of time within 2 meters of a confirmed or probable case.)
- Laboratory worker who processed body fluids or tissues of a probable or confirmed EVD case,
- Direct exposure to human remains (e.g., through participation in funeral or burial rites) in a geographic area where an EVD outbreak is occurring,
- Direct exposure to human remains of a probable or confirmed EVD case,
- Direct contact with bats, primates or wild bush meat from an EVD-affected country, or
- Other suspicious contacts identified by Public Health.

[1] Clinical illness: an individual presenting with at least one of the following symptoms:

- elevated body temperature
- subjective fever
- malaise
- myalgia
- headache
- arthralgia
- fatigue
- loss of appetite
- conjunctival redness
- sore throat
- chest pain
- abdominal pain
- nausea
- vomiting
- diarrhea that can be bloody
- bleeding not related to injury
- hemorrhage
- erythematous maculopapular rash on the trunk

[2] Healthcare workers: defined as individuals who provide health care or support services, such as nurses, physicians, dentists, nurse practitioners, paramedics, some emergency first responders, allied health professionals, unregulated healthcare providers, clinical instructors and students, volunteers and housekeeping staff; have varying degrees of responsibility related to the health care they provide, depending on their level of education and their specific job/responsibilities. Household carers perform similar functions but in non-health care settings.

Reporting Requirements

1. **Physicians, Health Practitioners and others**
   A physician, health practitioner or person in charge of an institution shall in accordance with Sections 22(1) and 22(2) of the *Public Health Act*, notify the Medical Officer of Health (MOH)(or designate) of the health zone, of all confirmed, probable and suspect cases by the Fastest Means Possible (FMP) i.e., direct voice communication.

2. **Laboratories**
   All laboratories, including the National Microbiology Laboratory (NML) and the Provincial Laboratory for Public Health (ProvLab), shall in accordance with Section 23 of the *Public Health Act,* report all laboratory results for Ebola virus tests including negatives by FMP i.e., direct voice communication to the:
   - Chief Medical Officer of health (CMOH) (or designate),
   - Zone MOH (or designate) and
   - Attending/ordering physician.

3. **Alberta Health Services and First Nations and Inuit Health Branch (FNIHB)**
   - The MOH (or designate) of the zone where the case currently resides shall notify the CMOH (or designate) of all confirmed, probable and suspect cases by the FMP i.e., direct voice communication.
   - For in-zone Alberta resident cases:
     - The MOH (or designate) of the zone where the case currently resides shall forward the preliminary Public Health Agency of Canada's *Ebola Case Report Form* of all confirmed, probable and suspect cases to the CMOH (or designate) immediately upon notification.
       - Updated forms should be sent to the CMOH (or designate) when more information becomes available.
     - The MOH (or designate) of the zone where the case currently resides shall forward the preliminary *Notifiable Disease Report* (NDR) of all confirmed and probable cases to the CMOH (or designate) within one week of notification and the final NDR (amendment) within two weeks of notification.
   - For out-of-zone Alberta resident cases:
     - The MOH (or designate) first notified shall notify the MOH (or designate) of the zone where the client currently resides by FMP i.e., direct voice communication and then follow up with either mail, fax or electronic transfer of a copy of the positive laboratory report.
   - For out-of-province and out-of-country non-Alberta resident cases:
     - For non-Alberta residents, where the infection was likely acquired within Alberta, the MOH (or designate) of the zone shall forward the preliminary NDR of all confirmed cases to the CMOH (or designate) within one week of notification and the final NDR (amendment) within two weeks of notification.
     - For non-Alberta residents, where the infection was likely acquired outside Alberta, the following information should be forwarded to the CMOH (or designate) by phone, fax or electronic transfer within 48 hours (two days) including:
       - name,
       - date of birth,
       - out-of-province health care number,
       - out-of-province address and phone number,
       - attending physician (locally and out-of-province) and
       - positive laboratory report (faxed).

4. Additional Reporting Requirements

- The zone MOH (or designate) shall notify the CMOH by FMP i.e., direct voice communication where there is a suspicion of an exposure of concern.
- In the case of an exposure of concern (e.g., intentional release), the CMOH will notify the Alberta Security and Strategic Intelligence Support Team (ASSIST) Duty Officer at 780-644-2680 and Alberta Health Emergency Preparedness on Call at ahweoc@gov.ab.ca.

Etiology

Ebola haemorrhagic fever, also Ebola virus disease (EVD), is caused by *ebolavirus* and is a member of the Filoviridae family. There are five species of Ebola based on where it was discovered:[3-5]

- Zaire ebolavirus (EBOV),
- Sudan ebolavirus (SUDV),
- Tai Forest ebolavirus (TAFV),
- Bundibugyo ebolavirus (BDBV) and
- Reston ebolavirus (RESTV).

Clinical Presentation

EVD is a severe, acute viral illness that is characterized by abrupt onset of fever, malaise, myalgia and headache followed by pharyngitis, vomiting, and diarrhea.[6,7] Other symptoms that have been reported include chest pain, cough, lymphadenopathy, photophobia, and conjunctival injection. About 50% of cases develop a maculopapular rash on the trunk within 5 days of symptom onset. About 5 – 7 days after symptoms onset, 40 – 50% of cases will develop bleeding manifestations (e.g., mucous membrane hemorrhages, hematemesis, bloody diarrhea, oozing of blood at puncture sites).[8]

Central nervous system findings include psychosis, delirium, coma, seizures.[3,9-15] Shock (with DIC and end-organ failure) often ensues during second week of illness. Massive bleeding occurs late in the clinical course in fatal cases. Other complications include illness-induced abortion among pregnant women, hearing loss, orchitis, pericarditis, suppurative parotitis, unilateral vision loss and migratory arthritis. If recovery doesn't occur then death will occur in 7 – 16 days due to multiple organ dysfunction syndrome.

If recovery occurs, convalescence may be complicated by the occurrence of myelitis, recurrent hepatitis, psychosis or uveitis.[16]

The case fatality rate of EVD varies by species:[17]

- Ebola-Zaire, 36 – 90%
- Ebola-Sudan, 41 – 71%
- Ebola-Tai Forest, only one case who survived
- Ebola-Bundibugyo, 25 - 51%
- Ebola-Reston, 0% (not known to cause clinical disease in humans)

Diagnosis

Any and all laboratory testing of a suspected EVD case should be done in consultation with the Zonal MOH and the Virologist/Microbiologist on call. The decision for specimen collection and testing should be based on the epidemiological risk factor(s) and clinical status of the patient. The collection, handling, transport and analysis should strictly follow the procedures outlined in *AHS Laboratory Services Ebola Laboratory Strategy*.[18]

The diagnosis of EVD can be confirmed by one or more of the following diagnostic markers: (i) presence of virus-specific RNA by RT-PCR, (ii) isolation of virus and (iii) presence of virus-specific antibodies.[17] Currently PT-PCR is the first line test for diagnosing EVD.

As Ebola virus may not be detectable in blood within the first three days after the onset of fever, virus isolation and RT-PCR tests may be negative if testing is done before this 3 day threshold. To reliably rule out EVD, repeat testing three days after onset of fever should be considered.[15,18]

Similar to the Ebola RT-PCR and virus isolation tests, the antibody response in Ebola specific serology tests will likely not be present very early post-fever onset. However detection of Ebola specific antibodies in an affected patient is considered to be a good prognostic indicator for successful recovery.

Ebola RT-PCR testing is available at ProvLab, a containment level 3 facility. Positive Ebola RT-PCR results from ProvLab require confirmation from NML. Negative Ebola RT-PCR results from ProvLab should be assessed in the overall clinical and epidemiologic context of a particular case for a decision as to whether the patient should be removed from isolation or not. The MOH-clinical-lab team may make this decision prior to receipt of a confirmatory Ebola negative result from NML.

No virus culture should be attempted outside of NML, a containment level 4 laboratory.

Epidemiology

Reservoir

The natural reservoir of *ebolavirus* is thought to be forest-dwelling fruit bats as viral RNA has been found in 3 bat species in central Africa.[7] Bats are also a likely candidate as a reservoir because the virus has been shown to be non-lethal to them. Four of the five subtypes in Africa have been found in animal hosts native to Africa. The fifth subtype, Ebola-Reston, is more likely associated with an animal host (pig, primate) from the Philippines.[19]

Transmission[7,17]

- The first patient tends to become infected through contact with the blood, secretions, organs or other bodily fluids of an infected animal.
- Further transmission can happen in several ways:
  - Person-to-person transmission via direct contact with the blood, secretions, organs or other bodily fluids of infected people,
  - Indirect contact via objects, such as needles, that have been contaminated with infected secretions,
  - Burial ceremonies where mourners have direct contact with the body of the deceased person can also play a role in the transmission of Ebola.[17]

Incubation Period

Symptoms take between 2 – 21 days to appear, usually 4 – 9 days.[5,20]

Period of Communicability

Cases are not considered to be communicable before the onset of symptoms. From the onset of symptoms, communicability increases as the severity of illness progresses and the case remains communicable as long as blood and body fluids contain the virus. This includes the post-mortem period.

A confirmed case of EVD is considered not be infectious to the community once their clinical condition improves significantly, they are free of fever, diarrhea, vomiting, coughing and bleeding for three or more days and they have 2 confirmed negative blood PCR tests 48 hours apart, with at least one test being done 3 days or more after onset of symptoms.[15,21,22]

Viral shedding is known to occur in the semen of male cases during the convalescence stage. Live virus has been isolated in seminal fluid up to 82 days after illness onset.[23] For this reason male cases should abstain from sexual intercourse for 15 weeks after the date of symptom onset.[24]

Host Susceptibility

All ages are susceptible.[7] Case mortality tends to be higher in pregnant women, younger children, individuals with pre-existing immunodeficiencies and certain gene alleles (B*67 and B*15).[25-27] In the current outbreak in West Africa, a sharp increase in mortality in infected individuals over 40 years of age, even in the absence of co-existing conditions, has been observed.[28] Many fatalities are due to dehydration caused by gastrointestinal symptoms.[29]

It is not known why some people recover from EVD while others do not.

Low levels of baseline seropositivity have been demonstrated in outbreak areas indicating prior immunity and cross-reactivity between different Ebola subtypes has been documented.[30,31]

Occurrence

General

EVD occurs mainly in areas surrounding rainforests in central Africa.[5] There have been a number of outbreaks in several African countries over the past few decades, some being notable for their high mortality rates. Beginning in March 2014, an outbreak of Ebola has been reported in several Western African countries and it has become the largest outbreak since Ebola was first identified in 1976.[17]

Canada

EVD is nationally notifiable in Canada. There has never been a case reported in Canada.

Alberta

EVD is notifiable in Alberta. There has never been a case reported in Alberta.

Key Investigation

Single case/cluster

- Confirm that the diagnosis meets the Alberta Health confirmed case definition.
- Review clinical presentation and history to determine possible source of infection of the case.
- Investigate possible exposures during the 21 days before onset, including a history of:[24]
  - Residence in or travel to an area where EVD transmission is active,
  - HCW/personnel, patient or visitor who spent time in a setting where EVD confirmed cases are being assessed or cared for,
  - Household member of a confirmed EVD case,
  - Laboratory worker who has processed body fluids or tissues of a confirmed EVD case,
  - Direct exposure to human remains of a confirmed EVD case,
  - Direct exposure to any human remains (e.g., through participation in funeral or burial rites) in a geographic area where an EVD outbreak is occurring,
  - Direct contact with bats, primates or other wild animals from EVD-affected country,[5,25]
  - Any other direct or indirect exposure to a confirmed case.
- Identify Close Contacts of the case of EVD:
  - A Close Contact is defined as an individual with one or more of the following high risk exposures:[24]
    - who, since the patient's symptom onset, has provided care to the patient (including a HCW, family member, friend, funeral worker, or volunteer), or who has had other close physical contact with the patient or deceased body, that may have resulted in

unprotected exposure to blood or body fluids from the patient directly or indirectly through contaminated surfaces or equipment;

OR

- who has worked in a laboratory handling specimens from EVD patients and may have had unprotected exposure to these specimens through the course of their work.

- Identify any contact with animals since symptom onset.

Note: *If a close contact, when first identified, is found to have clinical evidence of EVD illness that developed within 21 days following the last close contact with the case, the individual should be managed as a probable case.*

Control

Management/Treatment of a Case

- Upon identification of an individual meeting the suspect or probable case definition, provide the individual with information as required and in consultation with the local MOH, regarding when, where and how (e.g. mode of transport) to go for medical assessment and instruct the individual to report travel history or epidemiological risk factor(s) immediately upon presenting to a health care setting. The health care facility should be notified prior to the arrival of the individual so that the facility can ensure appropriate infection prevention and control measures are in place to safely assess the individual.
- Strict enhanced contact and droplet precautions as outlined by the Public Health Agency of Canada in Infection Prevention and Control Expert Working Group: Advice on Infection Prevention and Control Measures for Ebola Virus Disease in Healthcare Settings apply until EVD is ruled out for a suspect or probable case or until the clinical condition of a confirmed case improves significantly and the case is free of fever, diarrhea, vomiting, coughing and bleeding for three or more days and has had two confirmed negative blood PCR tests 48 hours apart, with at least one test being done 3 days or more after onset of symptoms.[21,22,32]
- Where possible, aerosol-generating medical procedures (AGMPs) should not be performed on suspected, probable or confirmed cases of EVD. Fit tested N95 respirator masks must be worn when performing AGMPs and these procedures ideally are best performed in negative pressure rooms. Potential AGMPs include:[33]
  - Endotracheal intubation,
  - Bronchoscopy,
  - Airway suctioning,
  - Positive pressure ventilation via face mask,
  - High frequency oscillatory ventilation,
  - Central line insertion, or
  - Diagnostic sputum induction.
- Implement a buddy system for healthcare personnel when caring for suspect, probable and confirmed EVD cases and when donning and doffing PPE.
- Conduct active daily monitoring of suspect, probable and confirmed cases for duration of illness or until laboratory investigation has ruled out EVD. Update and submit the *PHAC Ebola Case Report Form* to Alberta Health when new information is available.
- Currently there are no approved antiviral treatments for EVD. However new experimental treatments are being developed and evaluated.[7,17,28]
- Supportive care, including aggressive fluid intake of at least 4 liters per day, maintenance of fluid and electrolytes, mechanical ventilation, dialysis and treatment of secondary infections, is important for the management of confirmed cases.[34]
- Anticoagulant therapies, aspirin, non-steroidal anti-inflammatory medications, and intramuscular injections are contraindicated.[34]

- Environmental terminal decontamination of the residence and community facilities visited by a confirmed case while he/she was symptomatic must be ordered for cases identified in the community as per the Section 35 of the *Public Health Act*.
- Management of a convalescent confirmed case should be done on a case by case basis in consultation with an infectious disease specialist and Public Health. The management should include counselling on the risk of transmission of EVD through body fluids such as semen. Abstinence from sexual contact should be strongly advised for at least 15 weeks following onset of illness.[24]

Deceased Cases[35,36]

- All remains of deceased confirmed cases of EVD must be handled in accordance with Alberta's *Bodies of Deceased Persons Regulation*.
- Only personnel trained in handling infected deceased persons, and wearing appropriate PPE for enhanced contact precautions should touch or move any Ebola infected deceased person. In addition, facial protection may be considered if splash with body fluid is anticipated. PPE should be donned before contact with the body, worn during the process of placement in body bag and should be removed immediately after and discarded as regulated medical waste.
- Contact with a deceased person with EVD should be kept to a minimum.
  - At the site of death, the body should be labeled in accordance with the *Bodies of Deceased Persons Regulation*. Any intravenous lines or endotracheal tubes should be left in place. The body should not be sprayed, washed or embalmed. It should be placed in a leak proof plastic body bag in a way that prevents contamination of the outside of the bag and zippered shut.
  - Once zippered shut the body bag should not be opened. The bagged body should be placed in a hermetically sealed container as soon as practically possible after death, preferably at the site of death. The hermetically sealed container must be labeled in accordance with the *Bodies of Deceased Persons Regulation*.
  - Once the body is removed from the site of death, the site of death must be cleaned and disinfected.
  - The body may not be viewed as the hermetically sealed container must not be opened.
  - Cremation is preferable. If that is not possible, the body should be buried in the hermetically sealed container promptly.[17,36]
  - Transportation of remains should be minimized as much as possible. Vehicles used for transporting the body should be cleaned and disinfected in accordance with the *Bodies of Deceased Persons Regulation*.
  - Autopsies should be avoided. If an autopsy is necessary it should involve extensive consultation with the Autopsy team, Public Health and IPC. Aerosol-generating procedures (such as bone sawing) should be avoided during autopsies if possible. Otherwise, N95 respirator masks and negative-pressure rooms should be used.[37,38]

Management of Close Contacts

- Due to the severity of EVD and the lack of treatment, a robust public health response to identify close contacts of confirmed EVD cases must occur promptly.
- A close contact is defined as an individual:
  - who, since the onset of symptoms, has provided care to a confirmed case or who has had other close physical contact with the case or deceased body, that may have resulted in exposure to blood or other body fluids from the case. This may include but not be limited to healthcare worker, family member, funeral worker, friend or volunteer;

OR

  - who has had contact with surfaces or equipment contaminated with blood or body fluids of a confirmed case;

  OR

  - who has worked in a laboratory handling specimens from confirmed cases and may have had exposure to these specimens through the course of their work.
- All close contacts should monitor or be monitored twice a day for 21 days from last close contact with the confirmed case for the development of fever or other EVD symptoms.
- All close contacts must be:
  - Assessed to determine the risk of the exposure.
  - Assessed for symptoms of EVD. If the contact is found to have clinical evidence of EVD illness that developed within 21 days following last close contact with the confirmed case, the individual should be managed as a probable case.
  - Educated on the signs and symptoms of EVD as well as how to measure body temperature accurately.
  - Advised not to take any antipyretic medication during the 21 day monitoring period if possible.
  - Advised should a fever or other symptoms develop during the 21 day monitoring period, to self-isolate immediately and call public health for further direction.
- Management of close contacts and the specifics of the quarantine applied must be based on assessed risk and is at the discretion of the local MOH. Based on the risk of the exposure and expected compliance with recommendations, the specifics of the quarantine may include daily active monitoring, direct active monitoring, restrictions on air travel and/or other public conveyances, movement in the community, participation in community congregate activities and/or restrictions to a specific location such as contact's home or facility, with the minimum being daily active monitoring (i.e., phone call by Public Health to contact) to ensure self-monitoring is being performed twice a day and a notification requirement for travel outside of their zone.
- Close contacts should be advised to avoid visiting farms with livestock for the 21 day monitoring period.
- Close contacts who possess companion pets should be encouraged to find alternative housing for them for the 21 day monitoring period.
- There is no licensed prophylaxis or vaccine available for protection against EVD.[3,17,39]

Management of Animal Contacts

- When contact with animals (companion or livestock) is identified for a confirmed case, the Public Health Veterinarian must be consulted to perform a risk assessment and implement measures as required.

Management of Travelers Returning from Ebola Affected Areas

- Should local Public Health or Alberta Health become aware of a returning traveler from an Ebola affected area (through the traveler contacting Public Health through their own initiative, or as ordered by Quarantine Officers (QO)), the following should occur:
  - If by QO, the QO will notify the CMOH and local MOH (or designate).
  - If notified by the traveller, the local MOH (or designate) will notify the CMOH
  - The local MOH or designate shall conduct a risk assessment, including confirmation of travel and exposure history and symptom inquiry, as soon as possible. Based on this risk assessment the MOH will determine how best to manage the traveler.
  - If the traveler is symptomatic or if in the opinion of the MOH, the traveler needs to be isolated in a facility for further assessment, the MOH shall ensure isolation (and

testing/treatment as required) takes place and the CMOH (or designate) is informed by FMP.
    - If the traveler is asymptomatic, the MOH, based on assessed risk and expected compliance with recommendations, may order the traveler to self-monitor twice a day for fever and other EVD symptoms and to report to local Public Health on a regular basis for 21 days from departure from an Ebola affected area. The MOH, at their discretion and in consultation with the CMOH, may apply additional measures.
    - The MOH shall require the traveler to report any planned travel during the 21 day monitoring period to local Public Health
    - The MOH (or designate) shall ensure travelers are provided with information on the signs and symptoms of EVD and instructions on what to do if symptoms develop including immediate self-isolation.

Airline Travel[40]

- There is no evidence to support the transmission of EVD in airplanes by asymptomatic passengers. However passengers infected while visiting Ebola affected areas could arrive while incubating the disease and develop symptoms compatible with EVD after arrival.
- The risk of transmission with an infected symptomatic passenger is low in the early stages of symptoms and increases with the later stages of the disease with increasing viral titers and increased viral shedding.[20]
- The risk assessment of possible transmission of EVD on an aircraft by a symptomatic passenger should be undertaken on a case-by-case basis through discussion between the CMOH and the local MOH.
    - This should take into account information on the clinical status of the index case, the epidemic situation of the country where the index case most likely acquired the infection, the possible exposure of the index case and how long the event has been detected after the flight.
- It is recommended that passenger trace back be undertaken only if the index case had symptoms during the flight and the flight was within 21 days after potential exposure.
    - The trace back should only be done after confirmation of the infected passenger in conjunction with the assistance of the Quarantine Officers;
    - Passengers and crew with direct contact, seat neighbours (at a minimum +/− 1 seat), crew and cleaning personnel of the section of the plane where the infected passenger was seated should be included in the trace back, even if exposure to body fluids was not reported.[20,40]

Preventive Measures

- There is no vaccine or prophylaxis currently licensed for the prevention of EVD. Several experimental vaccines have been developed and are currently being trialed.
- Educate travelers to foreign countries on the following:
    - Signs and symptoms of EVD,
    - What to do if considering travel abroad: PHAC Travel Health Notices.

Resources

- Alberta Health: Ebola
- Alberta Health Services (AHS): Ebola
- Public Health Agency of Canada (PHAC): Ebola
- Centers for Disease Control and Prevention (CDC): Ebola
- World Health Organization (WHO): Ebola

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