Ministry of Health and Long-Term Care

Infectious Diseases Protocol

Appendix A: Disease-Specific Chapters

Chapter: Hemorrhagic fevers caused by: i) Ebola virus and ii) Marburg virus, iii) Lassa Fever, and (iv) Other viral causes including bunyaviruses, arenaviruses and flaviviruses

Effective: February 2019

Ontario

Hemorrhagic fevers caused by: i) Ebola virus and ii) Marburg virus iii) Lassa Fever, and (iv) Other viral causes including bunyaviruses, arenaviruses and flaviviruses

☒ Communicable

☒ Virulent

Health Protection and Promotion Act:
O. Reg. 135/18 (Designation of Diseases)

1.0 Aetiologic Agent

Viruses from several distinct families can cause viral hemorrhagic fever (VHF). They are all ribonucleic acid (RNA) viruses, and are all enveloped in a fatty lipid coating. The Ebola and Marburg viruses, are two antigenically distinct **filoviruses**. In Africa, 4 different subtypes of the Ebola virus have been associated with human illness. Members of other viral families causing VHF include **bunyaviruses** (hantaviruses, Crimean Congo hemorrhagic fever viruses, Rift Valley fever virus), **arenaviruses** (Lassa virus, Lujo virus, Guanarito, Machupo, Junin, and Sabia viruses) and **flaviviruses** (Yellow Fever virus, Dengue virus, Kyasanur Forest virus, Omsk virus).[1]

2.0 Case Definition

2.1 Surveillance Case Definition

Refer to Appendix B for Case Definitions.

2.2 Outbreak Case Definition

The outbreak case definition varies with the outbreak under investigation. Please refer to the *Infectious Diseases Protocol, 2018* (or as current) for guidance in developing an outbreak case definition as needed.

The outbreak case definitions are established to reflect the disease and circumstances of the outbreak under investigation. The outbreak case definitions should be developed for each individual outbreak based on its characteristics, reviewed during the course of the outbreak, and modified if necessary, to ensure that the majority of cases are captured by the definition. The case definitions should be created in consideration of the outbreak definitions.

Outbreak cases may be classified by levels of probability (*i.e.* confirmed and/or probable).

3.0 Identification

3.1 Clinical Presentation

Viral hemorrhagic fevers are associated with an acute onset of fever, severe illness and hemorrhagic symptoms including hemorrhagic or purpuric rash, epistaxis, hematemesis, hemoptysis, blood in stool and other hemorrhagic symptoms.[2]

In severe and fatal forms, the hemorrhagic diathesis is often accompanied by hepatic damage, renal failure, central nervous system (CNS) involvement and terminal shock with multi-organ dysfunction.[3]

In the case of dengue fever, clinical presentation is mild in comparison to dengue hemorrhagic fever including fever, headache, myalgia, bone pain, macular or maculopapular rash, nausea and vomiting.[3] Whereas cases of dengue hemorrhagic fever are reportable, cases of dengue fever without identified hemorrhagic manifestations are not reportable.

In cases of Lassa fever about 80% of human infections are mild or asymptomatic and the remaining have severe multisystem disease. Patients present with malaise, fever, headache, sore throat, cough, nausea, vomiting, diarrhea, myalgia, and chest and abdominal pain.[3]

3.2 Diagnosis

See Appendix B for diagnostic criteria relevant to the Case Definitions.

For further information about human diagnostic testing, contact the Public Health Ontario Laboratories or refer to the Public Health Ontario Laboratory Services webpage: http://www.publichealthontario.ca/en/ServicesAndTools/LaboratoryServices/Pages/default.aspx

Note: Any testing related to suspect VHF should be carried out under level 4 containment facilities (National Microbiology Laboratory) due to issues of safety, security, expertise, and personnel vaccination.

4.0 Epidemiology

4.1 Occurrence

Viral hemorrhagic fevers are not endemic to Ontario and to date no cases have been reported.

Ebola has been isolated in Sudan, Democratic Republic of Congo, Uganda, Cotê d'Ivoire, Gabon, Uganda, Guinea, Liberia, Sierra Leone and Nigeria. Marburg has been isolated in Uganda, South Africa, Kenya, Democratic Republic of Congo and Angola.[3]

Dengue virus transmission is endemic in most countries located in the tropics and subtropics. In dengue endemic areas, transmission occurs year-round with peak disease incidence usually occurring during the rainy season and in areas of high *Aedes aegypti* prevalence.[3]

Lassa fever is endemic to Guinea, Liberia, regions of Nigeria and Sierra Leone.[3]

Please refer to Public Health Ontario's (PHO) Reportable Disease Trends in Ontario reporting tool and other reports for the most up-to-date information on infectious disease trends in Ontario.

http://www.publichealthontario.ca/en/DataAndAnalytics/Pages/DataReports.aspx

For additional national and international epidemiological information, please refer to the Public Health Agency of Canada (PHAC) and the World Health Organization.

4.2 Reservoir

Fruit bats in Africa are believed to be the reservoir for Ebola and Marburg infections. Forest-dwelling fruit bats, multiple species are the source of Ebola viruses and cave-dwelling fruit bats, specifically the *Rousettus aegyptiacus* species are believed to be the reservoir for Marburg viruses.[3]

For dengue fever, in tropical urban centres, a cycle between humans and *Aedes Aegypti* mosquito sustains the viruses. It is also thought that in South-East Asia and West African forest the reservoir for the viruses is a monkey/mosquito cycle.[3]

For Lassa fever, rodents in the genus *Mastomys,* in Africa, are the reservoir.[3]

4.3 Modes of Transmission

Filovirus infection is believed to occur from inadvertent exposure to infected bat excreta or saliva following entry into roosting areas. Nonhuman primates, especially gorillas and chimpanzees, and other wild animals may become infected from bat contact and serve as intermediate hosts that transmit filoviruses to humans through contact with their blood and bodily fluids, usually associated with hunting and butchering.[4]

For Ebola and Marburg, person to person transmission occurs by direct contact with infected blood, urine, vomit, diarrhea, secretions, organs or semen. Risk is highest during the late stages of illness when the infected person is vomiting, having diarrhea or haemorrhaging and post-mortem contact with bodily fluids. Risk during the asymptomatic incubation period is low.[3] Filoviruses are not spread through the air or by water.[4] Nosocomial infections have been frequent; virtually all patients who acquired infection from contaminated syringes and needles have died.[3]

For dengue hemorrhagic fever, no direct person to person spread; persons are infective for mosquitoes (principally *Aedes Aegypti*, similar to the malaria cycle) from shortly before the febrile period to the end thereof, usually 3-5 days. The mosquito becomes infective 8-12 days after the viremic blood-meal and remains so for life.[3]

For Lassa fever, primarily through aerosol or direct contact with excreta of infected rodents deposited on surfaces such as floors, beds or in food and water. It can also be spread person to person through sexual contact and in hospitals from infected persons' pharyngeal secretions, blood, or urine or from contaminated needles, or in laboratory accidents.[3]

4.4 Incubation Period

Ebola and Marburg virus diseases: Probably 5 to 15 days.[3]

Dengue: From 3-14 days, commonly 4-7 days.[3]

Lassa: Commonly 6-21 days.[3]

4.5 Period of Communicability

Ebola and Marburg are communicable as long as blood and secretions contain virus. Ebola virus was isolated from seminal fluid on the 61st day after onset of illness in a laboratory acquired case.[3]

For dengue hemorrhagic fever, patients are infective for mosquitoes during their period of viremia, from shortly before, until the end of the febrile period. The mosquito becomes infective 8-12 days after the viremic blood-meal and remains so for life.[3] There is no person-person transmission of dengue.

For Lassa fever, person to person spread may theoretically occur during the acute febrile phase when virus is present in secretions and excretions. Virus can be excreted in urine for 3-9 weeks from onset of illness and can be spread by sexual contact through semen for up to 3 months after infection.[3]

4.6 Host Susceptibility and Resistance

All ages are susceptible.[3]

Recovery from infection with one dengue virus serotype provides lifelong homologous immunity but only short-term protection against other serotypes and may exacerbate disease upon subsequent infections potentially leading to Dengue *Hemorrhagic* Fever (as opposed to Dengue Fever).[3]

5.0 Reporting Requirements

As per Requirement #3 of the "Reporting of Infectious Diseases" section of the *Infectious Diseases Protocol, 2018* (or as current), the minimum data elements to be reported for each case are specified in the following:

- *Ontario Regulation 569* (Reports) under the *Health Protection and Promotion Act* (HPPA);[5]
- The iPHIS User Guides published by PHO; and
- Bulletins and directives issued by PHO.

6.0 Prevention and Control Measures

6.1 Personal Prevention Measures

The PHAC recommends travelers in areas with Ebola avoid direct contact with blood or bodily fluids of a person or corpse infected with the Ebola virus. Also, avoid contact with or handling an animal suspected of having Ebola hemorrhagic fever.[6]

Check travel health notices for specific recommendations:

http://www.phac-aspc.gc.ca/tmp-pmv/notices-avis/index-eng.php

Basic personal measures to prevent mosquito bites are strongly recommended in terms of dengue/Dengue Hemorrhagic Fever prevention.[3]

6.2 Infection Prevention and Control Strategies

Public Health response will be under the direction of provincial and federal jurisdiction.

Refer to PHO's website at www.publichealthontario.ca to search for the most up-to-date information on Infection Prevention and Control.

For Lassa fever additional strategies include:

- Strict droplet and contact precautions for hospitalized cases and negative pressure room with door closed and airborne precautions if case has pneumonia.[3]

6.3 Management of Cases

In addition to the requirements set out in the Requirement #2 of the "Management of Infectious Diseases – Sporadic Cases" and "Investigation and Management of Infectious Diseases Outbreaks" sections of the *Infectious Diseases Protocol, 2018* (or as current), the board of health shall investigate cases to determine the source of infection. Refer to Section 5: Reporting Requirements above for relevant data to be collected during case investigation.

Clinical management of VHF and Dengue Hemorrhagic Fever (DHF), in the latter especially if complicated by dengue shock syndrome, would be the responsibility of medical specialists such as infectious disease specialist.

6.4 Management of Contacts

Contacts of DHF are not at-risk, given the absence of person-person transmission.[3]

For Ebola, Marburg and Lassa fever contacts include: people living with, caring for, testing laboratory specimens from or having close/intimate contact with the case, in the three weeks after the onset of illness.[3] Establish close surveillance of contacts including taking body temperature twice daily for three weeks after last exposure and if temperature above 38.3 °C or 101 °F, hospitalize immediately while following the infection prevention and control measures described above. Determine contacts place of residence during 3 weeks prior to onset and search for unreported or undiagnosed cases.[3]

6.5 Management of Outbreaks

Please see the *Infectious Diseases Protocol, 2018* (or as current) for the public health management of outbreaks or clusters in order to identify the source of illness, manage the outbreak and limit secondary spread.

Given the severity and rarity of hemorrhagic fevers, a single confirmed case constitutes an outbreak.

7.0 References

1. Centers for Disease Control and Prevention. Viral Hemorrhagic Fevers (VHFs) [Internet]. Atlanta, GA: U.S. Department of Health & Human Services 2014 [updated January 29, 2014; cited August 10, 2018]. Available from: https://www.cdc.gov/vhf/index.html
2. World Health Organization, Department of Communicable Disease Surveillance and Response. WHO Recommended Surveillance Standards. 2nd ed. Geneva: World Health Organization; 1999. Available from: http://www.who.int/csr/resources/publications/surveillance/WHO_CDS_CSR_ISR_99_2_EN/en/
3. Heymann DL, editor. Control of Communicable Diseases Manual. 20 ed. Washington, D.C: American Public Health Association; 2015.
4. Committee on Infectious Diseases, American Academy of Pediatrics. Section 3: Summaries of Infectious Diseases: Hemorrhagic Fevers Caused By Filoviruses - Ebola and Marburg. In: Kimberlin DW, Brady MT, Jackson MA, Long SS, editors. Red Book: 2018 Report of the Committee on Infectious Diseases. 31 ed. Itasca, IL: American Academy of Pediatrics; 2018.
5. Health Protection and Promotion Act, R.S.O. 1990, Reg. 569, Reports, (2018). Available from: https://www.ontario.ca/laws/regulation/900569
6. Government of Canada. Ebola virus disease: Prevention and risks [Internet]. Ottawa, ON: Her Majesty the Queen in Right of Canada; 2018 [updated July 19, 2018; cited August 10, 2018]. Available from: https://www.canada.ca/en/public-health/services/diseases/ebola/prevention-ebola.html

8.0 Document History

Table 1: History of Revisions

Revision Date	Document Section	Description of Revisions
May 2014	Document Title	Document title updated from “Disease: Hemorrhagic fevers, including: i) Ebola virus disease; ii) Marburg virus disease, and iii) Other viral causes” to “Disease: Hemorrhagic fevers caused by: i) Ebola virus and ii) Marburg virus and iii) Other viral causes including bunyaviruses, arenaviruses and flaviviruses.”
May 2014	1.0 Aetiologic Agent	Entire section updated.
May 2014	2.2 Outbreak Case Definition	Entire section updated.
May 2014	3.1 Clinical Presentation	Entire section updated.
May 2014	3.2 Diagnosis	Deleted “Diagnosis is usually through a combination of laboratory tests…” Deleted “Refer to the Ontario VHF Contingency Plan, 2002 for specific information on diagnostic testing.”
May 2014	4.1 Occurrence	Addition of second and third paragraphs.
May 2014	4.2 Reservoir	First paragraph, second sentence changed from “In Africa, human index cases have been linked to monkeys, chimpanzees, gorillas, duikers, and porcupines and other animals found dead in the rain forests” to “In Africa, human index cases have been linked to exposure to monkeys, chimpanzees, gorillas, duikers, and porcupines and other animals found dead or killed in the rain forests.” Second paragraph updated.
May 2014	4.3 Modes of Transmission	First paragraph, “Ebola” and “Marburg” changed to “ebola” and “marburg”. First paragraph, second sentence, addition of “…and post-mortem contact with bodily fluids.” Second paragraph, “Ebola” changed to “ebola”. Deletion of “For Dengue, bite of infective mosquitoes…” Addition of last paragraph “For dengue hemorrhagic fever, no direct…”

Revision Date	Document Section	Description of Revisions
May 2014	4.5. Period of Communicability	First paragraph, first sentence, addition of “Ebola and Marburg are communicable” at the beginning of the sentence. Addition of second paragraph. Deletion of “For dengue fever, no direct person to person spread…”
May 2014	4.6 Host Susceptibility and Resistance	Addition of “Host” to section title. Second sentence changed from “Recovery from infection with one serotype…” to “Recovery from infection with one dengue virus serotype…” Second sentence, addition of “leading to Dengue Hemorrhagic Fever (as opposed to Dengue Fever)” at the end of the sentence.
May 2014	5.1 To local Board of Health	Entire section updated.
May 2014	5.2 To the Ministry of Health and Long-Term Care (the Ministry) or Public Health Ontario (PHO), as specified by the Ministry	Section title updated. First paragraph changed from “The board of health shall notify the PHD of the MOHLTC…” to “The board of health shall notify PHO immediately…” Second paragraph, changed from “Report only case classifications specified in the case definition to PHD” to “Report only case classifications specified in the case definition” Addition of last paragraph.
May 2014	6.1 Personal Prevention Measures	Entire section updated.
May 2014	6.2 Infection Prevention and Control Strategies	Entire section updated.
May 2014	6.3 Management of Cases	Entire section updated.
May 2014	6.4 Management of Contacts	Entire section updated.
May 2014	6.5 Management of Outbreaks	Deletion of “Refer to the Ontario VHF Contingency Plan.”
May 2014	7.0 References	Updated.
May 2014	8.0 Additional Resources	Updated.

Revision Date	Document Section	Description of Revisions
February 2019	General	Minor revisions were made to support the regulation change to Diseases of Public Health Significance, including merging Lassa Fever into the chapter. Common text included in all Disease Specific chapters: Surveillance Case Definition, Outbreak Case Definition, Diagnosis, Reporting Requirements, Management of Cases, and Management of Outbreaks. The epidemiology section and references were updated and Section 8.0 Additional Resources was deleted.
February 2019	1.0 Aetiologic Agent	Added: “They are all ribonucleic acid (RNA) viruses, and are all enveloped in a fatty lipid coating.” Updated to 4 different subtypes of the Ebola virus have been associated with human illness.
February 2019	4.2 Reservoir	Reservoir for Ebola and Marburg updated.
February 2019	4.3 Modes of Transmission	Modes of transmission for Ebola and Marburg updated.
February 2019	4.4 Incubation Period	Incubation period for Ebola and Marburg updated.
February 2019	6.4 Management of Contacts	Entire section updated.


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