21-ID-04

Committee: Infectious Disease

Title: Update to Public Health Reporting and National Notification of Viral Hemorrhagic Fever (VHF) caused by Ebola or Marburg viruses, Old World arenaviruses (Lassa and Lujo viruses), New World arenaviruses (Guanarito, Machupo, Junin, Sabia, and Chapare viruses), or Crimean-Congo hemorrhagic fever virus

☒Check this box if this position statement is an update to an existing standardized surveillance case definition and include the most recent position statement number here: _10-ID-19__.

Synopsis:
This position statement recommends updating the Viral Hemorrhagic Fever case definition by modifying the fever threshold to ≥38ºC, adding Chapare virus, and amending the epidemiologic linkage criteria for sexual exposure to semen by removing time period around source case's illness onset.

I. Statement of the Problem

Viral Hemorrhagic Fever (VHF), caused by filoviruses (Ebola and Marburg viruses), Old World arenaviruses (Lassa virus and Lujo viruses), New World arenaviruses (Guanarito, Machupo, Junin, Sabia, and Chapare viruses), or Crimean Congo hemorrhagic fever virus, was added to the Nationally Notifiable Condition list in June of 2009. The 2010 position statement defined fever as a core body temperature >40ºC. Following domestic transmission of Ebola virus in 2014, CDC amended the fever threshold to ≥38ºC/100.4ºF. In 2019, investigation of viral hemorrhagic fever cases in Bolivia were determined to be caused by Chapare virus and human-to-human transmission of the virus was documented for the first time[1]. Additionally, Ebola virus has been found to persist in the semen of EVD patients after clinical recovery for longer than 10 weeks of onset of illness. This position statement recommends: 1) modifying the fever threshold to ≥38ºC/100.4ºF, 2) adding Chapare virus to those reportable under this position statement, and 3) amending the epidemiologic linkage criteria for sexual exposure within the past 3 weeks to semen from a confirmed acute or clinically recovered case of VHF to remove the stipulated time period of exposure within 10 weeks of the VHF case's onset of illness.

II. Background and Justification

Background

Viral hemorrhagic fevers (VHFs) refer to a group of illnesses that are caused by several families of viruses, including filoviruses (Ebola and Marburg viruses), Old World arenaviruses (Lassa and Lujo viruses), New World arenaviruses (e.g. Guanarito, Machupo, Junin, Sabia, and Chapare viruses), and Crimean Congo hemorrhagic fever virus. This position statement proposes three key updates to the previous 10-ID-19 position statement on VHFs: 1) modify the definition for fever from >40ºC to ≥38ºC/100.4ºF, 2) add Chapare virus, a re-emerging New World arenavirus, to those reportable under this position statement, and 3) amend the epidemiologic linkage criteria for exposure within the past 3 weeks to semen from a confirmed acute or clinically recovered case of VHF to remove the stipulated time period of exposure within 10 weeks of the VHF case's onset of illness.

Justification

The fever threshold set in the previous position statement defined fever as a core body temperature >40ºC. In 2014, following domestic transmission of Ebola virus in the United States, CDC amended the fever threshold for Ebola and other viral hemorrhagic fevers to ≥38ºC/100.4ºF for increased sensitivity. In 2017, 42 Code of Federal Regulations parts 70/71 was amended to define fever for nationally notifiable diseases as ≥38ºC/100.4ºF.

In 2003, a cluster of hemorrhagic fever was reported in a rural area of Bolivia. Clinical specimens were available for only one fatal case for whom epidemiologic data were limited. Chapare virus, a novel New World arenavirus and cause of Chapare hemorrhagic fever (CHHF)[2], was identified as the causative agent. No cases of CHHF were reported until 2019, when an investigation of hemorrhagic fever cases involving healthcare workers determined the cause to be Chapare virus, and human-to-human transmission of the virus was documented for the first time[1]. Clinically, CHHF presents similarly to other VHFs[3]. The case fatality rate of this outbreak was 60% (3/5), with secondary and tertiary transmission occurring among healthcare workers[1]. Laboratory testing identified a possible rodent reservoir with large geographic distribution[1], raising concern for future outbreaks and highlighting a need for heightened awareness among clinicians and increased surveillance for Chapare virus and other causes of VHFs in the region.

Ebola virus can persist in the semen in EVD patients after clinical recovery. Ebola virus has been detected in seminal fluid of an EVD survivor by rRT-PCR up to 3.3 years after onset of disease and cultured from semen as long as 82 days after illness onset. In additional, sexual transmission of Ebola virus by EVD survivors has been documented[4-7]. In three instances, the time from clinical recovery of the survivor to the time they transmitted the virus sexually to a partner was 5 months[4], 11 months[8], and 17 months[6]. Therefore, it is prudent to amend the epidemiologic linkage criteria for "exposure within the past 3 weeks to semen from a confirmed acute or clinically recovered case of VHF" by removing the time period of exposure "within 10 weeks of onset of illness."

III. Statement of the desired action(s) to be taken

CSTE recommends the following actions:

1. Implement a standardized surveillance case definition for viral hemorrhagic fever.
    A. Utilize standard sources (e.g. reporting*) for case ascertainment for viral hemorrhagic fever. Surveillance for viral hemorrhagic fever should use the recommended sources of data to the extent of coverage presented in Section V.

    B. Utilize standardized criteria for case ascertainment for viral hemorrhagic fever presented in Section VI and Table VI in Technical Supplement.

    C. Utilize standardized criteria for case classification for viral hemorrhagic fever presented in Section VII and Table VII in Technical Supplement.

2. Utilize standardized criteria for case ascertainment and classification (based on Sections VI and VII and Technical Supplement) for Viral Hemorrhagic Fever and **update** Viral Hemorrhagic Fever on the *Nationally Notifiable Condition List*
    ☒ Immediately notifiable, extremely urgent (within 4 hours) only when intentional release is suspected as the cause of infection
    ☒ Immediately notifiable, urgent (within 24 hours)
    ☐ Routinely notifiable
    ☐ No longer notifiable

3. CSTE recommends that all States and Territories enact laws (statute or rule/regulation as appropriate) to make this disease or condition reportable in their jurisdiction. Jurisdictions (e.g. States and Territories) conducting surveillance (according to these methods) should submit case notifications** to CDC.

4. Expectations for Message Mapping Guide (MMG) development for a newly notifiable condition: the National Notifiable Diseases Surveillance System (NNDSS) is transitioning to HL7-based messages for case notifications; the specifications for these messages are presented in MMGs. When CSTE recommends a new condition be made nationally notifiable, CDC must obtain Office of Management and Budget Paperwork Reduction Act (OMB PRA) approval prior to accepting case notifications for the new condition. Under anticipated timelines, notification using the Generic V2 MMG would support transmission of the basic demographic and epidemiologic information common to all cases and could begin with the new *MMWR* year following the CSTE annual

conference. Input from CDC programs and CSTE would prioritize development of a disease-specific MMG for the new condition among other conditions waiting for MMGs.

5. CDC should publish data on Viral Hemorrhagic Fever as appropriate (see Section IX).

   CSTE recommends the following case statuses be included in the CDC Print Criteria:

   ☒Confirmed
   ☐Probable
   ☒Suspect
   ☐Unknown

6. CSTE recommends that all jurisdictions (e.g. States, Localities, or Territories) with legal authority to conduct public health surveillance follow the recommended methods outlined in this recommendation and in the accompanying standardized surveillance position statement.

   *Reporting: process of a healthcare provider or other entity submitting a report (case information) of a condition under public health surveillance TO local, state, or territorial public health.
   **Notification: process of a local or state public health authority submitting a report (case information) of a condition on the *Nationally Notifiable Conditions List* to CDC.

IV. Goals of Surveillance

To provide information on the temporal, geographic, and demographic occurrence of viral hemorrhagic fever to facilitate its prevention and control.

V. Methods for Surveillance: Surveillance for viral hemorrhagic fever should use the recommended sources of data and the extent of coverage listed in Table V.

Table V. Recommended sources of data and extent of coverage for ascertainment of cases of viral hemorrhagic fever.

Source of data for case ascertainment	Coverage	
	Population-wide	Sentinel sites
Clinician reporting	X	
Laboratory reporting	X	
Reporting by other entities, specify: hospitals	X	
Death certificates	X	
Hospital discharge or outpatient records	X	
Data from electronic medical records	X	
Telephone survey		
School-based survey		
Other, specify:		

VI. Criteria for case ascertainment

A. Narrative: A description of suggested criteria for case ascertainment of a specific condition.

A1. Clinical Criteria for Reporting

A person with epidemiologic risk factor(s)* with the following clinical findings:

- Fever ≥38°C/100.4°F
  AND
- One or more of the following clinical findings:
  - severe headache
  - muscle pain

- erythematous maculopapular rash on the trunk with fine desquamation 3–4 days after rash onset
- vomiting
- diarrhea
- abdominal pain
- bleeding not related to injury
- thrombocytopenia
- pharyngitis (Arenavirus only)
- proteinuria (Arenavirus only)
- retrosternal chest pain (Arenavirus only)

** Clinical criteria must be paired with epidemiologic linkage criteria to trigger a report to public health.*

A2. Laboratory Criteria for Reporting

A person for whom a diagnostic test specific for VHF** has been ordered.

***VHF refers to viral hemorrhagic fever caused by either Ebola or Marburg viruses, Old World arenaviruses (Lassa and Lujo viruses), New World arenaviruses (Guanarito, Machupo, Junin, Sabia, and Chapare viruses), or Crimean-Congo hemorrhagic fever virus.*

A3. Epidemiologic Linkage Criteria for Reporting

A person with clinically compatible symptoms* with one or more of the following epidemiologic risk factors:

- contact within the past 3 weeks with blood or other body fluids of a patient with VHF
- residence in—or travel within the past 3 weeks to—a VHF endemic area or area with active transmission
- work within the past 3 weeks in a laboratory that handles VHF specimens
- work within the past 3 weeks in a laboratory that handles bats, rodents, or primates from a VHF endemic area or area with active transmission
- sexual exposure within the past 3 weeks to semen from a confirmed acute or clinically recovered case of VHF

** Epidemiologic linkage criteria must be paired with clinical criteria to trigger a report to public health.*

A4. Vital Records Criteria for Reporting

- A person whose death certificate lists VHF (i.e., Ebola, Lassa, Marburg, Lujo, New World arenavirus (Guanarito, Machupo, Junin, Sabia, and Chapare viruses), or Crimean-Congo hemorrhagic fever viruses) as a cause of death or a significant condition contributing to death.

Other recommended reporting procedures

- All cases (suspected or confirmed) of viral hemorrhagic fever should be reported.
- Reporting should be on-going and routine.
- Reporting should be immediate.

B. Disease-specific data elements to be included in the initial report

Epidemiologic:

- contact within the past 3 weeks with blood or other body fluids of a patient with VHF
- residence in—or travel within the past 3 weeks to—a VHF endemic area or area with active transmission
- work within the past 3 weeks in a laboratory that handles VHF specimens

- work within the past 3 weeks in a laboratory that handles bats, rodents, or primates from a VHF endemic area or area with active transmission
- sexual exposure within the past 3 weeks to semen from a confirmed acute or clinically recovered case of VHF

VII. Case Definition for Case Classification

A. Narrative: Description of criteria to determine how a case should be classified.

A1. Clinical Criteria

An illness with acute onset of:

- Fever ≥38°C/100.4°F
  AND
- One or more of the following clinical findings:
  - severe headache
  - muscle pain
  - erythematous maculopapular rash on the trunk with fine desquamation 3–4 days after rash onset
  - vomiting
  - diarrhea
  - abdominal pain
  - bleeding not related to injury
  - thrombocytopenia
  - pharyngitis (Arenaviruses only)
  - proteinuria (Arenaviruses only)
  - retrosternal chest pain (Arenaviruses only)

A2. Laboratory Criteria

Any one of the following:

- Detection of VHF* viral antigens in blood by ELISA.
- VHF viral isolation in cell culture for blood or tissues.
- Detection of VHF-specific genetic sequence by RT-PCR from blood or tissues.
- Detection of VHF viral antigens in tissues by immunohistochemistry.

** VHF refers to viral hemorrhagic fever caused by either Ebola or Marburg viruses, Old World arenaviruses (Lassa and Lujo viruses), New World arenaviruses (Guanarito, Machupo, Junin, Sabia, and Chapare viruses), or Crimean-Congo hemorrhagic fever virus.*

A3. Epidemiologic Linkage

One or more of the following exposures **within the 3 weeks before onset of symptoms**:

- Contact with blood or other body fluids of a patient with VHF
- Residence in—or travel to—a VHF endemic area or area with active transmission
- Work in a laboratory that handles VHF specimens
- Work in a laboratory that handles bats, rodents, or primates from a VHF endemic area or area with active transmission
- Sexual exposure to semen from a confirmed acute or clinically recovered case of VHF

A4. Case Classifications

Confirmed: Meets laboratory criteria.

Probable: N/A

Suspect: Meets clinical criteria AND epidemiologic linkage criteria.

B. Criteria to distinguish a new case of this disease or condition from reports or notifications which should not be enumerated as a new case for surveillance
A new case of VHF should be enumerated only if not previously counted as a case of VHF caused by the same virus as determined by laboratory evidence.*

**Among the VHFs included in this position statement, reinfection with the same virus species has not been documented. There is a theoretical possibility that a VHF (ex. Ebola) survivor could be infected by a virus that causes one of the other VHFs included in this position statement (ex. Lassa fever, Crimean-Congo hemorrhagic fever, etc.).*

VIII. Period of Surveillance

Surveillance should be ongoing.

IX. Data sharing/release and print criteria

CSTE recommends the following case statuses* be included in the 'case' count released outside of the public health agency:

☒Confirmed
☐Probable
☒Suspect
☐Unknown

* Which case statuses are included in the case counts constitute the "print criteria."

Jurisdictions (e.g., States and Territories) conducting surveillance under this case definition can voluntarily submit de-identified case information to CDC, if requested and in a mutually agreed upon format.

Production of national data summaries and national data re-release for non-NNCs:

- Prior to release of national data summaries CDC should follow the CDC/ATSDR Policy on Releasing & Sharing Data, issued on April 16, 2003 and referenced in 11-SI-01 and custodians of such data should consult the CDC-CSTE Intergovernmental Data Release Guidelines Working Group report (www.cste2.org/webpdfs/drgwgreport.pdf) which contains data release guidelines and procedures for CDC programs re-releasing state, local, or territorial-provided data.
- CDC programs have a responsibility, in collaboration with states, localities, and territories, to ensure that CDC program-specific data re-release procedures meet the needs of those responsible for protecting data in the states and territories.

- Notification to CDC should be immediate-extremely urgent for suspected or confirmed cases when an intentional release is suspected as the cause of infection.
- Notification should be immediate-urgent for all other suspected and confirmed cases.
- Immediate notifications of VHF cases of international concern by the CDC's Special Pathogens Branch to WHO will occur for confirmed cases in accordance with the International Health Regulations.

X. Revision History

Position Statement ID	Section of Document	Revision Description
10-ID-19	Definition of Viral Hemorrhagic Fever	For the purposes of this position statement, updated and clarified definition of VHF to include Chapare virus: *VHF refers to viral hemorrhagic fever caused by either Ebola or Marburg viruses, Old World arenaviruses (Lassa and Lujo viruses), New World arenaviruses (Guanarito, Machupo, Junin, Sabia, and Chapare viruses), or Crimean-Congo hemorrhagic fever virus*

10-ID-19	A1- Clinical Criteria for Reporting	Amend definition of fever to ≥38ºC
10-ID-19	A3. Epidemiologic Linkage Criteria for Reporting	DELETED time frame for exposure to semen from an acute or clinically recovered VHF patient
10-ID-19	Table V	Specified other reporting sites

XI. References

1. Mafayle RL*, Morales-Betoulle M*, Romero C*, Cossaboom CM*, et al. Chapare hemorrhagic fever in Bolivia, 2019: nosocomial transmission, viral persistence in humans, and virus detection in *Oligoryzomys microtis* rodents. In preparation.
2. Delgado S, Erickson BR, Agudo R, et al. Chapare virus, a newly discovered arenavirus isolated from a fatal hemorrhagic fever case in Bolivia. PLoS Pathog 2008;4(4):e1000047. DOI: 10.1371/journal.ppat.1000047.
3. Escalera-Antezana JP, Rodriguez-Villena OJ, Arancibia-Alba AW, Alvarado-Arnez LE, Bonilla-Aldana DK, Rodriguez-Morales AJ. Clinical features of fatal cases of Chapare virus hemorrhagic fever originating from rural La Paz, Bolivia, 2019: A cluster analysis. Travel Med Infect Dis 2020:101589. DOI: 10.1016/j.tmaid.2020.101589.
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5. Deen GF, Broutet N, Xu W, et al. Ebola RNA Persistence in Semen of Ebola Virus Disease Survivors - Final Report. N Engl J Med 2017;377(15):1428-1437. DOI: 10.1056/NEJMoa1511410.
6. Diallo B, Sissoko D, Loman NJ, et al. Resurgence of Ebola Virus Disease in Guinea Linked to a Survivor With Virus Persistence in Seminal Fluid for More Than 500 Days. Clin Infect Dis 2016;63(10):1353-1356. DOI: 10.1093/cid/ciw601.
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Technical Supplement

Table VI. Table of criteria to determine whether a case should be reported to public health authorities.

Criterion	Viral Hemorrhagic Fever^	
Clinical Criteria for Reporting		
Fever (≥38°C/100.4°F)		N
Severe headache		O
Muscle pain		O
Erythematous maculopapular rash on the trunk with fine desquamation 3–4 days after rash onset		O
Vomiting		O
Diarrhea		O
Abdominal pain		O
Bleeding not related to injury		O
Thrombocytopenia		O
Pharyngitis		O1
Proteinuria		O1
Retrosternal chest pain		O1
Laboratory Criteria for Reporting		
Test order for any diagnostic test specific for VHF	S*	
Epidemiological Linkage Criteria for Reporting		
Contact within the past 3 weeks with blood or other body fluids of a patient with VHF		O
Residence within the past 3 weeks in a VHF endemic area or area with active transmission		O
Travel within the past 3 weeks to a VHF endemic area or area with active transmission		O
Work within the past 3 weeks in a laboratory that handles VHF specimens		O
Work within the past 3 weeks in a laboratory that handles bats, rodents, or primates from a VHF endemic area or area with active transmission		O
Sexual exposure within the past 3 weeks to semen from a confirmed acute or clinically recovered VHF case		O
Vital Records Criteria for Reporting		
Death certificate lists viral hemorrhagic fever as a cause of death or a significant condition contributing to death	S	

Notes:

^VHF = viral hemorrhagic fever caused by either Ebola or Marburg viruses, Old World arenaviruses (Lassa and Lujo viruses), New World arenaviruses (Guanarito, Machupo, Junin, Sabia, and Chapare viruses), or Crimean-Congo hemorrhagic fever virus.

S = This criterion alone is SUFFICIENT to report a case.

N = All “N” criteria in the same column are NECESSARY to report a case.

O = At least one of these “O” (ONE OR MORE) criteria in **each category** (categories=clinical evidence, laboratory evidence, and epidemiological evidence) **in the same column**—in conjunction with all “N” criteria in the same column—is required to report a case.

1 = Additional criteria that apply only to the Arenaviruses (Lassa, Lujo or new world arenaviruses including Junin, Machupo, Sabia, Guanarito, or Chapare)

* A requisition or order for any of the “S” laboratory tests is sufficient to meet the reporting criteria.

Table VII. Classification Table: Criteria for defining a case of Viral Hemorrhagic Fever*.

Criterion	Suspect	Confirmed
Clinical Evidence		
Fever (≥38°C/100.4°F)	N	
Severe headache	O	
Muscle pain	O	
Erythematous maculopapular rash on the trunk with fine desquamation 3–4 days after rash onset	O	
Vomiting	O	
Diarrhea	O	
Abdominal pain	O	
Bleeding not related to injury	O	
Thrombocytopenia	O	
Pharyngitis	O1	
Proteinuria	O1	
Retrosternal chest pain	O1	
Laboratory Evidence		
Detection of VHF viral antigens in blood by ELISA		S
VHF viral isolation in cell culture for blood or tissues		S
Detection of VHF-specific genetic sequence by RT-PCR from blood or tissues		S
Detection of VHF viral antigens in tissues by immunohistochemistry		S
Epidemiologic Linkage Evidence		
Contact within the 3 weeks before onset of symptoms with blood or other body fluids of a patient with VHF	O	
Residence within the 3 weeks before onset of symptoms in a VHF endemic area or area with active transmission	O	
Travel within the 3 weeks before onset of symptoms to a VHF endemic area or area with active transmission	O	
Work within the 3 weeks before onset of symptoms in a laboratory that handles VHF specimens	O	
Work within the 3 weeks before onset of symptoms in a laboratory that handles bats, rodents, or primates from a VHF endemic area or area with active transmission	O	
Sexual exposure within the 3 weeks before onset of symptoms to semen from a confirmed acute or clinically recovered VHF case	O	
Criteria to distinguish a new case:		
Not previously counted as a case of VHF caused by the same virus detected by laboratory evidence.	N/A	N

Notes:

*VHF refers to viral hemorrhagic fever caused by either Ebola or Marburg viruses, Old World arenaviruses (Lassa and Lujo viruses), New World arenaviruses (Guanarito, Machupo, Junin, Sabia, and Chapare viruses), or Crimean-Congo hemorrhagic fever virus.

S = This criterion alone is SUFFICIENT to classify a case.

N = All "N" criteria in the same column are NECESSARY to classify a case. A number following an "N" indicates that this criterion is only required for a specific disease/condition subtype (see below). If the absence of a criterion (i.e., criterion NOT present) is required for the case to meet the classification criteria, list the absence of criterion as a necessary component.

O = At least one of these "O" (ONE OR MORE) criteria in **each category** (categories=clinical evidence, laboratory evidence, and epidemiologic evidence) **in the same column**—in conjunction with all "N" criteria in the same column—is required to classify a case. A number following an "O" indicates that this criterion is only required for a specific disease/condition subtype.

1 = Additional criteria that apply only to Arenaviruses (Lassa, Lujo or new world arenaviruses, including Junin, Machupo, Sabia, Guanarito, Chapare)