09-ID-18

Committee: Infectious

Title: Add Viral Hemorrhagic Fever (VHF) caused by Ebola or Marburg viruses, Lassa virus, new world Arenaviruses (Guanarito, Machupo, Junin, Sabia), or Crimean-Congo hemorrhagic fever to the Nationally Notifiable Condition list.

I. Statement of the Problem

CSTE position statement 07-EC-02 recognized the need to develop an official list of nationally notifiable conditions and a standardized reporting definition for each condition on the official list. The position statement also specified that each definition had to comply with American Health Information Community recommended standards to support "automated case reporting from electronic health records or other clinical care information systems." In July 2008, CSTE identified sixty-eight conditions warranting inclusion on the official list, each of which now requires a standardized reporting definition.

II. Background and Justification

Background[1]

Viral hemorrhagic fevers are a group of febrile illnesses caused by several distinct families of viruses, all of which are enveloped and have RNA genomes. The group includes the filoviruses, Ebola and Marburg, Lassa fever virus, the New World arenaviruses (Guanarito, Machupo, Junin, and Sabia), and Rift Valley fever and Crimean Congo hemorrhagic fever viruses. Humans are not the natural reservoir for any of these viruses, and human cases or outbreaks of hemorrhagic fevers caused by these viruses occur sporadically and irregularly. Humans are initially infected when they come into contact with infected hosts, but with some viruses humans can transmit the virus to other humans after the initial transmission from the natural host. Although some types cause relatively mild illnesses, many of these viruses can cause severe, life-threatening disease. Severe illness is characterized by vascular damage and increased permeability, multi-organ failure, and shock. This position statement addresses hemorrhagic fevers caused by two filoviruses, Ebola and Marburg, arenaviruses (including Guanarito, Machupo, Junin, Sabia, and Lassa) and Crimean Congo hemorrhagic fever caused by the bunyavirus, Nairovirus. Two other related syndromes—hantavirus pulmonary syndrome and yellow fever—are addressed in their own position statements.

Ebola and Marburg are filoviruses that belong to the family *Filoviridae* and can cause severe hemorrhagic fever in humans and nonhuman primates. Confirmed cases of Ebola hemorrhagic fever have been reported in the Republic of Congo, Côte d'Ivoire, Liberia, Democratic Republic of Congo, Gabon, Sudan, and Uganda. Occupational infection of laboratory workers resulting

[1] Much of the material in the background is directly quoted from Rollin and Ksiazek's sub-chapter on viral hemorrhagic fevers in *Health Information for International Travel 2008*. See the References for further information on this source.

from needle-stick injury has occurred in England and Russia. Marburg virus is also indigenous to Africa. Although the precise geographic range for Marburg virus is unknown, it includes at least parts of Uganda, western Kenya, Democratic Republic of Congo, and Angola. The reservoir hosts for Ebola and Marburg viruses have not yet been identified, although fruit bats are strongly suspected. Outbreaks can occur when a patient who has been exposed to that unknown reservoir species or an infected nonhuman primate transmits the virus to others in a community. Within that community, the outbreak often becomes amplified in the health-care setting.

A virus transmitted from asymptomatically infected rodents to humans causes Lassa fever. Although most infections are mild, some are severe, causing a hemorrhagic fever that is often fatal. Lassa fever is limited to rural areas of West Africa, with hyper-endemic areas in eastern Sierra Leone, Guinea, Liberia, and Nigeria. Peri-domestic exposure to infected rodents is the most likely source of human infection. Transmission to humans can occur via inhalation of primary aerosols from rodent urine, by ingestion of rodent-contaminated food, or by direct contact of broken skin with rodent excreta. Rodent infestation facilitated by inappropriate food storage increases the risk of human infection. Person-to-person spread of Lassa virus has also been described, most notably by large droplet and contact transmission in the hospital setting. Airborne transmission is not believed to be an important route of infection from person to person. Laboratory handling of infectious specimens and contact with contaminated medical equipment are also associated with transmission.

The Arenaviridae are a family of viruses whose members are generally associated with rodent-transmitted disease in humans. Each virus usually is associated with a particular rodent host species in which it is maintained. Arenavirus infections are relatively common in humans in some areas of the world and can cause severe illnesses. One arenavirus, Lassa, was described above. New world arenaviruses include Guanarito, Machupo, Junin, and Sabia). Human infection occurs through exposure to excretions of infected rodents. Some arenavirus infections are associated with secondary person-to-person transmission especially in health care settings.

Crimean-Congo hemorrhagic fever (CCHF) is caused by infection with a tick-borne virus (Nairovirus) in the family Bunyaviridae. Crimean-Congo hemorrhagic fever is found in Eastern Europe, particularly in the former Soviet Union and throughout the Mediterranean, in northwestern China, central Asia, southern Europe, Africa, the Middle East, and the Indian subcontinent. Ixodid (hard) ticks, especially those of the genus, *Hyalomma*, are both a reservoir and a vector for the CCHF virus. Numerous wild and domestic animals, such as cattle, goats, sheep and hares, serve as amplifying hosts for the virus. Transmission to humans occurs through contact with infected animal blood or ticks. CCHF can be transmitted from one infected human to another by contact with infectious blood or body fluids. Documented spread of CCHF has also occurred in hospitals due to improper sterilization of medical equipment, reuse of injection needles, and contamination of medical supplies.

Because of their potential for high mortality rates in infected persons and their potential for transmission from person to person, Lassa virus and some other arenaviruses and filoviruses causing viral hemorrhagic fever have been designated as category A possible bioterrorism agents.

Justification

Viral hemorrhagic fever meets the definition of a nationally and **immediately** notifiable condition—as specified in CSTE position statement 08-EC-02—for the following reason(s):

- The condition has special importance for international health regulations (IHR).
- The condition is included on the list of Category A possible bioterrorism agents and toxins.
- A majority of state and territorial jurisdictions—or jurisdictions comprising a majority of the US population—have laws or regulations requiring **immediate** reporting of viral hemorrhagic fever to public health authorities.
- The Centers for Disease Control and Prevention (CDC) requests **immediate-extremely urgent** notification of any cases of viral hemorrhagic fever suspected of being intentional. For all other cases of viral hemorrhagic fever, notification will be **immediate-urgent**. The CDC has condition-specific policies and practices concerning its response to, and use of, notifications.

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

1) Viral hemorrhagic fever caused by Ebola or Marburg viruses, Lassa virus, new world Arenaviruses (Guanarito, Machupo, Junin, Sabia), or Crimean-Congo hemorrhagic fever should be added to the Nationally Notifiable Condition list.
2) CSTE requests that CDC adopt this standardized reporting definition for viral hemorrhagic fever to facilitate more timely, complete, and standardized local and national reporting of this condition.

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 sources of data and the extent of coverage listed in Table V below.

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

	Coverage	
Source of data for case ascertainment	Population-wide	Sentinel sites
clinician reporting	x	
laboratory reporting	x	

reporting by other entities (e.g., hospitals, veterinarians, pharmacies)	x
death certificates	x
hospital discharge or outpatient records	x
extracts from electronic medical records	x
telephone survey	
school-based survey	
other _____	

VI. Criteria for Reporting

Reporting refers to the process of healthcare providers or institutions (e.g., clinicians, clinical laboratories, hospitals) submitting basic information to governmental public health agencies about cases of illness that meet certain reporting requirements or criteria. The purpose of this section is to provide those criteria that should be used by humans and machines to determine whether a specific illness should be reported.[2]

A. Narrative description of criteria to determine whether a case should be reported to public health authorities

Report any illness to public health authorities that meets any of the following criteria:

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

2. A person with ALL of the following findings:
   - a fever > 40°C;
   - 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
     - pharyngitis (arenavirus only)
     - diarrhea
     - bleeding not related to injury
     - thrombocytopenia
     - proteinuria (arenavirus only)
     - retrosternal chest pain (arenavirus only)
   - one or more of the following epidemiological risk factors:

[2] "Human-based" criteria (described below under "A. Narrative") can be applied by medical care providers and laboratory staff based on clinical judgment and clinical diagnosis. Machine-based criteria (described below under "B. Table") can be applied using computerized algorithms that operate in electronic health record systems, including computerized records of laboratory test orders and laboratory test results.

- 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
- work within the past 3 weeks in a laboratory that handles VHF specimens
- work within the past 3 weeks in a laboratory that handles primates from endemic areas
- exposure within the past 3 weeks to semen from a confirmed acute or convalescent case of VHF within 10 weeks of the person's onset of illness

4. A person whose death certificate lists VHF (i.e., Ebola, Lassa, Marburg, new world Arenavirus, or Crimean-Congo hemorrhagic fever) 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. Table of criteria to determine whether a case should be reported to public health authorities

Table VI-B. Proposed Table of criteria to determine whether a case should be reported to public health authorities. Note: The following criteria are proposed for evaluation before general implementation. For purposes of currently implementing reporting the narrative description in VI-A, should be used.

Criterion	Reporting		
Clinical Presentation			
fever (> 40°C)		N	
severe headache		O	
muscle pain		O	
erythematous maculopapular rash on the trunk with fine desquamation 3–4 days after rash onset		O	
retrosternal chest pain		O1	
pharyngitis (sore throat)		O1	
vomiting		O	
diarrhea		O	
bleeding not related to injury		O	
proteinuria		O1	
thrombocytopenia		O	

Laboratory findings			
detection of VHF viral antigens in blood or tissues by ELISA	S*		
VHF viral isolation in cell culture from blood or tissues	S*		
detection of VHF viral genes (RT-PCR) from blood or tissues	S*		
Detection of VHF viral antigens in tissues by immunohistochemistry	S*		
Detection of IgM or IgG in blood by ELISA	S*		
Epidemiological risk factors			
contact with blood or other body fluids of a patient with VHF within the past 3 weeks		O	
residence in—or travel within the past 3 weeks to—a VHF endemic area		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 primates from endemic areas		O	
exposure within the past 3 weeks to semen from a confirmed acute or convalescent VHF case within 10 weeks of the person's onset of illness		O	

Notes:
VHF = viral hemorrhagic fever caused by Ebola, Lassa, or Marburg virus, a new world arenavirus or Congo-Crimean hemorrhagic fever.
S = This criterion alone is sufficient to report a case
N = All "N" criteria in the same column—in conjunction with at least one of any "O" criteria in each category (e.g., clinical presentation and laboratory findings) in the same column—are required to report a case. A number following an "N" indicates that this criterion is only required for a specific clinical presentation (see below).
O = At least one of any "O" criteria in each category (e.g., clinical presentation and laboratory findings) in the same column—in conjunction with all other "N" criteria in the same column—is required to report a case. A number following an "O" indicates that this criterion is only required for a specific clinical presentation (see below).
1 = Arenaviruses (Lassa or new world arenaviruses including Junin, Machupo, Sabia, or Guanarito)

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

C. Disease Specific Data Elements:

Disease-specific data elements to be included in the initial report are listed below.

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
work within the past 3 weeks in a laboratory that handles VHF specimens
work within the past 3 weeks in a laboratory that handles primates from endemic areas
exposure within the past 3 weeks to semen from a confirmed acute or convalescent case of VHF within 10 weeks of the person's onset of illness

VII. Case Definition for Case Classification

A. Narrative description of criteria to determine whether a case should be classified as confirmed or suspected (possible) is provided:

[Note: There is no CSTE-CDC case definition for VHF. The definition below was created for this position statement.]

Clinical presentation criteria

An illness with acute onset with ALL of the following clinical findings:

- fever > 40°C
- 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
  - pharyngitis (Arenaviruses only)
  - abdominal pain
  - bleeding not related to injury
  - retrosternal chest pain (Arenaviruses only)
  - proteinuria (Arenaviruses only)

Laboratory criteria for diagnosis

One or more of the following laboratory findings:

- detection of VHF viral antigens in blood by ELISA antigen detection
- VHF viral isolation in cell culture for blood or tissues
- detection of VHF viral genes using reverse transcriptase with polymerase chain reaction amplification (RT-PCR) from blood or tissues
- detection of VHF viral antigens in tissues by immunohistochemistry

Note: VHF refers to viral hemorrhagic fever caused by either Ebola, Lassa, or Marburg virus, a new world arenavirus, or Crimean-Congo hemorrhagic fever.

Criteria for 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
- work in a laboratory that handles VHF specimens
- work in a laboratory that handles primates from endemic areas

OR

Exposure within the past 3 weeks to semen from a confirmed acute or convalescent case of VHF within the 10 weeks of onset of symptoms

Case classification

Suspect: Case meets the clinical and epidemiologic linkage criteria

Confirmed: Case meets the clinical and laboratory criteria

B. Classification Tables

Table VII-B lists the criteria that must be met for a case to be classified as confirmed or suspected (possible).

Table VII-B. Proposed table of criteria to determine whether a case is classified. Note: The following criteria are proposed for evaluation before general implementation. For purposes of current notification, the narrative description in VII-A, should be used.

	Case Definition		
Criterion	Confirmed	Probable	Suspected
Clinical Presentation			
fever (> 40°C)	N		N
severe headache	O		O
muscle pain	O		O
erythematous maculopapular rash on the trunk with fine desquamation 3–4 days after rash onset	O		O
retrosternal chest pain	O1		O1
pharyngitis (sore throat)	O1		O1
vomiting	O		O
diarrhea	O		O
bleeding not related to injury	O		O
proteinuria	O		O1

thrombocytopenia	O		O
Laboratory findings			
detection of VHF viral antigens in blood or tissues by ELISA antigen detection	S		
VHF viral isolation in cell culture from blood or tissues	S		
detection of VHF viral genes (RT-PCR) from blood or tissues	S		
Detection of VHF viral antigens in tissues by immunohistochemistry	S		
Detection of IgG in blood by CDC ELISA			
Epidemiological risk factors			
contact with blood or other body fluids of a patient with VHF within the past 3 weeks			O
residence in—or travel within the past 3 weeks to—a VHF endemic area			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 primates from endemic areas			O
exposure within past 3 weeks to semen from a confirmed acute or convalescent VHF case within 10 weeks of onset of illness			O

Notes:
VHF = viral hemorrhagic fever caused by Ebola, Lassa, or Marburg virus, a new world Arenavirus, or Congo-Crimean hemorrhagic fever.
S = This criterion alone is sufficient to classify a case
N = All "N" criteria in the same column—in conjunction with at least one of any "O" criteria in each category (e.g., clinical presentation and laboratory findings) in the same column—are required to classify a case. A number following an "N" indicates that this criterion is only required for a specific clinical presentation (see below).
O = At least one of any "O" criteria in each category (e.g., clinical presentation and laboratory findings) in the same column—in conjunction with all other "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 clinical presentation (see below).
* A requisition or order for any of the "S" or "N" laboratory tests is sufficient to meet the reporting criteria.
1 = Arenavirus (Lassa or new world arenaviruses, including Junin, Machupo, Sabia, Guanarito)

VIII. Period of Surveillance

Surveillance should be on-going.

IX. Data sharing/release and print criteria

- 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. References

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