

# Viral Hemorrhagic Fevers

## Investigative Guidelines

September 2019

### REPORT IMMEDIATELY

Note: In setting of a known Ebola outbreak, use Ebola Investigative Guideline. For dengue, consult ACDP.

## 1. DISEASE REPORTING

### 1.1 Purpose of Reporting and Surveillance

1. To identify potential foci of viral hemorrhagic fever (VHF) agents (such as laboratory specimens, ill non-human primates, or clusters of illness around an imported case).
2. To identify sources of transmission and geographical areas of risk outside of Oregon.
3. To determine the magnitude of risk to humans and animals.
4. To stop transmission from all such sources and geographic areas.
5. To identify cases as early as possible to prevent transmission to other persons or animals.
6. To identify cases and clusters of human illness that may be associated with a bioterrorist event.

### 1.2 Laboratory and Physician Reporting Requirements

1. Laboratories and physicians are required to report any known or suspected case of VHF **immediately** to the local public health authority (LPHA) as an “unusual disease or condition of public health significance”.
2. If this is not possible, such cases should be reported to the Oregon Acute Communicable Disease Prevention Section (ACDP) at 971-673-1111.
3. Report any potential exposure to an agent that could cause VHF.

### 1.3 Local Public Health Authority Reporting and Follow-Up Responsibilities

1. Report all confirmed, or suspect cases or illness suggestive of VHF immediately to ACDP.
2. Consult with ACDP about strategies for enhanced surveillance, contact investigation, and monitoring.
3. Work with local providers and facilities to ensure compliance with respiratory and contact isolation procedures in care of patients with suspected VHF or confirmed disease with a communicable VHF.

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4. Assure all contacts potentially exposed to a VHF case-patient are identified, educated, and placed under adequate surveillance for the period when symptoms are most likely to arise.
5. Complete the reporting forms, surveillance and follow-up forms, and otherwise document investigation, outreach, active surveillance, and completeness of containment efforts.
6. Consult with ACDP prior to closing case and contact investigation activities for each suspected or confirmed VHF case.

### 1.4 Oregon Public Health Division (OPHD) Responsibilities

1. Provide consultation to LPHA, public health, Tribal, and private health sector professionals concerning:
  - Isolation of cases and potential cases;
  - Diagnostic evaluation, treatment, and clinical monitoring;
  - Required reporting and surveillance activities;
  - Contact identification and follow-up;
  - Interjurisdictional tracking of cases and contacts who move out of county or State of Oregon jurisdiction;
  - Development and maintenance of adequate tools to coordinate case and contact surveillance, and assure adequacy of response activities;
  - Provision of surge capacity if a VHF outbreak and contact investigation overwhelm the resources of the LPHA.
2. Facilitate expert consultation with infectious disease specialists and CDC.
3. Coordinate specimen collection with the LPHA and Oregon State Public Health Laboratory (OSPHL) to assure confirmation of suspected VHF cases and early identification of disease in symptomatic contacts and others.

## 2. THE DISEASE AND ITS EPIDEMIOLOGY

### 2.1 Etiologic Agent

VHFs include numerous zoonotic diseases, all of which can cause a hemorrhagic syndrome in humans. Because of its high fatality rate, past outbreaks, and the occasional importation of the virus into the United States in non-human primates, Ebola hemorrhagic fever has been most publicized in the United States. VHFs are known to be caused by viruses from four families. All are RNA, enveloped viruses.

- Filoviruses: Ebola and Marburg [Category A];
- Arenaviruses: Lassa, Junín (Argentine HF), Chapare HF, Lujo HF, Machupo (Bolivian HF), Sabiá (Brazilian HF) Guanarito (Venezuelan HF) [Category A];
- Bunyaviruses: Crimean-Congo HF, Dobrava HF, Hantaan HF, Saaremaa HF, Puumala HF, Rift Valley HF, Seoul HF;
- Flaviviruses: Alkhurma HF, Dengue, Yellow Fever, Omsk HF, Kyasanur Forest Disease.

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## 2.2 Description of Illness

Though signs and symptoms vary, VHF is usually characterized by onset of high fever, headache, muscle aches, and fatigue. The duration of illness ranges from a few days to weeks. As the disease progresses, symptoms may include petechiae, bruising, swelling around the eyes, flushing, shock, sustained fever, and sweats. Bleeding occurs from mucous membranes and may present as nosebleeds, bleeding gums, bloody vomit, bloody urine, and blood in stools or sputum. Patients often go into shock, with multi-organ dysfunction. Encephalopathy, hepatitis, tremors, and reduced white blood cell and platelet levels are frequently seen. Renal failure may occur.

The differential diagnosis includes a variety of viral and bacterial diseases: influenza, hepatitis, staphylococcal or other bacterial sepsis, toxic shock syndrome, rubella, measles, and hemorrhagic smallpox, among others. Non-infectious diseases that present with bleeding also must be excluded (e.g., hemolytic uremic syndrome and leukemia). Mortality rates for VHF's vary depending on the agent and strain and can range from 10% to 90%. In Lassa VHF, sensorineural hearing loss affects about one-third of patients, with only half recovering hearing after 1–3 months.

## 2.3 Reservoirs

Many wild and domestic animals, ticks, and mosquitoes are known to carry viruses that cause VHF, although the reservoirs have not been identified for all VHF agents. Rodents are known to be carriers of Omsk HF, VHF-associated arenaviruses and most VHF-associated bunyaviruses. Some ticks can harbor Alkhurma, Crimean-Congo HF, and Kyasanur Forest Disease viruses. Livestock (cattle, sheep, goats, and camels) can carry bunyaviruses that cause VHF (Rift Valley, Crimean-Congo HF).

Primates are the only non-human animals known to have been affected by Ebola and Marburg disease. However, because these infections are associated with rapid and often fatal illness in these animals, they are not considered reservoirs. Fruit bats, on the other hand, are likely reservoirs for Ebola and Marburg.

## 2.4 Modes of Transmission

Depending on the virus, initial human cases in VHF outbreaks typically involve exposure to affected reservoir rodents or their spoor (arenaviruses, Omsk HF, Lassa HF) reservoir bats or infected bushmeat (Ebola, Marburg), infected livestock (Rift Valley Fever, Crimean-Congo HF), ticks (Alkhurma, Omsk HF, Crimean-Congo HF) or mosquitoes (yellow fever, dengue, Rift Valley Fever). **Several VHF infections can subsequently be transmitted via person-to-person contact (Ebola, Marburg, Lassa, Lujo and other arenaviruses, Crimean-Congo HF).**

In these situations, infection can result from direct contact with infectious body fluids or contaminated fomites. Sexual transmission of Ebola and Lassa fever has been documented. Unsterilized medical equipment has been implicated in spread of several communicable VHF's. In rare cases, lab workers have been

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infected through handling of specimens. Airborne spread has never been documented.

### 2.5 Incubation Period

The incubation periods for various VHFs range from 2 to 21 days, with an average of 3 to 10 days.

### 2.6 Period of Communicability or Infectious Period

To be honest, the evidence isn't great. No VHF infection has been reported in persons who had contact with a case only during the incubation period (that is, before onset of fever). For communicable VHF agents, viral load and risk for transmission appear greatest during the later stages of illness. It seems prudent, however, to assume that individuals ill with suspected VHF or confirmed, communicable VHF are infectious throughout the clinical course. Anyone, including healthcare and laboratory personnel, who has had close contact with a symptomatic case's secretions (or with body fluids of a high-risk symptomatic contact of a case) in the absence of appropriate infection control precautions should be placed under medical surveillance with fever watch for 21 days after last exposure. Virus may remain in the blood and secretions for months after an individual recovers. WHO currently recommends that male EVD survivors refrain from unprotected sexual activity for at least 12 months after symptom onset or until their semen has twice tested negative for Ebola. Contaminated bedding, clothing, and medical equipment may remain infectious for several days.

### 2.7 Epidemiology

Various VHFs are enzootic in different geographic regions, specifically in sub-Saharan Africa (Ebola, Marburg, Lassa, Rift Valley Fever), Europe (Crimean-Congo HF, Puumala, Saaremaa, Dobrava), Asia (Crimean-Congo HF, Hantaan), or the Americas (New World arenaviruses such as Junín, Machupo). For most VHFs, human infections are rare, and outbreaks, when they occur, tend to be sporadic. Outbreaks of Ebola hemorrhagic fever in imported non-human primates used for research have occurred in the U.S. In one instance, individuals working with infected primates developed antibody to Ebola, suggesting exposure, but the individuals did not become clinically ill. There is speculation that this particular strain of Ebola virus (called Ebola Reston) may be unable to cause clinical disease in humans.

### 2.8 Treatment

As of 2019, there are no FDA-approved medications for treatment of Marburg or Ebola virus infections.

There is, however, plenty of activity in this area, and some medications and vaccines are being used in outbreak settings. Stay tuned. There is no effective treatment for most diseases caused by VHF agents other than supportive care. Maintaining fluid and electrolyte balance, circulatory volume, and blood pressure are important. Mechanical ventilation, dialysis, and anti-seizure treatment may be required. Injections, aspirin, and all anticoagulants are contraindicated, and steroids are not indicated. Ribavirin may be helpful with arenavirus and bunyavirus

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infections, but this drug has not been shown to be useful against filovirus or flavivirus infections.

### 3. CASE DEFINITIONS, DIAGNOSIS AND LABORATORY SERVICES

#### 3.1 Confirmed Case Definition

Fever  $>40^{\circ}\text{C}$ , plus one or more of the following:

- Severe headache, muscle pain, vomiting, diarrhea, abdominal pain, bleeding not related to injury, thrombocytopenia, or a red maculopapular rash on the trunk with fine desquamation 3-4 days after rash onset.

For arenaviruses, the following are also qualifying signs and symptoms: pharyngitis, retrosternal chest pain, and proteinuria.

Plus at least one of the following laboratory findings:

- Detection of VHF viral antigens by enzyme-linked immunosorbent assay (ELISA),
- VHF viral isolation in cell culture for blood or tissues,
- Detection of VHF-specific genetic sequence by reverse transcription-polymerase chain reaction (RT-PCR) from blood or tissues, or
- Detection of VHF viral antigens in tissues by immunohistochemistry

#### 3.2 Suspect Case Definition

Meets clinical criteria listed above, plus experienced one or more of the following exposures in the three weeks before onset of symptoms:

- Contact with blood or other bodily 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 bats, rodents, or primates from enzootic areas, or
- Exposure to semen from a confirmed acute or convalescent case of VHF within 10 weeks of that person's onset of symptoms

#### 3.3 Services Available at the Oregon State Public Health Laboratory (OSPHL)

The OSPHL can facilitate testing for VHF through CDC or other public health laboratories. If testing is needed, contact the ACDP Epi on-call to arrange this. Once testing is approved, OSPHL staff (503-693-4100) will provide guidance on what specimens to send, as well as where and how to send them.

### 4. ROUTINE CASE INVESTIGATION

If a suspect or confirmed case of VHF is reported, or there is potential exposure to an agent that could cause VHF, call the ACDP epidemiologist immediately, day or night, at 971-673-1111.

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Case investigation of VHF in Oregon residents will involve close collaboration between ACDP epidemiologists and LHD staff. If a bioterrorist event is suspected, we will be inundated by people from CDC so fast it will make your head swim. Working closely with ACDP and, more than likely, CDC, the LHD Communicable Disease staff will be involved in the investigation of any VHF case living within their communities. As noted previously, some VHFs (Ebola, Marburg, Lassa, Crimean-Congo) are communicable. Some aren't. In the absence of lab confirmation that the illness is caused by a non-communicable virus, we should assume communicability and proceed with contact investigation as outlined below.

Contacts at risk for VHF infection must be identified, located, interviewed, and assessed for symptoms of illness. Local health department staff will do rapid screening of contacts for symptoms of illness. (See checklist on final page.) They can also advise each contact to monitor his or her temperature and can review key symptoms to guide decision-making about medical referral.

### 4.1 Investigation Activities

1. **Stay Safe.** If you can collect needed information without entering the patient's room (for instance, by phone), this is certainly a reasonable way to avoid infection. Observe recommended hospital infection prevention practices and personal protective equipment if entering an ill patient's room.
2. Complete the case report form. See [www.oregon.gov/oha/PH/DISEASESCONDITIONS/DISEASESAZ/Documents/vhf-case-report-form.pdf](http://www.oregon.gov/oha/PH/DISEASESCONDITIONS/DISEASESAZ/Documents/vhf-case-report-form.pdf) Most of the information on the form can be obtained from the healthcare provider or the medical record. In Orpheus, for each VHF case or suspect, record "Viral Hemorrhagic Fever" as the disease being reported. For initial suspects and cases, and in early phase of symptoms, lab results may not be available. When possible, record the type of VHF (e.g., Ebola, Marburg, Lassa, etc.).
3. Record demographic and clinical information about the suspected or confirmed case patient. Interviews most likely will be done with close household members, as the patient may be too ill to provide adequate information. Use the case report form to collect the following data for each case:
  - Name, age, race/ethnicity, address, phone numbers;
  - Parent/guardian information, if applicable;
  - Clinical data, including signs and symptoms, date of onset, date of diagnosis, duration;
  - Status (hospitalized, at home, deceased).
4. List information about the healthcare providers attending the case patient:
  - Name and phone number of the hospital where the case is or was hospitalized;

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- Name and phone number of the attending physician;
  - Name and phone number of the infection control official at the hospital;
  - If the patient was seen by a healthcare provider before hospitalization, or seen at more than one hospital, get those names and phone numbers too;
  - Name of any person or agency involved in transporting the patient while symptomatic.
5. Document all activities, including travel, during the 21 days prior to symptom onset. This can provide clues to how, where, and when the case may have been exposed
  6. Also, document activities of the case-patient between onset of symptoms and when the patient enters medical isolation. This will help to identify, assess, and monitor all contacts who spent time with the infected person. Monitoring is particularly important for all those who had physical contact with the ill patient. Institute surveillance of VHF contacts for a period of 21 days after the last known exposure to the case patient.
    - For Ebola and Marburg filoviruses, institute fever watches for all persons who had any direct physical contact with the ill patient's blood, secretions, organs, or semen. Airborne transmission has not been documented. Nosocomial infections have resulted from contaminated needles and syringes.
    - Identify all persons who spent time in the same close air space (within 6 feet) with the ill patient, in each of the patient's social settings, and alert them to the need for fever watch. (See #7 below.) Ask about household and other sleeping places, worksites, and places of leisure activities (church, clubs, sports teams, frequently visited households of friends, etc.).
    - For travel history, identify any contacts ill with symptoms suggesting VHF during any travel that occurred in the 21 days before the onset of symptoms to assess where and when infection might have occurred. Determine the date(s) and geographic area(s) traveled to. List all people who had close contact with the case-patient during travel during the infectious period (car, bus, airplane, etc.).
  7. Educate possible contacts about VHF transmission and the need to self-monitor for fever, as well as for symptoms suggestive of VHF infection, for 21 days after the most recent exposure to the case-patient. Make plans for immediate medical evaluation should symptoms develop but have them alert the provider that they are coming, to avoid exposure to others.
    - Asymptomatic contacts should monitor temperatures twice daily during the surveillance period. The LHD should establish telephone, remote-visual, or home visit monitoring of this temperature surveillance.
    - If a contact develops a body temperature over 101°F, arrange for prompt medical evaluation with strict isolation precautions.
    - Interview any symptomatic contacts for their close contacts.
    - Interview, assess, and monitor secondary contacts to VHF cases.
    - Asymptomatic contacts may continue their routine daily activities but are

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advised not to travel outside of the home community during the surveillance period.

- Visitors should be discouraged in households where close contacts are under surveillance for clinical symptoms after exposure to a VHF patient.

### 5. CONTROLLING FURTHER SPREAD

#### 5.1 Personal Preventive Measures

All people at risk of VHF infection because of occupational or household contact with VHF patients need instruction on frequent and thorough hand hygiene, the use of gloves and other personal protective barrier equipment including respiratory protection to prevent exposure to blood and body fluids, and safe methods of waste disposal.

Several strategies could help prevent exposure to VHF agents:

- Avoiding non-essential travel to areas with known outbreaks of VHF;
- Laboratory workers who handle specimens suspected of containing the agents of VHFs should practice enhanced precautions to avoid exposures;
- Persons working with imported non-human primates (NHPs) should know the signs of VHF in them and immediately report any suspected cases of VHF in NHPs to ACDP (971-673-1111).

#### 5.2 Isolation of VHF cases

Suspect VHF cases and those with confirmed, communicable VHF infections must be isolated, and all persons caring for them must observe strict standard, contact, and droplet precautions, typically supplemented by respiratory protection using powered air purifying respirators (PAPRs).

- Healthcare professionals are at risk from accidental percutaneous and mucous membrane exposures to blood and body fluids. They should pay special attention to the use of barrier/contact precautions in care of the patient, and in cleaning or disposal of anything the patient may have touched or contaminated.
- CDC recommends use of at least an N95 respirator or PAPR during care of confirmed Ebola patients and those with suspected Ebola disease who are unstable. It also seems prudent when possibly aerosol-generating procedures (endotracheal intubation, sputum induction, bronchoscopy, airway suctioning, or positive pressure ventilation by face mask) are performed.
- Patients with VHF who have respiratory symptoms should wear a surgical mask whenever transported through areas where others may not have personal protective equipment.

#### 5.3 Period of Isolation of Patient

Patients should be isolated until they are clinically well, and then monitored for at least three weeks.

Because blood and secretions may contain virus for anywhere from weeks to months after VHF illness, recovering patients must be educated and monitored



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for infectiousness (specific lab monitoring of specimens should be determined by expert clinician consultation).

The World Health Organization recommends that male survivors of Ebola infection “practice safer sex” (i.e., avoid unprotected sex) for 12 months from symptom onset, or until their semen tests negative twice for Ebola virus. Recovering patients with other confirmed, communicable VHF should refrain from sexual activity for at least three months after clinical recovery.

### **5.4 Follow-up of Cases**

Patients recovering from VHF should be monitored clinically during convalescence. Those with Lassa infections are at risk of deafness, and hearing acuity should be monitored during recovery.

### **5.5 Protection of Contacts of a Case**

Healthcare workers and other contacts of confirmed or suspected cases of VHF should practice recommended precautions to reduce their risk of acquiring VHF. Anyone, including healthcare and laboratory personnel, who has had contact with a case’s secretions (or with body fluids of high-risk symptomatic contacts of a case) without using appropriate personal protective equipment should be placed under medical surveillance with fever watch for 21 days after last exposure.

### **5.6 Vaccines and Antiviral Prophylaxis**

Ribavirin has a possible role in post-exposure prophylaxis for contacts with high-risk (i.e., body fluid) exposures to Lassa fever patients. That said, there are no FDA-approved medications for prophylaxis of VHFs. As of 2019, the only FDA-approved vaccine active against a VHF agent is for yellow fever, although vaccines against Ebola have been used in outbreak settings.

### **5.7 Environmental Measures**

Depending on the VHF agent involved, it may be useful to enhance vector control for specific reservoir animals during a VHF outbreak. Consult with the State ACDP public health veterinarian for specific recommendations. Households where VHF patients have been identified, or recovering patients are living, must receive targeted teaching about personal hygiene, waste disposal, and limiting exposure to possibly infected materials or animals.

### **5.8 Infection Control**

With the lack of effective therapy or preventive vaccines against most VHF agents, efforts to prevent transmission rely on careful, vigilant infection control measures.

#### **1. Isolation**

Suspected VHF cases must be immediately reported to the infection control professional within a healthcare facility, and isolated promptly.

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- Isolate the patient in a private room, with a private bathroom, or, if not possible, use group rooms housing VHF patients in the same wing or area of the facility.
  - Limit staff caring for patient to those with needed training in relevant infection precautions, and with full protective equipment.
  - Keep door to the room closed at all times.
  - No visitors, except for a limited number of family members, with full PPE for universal, contact, and droplet precautions and at least N95 respirator or PAPR.
  - Patients with respiratory symptoms should wear a surgical mask any time they move through an area where others might be.
2. Personal Protective Barrier Precautions
    - Strict hand hygiene plus double gloves;
    - Gowns; consider impermeable gowns, shoe and leg coverings if there is substantial risk of blood or other bodily fluid exposure;
    - Goggles and PAPR or N95 with face shield if within 6 feet of patient.
  3. Surveillance of healthcare workers and laboratory personnel potentially exposed to VHF
    - Monitor healthcare workers and laboratory workers with possible exposure to VHF agents for 21 days after exposure to a symptomatic patient (or infectious material from the patient). If fever or other symptoms develop, arrange prompt medical evaluation.
  4. Contact with deceased infected patients has been found to be a source of transmission in some VHF outbreaks.
    - Mortuary personnel need to be alerted to any suspect or confirmed VHF case. It is recommended that only trained personnel handle bodies of deceased VHF fever patients, using infection control procedures as during care of ill persons. Autopsies should be discouraged, or performed only by specially trained persons, wearing maximum respiratory protection equipment, in negative-pressure rooms, to guard against aerosols generated. No embalming should be done. Prompt burial or cremation is recommended.

## 6. SPECIAL SITUATIONS

Long story short: Any case of VHF we investigate is a special situation. Just give us a call. We'll work through it together.

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### 7. REFERENCES

- CDC. Viral Hemorrhagic Fevers. Accessed July 16, 2019 at:  
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- CDC. Infection Prevention and Control Recommendations for Hospitalized Patients Under Investigation (PUIs) for Ebola Virus Disease (EVD) in U.S. Hospitals.  
[www.cdc.gov/vhf/ebola/clinicians/evd/infection-control.html](http://www.cdc.gov/vhf/ebola/clinicians/evd/infection-control.html)
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- Bausch DG, CM Hadi, SH Khan, JJJ Lertora. Review of the Literature and Proposed Guidelines for the Use of Oral Ribavirin as Postexposure Prophylaxis for Lassa Fever. *Clinical Infectious Disease* 2010;51(12):1435-1441.

### UPDATE LOG

- 2019: Section 2.1: updated list of VHF. Updated Sections 2.3 2.4, 2.6, and 2.8: reservoirs, routes of transmission, period of communicability, and treatment. Updated information on infection prevention in Sections 4.1, 5.2, 5.4, and 5.7. Minor edits; links to references added.
- 2014: Typos corrected. Sec. 3.1: temperature component of Ebola case definition updated. Sec. 3.3: guidance on lab specimen shipment updated. Sec. 4.1: language on obtaining history of possible exposure to VHF during travel clarified. (Leman)
- 2013: Updated infection control guidance, ACDP contact information. Updated case definition. Updated information on treatment and prophylaxis. Revised *Contact Symptom Checklist*. Edits throughout to improve clarity. (Leman)
- 2004: Original Document

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## Contact Interview Checklist

Name: \_\_\_\_\_  
Last First MI

Orpheus # of Epi-linked Case \_\_\_\_\_

Sex  Female  Male Ethnicity: Latino?  yes  no  unknown

Race  AI/AN  Asian  Black  Pacific Islander  white  
 Refused  Unknown  Other \_\_\_\_\_

Date of birth   /  /    
m d y

Most recent exposure date   /  /    
m d y

Nature of Exposure:  Body fluid contact  W/in 6 ft. while case was ill  Neither of these  
 Healthcare worker  Laboratorian  Family member  
 Other

Any of these signs and symptoms?

- Fever  Fatigue
- Weakness  Headache
- Irritability  Muscle aches
- Dizziness  Nausea / vomiting
- Rash  Diarrhea
- Flushing  Low blood pressure (shock)
- Sweats  Sore throat
- Any bleeding/bruising in absence of injury?
- Swelling around eyes
- Redness of eyes

On-going exposure likely?  yes  no

Education on standard, contact, and droplet precautions given, if on-going exposure predicted.