Viral Hemorrhagic Fever (VHF)

Revised 03/27/2011

Epidemiology

The viral hemorrhagic fevers are a diverse group of illnesses caused by RNA viruses from four viral families linked by a clinical syndrome. The Arenaviridae include the etiologic agents of Argentine, Bolivian and Venezuelan hemorrhagic fevers and Lassa fever. The Bunyaviridae include the members of the Hantavirus genus, the Congo-Crimean hemorrhagic fever virus from the Nairovirus genus and the Rift Valley fever virus from the Phlebovirus genus; the Filoviridae include Ebola and Marburg viruses; the Flaviviridae include dengue and yellow fever viruses. These viruses are spread in a variety of ways; some may be transmitted to humans through a respiratory portal of entry. Because these viruses are so diverse and occur in different geographic locations endemically, their full history is beyond the scope of this manual.

Arenaviridae:
- Argentine hemorrhagic fever (AHF), caused by the Junin virus, was first described in 1955 in corn harvesters. From 300 to 600 cases per year occur in areas of the Argentine pampas.
- Bolivian, Brazilian and Venezuelan hemorrhagic fevers are caused by the related Machupo, Guanarito and Sabia viruses.
- Lassa virus causes disease in West Africa. These viruses are transmitted from their rodent reservoirs to humans by the inhalation of dusts contaminated with rodent excreta.

Bunyaviridae:
- Congo-Crimean hemorrhagic fever (CCHF) is a tick-borne disease that occurs in the Crimea and in parts of Africa, Europe and Asia. It can also be spread by contact with infected animals and in healthcare settings.
- Rift Valley fever (RVF) is a mosquito-borne disease that occurs in Africa.
- The hantaviruses are rodent-borne viruses with a wide geographic distribution. Hantaan and closely related viruses cause hemorrhagic fever with renal syndrome (HFRS, also known as Korean hemorrhagic fever or epidemic hemorrhagic fever). This is the most common disease due to hantaviruses. It was described prior to World War II in Manchuria along the Amur River, among United Nations troops during the Korean conflict and subsequently in Japan, China and in the Russian Far East. Severe disease also occurs in some Balkan states, including Bosnia, Serbia and Greece. Nephropathia epidemica is a milder disease that occurs in Scandinavia and other parts of Europe and is caused by strains carried by bank voles. In addition, newly described hantaviruses cause Hantavirus Pulmonary Syndrome (HPS) in the Americas. The hantaviruses are transmitted to humans by the inhalation of dusts contaminated with rodent excreta.

Filoviridae:
- Ebola hemorrhagic fever was first recognized in the western equatorial province of the Sudan and the nearby region of Zaire in 1976. A second outbreak occurred in Sudan in 1979 and in 1995, a large outbreak (316 cases) developed in Kikwit, Zaire from a single index case. Subsequent epidemics have also occurred in Gabon, the Ivory Coast, Uganda and the Republic of Congo.
There are five species of Ebola: Zaire, Sudan, Ivory Coast, Reston and Bundibugyo. The African strains cause severe disease and death, with case fatality rates that vary by viral species (Bundibugyo ~35%, Sudan 40% - 50%, Zaire 80% - 90%). It is not known why this disease appears infrequently. A related virus (Ebola Reston) was isolated from monkeys imported into the United States from the Philippines in 1989 and subsequently developed hemorrhagic fever. While subclinical infections occurred among exposed animal handlers, Ebola Reston has not been identified as a human pathogen, though it recently has been shown to cause disease in pigs.

- Marburg epidemics have occurred on eight occasions: six times in Africa and twice in Europe. The first recognized outbreak occurred in Marburg, Germany and Yugoslavia among people exposed to African green monkeys and resulted in 31 cases and seven deaths. Case fatality rates in Marburg outbreaks have varied from 21% to nearly 90%. There is only one species of Marburg virus, though there are several strains.

- Filoviruses can be spread from human to human by direct contact with infected blood, secretions, organs, or semen. Ebola Reston apparently spread from monkey to monkey, and from monkeys to humans by the respiratory route. The natural reservoirs of the filoviruses are unknown, but recent evidence strongly implicates bats as either the reservoir or as intermediate host.

*Flaviviridae:*

- Yellow fever and dengue are two mosquito-borne fevers that have great importance in the history of military campaigns and military medicine, as well as in port cities engaging in commerce with the tropics, such as New Orleans.

- Tick-borne flaviviruses include the agents of Kyasanur Forest disease in India and Omsk hemorrhagic fever in Siberia.

**Clinical Description**

Common symptoms are fever, myalgia and prostration. Physical examination may reveal only conjunctival injection, mild hypotension, flushing and petechial hemorrhages. Full-blown VHF typically evolves to shock and generalized mucous membrane hemorrhage and often is accompanied by evidence of pulmonary hematopoietic and neurologic involvement. Renal insufficiency is proportional to cardiovascular compromise, except in HFRS, which features renal failure as an integral part of the disease process.

The clinical syndrome that these viruses may cause is VHF. However, this syndrome is variable in its presentation. Bleeding may be an uncommon feature and not very impressive when it occurs (as in dengue hemorrhagic fever or Rift Valley fever) or it may present as copious life threatening hemorrhage, as is Crimean Congo hemorrhagic fever. The progression to a septic shock-like picture may be due to a combination of increases in vascular permeability, vasodilation, decreased myocardial function and fluid loss.

VHF should be suspected in any patient presenting with a severe febrile illness and evidence of vascular involvement (postural hypotension, petechiae, easy bleeding, flushing of face and chest, non-dependent edema), who has traveled to an area where the virus is known to occur, or where intelligence information suggests a biological warfare threat. Symptoms and signs suggesting additional organ system involvement are common (headache, photophobia, pharyngitis, cough, nausea or vomiting, diarrhea, constipation, abdominal pain, hyperesthesia, dizziness, confusion, tremor), but usually do not dominate the picture with the exceptions in the following listing under “Clinical Features.” A positive tourniquet test has been particularly useful in dengue hemorrhagic fever, but should be sought in other hemorrhagic fevers as well.

Not all infected patients develop VHF. There is both divergence and uncertainty about which host factors and viral strain characteristics might be responsible for the mechanisms of disease. For example, an immunopathogenic mechanism has been identified for dengue hemorrhagic fever, which usually occurs among patients previously infected with a heterologous dengue serotype. Antibodies directed against the previous strain enhances uptake of the dengue virus by circulating monocytes. These cells express viral
antigens on their surfaces. Lysis of the infected monocytes by cytotoxic T-cell responses results in the release of pro-inflammatory cytokines, pro-coagulants and anticoagulants, which in turn results in vascular injury and permeability, complement activation and a systemic coagulopathy.

Diffuse or disseminated intravascular coagulation (DIC) has been implicated in Rift Valley, Marburg and Ebola fevers, but in most VHF's the etiology of the coagulopathy is multifactorial (e.g., hepatic damage, consumptive coagulopathy and primary marrow injury to megakaryocytes).

**Clinical Features:**

Apart from epidemiologic and intelligence information, some distinctive clinical features may suggest a specific etiologic agent.

- While hepatic involvement is common among the VHF's, a clinical picture dominated by jaundice and other features of hepatitis is only seen in some cases of Rift Valley fever, Congo-Crimean and yellow fever.
- Kyasanur Forest disease and Omsk hemorrhagic fever are notable for pulmonary involvement and a biphasic illness with subsequent CNS manifestations.
- Lassa fever can cause severe peripheral edema due to capillary leak, but hemorrhage is uncommon.
- Hemorrhage is commonly caused by the South American arenaviruses. Severe hemorrhage and nosocomial transmission are typical for Congo-Crimean HF.
- Retinitis is not uncommonly seen as a late feature of Rift Valley fever. Hearing loss is common among Lassa fever survivors.

Classic HFRS has a severe course that progresses sequentially from fever through hemorrhage, shock, renal failure and polyuria. Nephropathia endemica features prominent fever, myalgia, abdominal pain and oliguria, without shock or severe hemorrhagic manifestations. North American cases of Hantavirus Pulmonary Syndrome (HPS) due to the Sin Nombre virus lack hemorrhagic manifestations and renal failure, but nevertheless carry a very high mortality due to rapidly progressive and severe pulmonary capillary leak, which presents as ARDS. These syndromes may overlap. Subclinical or clinical pulmonary edema may occur in HFRS and nephropathia endemica, while HFRS has complicated HPS due to South American hantaviruses and the Bayou and Black Creek Canal viruses in North America.

Mortality may be substantial, ranging from 0.2% percent for nephropathia endemica, to 50% to 90% among Ebola victims.

**Diagnosis:** Definitive diagnosis rests on specific virologic techniques.

A detailed travel history and a high index of suspicion are essential in making the diagnosis of VHF:

- Patients with arenavirus or hantavirus infections often recall having seen rodents during the presumed incubation period; since the viruses are spread to man by aerosolized excreta or environmental contamination, actual contact with the reservoir is not necessary.
- Large mosquito populations are common during Rift Valley fever or flavivirus transmission, but a history of mosquito bite is too common to be of diagnostic importance.
- Tick bites or nosocomial exposure are of some significance in suspecting Congo-Crimean HF.

The clinical laboratory can be very helpful. Thrombocytopenia (exception: Lassa), and leukopenia (exceptions: Lassa, Hantaan and some severe CCHF cases) are the rule. Proteinuria and/or hematuria are common and their presence is the rule for Argentine HF, Bolivian HF and HFRS. High AST elevation correlates with severity of Lassa fever. Jaundice is a poor prognostic sign in yellow fever.

In most geographic areas, the major item in the differential diagnosis is malaria. It must be borne in mind that parasitemia in patients partially immune to malaria, does not prove that symptoms are due to malaria. Other items in the differential may include typhoid fever, nontyphoidal salmonellosis, leptospirosis,
rickettsial infections, shigellosis, relapsing fever, fulminant hepatitis and meningococcemia. Additional illnesses which could mimic VHF include acute leukemia, lupus erythematosus, idiopathic or thrombotic thrombocytopenic purpura, hemolytic uremic syndrome and the multiple causes of disseminated intravascular coagulation.

Definitive diagnosis in an individual case rests on specific virologic diagnosis. Most patients have readily detectable viremia at presentation (exception: hantaviral infections). Rapid enzyme immunoassays can detect viral antigens in acute sera from patients with Argentine HF, Lassa fever, Rift Valley fever, Congo-Crimean HF and yellow fever. Lassa- and Hantaan-specific IgM often are detectable during the acute illness. Diagnosis by virus cultivation and identification will require three to ten days or longer. With the exception of dengue, specialized microbiologic containment is required for safe handling of these viruses. Appropriate precautions should be observed in collection, handling, shipping and processing of diagnostic samples. The Centers for Disease Control and Prevention (CDC) has diagnostic laboratories functioning at the highest (BL-4 or P-4) containment level.

**Laboratory Tests**

Methods of diagnosis at specialized laboratories include antigen detection by ELISA, IgM antibody detection by antibody-capture ELISA, RT-PCR and viral isolation. Antigen detection (by ELISA), and RT-PCR are the most useful diagnostic techniques in the acute clinical setting. Viral isolation is of limited value because it requires a biosafety level IV laboratory.

Either the presence of IgM or a four-fold rise in titer of IgG antibody between acute and convalescent phase serum samples are diagnostic of these viral illnesses, but antibody-capture ELISA is of limited value in early diagnosis because antibodies to these viruses usually do not appear until onset of recovery, approximately at the second week of illness.

**SURVEILLANCE**

Viral Hemorrhagic Fevers (VHFs) are all reportable conditions. They should be reported immediately by phone upon recognition that a case, a suspected case, or a positive laboratory result is known.

**Treatment**

Intensive supportive care may be required. Antiviral therapy with ribavirin may be useful in several of these infections. Convalescent plasma may be effective in Argentine hemorrhagic fever (available only as IND under protocol).

General principles of supportive care apply to hemodynamic, hematologic, pulmonary and neurologic manifestations of VHF, regardless of the specific etiologic agent. These patients all require intensive care, but the efficacy in changing patient outcomes is variable (very good in dengue hemorrhagic fever, not very effective in yellow fever). Management of these diseases is similar to the management of septic shock. Health care providers employing vigorous fluid resuscitation of hypotensive patients must be mindful of the propensity of some VHFs (e.g., HFRS) for pulmonary capillary leak. Pressor agents are frequently required. The use of intravascular devices and invasive hemodynamic monitoring must be carefully considered in the context of potential benefit versus the risk of hemorrhage. Restlessness, confusion, myalgia and hyperesthesia should be managed by conservative measures, and the judicious use of sedatives and analgesics. Secondary infections may occur as with any patient undergoing intensive care utilizing invasive procedures and devices, such as intravenous lines and indwelling catheters.

The management of clinical bleeding should follow the same principles as for any patient with a systemic coagulopathy, assisted by coagulation studies. Intramuscular injections, aspirin or any NSAIDs and other anticoagulant drugs should be avoided.
The antiviral drug ribavirin is available for therapy of Lassa fever, HFRS, Congo-Crimean HF and Rift Valley fever. Separate Phase III efficacy trials have indicated that parenteral ribavirin reduces morbidity in HFRS and lowers both the morbidity and mortality of Lassa fever. In the HFRS field trial, treatment was effective if begun within the first four days of fever and continued for a seven-day course. A compassionate use protocol, utilizing intravenous ribavirin as a treatment for Lassa fever, is sponsored by the CDC. Doses are slightly different and continued for a ten-day course; treatment is most effective if begun within seven days of onset, so early diagnosis and treatment initiation is key in diseases where this drug is effective. The only significant side effect of ribavirin is a modest anemia due to a reversible inhibition of erythropoiesis and mild hemolysis. Although ribavirin is teratogenic in laboratory animals, the potential benefits must be weighed against the potential risks to pregnant women with grave illness due to one of these VHFs. Safety in infants and children has not been established. Ribavirin has poor \textit{in vitro} and \textit{in vivo} activity against the filoviruses (Ebola and Marburg), and the flaviviruses (dengue, yellow fever, Omsk HF and Kyanasur Forest Disease).

Argentine HF responds to therapy with two or more units of convalescent plasma containing adequate amounts of neutralizing antibody and given within eight days of onset. This therapy is investigational and available only under protocol.

**Case Definition**

Since VHF has multiple disease etiologies, no single case definition is available.

**Prevention**

**Vaccine**

The only licensed VHF vaccine is yellow fever vaccine, which is mandatory for travelers to endemic areas of Africa and South America.

Argentine hemorrhagic fever vaccine is a live, attenuated, investigational vaccine developed at the United States Army Medical Research Institute for Infectious Diseases (USAMRIID), which has proved efficacious both in an animal model and in a field trial in South America, and seems to protect against Bolivian hemorrhagic fever as well.

Both inactivated and live-attenuated Rift Valley fever vaccines are currently under investigation. There is also a veterinary vaccine available for livestock.

An investigational vaccinia-vectored Hantaan vaccine is offered to laboratory workers at USAMRIID.

**Prophylactic ribavirin**

May be effective for Lassa fever, Rift Valley fever, CCHF and possibly HFRS (available only as IND under protocol – see below). A Department of Defense compassionate use protocol exists for prophylactic administration of oral ribavirin to high risk contacts (direct exposure to body fluids) of Congo-Crimean HF patients. A similar post-exposure prophylaxis strategy has been suggested for high contacts of Lassa fever patients. Most patients will tolerate this dose well, but patients should be under surveillance for breakthrough disease (especially after drug cessation) or adverse drug effects (principally anemia). Exposed contacts to CCHF or Lassa Fever under follow-up should have prompt initiation of IV ribavirin therapy if they develop symptoms.

**Exposure management**

Persons with percutaneous or mucocutaneous exposure to blood, body fluids, secretions, or excretions from a patient with suspected VHF should immediately wash the affected skin surfaces with soap and water. Mucous membranes should be irrigated with copious amounts of water or saline.
Close personal contacts or medical personnel exposed to blood or secretions from VHF patients (particularly Lassa fever, CCHF and filoviral diseases), should be monitored for symptoms, fever and other signs during the established incubation period.

**Travel exposure**

Travelers may have been exposed during flights or other modes of transportation. The following are the risk categories for travel exposure:

**High risk**
- Exposure from a percutaneous injury (e.g., a needlestick or cut with a sharp object) to blood, tissue or other body fluids that are potentially infectious (e.g., urine, vomitus, stool)
- Exposure from direct, unprotected contact with potentially infectious material (e.g., touching vomitus with an ungloved hand)
- Exposure via mucosal exposure (e.g., to eyes, nose, mouth) to splashes or droplets of potentially infectious blood and body fluids or sexual contact with a symptomatic patient.

**Low risk**
- Sharing a room or seated in a vehicle within six feet (i.e., coughing distance) of a potentially infectious patient, without direct contact with potentially infectious material
- Providing routine medical care while using personal protective equipment appropriately
- Routine cleaning and laundry of contaminated linens and surfaces while using personal protective equipment appropriately
- Transport of a potentially infectious patient or specimen without direct contact with potentially infectious material
- Handling of clinical specimens while using personal protective equipment appropriately

Contacts should monitor their health for 21 days following exposure and seek medical attention immediately, if fever or any other early sign or symptom of VHF develops.

**Prevention of Exposure**

<table>
<thead>
<tr>
<th>Family</th>
<th>Virus</th>
<th>Standard Procedure</th>
<th>Mask and Eye Protection Within 3 Feet</th>
<th>Airborne Transmission- Use of HEPA-Filtered Respirator (Only if Prominent Cough, Vomiting, Diarrhea, or Hemorrhage)</th>
<th>Private Room (Only if Significant Cough, Hemorrhage, or Diarrhea)</th>
<th>Mosquito Proofing</th>
<th>Special Cautions-Virus Present in Blood or Excreta</th>
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</thead>
<tbody>
<tr>
<td>Filoviridae</td>
<td>Ebola</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<tr>
<td></td>
<td>Marburg</td>
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<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Bunyaviridae</td>
<td>CCHF</td>
<td>X</td>
<td>X</td>
<td>X</td>
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</tr>
<tr>
<td></td>
<td>Rift Valley Fever</td>
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<td>X</td>
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<td>X</td>
<td>X</td>
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<tr>
<td></td>
<td>Hantavirus</td>
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<td></td>
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</tr>
<tr>
<td>Arenaviridae</td>
<td>Lassa</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td></td>
<td>South American Viruses</td>
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<td></td>
<td></td>
<td></td>
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<td>X</td>
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<tr>
<td>Flaviviridae</td>
<td>Dengue</td>
<td>X</td>
<td></td>
<td>X</td>
<td></td>
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</tr>
<tr>
<td></td>
<td>Yellow Fever</td>
<td>X</td>
<td></td>
<td>X</td>
<td>X</td>
<td></td>
<td>X</td>
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</table>
### Viral Hemorrhagic Fever Case Investigation Form

<table>
<thead>
<tr>
<th>ID Number</th>
<th>Interviewer</th>
<th>Job title</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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</tr>
</tbody>
</table>

**Interview date**

**Person interviewed**

Patient  Other

**Describe relationship if other**

**Demographic information**

<table>
<thead>
<tr>
<th>Last name</th>
<th>First name</th>
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</thead>
<tbody>
<tr>
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</tbody>
</table>

**Sex**

- Male
- Female

**Date of birth**

**Age**

**Ethnicity**

- African
- Asian

**Nationality**

**Home phone**

**Other phone**

**Street**

**City**

**Zip**

**Country**

**How many people reside in the same household?**

- 1
- 2
- 3
- 4

- 5
- 6
- 7
- 8

- 9
- 10
- 11
- 12

**List Name, Age, Relationship**

**Household pets**

- Indoor
- Outdoor
- Both

**Any pet died recently (describe)**

---

**Occupation/Hobby**

**Brief description of job**

- Lab worker/technician: yes no unknown
- Taxidermist: yes no unknown
- Veterinarian: yes no unknown
- Farmer: yes no unknown
- Abattoir: yes no unknown
- Butcher: yes no unknown
- Other food prep: yes no unknown

**Address**

**City**

**Department**

**Floor/Room**

**Hobby**

- Do you work with fibers/wool/animal skin/or other animal product? yes no unknown
- Have you been camping in past two months? yes no unknown
- Have you stayed in cabins in the past two months? yes no unknown
- Have you been hunting? yes no unknown
- Have you skinned or dressed and animal? yes no unknown
- Have you had an animal stuffed or mounted? yes no unknown

**Clinical information**

**Date onset**

**History of present illness**

**Chief complaint**

- Cough: yes no unknown
- Hemoptysis: yes no unknown
- Breath shortness: yes no unknown
- Cyanosis: yes no unknown
- Adenopathies: yes no unknown
- Fever: yes no unknown
- Antipyretics taken: yes no unknown
- Sputum: yes no unknown
- Chest pain: yes no unknown
- Stridor /Wheezing: yes no unknown
- Conjunctivitis: yes no unknown
- Location: yes no unknown
- Max Temp: yes no unknown
- Headache: yes no unknown
<table>
<thead>
<tr>
<th>Symptom</th>
<th>Yes</th>
<th>No</th>
<th>Unknown</th>
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<tbody>
<tr>
<td>Stiff neck</td>
<td>yes</td>
<td>no</td>
<td>unknown</td>
</tr>
<tr>
<td>Fatigue</td>
<td>yes</td>
<td>no</td>
<td>unknown</td>
</tr>
<tr>
<td>Altered mental status</td>
<td>yes</td>
<td>no</td>
<td>unknown</td>
</tr>
<tr>
<td>Sore throat</td>
<td>yes</td>
<td>no</td>
<td>unknown</td>
</tr>
<tr>
<td>Nausea</td>
<td>yes</td>
<td>no</td>
<td>unknown</td>
</tr>
<tr>
<td>Rash</td>
<td>yes</td>
<td>no</td>
<td>unknown</td>
</tr>
<tr>
<td>Past Medical History:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Do you have a regular physician?</td>
<td>yes</td>
<td>no</td>
<td>unknown</td>
</tr>
<tr>
<td>If yes, name: phone number: (xxx) xxx-xxxx</td>
<td></td>
<td></td>
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<tr>
<td>Are you allergic to any medications?</td>
<td>yes</td>
<td>no</td>
<td>unknown</td>
</tr>
<tr>
<td>If yes, list:</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Are you currently taking any medications:</td>
<td>yes</td>
<td>no</td>
<td>unknown</td>
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<tr>
<td>If yes, list:</td>
<td></td>
<td></td>
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<tr>
<td>Have you had any wound or lesion in the past several months?</td>
<td>yes</td>
<td>no</td>
<td>unknown</td>
</tr>
<tr>
<td>If yes, where: appearance:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>yes</td>
<td>no</td>
<td>unknown</td>
</tr>
<tr>
<td>Neurologic condition</td>
<td>yes</td>
<td>no</td>
<td>unknown</td>
</tr>
<tr>
<td>Diabetes</td>
<td>yes</td>
<td>no</td>
<td>unknown</td>
</tr>
<tr>
<td>Cardiac disease</td>
<td>yes</td>
<td>no</td>
<td>unknown</td>
</tr>
<tr>
<td>Seizures</td>
<td>yes</td>
<td>no</td>
<td>unknown</td>
</tr>
<tr>
<td>Other pulmonary disease</td>
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<td>no</td>
<td>unknown</td>
</tr>
<tr>
<td>Malignancy</td>
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<td>no</td>
<td>unknown</td>
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<tr>
<td>Currently on treatment:</td>
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<td>unknown</td>
</tr>
<tr>
<td>HIV infection</td>
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<td>no</td>
<td>unknown</td>
</tr>
<tr>
<td>Currently pregnant</td>
<td>yes</td>
<td>no</td>
<td>unknown</td>
</tr>
<tr>
<td>Other immunocompromising condition (e.g., renal failure, cirrhosis, chronic steroid use)</td>
<td>yes</td>
<td>no</td>
<td>unknown</td>
</tr>
<tr>
<td>Social History:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current alcohol abuse:</td>
<td>yes</td>
<td>no</td>
<td>unknown</td>
</tr>
<tr>
<td>Past alcohol abuse:</td>
<td>yes</td>
<td>no</td>
<td>unknown</td>
</tr>
<tr>
<td>Current injection drug use:</td>
<td>yes</td>
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<tr>
<td>Past injection drug use:</td>
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<td>no</td>
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</tr>
<tr>
<td>Current smoker:</td>
<td>yes</td>
<td>no</td>
<td>unknown</td>
</tr>
<tr>
<td>Former smoker:</td>
<td>yes</td>
<td>no</td>
<td>unknown</td>
</tr>
</tbody>
</table>
Other illicit drug use:  yes  no  unknown
If yes, specify:

Hospital Information:

Hospitalized:  yes  no
Name of hospital:
Date of admission:  /  /  date of discharge:  /  /
Attending physician Last name:  First name:
Office telephone: (xxx)xxx-xxxx  pager: (xxx)xxx-xxxx  fax: (xxx)xxx-xxxx

Medical Record Abstraction:

Medical record number:
Hospital name:
Ward/room number:
Admission diagnosis (es):
  1)
  2)
  3)

Physical Exam:

Admission vital signs:
  Temp: (oral / rectal °F / °C ) heart rate: resp. rate: b/p:
Mental status:  normal  abnormal  not noted
If abnormal, describe:
Respiratory status:  normal spontaneous  respiratory distress  ventilatory support
If abnormal, check all that apply:
  rales  stridor/wheezing  decreased or absent
  Other (specify:)
Skin:  normal  abnormal  not noted
If abnormal, check all that apply:
  edema  chest wall edema  cyanosis  erythema
  petechiae  sloughing/necrosis  purpura  rash
If rash present, describe type and location on body:

Other abnormal physical findings (describe):

Diagnostic Studies:

<table>
<thead>
<tr>
<th>Test</th>
<th>Results of Tests Done on Admission Date( / / )</th>
<th>Abnormal Test Result at Any Time (specify date mm/dd/yy)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin (hb)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hematocrit (hct)</td>
<td></td>
<td></td>
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<tr>
<td>Platelet (plt)</td>
<td></td>
<td></td>
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<tr>
<td>Total white blood cell</td>
<td></td>
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<tr>
<td>(wbc)</td>
<td></td>
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<tr>
<td>Wbc differential:</td>
<td></td>
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<tr>
<td>Test</td>
<td>Results of Tests Done on Admission Date ( / / )</td>
<td>Abnormal Test Result at Any Time (specify date mm/dd/yy)</td>
</tr>
<tr>
<td>------------------------------</td>
<td>-------------------------------------------------</td>
<td>--------------------------------------------------------</td>
</tr>
<tr>
<td>Respiratory secretions:</td>
<td>expectorated sputum</td>
<td>expectorated sputum</td>
</tr>
<tr>
<td></td>
<td>induced sputum</td>
<td>induced sputum</td>
</tr>
<tr>
<td></td>
<td>bronchial alveolar lavage (bal)</td>
<td>bronchial alveolar lavage (bal)</td>
</tr>
<tr>
<td></td>
<td>tracheal aspirate</td>
<td>tracheal aspirate</td>
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<tr>
<td></td>
<td>Specimen type:</td>
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<tr>
<td></td>
<td>expectorated sputum</td>
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<td></td>
<td>induced sputum</td>
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<td></td>
<td>bronchial alveolar lavage (bal)</td>
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<td></td>
<td>tracheal aspirate</td>
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<td></td>
<td>Gram stain (check all that apply)</td>
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<td></td>
<td>pmns</td>
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<td></td>
<td>epithelial cells</td>
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<tr>
<td></td>
<td>gram positive cocci</td>
<td></td>
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<tr>
<td></td>
<td>gram negative cocci</td>
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<tr>
<td></td>
<td>gram positive rods</td>
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<tr>
<td></td>
<td>gram negative coccobacilli</td>
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<tr>
<td></td>
<td>gram negative rods</td>
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<tr>
<td></td>
<td>gram negative rods with bipolar staining (safety pins)</td>
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<tr>
<td></td>
<td>other ( / / )</td>
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<tr>
<td>Respiratory secretions:</td>
<td>positive (specify)</td>
<td>positive (specify)</td>
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<tr>
<td></td>
<td>negative</td>
<td>negative</td>
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<td></td>
<td>pending</td>
<td>pending</td>
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<tr>
<td></td>
<td>not done</td>
<td>not done</td>
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<tr>
<td>Respiratory secretions:</td>
<td>positive (specify)</td>
<td>positive (specify)</td>
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<td>negative</td>
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<td>pending</td>
<td>pending</td>
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<tr>
<td></td>
<td>not done</td>
<td>not done</td>
</tr>
<tr>
<td>Respiratory secretions:</td>
<td>positive (specify)</td>
<td>positive (specify)</td>
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<td>negative</td>
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<td>pending</td>
<td>pending</td>
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<tr>
<td></td>
<td>not done</td>
<td>not done</td>
</tr>
<tr>
<td>Respiratory secretions:</td>
<td>positive</td>
<td>positive</td>
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<tr>
<td></td>
<td>negative</td>
<td>negative</td>
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<td></td>
<td>pending</td>
<td>pending</td>
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<tr>
<td></td>
<td>not done</td>
<td>not done</td>
</tr>
</tbody>
</table>
Respiratory secretions:  
Other test (e.g., dfa, pcr, etc)  
( / / )

Chest radiograph  
normal  
unilateral, lobar/consolidation  
bilateral, lobar/consolidation  
interstitial infiltrates  
widened mediastinum  
pleural effusion  
other  
( / / )

Legionella urine antigen  
positive  
negative  
pending  
not done  
( / / )

### Test Results of Tests Done on Admission Date ( / / )  
Abnormal Test Result at Any Time (specify date mm/dd/yy)

Other pertinent study results  
(e.g., chest ct, pleural fluid)  
( / / )

Other pertinent study results  
(e.g., toxin assays)  
( / / )

Pulmonology consulted: yes no unknown  
Date of exam: ( / / )

Name of neurologist: last name first name  
Telephone (xxx)xxx-xxxx or beeper number ( xxx)xxx-xxxx  

Infectious disease consult: yes no unknown  
Date of exam: ( / / )

Name of id physician: last name first name  
Telephone (xxx)xxx-xxxx or beeper number ( xxx)xxx-xxxx  

Hospital course:  
a. antibiotics: yes no unknown  
If yes, check all that apply:  
amoxicillin  
ampicillin  
ampicillin and sulbactum (unasyn)  
augmentin (amoxicillin and clavulanate)  
azithromycin (zithromax)  
cefazolin (ancef, kefzol)  
cefuroxime (ceftin)  
cefalexin (keflex, keftab)  
ciprofloxacin (cipro)  
clarithromycin (biaxin)  
doxycycline (doryx, vibramycin)  
erythromycin (e-mycin, ery-tab, eryc)
cefepime (maxipime)  gentamicin (garamycin)
cefotaxime (xelonal)  levofloxacin (levaquin)
cefotetan (cefotan)  nafcillin
cefoxitin (mefoxin)  ofloxacin (floxin)
ceftazidime (fortaz, tazicef, tazidime)  streptomycin
ceftizoxime (cefixox)  ticarcillin and clavulanate (timentin)
ceftriaxone (rocephin)  trimethoprim-sulfamethoxazole (bactrim, cotrim, tmp/smx)
other

b. antivirals: yes no unknown
If yes, check all that apply:
acyclovir (zovirax)
amantadine (symmetrel)
oseltamivir (tamiflu)
rinamidine (flumadine)
zanamivir (relenza)
other

c. did patient require intensive care: yes no unknown
If patient was admitted to intensive care unit:
a. length of stay in icu, in days:
b. was patient on mechanical ventilation: yes no unknown

Working or discharge diagnosis (es):
1)
2)
3)

Outcome:
recovered/discharged
died
still in hospital: improving? worsening?

Additional comments:

Risk Exposure Questions

The following questions pertain to the two week period prior to the onset of your illness/symptoms:

Occupation (provide information for all jobs/ volunteer duties)
1. Please briefly describe your job/ volunteer duties:
2. Does your job involve contact with the public? : yes no
If “yes”, specify
3. Does anyone else at your workplace have similar symptoms? yes no unknown
If “yes”, name and approximate date on onset (if known)
**Knowledge of other ill persons**

4. Do you know of other people with similar symptoms? :  yes  no  unknown

(If yes, please complete the following questions)

<table>
<thead>
<tr>
<th>Name of Ill Person</th>
<th>Age</th>
<th>Sex</th>
<th>Address</th>
<th>Phone</th>
<th>Date of Onset</th>
<th>Relation to you</th>
<th>Did they seek medical care?</th>
<th>Where?</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
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</tbody>
</table>

**Travel***

*travel is defined as staying overnight (or longer) at somewhere other than the usual residence

8. Have you traveled anywhere in the last two weeks? :  yes  no  unknown

   Dates of travel:  / /  to  / /

   Method of transportation for travel:

   Where did you stay?

   Purpose of travel?

   Did you do any sightseeing on your trip? :  yes  no

      If yes, specify:

   Did anyone travel with you? :  yes  no

      If yes, specify:

   Are they ill with similar symptoms? :  yes  no  unknown

      If yes, specify:

   Information for additional trips during the past two weeks:

<table>
<thead>
<tr>
<th>Category</th>
<th>y/n/u</th>
<th>Description of activity</th>
<th>Location of activity</th>
<th>Date of activity</th>
<th>Time of activity (start, end)</th>
<th>Others ill? (y/n/u)</th>
</tr>
</thead>
<tbody>
<tr>
<td>9. Airports</td>
<td></td>
<td></td>
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<tr>
<td>10. Beaches</td>
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<td>11. Bars/clubs</td>
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<td>12. Campgrounds</td>
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<tr>
<td>13. Carnivals/circus</td>
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<tr>
<td>14.</td>
<td>Casinos</td>
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<tr>
<td>15.</td>
<td>Family planning clinics</td>
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<tr>
<td>16.</td>
<td>Government office building</td>
<td></td>
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<tr>
<td>17.</td>
<td>Gym/workout facilities</td>
<td></td>
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<tr>
<td>18.</td>
<td>Meetings or conferences</td>
<td></td>
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<tr>
<td>19.</td>
<td>Movie theater</td>
<td></td>
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<tr>
<td>20.</td>
<td>Museums</td>
<td></td>
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<tr>
<td>21.</td>
<td>Parks</td>
<td></td>
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<tr>
<td>22.</td>
<td>Parties (including raves, prom, etc)</td>
<td></td>
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<tr>
<td>23.</td>
<td>Performing arts (i.e. concert, theater, opera)</td>
<td></td>
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<tr>
<td>24.</td>
<td>Picnics</td>
<td></td>
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<tr>
<td>25.</td>
<td>Political events (including rallies)</td>
<td></td>
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<tr>
<td>26.</td>
<td>Religious gatherings</td>
<td></td>
<td></td>
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<tr>
<td>27.</td>
<td>Shopping malls</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>28.</td>
<td>Sporting event</td>
<td></td>
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<tr>
<td>29.</td>
<td>Street festivals, flea markets, parades</td>
<td></td>
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<tr>
<td>30.</td>
<td>Tourist attractions (i.e. french quarter, aquarium)</td>
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</tr>
</tbody>
</table>

**Public functions/venues (during 2 weeks prior to symptom onset)**

**Transportation**

Have you used the following types of transportation in the two weeks prior to onset?

31. Bus/streetcar: yes  no  unknown
    Frequency of this type of transportation: daily  weekly  occasionally  rarely
    Bus number: origin:
    Any connections?  yes  no (specify: location: bus#:  )
    Company providing transportation: destination:

32. Train: yes  no  unknown
    Frequency of this type of transportation: daily  weekly  occasionally  rarely
    Route number: origin:
    Any connections?  yes  no (specify: location: route#:  )
    Company providing transportation: destination:
33. Airplane: yes  no  unknown
   Frequency of this type of transportation:  daily  weekly  occasionally  rarely
   Flight number:  origin:  
   Any connections?  yes  no (specify:  location:  flight#:  )
   Company providing transportation:  destination:  

34. Ship/boat/ferry: yes  no  unknown
   Frequency of this type of transportation:  daily  weekly  occasionally  rarely
   Ferry number:  origin:  
   Any connections?  yes  no (specify:  location:  ferry#:  )
   Company providing transportation:  destination:  

35. Van pool/shuttle: yes  no  unknown
   Frequency of this type of transportation:  daily  weekly  occasionally  rarely
   Route number:  origin:  
   Any connections?  yes  no (specify:  location:  route#:  )
   Company providing transportation:  destination:  

**Food and Beverage**

36. During the two weeks before your illness, did you eat at any of the following food establishments or private gatherings with food or beverages?

<table>
<thead>
<tr>
<th>Food Establishment</th>
<th>y/n</th>
<th>Name of establishment</th>
<th>Location of meal</th>
<th>Date of meal</th>
<th>Time of meal (start, end)</th>
<th>Food and drink (items consumed)</th>
<th>Others ill? (y/n/u)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cafeteria at school, hospital, or other</td>
<td></td>
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<tr>
<td>Casino or mall food court</td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>Grocery store or corner store</td>
<td></td>
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<tr>
<td>Concert, movie, or other entertainment</td>
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<tr>
<td>Dinner party, birthday party or other celebration</td>
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<tr>
<td>Gas station or convenience store</td>
<td></td>
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<tr>
<td>Plane, boat, train, or other</td>
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<tr>
<td>Picnic, barbecue, crawfish boil, or potluck</td>
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<tr>
<td>Outdoor farmers market, festival, or swap meet</td>
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<tr>
<td>Restaurant, fast-food, or deli</td>
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<tr>
<td>Sporting event or snack bar</td>
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<tr>
<td>Street-vended food</td>
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</tbody>
</table>
37. During the two weeks before your illness, did you consume any free food samples from…….?  
   Grocery store: yes, no, unknown  
   Race/competition: yes, no, unknown  
   Public gathering: yes, no, unknown  
   Private gathering: yes, no, unknown  

   If “yes” for any in question #37, provide date, time, location and list of food items consumed:  
   Date/time: 
   Location (name and address): 
   Food/drink consumed: 
   Others also ill?: yes, no, unknown  
   (explain): 

38. During the two weeks before your illness, did you consume any of the following products?  
   Vitamins: yes, no, unknown  
   Specify (include brand name): 
   Herbal remedies: yes, no, unknown  
   Specify (include brand name): 
   Diet aids: yes, no, unknown  
   Specify (include brand name): 
   Nutritional supplements: yes, no, unknown  
   Specify (include brand name): 
   Other ingested non-food: yes, no, unknown  
   Specify (include brand name): 

39. During the two weeks before your illness, did you consume any unpasteurized products (i.e. milk, cheese, fruit juices)? yes, no, unknown  
   If yes, specify name of item:  
   Date/time: 
   Location (name and address): 
   Were others also ill?: yes, no, unknown  
   (explain): 

40. During the two weeks before your illness, did you purchase food from any internet grocers?  
   yes, no, unknown  
   If yes, specify date / time of delivery: store/site: 
   Items purchased: 

41. During the two weeks before your illness, did you purchase any mail order food?  
   yes, no, unknown  
   If yes, specify date/time of delivery: 
   Store purchased from: items purchased: 

42. Please check the routine sources for drinking water (check all that apply):
community or municipal
well (shared)
well (private family)
bottled water (specify brand:)
other (specify:)

**Aerosolized Water**

43. During the two weeks prior to illness, did you consume water from any of the following sources (check all that apply):
- wells
- lakes
- streams
- springs
- ponds
- creeks
- rivers
- sewage-contaminated water
- street-vended beverages (made with water or ice and sold by street vendors)
- ice prepared w/ unfiltered water (made with water that is not from a municipal water supply or that is not bottled or boiled)
- unpasteurized milk
- other (specify:)

If “yes” for any in question #43, provide date, time, location and type of water consumed:
- Date/time:
- Location (name and address):
- Type of water consumed:
- Were others also ill?:  yes, no, unknown

(explain):

44. During the two weeks prior to illness, did you engage in any of the following recreational activities (check all that apply):
- swimming in public pools (e.g., community, municipal, hotel, motel, club, etc)
- swimming in kiddie/wading pools
- swimming in sewage-contaminated water
- swimming in fresh water, lakes, ponds, creeks, rivers, springs, sea, ocean, bay (please circle)
- wave pools? water parks? waterslides? surfing
- rafting? boating? hot tubs (non-private)? whirlpools (non-private)?
- jacuzzis (non-private)?
- other (specify:)

If “yes” for any in question #44, provide date, time, location and type of activity:
- Date/time:
- Location (name and address):
- Type of water consumed:
- Were others also ill?:  yes, no, unknown

(explain):

45. During the two weeks prior to illness, were you exposed to aerosolized water from any of the following non-private (i.e., used in hospitals, malls, etc) sources (check all that apply):
- air conditioning at public places
- whirlpool spas
- respiratory devices
- hot tub
- vaporizers
- spa baths

(explain):
humidifiers
creek and ponds
misters
decorative fountains
other (please explain)

If “yes” for any in question #45, provide date, time and location of exposure to aerosolized water:
Date/time:
Location (name and address):
Explanation of aerosolized water:
Others also ill; yes, no, unknown
(explain):

Recreation (activities that are not related to work)
46. In the past two weeks, did you participate in any outdoor activities?
   yes, no, unknown
   If “yes”, list all activities and provide locations)

47. Do you recall any insect or tick bites during these outdoor activities?
   yes, no, unknown
   (If “yes”, list all activities and provide locations of activities)

48. Did you participate in other indoor recreational activities (i.e. clubs, crafts, etc that did not occur in a private home)? yes, no, unknown
   (List all activities and provide location)

Vectors
49. So you recall any insect or tick bites in the last two weeks? yes, no, unknown
   Date(s) of bite(s): bitten by: mosquito, tick, flea, fly, other:
   Where were you when you were bitten?

50. Have you had any contact with wild or domestic animals, including pets? yes, no, unknown
   Type of animal:
   Explain the nature of contact:
   Is / was the animal ill recently; yes, no, unknown
   If yes please describe the animal’s symptoms:
   Date / time of contact:
   Location of contact:

51. To your knowledge, have you been exposed to rodents/rodent droppings in the last two weeks? yes, no, unknown
   If yes, explain type of exposure:
   Date/time of exposure:
   Location where exposure occurred:
Individual has had physical contact or contact with the body fluids of a confirmed Viral Hemorrhagic Fever (VHF) case within three weeks of the onset of symptoms.

**YES**

Is contact experiencing fever (oral temp. >100.4°F/ 38°C)?

**NO**

Continue temperature checks two times per day for 21 days following last exposure to a case.

**YES**

Consider the contact to be a new case. Refer the patient for medical care. Patient should remain in isolation and if possible wear a mask while waiting for transportation to an isolation facility.

**Educate household about VHF transmission risks and precautions**