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Viral Hemorrhagic Fever (VHF)

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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 Kyanasur 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 diisseminated intravascular coagulation (DIC) has been implicated in Rift Valley, Marburg and Ebola fevers, but in most VHFs 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 VHFs, 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.
- Kyanasur 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 nephropathica 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 *in vitro* and *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

Family	Virus	Standard Procedure	Mask and Eye Protection Within 3 Feet	Airborne Transmission- Use of HEPA-Filtered Respirator (Only if Prominent Cough, Vomiting, Diarrhea, or Hemorrhage)	Private Room (Only if Significant Cough, Hemorrhage, or Diarrhea)	Mosquito Proofing	Special Caution- Virus Present in Blood or Excreta
Filoviridae	**Ebola**	X	X	X	X		X
	Marburg	X	X	X	X		X
Bunyaviridae	**CCHF**	X	X	X	X		X
	Rift Valley Fever	X	X	X	X		X
	Hantavirus	X					
Arenaviridae	**Lassa**	X	X	X	X		X
	South American Viruses	X					X
Flaviviridae	**Dengue**	X				X	
	Yellow Fever	X				X	X

Viral Hemorrhagic Fever Case Investigation Form

ID Number	Interviewer		Job title	
Interview date				
Person interviewed			□ patient □ other	
Describe relationship if other				
Demographic information	Last name		First name	
Sex Male Female	Date of birth	Age	Ethnic W . African . Asian	
Nationality		Home phone	Other phone	
Street		City	Zip	Country
How many people reside in the same household?		List Name, Age, Relationship		
1	5		9	
2	6		10	
3	7		11	
4	8		12	
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		
Occupation Place Name			. Work . School	
Address		City	Zip	Country
Address		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	Sputum	. yes no unknown	
Hemoptysis	. yes no unknown	Chest pain	. yes no unknown	
Breath shortness	. yes no unknown	Stridor /Wheezing	. yes no unknown	
Cyanosis	. yes no unknown	Conjunctivitis	. yes no unknown	
Adenopathies	. yes no unknown	Location		
Fever	. yes no unknown	Max Temp		
Antipyretics taken	. yes no unknown	Headache	. yes no unknown	

Stiff neck	¨ yes ¨ no ¨ unknown	Muscle aches	¨ yes ¨ no ¨ unknown
Fatigue	¨ yes ¨ no ¨ unknown	Joint pains	¨ yes ¨ no ¨ unknown
Altered mental status	¨ yes ¨ no ¨ unknown	Unconscious/Unresponsive	¨ yes ¨ no ¨ unknown
Sore throat	¨ yes ¨ no ¨ unknown	Diarrhea	¨ yes ¨ no ¨ unknown
Nausea	¨ yes ¨ no ¨ unknown	Vomiting	¨ yes ¨ no ¨ unknown
Rash	¨ yes ¨ no ¨ unknown	Describe	
Other symptoms:			

Past Medical History:

Do you have a regular physician? ¨ yes ¨ no ¨ unknown
If yes, name: phone number: (xxx) xxx-xxxx
Are you allergic to any medications? ¨ yes ¨ no ¨ unknown
If yes, list:
Are you currently taking any medications: ¨ yes ¨ no ¨ unknown
If yes, list:
Have you had any wound or lesion in the past several months?
¨ yes ¨ no ¨ unknown
If yes, where: appearance:

Hypertension ¨ yes ¨ no ¨ unknown
Neurologicsl condition ¨ yes ¨ no ¨ unknown
Diabetes ¨ yes ¨ no ¨ unknown
Cardiac disease ¨ yes ¨ no ¨ unknown
Seizures ¨ yes ¨ no ¨ unknown
Other pulmonary disease ¨ yes ¨ no ¨ unknown
If yes, describe:

Malignancy ¨ yes ¨ no ¨ unknown
If yes, specify type:

Currently on treatment: ¨ yes ¨ no ¨ unknown
HIV infection ¨ yes ¨ no ¨ unknown
Currently pregnant ¨ yes ¨ no ¨ unknown
Other immunocompromising condition (e.g., renal failure, cirrhosis, chronic steroid use)
¨ yes ¨ no ¨ unknown
If yes, specify disease or drug therapy:

Other underlying condition(s):

Prescription medications:

Social History:

Current alcohol abuse: ¨ yes ¨ no ¨ unknown
Past alcohol abuse: ¨ yes ¨ no ¨ unknown
Current injection drug use: ¨ yes ¨ no ¨ unknown
Past injection drug use: ¨ yes ¨ no ¨ unknown
Current smoker: ¨ yes ¨ no ¨ unknown
Former smoker: ¨ yes ¨ no ¨ unknown

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:

Test	**Results of Tests Done on Admission Date(/ /)**	**Abnormal Test Result at Any Time (specify date mm/dd/yy)**
Hemoglobin (hb)		(/ /)
Hematocrit (hct)		(/ /)
Platelet (plt)		(/ /)
Total white blood cell (wbc)		(/ /)
Wbc differential:		(/ /)

% Granulocytes (pmns)		(/ /)
% Bands		(/ /)
% Lymphocytes		(/ /)
Renal function: bun/cr		(/ /)
Liver enzymes: alt/ast		(/ /)
Blood cultures:	□ positive (specify) □ negative □ pending □ not done (/ /)	□ positive (specify) □ negative □ pending □ not done (/ /)

Test	**Results of Tests Done on Admission Date(/ /)**	**Abnormal Test Result at Any Time (specify date mm/dd/yy)**
Respiratory secretions: Specimen type:	□ expectorated sputum □ induced sputum □ bronchial alveolar lavage (bal) □ tracheal aspirate	□ expectorated sputum □ induced sputum □ bronchial alveolar lavage (bal) □ tracheal aspirate (/ /)
Respiratory secretions: Gram stain (check all that apply)	□ pmns □ epithelial cells □ gram positive cocci □ gram negative cocci □ gram positive rods □ gram negative coccobacilli □ gram negative rods □ gram negative rods with bipolar staining (safety pins) □ other	□ pmns □ epithelial cells □ gram positive cocci □ gram negative cocci □ gram positive rods □ gram negative coccobacilli □ gram negative rods □ gram negative rods with bipolar staining (safety pins) □ other (/ /)
Respiratory secretions Analysis: bacterial culture	□ positive (specify) □ negative □ pending □ not done	□ positive (specify) □ negative □ pending □ not done (/ /)
Respiratory secretions Analysis: viral culture	□ positive (specify) □ negative □ pending □ not done	□ positive (specify) □ negative □ pending □ not done (/ /)
Respiratory secretions Analysis: influenza antigen	□ positive □ negative □ pending □ not done	□ positive □ negative □ pending □ not done (/ /)

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	□ normal □ unilateral, lobar/consolidation □ bilateral, lobar/consolidation □ interstitial infiltrates □ widened mediastinum □ pleural effusion □ other (/ /)
Legionella urine antigen	□ positive □ negative □ pending □ not done	□ 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)
□ cefixime (suprax)
□ cefotentan (cefotan)
□ cefotaxime (claforan)
□ cefoxitin (mefoxin)
□ ceftazidime (fortaz, tazicef, tazidime)
□ ceftizoxime (cefizox)
□ ceftriaxone (rocephin)
□ other

□ gentamicin (garamycin)
□ levofloxacin (levaquin)
□ nafcillin
□ ofloxacin (floxin)
□ streptomycin
□ ticarcillin and clavulanate (timentin)
□ trimethaprim-sulfamethoxazole (bactrim, cotrim, tmp/smx)
□ vancomycin (vancocin)

b. antivirals : □ yes □ no □ unknown
If yes, check all that apply:
□ acyclovir (zovirax)
□ amantadine (symmetrel)
□ oseltamivir (tamiflu)
□ rimantidine (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)

Name of Ill Person	Age	Sex	Address	Phone	Date of Onset	Relation to you	Did they seek medical care? Where?	Diagnosis

Ttravel*

*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:

Category	**y/n /u**	**Description of activity**	**Location of activity**	**Date of activity**	**Time of activity** (start, end)	**Others ill? (y/n/u)**
9. Airports						
10. Beaches						
11. Bars/clubs						
12. Campgrounds						
13. Carnivals/circus						

14. Casinos						
15. Family planning clinics						
16. Government office building						
17. Gym/workout facilities						
18. Meetings or conferences						
19. Movie theater						
20. Museums						
21. Parks						
22. Parties (including raves, prom, etc)						
23. Performing arts (i.e. concert, theater, opera)						
24. Picnics						
25. Political events (including rallies)						
26. Religious gatherings						
27. Shopping malls						
28. Sporting event						
29. Street festivals, flea markets, parades						
30. Tourist attractions (i.e. french quarter, aquarium)						

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***?

Food Establishment	**y/n /u**	**Name of establishment**	**Location of meal**	**Date of meal**	**Time of meal** (start, end)	**Food and drink** (items consumed)	**Others ill?** (y/n/u)
Cafeteria at school, hospital, or other							
Casino or mall food court							
Grocery store or corner store							
Concert, movie, or other entertainment							
Dinner party, birthday party or other celebration							
Gas station or convenience store							
Plane, boat, train, or other							
Picnic, barbecue, crawfish boil, or potluck							
Outdoor farmers market, festival, or swap meet							
Restaurant, fast-food, or deli							
Sporting event or snack bar							
Street-vended food							

Other food establishment							
Other private gathering							

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
□ respiratory devices
□ vaporizers
□ whirlpool spas
□ hot tub
□ spa baths

□ humidifiers
□ misters
□ other (please explain)

□ creek and ponds
□ decorative fountains

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

Iif "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 <u>indoor</u> 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

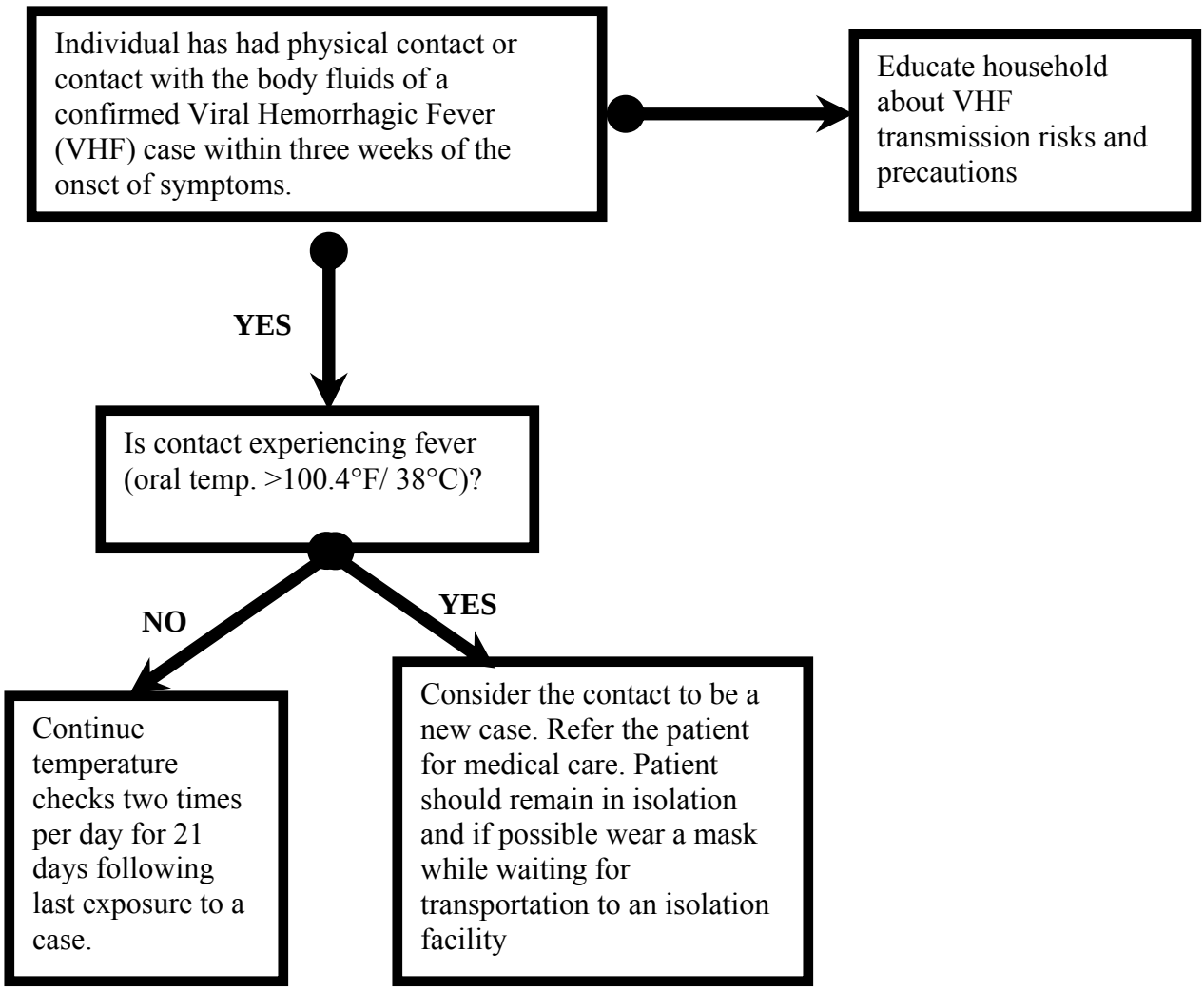
Date(s) of bite(s): bitten by: □mosquito □tick □flea □fly □other:
Where were you when you were bitten?

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.
Educate household about VHF transmission risks and precautions
YES
Is contact experiencing fever (oral temp. >100.4°F/ 38°C)?
NO
YES
Continue temperature checks two times per day for 21 days following last exposure to a case.
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