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# VIRAL HEMORRHAGIC FEVER:



# INITIAL MANAGEMENT OF SUSPECTED AND CONFIRMED CASES

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# Viral Hemorrhagic Fever: Initial Management of Suspected and Confirmed Cases

## INTRODUCTION

Every year the possibility exists that travelers with viral hemorrhagic fever (VHF) transmissible from person to person—Lassa, Ebola, Marburg, or Crimean-Congo hemorrhagic fever (CCHF)—may enter the United States. Among U.S. citizens, health professionals involved in the care of patients in Africa might be most likely to be exposed to agents of these diseases. Serologic studies have indicated, however, that missionaries and Peace Corps volunteers serving in Africa without obvious or frequent exposure to ill persons may also be exposed. Additionally, travelers may enter the United States asymptomatically infected with one of these viruses. Laboratory-acquired infection also remains a possibility in research or diagnostic facilities. Since guidelines concerning the approach to suspected cases of VHF were last published, in 1980 (*1*), approximately four cases of illness suspected of being VHF have occurred in the United States each year. None have been confirmed as VHF.

Although the source in nature of two (Ebola and Marburg) of the four viruses discussed in this document remains unknown, all four are capable of being transmitted from person to person, especially in the hospital setting. The communicability of these viruses in hospitals may vary considerably; however, the consequences of such transmission may be severe since case-fatality rates in hospital outbreaks have been high. The potential danger is increased by the fact that these illnesses begin with nonspecific symptoms that may be confused with other diseases. Therefore, appropriate barrier techniques designed to prevent transmission may not be instituted until late in the course of these illnesses, if at all. Finally, the lack of experience with these agents in the United States understandably results in confusion and anxiety on the part of physicians and other hospital personnel when a suspected importation occurs.

Since the earlier guidelines were published, additional clinical and laboratory observations have produced new information on the agents causing VHF and the illnesses they produce. Also, new information is available on treating patients with VHF. These guidelines are therefore offered to provide up-to-date information on these diseases, an organized approach to the suspected case of VHF, and guidelines concerning the handling of specimens and the care of patients. Also, a current list of persons available for consultation at CDC is included below. Because Lassa, Ebola, Marburg, and CCHF are the only hemorrhagic fevers for which person-to-person transmission has been documented, these guidelines will be limited to these four diseases. The reader is referred elsewhere for discussion of other agents that cause VHF in humans (*2*).

Further information and advice about the management of the patient with suspected VHF, control measures, and collection and shipment of diagnostic specimens are available on request from the following persons at CDC, Atlanta, Georgia. For all telephone numbers, dial 404-329 + extension:

1. Chief, Special Pathogens Branch, Division of Viral Diseases, Center for Infectious Diseases: Joseph B. McCormick, M.D. (ext. 3308).
2. Medical Epidemiologist, Office of the Director, Division of Viral Diseases, Center for Infectious Diseases: Jonathan E. Kaplan, M.D. (ext. 3095).
3. Director, Division of Viral Diseases, Center for Infectious Diseases: Frederick A. Murphy, D.V.M.(ext. 3574).
4. Acting Director, Office of Biosafety: John E. Forney, Ph.D. (ext. 3885).
5. After regular office hours and on weekends, the above-mentioned staff members may be contacted through the CDC duty officer (ext. 2888).

## LASSA FEVER

Lassa fever first came to medical attention in 1969 when three nurses working in missionary hospitals in Nigeria became ill. Two died in Nigeria, and the third patient, who was transported to the United States while still ill, survived (*3*). Two persons who worked in the laboratory in the United States where virologic studies were being done also became ill; one had worked with tissue cultures and infected mice, while the other had no known contact with the virus (*4,5*). Since that time Lassa fever has been shown to be endemic in many areas of West and Central Africa (*6*). The reservoir of infection, which is caused by an arenavirus, is the multimammate rat *Mastomys natalensis*. This rodent inhabits rural areas in sub-Saharan Africa and lives in and around human dwellings (*6, 7*).

Persons presumably acquire naturally occurring infections by contact with *M. natalensis*, either through handling the animal directly or by inhaling aerosolized excretions, such as urine. Subsequently, person-to-person transmission may occur within households and hospitals. Although one experience in Jos, Nigeria, has suggested that airborne transmission may occur (*8*), it is generally believed that direct contact with a patient or overt exposure to infective tissues, secretions, or excretions is necessary to transmit the infection from person to person.

The severity of illness appears to depend on the mode of transmission of the virus. Thus, in the community, where rodent-to-human transmission accounts for a substantial proportion of cases, the case-to-infection ratio may be as low as 1:30 (*9*). In the hospital, however, where transmission may occur by direct contact with infected secretions, excretions, or tissues, including inoculation with contaminated needles, this ratio is undoubtedly much higher. Case-fatality rates have ranged from 14% for sporadic cases in areas with endemic disease (*10*) to 52% for nosocomial outbreaks (*8*).

The incubation period of Lassa fever ranges from 6 to 21 days. Illness is usually heralded by fever, headache, myalgia, sore throat, and cough; chest and abdominal pain are also frequent complaints. In severe cases encephalopathy, hemorrhage, and shock may occur. Diagnosis can be made in three ways: by demonstrating a fourfold rise in titer of antibody to Lassa virus between acute-phase and convalescent-phase serum specimens with the indirect fluorescent antibody (IFA) technique, by detecting Lassa immunoglobulin M (IgM) antibodies, or by isolating Lassa virus from blood, urine, or throat (see HANDLING AND TRANSPORTING OF LABORATORY SPECIMENS). The diagnosis of Lassa is unlikely if no IgM or immunoglobulin G (IgG) antibody is detectable by the 14th day of illness, or if no virus is isolated from blood obtained during the first 7 days of illness. Virus isolation should be attempted only at laboratories equipped to handle viruses assigned to Biosafety Level 4 (*11*).

Treatment of Lassa fever is supportive and includes restoration of blood losses and maintenance of plasma volume, blood pressure, and electrolyte balance. Although immune plasma obtained from survivors of the disease has been used in severe cases, there are no data to confirm its efficacy. Preliminary data suggest that ribavirin, an antiviral compound, may be useful in the early stage of the illness (*12*). No Lassa fever vaccine is available.

Since the first recognized cases of Lassa fever in the United States in 1969, there has been one additional imported case of Lassa in this country, in 1976 (*13*). No secondary transmission following this case was noted despite intensive surveillance of close contacts. At least eight additional importations of Lassa fever have occurred in countries without endemic disease since recognition of the disease; however, no secondary transmission was identified after any of these importations (*14-20*). In four of these instances (*15,18-20*), the possibility of Lassa fever was not entertained until late in the course of illness or until after the patient had recovered, and barrier nursing techniques were not used during the acute stage of illness.

## EBOLA HEMORRHAGIC FEVER

Ebola hemorrhagic fever came to medical attention in 1976 when successive outbreaks occurred in Sudan and Zaire, comprising over 500 cases (*21,22*). The Sudan outbreak involved workers at a cotton factory, with subsequent spread in a hospital. Nosocomial transmission was associated with direct patient contact, and particularly with nursing a patient (*21*). The Zaire outbreak centered around an outpatient facility; contaminated needles were involved in disseminating infection in nearly half the cases (*22*). The case-fatality rates in these two outbreaks were 53% and 88%, respectively. A smaller outbreak (34 cases) was investigated in Sudan in 1979 (*23*). Serologic studies suggest that Ebola fever is endemic in limited areas of Sudan and Zaire, as well as the Central African Republic and Kenya (*24,25*). Both the reservoir of the virus in nature and the source of human infection remain unknown. Classification of Ebola virus in the family Filoviridae has been proposed (*26*).

Once Ebola infection develops in humans, person-to-person transmission may occur, both in the community and in the hospital. Intrafamilial spread outside the hospital appears to be related to close personal contact with a case (*22,23*); within the hospital, injections with contaminated needles have been implicated as well (*22*). Evidence suggests that airborne transmission is not important in the spread of Ebola infection (*21-23*).

The case-to-infection ratio of Ebola fever is unknown, but serologic studies suggest that mild or inapparent infection may be common in areas with endemic disease (*21,22*). Person-to-person transmission in medical facilities may result in a higher case-to-infection ratio (*22*). Case-fatality rates may be extremely high, as illustrated by the experiences in Zaire and Sudan (*21,22*).

The average incubation period of Ebola fever is estimated to be 6-9 days, with a range of 2-21 days. Ebola illness begins with sudden onset of fever, accompanied by headache, myalgia, sore throat, abdominal pain, and diarrhea. A maculopapular skin rash is commonly seen in fair-skinned patients. Hemorrhage, usually from the gastrointestinal (GI) tract, is very common. The diagnosis can be made serologically by the IFA test or, preferably, by isolation of Ebola virus from the blood in the acute phase of illness. As with Lassa fever, the diagnosis of Ebola fever is unlikely if virus is not isolated from blood obtained during the first 7 days of illness, or if antibody is not present by the 14th day of illness.

Treatment of Ebola illness is supportive. Immune plasma may be effective in reducing the level of viremia (*27*), but controlled studies to evaluate its effect on the outcome of illness have not been done. Evidence suggests that there is no cross-protection between the Zaire and Sudan strains of the virus (*28*), so immune plasma may have to be specific to be effective. No studies with ribavirin or other antiviral compounds have been undertaken.

There have been no documented imported cases of Ebola fever in the United States or Europe. However, one laboratory-acquired infection occurred in Great Britain in 1976 following accidental inoculation with infected guinea pig tissue (*29*); the patient survived, and no secondary transmission was detected (*30*).

## MARBURG VIRUS DISEASE

Marburg virus disease first came to medical attention in 1967 when 31 persons became ill in Europe following the importation of a group of African green monkeys from Uganda (*31-33*). Twenty-five of these patients were exposed directly to tissues from the monkeys. Six secondary cases occurred, all in persons who had direct contact with patients or their tissues. In 1975, a hitchhiker acquired Marburg infection in Rhodesia and then transmitted it to his girlfriend. She, in turn, transmitted it to a nurse in South Africa with whom she shared cigarettes, coffee cups, and handkerchiefs (*34,35*). A third outbreak of Marburg disease involved one primary and one secondary case (in the attending physician) in Kenya in 1980 (*36*), and a fourth involved a single case in South Africa in 1982 (*37*). Despite intensive investigation of these outbreaks, no natural reservoir of the Marburg virus has been identified, and the

area of endemicity has not been well defined. Morphologically, Marburg virus resembles the Ebola agent, but it is antigenically distinct. Classification in the family Filoviridae has been proposed (*26*).

Person-to-person transmission of Marburg disease has occurred in three of the four outbreaks that have been investigated. In each of these situations, transmission resulted from direct contact with an infected animal, an infected human, or infected tissues; there has been no evidence of airborne person-to-person transmission. The case-to-infection ratio of Marburg disease is unknown, but the case-fatality rate in the reported outbreaks has been 26%.

After an incubation period of 3-9 days, Marburg disease is heralded by fever, headache, myalgia, sore throat, dysphagia, vomiting, and diarrhea. A maculopapular skin rash is extremely common. Hemorrhage, usually from the GI tract, is a frequent finding, and disseminated intravascular coagulation (DIC) has been implicated in its pathogenesis. Diagnosis is made by IFA testing of serum specimens or by isolation of the virus from blood. As with Lassa and Ebola viruses, the diagnosis of Marburg virus disease is unlikely if virus is not isolated from blood obtained during the first 7 days of illness, or if antibody is not present by the 14th day of illness.

Treatment of Marburg virus disease is supportive. Immune plasma has been used, but its efficacy is unknown. Heparin may be useful in preventing DIC (*35*). No studies have evaluated the use of antiviral compounds in this disease.

Since the original Marburg disease outbreak, there have been no known cases of Marburg disease, either imported or laboratory acquired, in Europe or the United States.

## CRIMEAN-CONGO HEMORRHAGIC FEVER

Crimean hemorrhagic fever was first described in 1945, following an epidemic among field workers in the Crimea in the Soviet Union. The agent was isolated in 1945 (*38*), and subsequent studies showed that it was identical to a virus isolated in the Congo in 1956 (*39*); hence, the name Crimean-Congo hemorrhagic fever (CCHF). The disease is now known to be endemic throughout Eastern Europe, Africa, and Asia (*38*). Its natural reservoir is wild and domesticated mammals such as sheep, cattle, goats, and hares. Over 20 species of ticks have been found to be infected; however, illness is usually transmitted to humans by the bite of an ixodid (hard) tick of the genus *Hyalomma* (*38*). The CCHF agent has been classified as a bunyavirus.

Once a case of human CCHF occurs, person-to-person transmission is possible, particularly in the hospital setting; nosocomial outbreaks have occurred in several countries in which the disease is endemic, including the Soviet Union, Pakistan, India, and Iraq (*38,40-42*). Transmission is presumed to occur by direct contact with infective blood (*38,40,41*). There are no data to suggest that airborne transmission is an important mode of spread. The case-to-infection ratio in CCHF is unknown, but mild and inapparent infections do occur (*43*). The case-fatality rate ranges from 15% among sporadic cases (*43*) to 70% in nosocomial outbreaks (*42*).

After an incubation period of 3-6 days, illness is heralded by fever, chills, headache, myalgia, abdominal pain, and vomiting. Hemorrhage is a hallmark of the disease, and vascular collapse is common. Diagnosis is made serologically by the complement-fixation, indirect-hemagglutination, or IFA tests, or by isolation of the virus from blood. Failure to detect antibody by the 20th day of illness (the antibody response in CCHF may be delayed compared with that in other VHFs) or failure to isolate virus from blood obtained during the first 7 days of illness render the diagnosis unlikely.

Treatment is supportive. Although Suleiman (*41*) gained the impression that immune plasma may be effective, studies testing the efficacy of immune plasma have been inconclusive (*38*). The use of antiviral agents in CCHF has not been investigated.

No imported or laboratory-acquired cases of CCHF have been documented in countries without endemic disease.

## APPROACH TO A SUSPECTED CASE OF VHF

When confronted with a possible case of VHF, a physician should ask three questions: 1) Where has the patient been? 2) What time has elapsed between the patient's presence in the area with endemic VHF, or exposure to a person with VHF, and onset of illness? 3) What are the patient's symptoms? Careful history of the exact location of travel should be obtained. It is important to note that within the areas endemic for the various VHFs (Table 1), only specific types of exposure—direct or indirect contact with local animals or direct contact with ill persons or their tissues, secretions, or excretions—indicate the possibility of VHF. The vast majority of Americans visiting Africa and other areas with endemic VHFs will offer no history compatible with exposure to the organisms that cause VHF. Also, most travelers to urban areas, even though they may occasionally visit a rural area, will not come into contact with the virus reservoirs. An interval in excess of 3 weeks between possible exposure to VHF and onset of illness makes the diagnosis of VHF unlikely (Table 1). Since patients with VHF may present with nonspecific symptoms (fever, headache, myalgia), clinical diagnosis is very difficult, if not impossible. However, certain symptoms and signs in addition to these three (pharyngitis, conjunctivitis, vomiting, diarrhea, abdominal pain, and, most important, hemorrhagic manifestations and/or shock) should suggest the possibility of VHF (Table 1). Other febrile illnesses—malaria, typhoid fever, meningococcemia, arboviral and enteroviral infections, and leptospirosis—must be considered in the differential diagnosis.

If, having taken into account the above considerations, the physician feels the patient may have VHF, he/she should take the following actions immediately: 1) Place the patient in strict isolation, and 2) contact the local and state health departments and CDC.

## ISOLATION OF PATIENTS WITH SUSPECTED AND CONFIRMED VHF

Ideally, patients with suspected or confirmed VHF should be immediately placed in a special isolation unit (such as a Vickers Bed Isolator*) designed to prevent contamination of the area outside of the patient's immediate environment. Realistically, VHF will probably be suspected or diagnosed most frequently in medical facilities that have no specialized containment rooms or Vickers Isolators available. Most hospitals in the United States, however, have rooms in which it is possible to create negative pressure compared with the outside hall and in which air can be exhausted without recirculation to other rooms. Under these circumstances, strict isolation (*44*) should prevent transmission to others. If possible, the patient should remain in the hospital in which he/she is initially seen. If appropriate isolation cannot be arranged in this hospital, or if the hospital staff is logistically unprepared to care for a patient with VHF, transporting the patient to another institution, preferably a local one, must be considered. However, the risk to paramedical personnel and, more important, to the patient whose medical care will be delayed must be weighed carefully in making such a decision. It is recommended that the local and state health departments or CDC be consulted about the decision to move the patient to another institution and the means by which this may be accomplished.

To minimize the risk of transmitting VHF to health personnel caring for the patient, a number of precautions should be instituted:

1. The patient should be placed in a private room that is suitable for strict isolation and that can only be entered through an anteroom. Air from the patient's room should be at negative pressure compared with that of the outside hall, and it should be discharged without recirculation (the hospital engineer should confirm this before the room is used).

2. The anteroom, which should have hand-washing facilities, should be allocated for use by persons entering and leaving the patient's room. Air from this anteroom also should not recirculate to other parts of the hospital. The anteroom should contain supplies required for day-to-day care of the patient and supplies required for decontamination of materials taken from the patient's room (see Appendix).

*Use of trade names is for identification only and does not imply endorsement by the Public Health Service or the U.S. Department of Health and Human Services.

**Table 1. Clinical and epidemiologic characteristics of viral hemorrhagic fever**

| Characteristic | Lassa fever | Ebola hemorrhagic fever | Marburg virus disease | Crimean-Congo hemorrhagic fever |
|---|---|---|---|---|
| Endemic areas | West Africa (Guinea to Central Africa) | East Africa (Zaire, Sudan, Central African Republic, Kenya) | East Africa, South Africa | Eastern Europe, Asia, Africa |
| Etiologic-agent classification | Arenaviridae | Filoviridae (proposed) | Filoviridae (proposed) | Bunyaviridae |
| Reservoir in nature | Rodents (*Mastomys natalensis*) | ? | ? | Ticks (*Hyalomma* genus and others), wild and domesticated mammals |
| Modes of transmission | Rodent-to-human (virus excreted in urine); person-to-person | ? Person-to-person | ? Person-to-person | Tick bite; Person-to-person |
| Incubation period | 6-21 days | 2-21 days | 3-9 days | 3-6 days |
| **Symptoms** | **% of cases** | **% of cases** | **% of cases** | **% of cases** |
| Headache | 50-75 | 75-100 | 75-100 | 75-100 |
| Myalgia | 25-50 | 75-100 | 50-75 | 50-75 |
| Sore throat | 75-100 | 75-100 | 50-75 | 25-50 |
| Cough | 50-75 | 25-50 | 5-25 | 25-50 |
| Dysphagia | 5-25 | 5-25 | 25-50 | |
| Vomiting | 75-100 | 50-75 | 75-100 | 75-100 |
| Diarrhea | 25-50 | 75-100 | 75-100 | 25-50 |
| Chest pain | 25-50 | 50-75 | 5-25 | 5-25 |
| Abdominal pain | 50-75 | 75-100 | 5-25 | 75-100 |
| **Signs** | | | | |
| Fever | 75-100 | 75-100 | 75-100 | 75-100 |
| Conjunctivitis | 25-50 | 50-75 | 25-50 | 5-25 |
| Pharyngitis | 75-100 | 25-50 | 5-25 | 25-50 |
| Cervical lymphadenopathy | 25-50 | | 25-50 | |
| Abdominal tenderness | 50-75 | 25-50 | | 25-50 |
| Skin rash (macular) | 5-25 | 50-75 | 75-100 | |
| Hemorrhage (skin or gastrointestinal) | 25-50 | 75-100 | 25-50 | 75-100 |
| Shock | 25-50 | 25-50 | 25-50 | 50-75 |
| **Laboratory** | | | | |
| Leukopenia | 25-50 | 5-25 | 75-100 | 50-75 |
| Thrombocytopenia | | | 75-100 | 75-100 |
| Proteinuria | 50-75 | 50-75 | | 50-75 |
| Disseminated intravascular coagulation | | | 5-25 | 5-25 |

3. The external surfaces of all containers should be decontaminated before they are removed from the anteroom. Disposable linen, pajamas, and protective clothing worn by persons entering the patient's room (see below) should be double bagged in airtight bags, and the outside bag should be sponged with 0.5% sodium hypochorite solution (10% aqueous solution of household bleach) or a suitable phenolic disinfectant (such as Lysol*) before being removed from the anteroom. The bag and its contents should then be incinerated. Disposable items used in patient care/management, especially those involved in obtaining laboratory specimens (see HANDLING AND TRANSPORTING OF LABORATORY SPECIMENS) should be placed in a rigid plastic container containing 0.5% sodium hypochlorite. The outside of this container should be sponged with 0.5% sodium hypochlorite or a phenolic disinfectant before being removed from the patient's room. The container should then be autoclaved and discarded or incinerated.

4. Hospital traffic past the anteroom should be minimized, preferably by locating the room at the end of a corridor, and the door of the anteroom should be kept closed. A daily log should be kept of all persons entering the patient's room (the log should include adequate information for contacting these persons).

5. All persons entering the patient's room should wear the following disposable items: gowns, face masks, goggles, gloves, and head and shoe covers. Some persons may prefer to use full-face respirators equipped with high-efficiency particulate air (HEPA) filters, or nose and mouth respirators with HEPA filters plus goggles or face shield. These items may be stored either in the anteroom or immediately outside the door to the anteroom in the hallway. Protective clothing should be removed by the individual before he/she emerges from the anteroom into the outside hallway.

6. Routine management of the patient should be organized to limit traffic, including that of medical and nursing staff, into and out of the room. Patients who are ambulatory and have few symptoms should be encouraged to take care of themselves as much as possible (for example, noting their routine vital signs and making their beds).

7. The patient should use a chemical toilet, and all bodily secretions and excretions should be treated with 0.5% sodium hypochlorite before being removed from the room.

## VERIFICATION OF THE DIAGNOSIS OF VHF

Diagnosis of VHF can be confirmed by isolation of the causative virus from the blood of the patient or, in the case of Lassa fever, from the throat or urine. Diagnosis may also be made serologically, although antibodies are not usually present until the second week of illness. The Mobile Laboratory (see below) is equipped to perform serologic testing for the agents under discussion, but virus isolation must be done at a laboratory with appropriate containment facilities. The following guidelines pertain to obtaining the appropriate specimens for virus isolation.

## HANDLING AND TRANSPORTING OF LABORATORY SPECIMENS

### Collecting Specimens

The following initial specimens should be taken to confirm or rule out a diagnosis of VHF:

1. A throat swab placed in a plastic, screw-cap container in 1 ml of sterile, phosphate-buffered neutral saline, containing 1% human serum albumin or 25% rabbit serum albumin.

2. A clean-catch, midstream urine specimen obtained in a sterile container. Five milliliters of urine should be stabilized by the addition of either human serum albumin to a final concentration of 1% or rabbit serum albumin to a final concentration of 25% and placed in a plastic, screw-cap container.

3. Venous blood for antibody studies and virus isolation. Ten milliliters of clotted blood should be obtained in a sealed, plastic tube, if available (using vacutainers simplifies collection of multiple samples but may require using glass collection tubes). When obtaining the blood specimen, personnel should be acutely aware of the danger of accidental inoculation and of

sprays, spills, or aerosols (this obviously pertains to all specimens obtained from the patient for diagnostic purposes). Personnel should not attempt to replace the plastic needle guard on a used needle, but should discard the needle and syringe (or needle and vacutainer sleeve) into a rigid plastic container containing 0.5% sodium hypochlorite. The container should then be autoclaved and discarded or incinerated. To avoid unnecessary exposure of laboratory personnel, the blood specimen should not be centrifuged or separated.

The outside of each specimen container should be swabbed with 0.5% sodium hypochlorite or a phenolic disinfectant, and a label should be affixed with the patient's name, the date of the specimen, and the nature of the suspected infection. Specimens should then be double bagged in airtight bags and labeled similarly. Bags containing specimens should be sponged with a solution of 0.5% sodium hypochlorite or a phenolic disinfectant before being taken from the room.

### Packaging and Transporting Specimens

CDC (Office of Biosafety or contacts listed in the Introduction) or the state health department should be contacted for instructions on packaging, labeling, and shipping diagnostic laboratory specimens since shipment is subject to the applicable provisions of the Public Health Service interstate quarantine regulations (*45*). In general, specimens should be packaged as follows:

1. Place the specimen in a securely closed, watertight, primary container (screw-cap plastic test tube or vial), and seal the cap with tape. Heat-sealed plastic vials are also ideal primary containers for etiologic agents, provided they are formulated from a plastic that is not prone to shatter at temperatures of -20 C or lower.
2. Wrap the primary container with sufficient absorbent material (for example, paper towels or tissue) to absorb the entire contents in case the container breaks or leaks.
3. Place the wrapped, sealed primary container in a durable, watertight secondary container (screw-cap metal mailing tube or sealed metal can). Screw-cap metal mailing tubes should be sealed with tape. Several primary containers of specimens, each individually wrapped in absorbent material, may be placed in the secondary container, provided that the secondary container does not contain more than 50 ml of specimen material.
4. On the outside of the secondary container, place the specimen data forms, letters, and other information identifying or describing the specimen.
5. Place the secondary container and specimen information in an outer mailing tube or box.
6. Keep the specimens for virus isolation frozen, preferably by placing dry ice around the secondary container in the mailing tube or box (specimens should be frozen initially in a -20 C or -70 C freezer, not in dry ice).
7. Contact CDC or the state health department for advice on labeling and shipping.

## EXPOSURE OF LABORATORY PERSONNEL TO SPECIMENS

Laboratory personnel may have handled specimens from the patient during tests carried out early in the illness, before the diagnosis of VHF was considered. Additionally, once the diagnosis is considered, certain routine laboratory tests required for management of the patient may be necessary before the Mobile Laboratory is established (see CLINICAL MANAGEMENT OF PATIENTS WITH SUSPECTED VHF—THE MOBILE LABORATORY). Any person testing laboratory specimens from patients suspected of having VHF should wear surgical gloves and a full-face respirator with an HEPA filter. Care should be taken to minimize use of potentially hazardous procedures, such as ones that produce aerosols, and use of potentially hazardous equipment, such as glass microhematocrit tubes. Laboratory tests should be done in special areas with a Class 2A biological safety cabinet (*11*). All personnel who handled these specimens when not adequately protected should be placed under surveillance (see IDENTIFICATION, SURVEILLANCE, AND MANAGEMENT OF CONTACTS OF PATIENTS WITH VHF). The equipment used to carry out these tests should be decontaminated before being returned to routine use (see DECONTAMINATION PROCEDURES).

# CLINICAL MANAGEMENT OF PATIENTS WITH SUSPECTED VHF—THE MOBILE LABORATORY

## Case Management

The management of patients severely ill with VHF represents a major challenge to the practitioner of intensive-care medicine. The details of patient management cannot be covered in this document, and no attempt has been made to do so. A few general observations follow; further details may be obtained from the references.

The pathogenesis of VHFs is not clearly understood. Multiple organ systems may be affected by a viral infection that, although not highly inflammatory, is widely disseminated. A hallmark of these diseases is presence of high concentrations of virus in the blood for 2 weeks or longer. Many deaths occur among patients who are admitted during the second week of illness and who may be dehydrated and have low blood pressure. Thus, careful management of fluid and electrolyte balance from the onset of disease is perhaps the most important aid to recovery. Enzyme studies reveal that the liver is regularly affected, although it is doubtful that it is very often damaged sufficiently to cause death. The case-fatality rate in these diseases is higher for persons with overt bleeding than for those without hemorrhage. DIC has been documented only in patients with Marburg disease and CCHF, but its presence may help explain the clinical illness associated with the other hemorrhagic fevers as well. Detection and treatment of bleeding should be given high priority. Other acute problems that may occur include myocarditis and pericarditis, pleural effusion, intrauterine death, and spontaneous abortion.

Therapy is mainly supportive. Immune plasma obtained from persons who have survived the infection in question is frequently used for patients with VHF. However, the efficacy of such treatment has not been established. It is suggested that, if used, immune plasma should be administered early in the illness, preferably in the first week. The simultaneous presence of the virus and its naturally occurring antibodies in the blood of patients during the second week of illness suggests that some of the pathologic effects may be caused by deposition of antigen-antibody complexes. Administering immune plasma under such circumstances may only aggravate the patient's condition. Preliminary studies in Sierra Leone suggest that the antiviral agent ribavirin, if administered during the first week of illness, may be helpful in treating Lassa fever (*12*). This drug has not been studied in connection with the other hemorrhagic fevers.

## Mobile Laboratory

Any delay must be avoided in processing routine laboratory specimens necessary for care of the critically ill patient. In the past, however, there has been some reluctance to expose laboratory personnel or equipment to possible contamination with VHF viruses. Therefore, CDC has procured a Vickers Mobile Laboratory*, which can be transported within hours to any hospital in the United States where a person suspected of having VHF is hospitalized (*46*). A qualified laboratory technician experienced in working with VHF materials is available to accompany the laboratory equipment. The Mobile Laboratory includes facilities for performing routine hematologic and blood chemistry studies, coagulation studies, and urinalysis, as well as routine (bacterial) microbiologic cultures. Serologic studies for the agents causing VHF can be done in the Mobile Laboratory, but facilities are not adequate for attempting virus isolation. The laboratory is designed to facilitate the care of the ill patient so that transportation to another medical facility is unnecessary.

The Mobile Laboratory is to be installed in a hospital room with similar features to those of the patient's room and from which air can be exhausted to the outside of the hospital. It is preferable that this room be near the patient's room, have an anteroom or area for dressing, and have shower facilities. The room must have an 8-foot long table or counter with 4 feet of overhead clearance and an additional 8-10 linear feet of counterspace. Eight to ten electrical outlets will be required. Further information concerning the Mobile Laboratory can be obtained by contacting any of the persons listed in the INTRODUCTION.

### Autopsy and Handling of the Corpse

Careful consideration should be given to the potential risks and benefits of performing an autopsy on anyone suspected of having died from VHF. If an autopsy must be done, extreme precautions must be taken to prevent dissemination of the virus. Double gloves, cap and gown, waterproof apron and shoe coverings, and full-face respirators equipped with HEPA filters should be worn. Methods should be used to avoid or minimize aerosolization of tissues (e.g., bone should be cut with a hand saw rather than an electric saw). All effluents resulting from the autopsy should be decontaminated before they are washed down the drain, and the autopsy room should be decontaminated after the procedure.

The body should not be embalmed. Rather, the body should be placed in an airtight bag and either cremated or placed in a sealed casket for burial.

## DECONTAMINATION PROCEDURES

Conveyances (ambulances, for example), transport and bed isolation units, and hospital rooms can be decontaminated by applying a 0.5% sodium hypochlorite solution or a phenolic disinfectant to all exposed surfaces.

Patient care/management items (such as endoscopes) and laboratory equipment used to process specimens from patients with suspected VHF before the Mobile Laboratory is in place should be decontaminated before being returned to routine use. Surfaces in contact with potentially contaminated liquids, such as flow-through optical and sampling systems, can be decontaminated by flushing with 0.5% sodium hypochlorite. Sufficient solution should be used for the fluid to enter waste-disposal reservoirs in the instruments. Smaller reusable items, such as pipettes, should be immersed in 0.5% sodium hypochlorite and autoclaved. Disposable laboratory materials, such as pipette tips, plastic cuvettes, and excess specimens, should be placed in a rigid plastic container containing 0.5% sodium hypochlorite and autoclaved and discarded or incinerated.

## IDENTIFICATION, SURVEILLANCE, AND MANAGEMENT OF CONTACTS OF PATIENTS WITH VHF

A contact is defined as a person who has been exposed to an infected person or his/her secretions, excretions, or tissues in such a way as to be at risk of acquiring the infection. For VHF, this includes anyone who has been associated with an infected person—at any time from onset of fever to 3 weeks later—in any of the following ways:

1. Shared the same residence
2. Had face-to-face contact (within 3 feet) with the patient
3. Had skin or mucous membrane contact and/or a needle stick or other penetrating injury with the patient's secretions, excretions, blood, or tissues

CDC will work with state and local health authorities, as appropriate, to implement surveillance and management of contacts of patients with VHF. Initially, clinicians and hospital authorities should compile a list of individuals to be placed under surveillance, including their addresses and telephone numbers. The usual method of surveillance involves having the individual under surveillance record his/her temperature twice daily and report immediately any temperature of 101 F or greater or any symptoms of illness to the public health officer responsible for surveillance. Any person with a temperature of 101 F or more or other symptoms or signs suggestive of VHF within 3 weeks after exposure should be placed in isolation and treated as a suspected case.

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# APPENDIX

## Suggested List of Essential Supplies and Equipment To Be Kept in Anteroom Adjoining Patient's Room (Excluding Medications)

Equipment for full physical examination
Emergency equipment
Portable X-ray machine
Electrocardiogram machine
Intravenous equipment and supplies
Tourniquets
Dry gauze
Alcohol swabs
Needles and adapters
Syringes
Blood tubes for complete blood count, blood chemistry, and coagulation studies
Containers with Hanks' solution with 1% human serum albumin or 25% rabbit serum albumin for specimens of throat washing and urine
Printed specimen labels with patient's name
Marker pens
Plastic airtight bags, large and small
Large plastic trash bags
0.5% sodium hypochlorite (10% aqueous solution of household bleach), Lysol* solution
Chemical toilet
Urinals
Bed linen (disposable)
Pajamas (disposable)
Thermometers (disposable)
Toiletries, etc. (disposable)

*Use of trade names is for identification only and does not imply endorsement by the Public Health Service or the U.S. Department of Health and Human Services.

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