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Canadian Contingency Plan for Viral Hemorrhagic Fevers and Other Related Diseases

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Preface

The first Canadian Contingency Plan for Viral Hemorrhagic Fevers was written and published in 1978. The contents of the document did not change significantly over the next 10 years. However, in 1987, the task was begun to update the document to reflect the changing worldwide trends in infectious diseases. The current document specifically addresses evolving issues related to viral hemorrhagic fevers; however, it could also be applied to international outbreaks of other dangerous communicable diseases.

LCDC is grateful to all those who have contributed to the preparation of this document over the years .

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INTRODUCTION

The geographic distribution of many of these diseases, which are not usually found in Canada, indicates that individuals who present in this country with signs and symptoms consistent with an unusual or emerging communicable disease, such as acute viral hemorrhagic fever (VHF), will usually be travellers who have recently arrived in Canada. The majority of these suspected cases will have other conditions, which may also be travel-associated, that present with similar symptomatology. Surveillance activity associated with an outbreak of pneumonic plague in India in the autumn of 1994 demonstrated this fact. It was observed in Canada and elsewhere that individuals who have recently arrived from areas where unusual or emerging communicable diseases occur may present at different destinations with symptoms or illness requiring investigation and/or treatment[1,2]. Consequently, close attention to the differential diagnosis of illnesses in returned travellers is warranted.

A case of acute VHF has yet to be confirmed in Canada; however, there have been suspected acute cases, and confirmed convalescent cases have been reported. In addition, the recent recognition of locally acquired unusual or emerging communicable viral infections, such as hantavirus in North America, indicates that a reasonable index of suspicion is warranted in cases of seemingly obscure or undefined etiology and that these considerations need not be restricted solely to those individuals with exposure to foreign pathogens.

The original Canadian Contingency Plan was published on 1 March 1978 and revised in 1985, but not republished at that time. The Plan has now been revised for publication taking into account new information about the transmission of some of the VHFs and the use of antiviral agents for treatment and possibly prophylaxis.

Since the last revision of the contingency plan, new evidence about the transmissibility of Lassa fever by the respiratory route has been acquired. That information has made it possible to review some of the original recommendations regarding isolation practices[3,4]. Additionally, outbreaks of filovirus infections, both in non-human primates in North America and in humans in Africa, have significantly increased the understanding of aspects of those infections. Finally, there have been new evaluations of the uses of antiviral agents, such as ribavirin which may be effective in the treatment of Lassa fever and possibly some other VHFs[5].

The major focus of this document is directed at VHFs experience with the pneumonic plague outbreak in India indicates that some of the guidelines and procedures may be useful for other situations involving international outbreaks of dangerous communicable diseases.

Major differences between this plan and previous versions are as follows:

1. The recommendations for the use of containment isolator units have been abandoned. While recognizing that there may be some person-to-person transmission by, as yet, unknown routes, VHFs appear to be poorly transmitted by small droplet aerosols < 1 micron and the risk of infection during clinical care situations has been demonstrated to be reduced by use of strict standard infection control techniques.

2. Patients with suspected or proven VHF should no longer be transported to the National Defence Medical Centre, but should be hospitalized at the closest hospital with a suitable intensive care unit.

3. Routine laboratory tests should be performed in the hospital where the patient is admitted.

4. Procedures for handling laboratory specimens have been modified.

5. Ribavirin is recommended for treatment of Lassa fever, Rift Valley fever, Crimean-Congo hemorrhagic fever and hantaan virus infection.

6. Recommendations for disinfection of room and equipment after the patient has been transferred or discharged have been changed.

OBJECTIVE

The objective of the Plan is to present a guide for a coordinated response to the importation of suspected and confirmed cases of unusual or emerging communicable diseases, particularly VHFs, and to suggest appropriate management of cases and their contacts.

RATIONALE

While the majority of unusual or emerging communicable diseases are not indigenous to Canada[6], international travel provides the opportunity for the transport and introduction of these agents or infected individuals into the country. Additionally, as demonstrated by the recent recognition of hantavirus pulmonary syndrome in North America, local acquisition of an unusual or emerging communicable disease, while rare, remains possible. International travel is not a prerequisite for acquiring a serious communicable disease.

Many of the viral hemorrhagic viruses have high case-fatality rates. The management of patients and clinical contacts requires considerable care to prevent possible further transmission. In situations where the unusual or emerging communicable disease is highly infectious, contact tracing and identification may be required. A strongly suspected or

proven case of one of these diseases constitutes a potential public health emergency.

While the major focus of this plan is directed at diseases caused by viruses, many of the principles and operational practices can be applied to the control of unusual or emerging communicable bacterial diseases, e.g., pneumonic plague or international outbreaks of acute fatal disease of undetermined etiology.

The clinical management of these diseases and guidelines for their public health management in the United States have been described in "Update: Management of Patients with Suspected Viral Hemorrhagic Fever — United States"[7]. In general, the Canadian approach is similar to that taken by American authorities. It should be noted that the revisions in the above mentioned document have modified the guidelines for respiratory precautions and suggest a graduated containment approach that recognizes the increasing risk of infectiousness with the clinical progression of disease. This Canadian plan addresses issues specific to the Canadian approach.

THE RISK TO CANADA

The speed and volume of international travel and commerce have increased the risk that persons incubating any disease — including unusual or emerging communicable diseases — may arrive in Canada. Given the ease of modern air travel and the integration of international and domestic routes, passengers may arrive at many destinations in Canada shortly after leaving isolated or distant origins. Consequently, the presentation of one of these infections may occur in regions of the country where immediate access to specialist consultation may be difficult.

Appropriate control measures for situations involving these diseases are based both on an appreciation of the true risks associated with these communicable diseases as well as on a widespread understanding of the protocols in place to manage their occurrence, even if these events are rare or unlikely.

Unusual or emerging VHFs may be caused by members of the following virus groups:

- the Arenavirus group, including **Lassa, Junin, Sabia** and **Machupo** viruses[8,9]
- the Bunyavirus group, including **Crimean-Congo hemorrhagic fever** virus, and **Rift Valley fever** virus[10,11]
- the Filovirus group, including **Marburg** virus and **Ebola** virus[12-14], and
- the Flavivirus group including **Yellow fever** virus[15].

(The identification and classification of viral pathogens is a continuous process. The above noted listing indicates representative examples and is not meant to be definitive.)

As noted above, other imported communicable diseases of high infectivity and significant morbidity or mortality may require a coordinated national response in a manner similar to the unusual or emerging communicable viral diseases.

While many of VHFs were initially considered to be highly communicable between humans, this concept has not been substantiated. Although nosocomial transmission has occurred in areas with endemic disease, accumulated evidence shows that transmission of these viruses does not commonly occur through casual or remote contact[16-18]. Several importations to non-endemic countries have occurred without subsequent disease outbreaks. Indeed, with the exception of Marburg VHF, no secondary cases have been identified during importation episodes[4,6,10].

Body secretions and excretions, blood, semen, and tissue specimens from infected patients contain the virus. Evidence is accumulating to suggest that the risk of infection increases with the clinical progression of the disease. Persons at highest risk of secondary infection are those who are in closest contact with an infected person or his/her body fluids during the period of incubation and acute illness. Such persons include those with prolonged or close (face-to-face or exposure to secretions) contact with patients, those providing direct medical and nursing care, and laboratory workers handling the patient's specimens[7]. Data evaluating transmission by the respiratory route are scarce, but the possibility remains that such transmission may rarely occur with several of these or other viral agents.

A SUSPECTED CASE OF IMPORTED UNUSUAL OR EMERGING COMMUNICABLE DISEASE

The known areas of endemic transmission for Lassa, Ebola, and Marburg VHFs are exclusively in sub-Saharan Africa. Crimean-Congo VHF is transmitted throughout the Balkans and there is some serologic evidence of infection in Europe, China, central Asia, in the Indian subcontinent, the Middle East, and most of Africa. Other VHFs, such as those caused by the Junin, Sabia and Machupo viruses, are found in South America. In the absence of hospital or laboratory exposure these diseases are acquired almost exclusively in rural areas. Following an incubation period of 2 to 21 days, initial symptoms of all five VHFs are usually systemic and compatible with influenza: fever, myalgias, headache, and sometimes sore throat. At this point, such symptoms in a returning traveller who has a history of rural travel exposure, who has a history of contact with an ill individual or who has travelled to an area affected by an outbreak, could suggest a risk of VHF. However, the most likely diagnostic

possibilities would still be the following more common infectious diseases:

- **Bacterial**
  Typhoid, other enteric fevers, pyelonephritis, pneumonia, sepsis meningococcal disease, and leptospirosis.

- **Helminthic**
  Acute schistosomiasis, Katayama syndrome.

- **Protozoal**
  Malaria, amebic liver abscess.

- **Rickettsial**
  Typhus, Q fever, tickborne rickettsioses.

- **Viral**
  Mononucleosis, Dengue fever, hepatitis A, and acute HIV infection.

Conjunctivitis, petechiae, and in the case of filovirus infections, a morbilliform skin rash appear later and are more suggestive of VHF. It should be noted that these symptoms do not occur until the second week of illness. At this point, a reasonable suspicion of VHF would exist in the presence of a compatible travel history, the absence of a history strongly suggestive of other illnesses, and at least one negative blood smear for malaria. The investigations for malaria should be undertaken by those experienced in the interpretation. Additionally, it should be remembered that individuals with indigenous malaria immunity may have parasitemia but may be symptomatic for other reasons, including VHF. The additional signs of hemorrhage and shock are strongly suggestive of VHF.

LINES OF COMMUNICATION FOR SUSPECTED OR CONFIRMED CASES

The management of the presentation and the consequences of serious communicable diseases associated with travel requires the coordination of multiple jurisdictional responsibilities.

Local, provincial/territorial, national, and international action or measures may be indicated. Additionally, the rare nature of many of these diseases and the complexity of some of the diagnostic investigations limits the number of facilities available to deal appropriately with some of the threats posed by these infections.

Expedient, efficient, and coordinated communication is an essential component of this and any contingency plan.

Site of Case Identification

1. Ports of Entry

Imported unusual or emerging communicable diseases may be identified or suspected at Canadian Ports of Entry. An unusual or emerging communicable disease presenting on an aircraft or at a Port of Entry may be associated with considerable logistic and operational problems.

Imported diseases may present in one of two manners at Ports of Entry.

a. Advance warning from arriving aircraft

The presence of serious illness in aircraft passengers during flight is communicated to the airport of destination or diversion. Ground staff then transmit the information to appropriate destinations according to airport medical contingency plans.

This manner of identification is often sufficient to allow for advance notification of public health, transport, and hospital receiving personnel. Officials at the Port of Entry should immediately contact the Federal and Provincial/Territorial Response Coordinators.

b. Identification of ill persons during primary inspection

Arriving passengers are subject to inspection at Ports of Entry by either Canada Customs or Immigration officers. Persons who are noted to be ill may be referred for medical assistance and/or further medical evaluation. Both the Quarantine Act and the Immigration Act provide the authority for the medical examination and evaluation of individuals identified at Ports of Entry who are seriously ill.

In these situations prior notification of appropriate individuals and facilities is not possible. Contingency plans for the medical evaluation, isolation, contact notification and close liaison with local public health and hospital authorities were recently evaluated during the plague surveillance system and are currently functioning well.

Periodic testing and evaluation of the contingency plans in place to deal with arrivals with serious communicable disease is required to maintain an efficient system.

National quarantine services are provided at Ports of Entry by Health Canada. The official in charge should immediately notify the Federal and Provincial/Territorial Response Coordinators. Provincial/territorial and local public health staff should be responsible for follow-up of fellow travellers under surveillance. The Federal Response Coordinator will ensure that appropriate destination lists are obtained.

Quarantine health issues can be directed to the 24-hr LCDC Reference Line:

1-800-545-7661

2. Presentation Within the Local Health Care System

Suspected or identified cases who present at medical offices, clinics or hospitals will activate the provincial/territorial public health notification system as defined below.

To ensure a prompt and coordinated response to deal with the management of an unusual or emerging communicable disease, the following Response Coordinators have been designated:

- Provincial Response Coordinators are listed in the Appendix.
- The Federal Response Coordinator is the Director, Quarantine Health Services, Office of Special Health Initiatives, Laboratory Centre for Disease Control (LCDC), Health Protection Branch, Health Canada, Ottawa. Telephone, day: 613-957-8739; night: 1-800-545-7661. Fax: 613-952-8286.

If the patient's illness is compatible with or confirmed as an unusual or emerging communicable disease, it is incumbent upon the attending physician to discuss the situation immediately with the local Medical Officer of Health/Chef du département de santé communautaire who should, in turn, contact the Provincial/Territorial Response Coordinator (see the Appendix, p. 11).

If the attending physician is unable to contact the Medical Officer of Health/Chef du département de santé communautaire, the Provincial/Territorial Response Coordinator should be notified immediately. The Provincial/Territorial Response Coordinator should then notify the Federal Response Coordinator. If the Provincial/Territorial Response Coordinator and the Federal Response Coordinator agree that a reasonable or strong suspicion of VHF or a disease requiring similar control measures exists, then the procedures described in the rest of this document should be followed.

Cases arising at, or en route to, Canadian ports of entry should be reported by the Federal Quarantine Officer directly to the Federal Coordinator; this person, in turn, should immediately notify the appropriate Provincial/Territorial Coordinator. Following the evaluation of the situation, the Provincial/Territorial Coordinator will notify the appropriate Medical Officer of Health/Chef du département de santé communautaire.

In the rare instance of a medical evacuation to Canada from overseas of a patient with a suspected or proven unusual or emerging communicable disease, the Federal Response Coordinator should be contacted prior to the evacuation. The Federal Response Coordinator will notify the appropriate Provincial/Territorial Response Coordinator and the laboratory where diagnostic tests will be done.

If a VHF is first suspected by a physician at a hospital without an appropriate isolation room, or in the physician's office, or in a residential setting, etc., the Provincial/Territorial Response Coordinator and the local Medical Officer of Health/Chef du département de santé should arrange with the nearest appropriate hospital to have the patient transported there. Internal protocols within the hospital setting may need to be developed to address these situations in order to care safely for the patient and deal with the laboratory specimens. Assistance will be given to the hospital and the laboratory in establishing these protocols.

In hospitalized individuals where the diagnosis is suspected or in cases where a suspect case is being moved to a hospital, it is essential that the Infection Control Unit of that institution be immediately notified. Infection control officials will be instrumental in establishing and monitoring isolation practices and, in some centres, will notify appropriate public health personnel. In clinical situations, on-site advice and assistance may be obtained from experts in infectious diseases, infection control or tropical medicine. Due to the nature of the situation, the hospital administrators should be informed as well.

There should be ongoing and close communication between the attending physician(s), the local Medical Officer of Health/Chef du département de santé, the Provincial/Territorial Response Coordinator, the Federal Response Coordinator and the designated laboratory where diagnostic tests for VHF will be done.

The Provincial/Territorial Response Coordinator will be responsible to ensure that appropriate arrangements have been made by the local Medical Officerof Health/Chef du département de santé for transportation and isolation of suspect cases, that all appropriate staff have been notified, and that the ongoing communication referred to above occurs. The Coordinator should also notify other local public health staff who will be responsible for contact follow-up.

HOSPITALIZATION OF THE PATIENT

Throughout the course of a VHF illness, nosocomial transmission can occur directly (i.e., droplet), indirectly (e.g., instruments and hard surfaces), and possibly by aerosols. Viral shedding and its associated risks appear to increase from the incubation period through the last stages of infection[19].

The infection control team must be actively consulted and included in all decisions regarding patient isolation requirements, use of personal protective equipment and patient transport requirements.

Direct care givers should be limited to a small number of highly trained individuals. Students should not be included in the care team.

At a minimum, the laboratory dealing with the patient's specimens should be equipped with a biosafety cabinet and sealed aerosol-free centrifuge rotors (in this document a biosafety cabinet refers to a tested and certified Class II Biosafety Cabinet).

TRANSPORT OF THE PATIENT

The use of ambulance services for transportation from either a Port of Entry or a medical office or clinic to a hospital should be based on the clinical condition of the patient and after consultation with the local Medical Officer of Health/Chef du département de santé, and the standard practice of the jurisdiction. Movement of the patient by public transportation should be avoided. Where preliminary transportation has been by privately owned vehicle or by ambulance, the same vehicle, if available, should be used for further transportation.

For inter- or intra-hospital transport, transportation should be done as early as possible in the course of the disease. Because of increased mortality associated with transport[20], critically ill patients should not be transported. The use of ambulance services for transportation should be based on the clinical condition of the patient in consultation with the local Medical Officer of Health/Chef du département de santé.

Transport personnel must be informed of the patient's condition prior to moving. Because of the possible risk of the patient bleeding (e.g., from disconnected IVs, hemoptysis, scrapes, etc.), the increased risk of aerosolization of the virus from a blood spill and the close staff proximity to the patient, gloves, fluid-resistant gowns, fluid resistant masks and goggles are considered minimal equipment for transport staff. Transport should take place in a manner that minimizes patient contact with other persons (i.e., staff or patients).

The transport vehicle should be decontaminated promptly after use with a low-grade disinfectant (see "Disinfection of the Environment", p. 6).

MANAGEMENT OF THE PATIENT

There are five areas of concern: (1) patient isolation and protection of hospital staff; (2) laboratory tests and the collection of patient specimens; (3) laboratory processing of specimens; (4) performance of specific laboratory tests; and (5) treatment of the patient.

1. Patient Isolation and Protection of Hospital Staff

a. Isolation precautions for patients incubating or in early-stage VHF

During the incubation period there is little risk from body fluids other than blood. However, decisions with regard to isolation and precaution techniques should be made in anticipation of the patient's condition worsening. Given the unpredictability of the disease and the potential for clinical infectivity to increase, it may be prudent to upgrade the isolation precautions as soon as feasible[19].

The patient should be admitted to a private room. While a room with negative air flow is not necessary at this stage, it may be necessary if the disease progresses; therefore, admitting the patient to a room with negative air flow at this stage may circumvent transfer later. An anteroom, stocked with supplies, with facilities for handwashing and an area for donning protective equipment is useful.

Gowns and gloves are recommended for all persons who enter the room. Fluid-resistant masks and goggles or other eye protection are recommended if there is any possibility of a blood splash, minor or major (e.g., blood splashes and aerolization of blood can occur when starting an IV, emptying a suction container, taking blood for laboratory analysis, or dropping a container containing blood). Extreme vigilance is required to prevent needle sticks or other sharp injuries. Parenteral exposure has been associated with a high risk of transmission, a short incubation period and severe disease. Eliminate sharp instruments wherever possible. If feasible, use a needleless intravenous system.

Patient care equipment (e.g., thermometers, blood pressure cuffs, stethoscopes, commodes, etc.) should be dedicated to the patient. Use disposable supplies whenever possible. Soiled linens, clothing and protective clothing should be deposited in water-soluble plastic laundry bags that are closed in the room where used. The laundry bags should then be inserted into a designated red laundry bag (or a bag of another recognized colour). Heavily soiled laundry should be taken directly to the laundry (not placed in laundry chutes or other storage area). Soiled linen must go directly to the washing machine, with laundry bags placed directly into the water. Gowns, gloves, and masks should be worn by laundry workers.

Caregivers and visitors should wash their hands with an antiseptic solution (e.g., chlorhexidine 2%, povidone-iodine 10%, and chlorhexidine 0.5% on alcohol) after any patient contact and after leaving the patient's room .

b. Isolation of patients in advanced or end-stage VHF

Virus can infect many organs including those critical for virus dissemination, such as salivary glands, kidneys, bladder, sweat glands, and lungs[19]. Hemorrhage may be a prime feature of the clinical course with intense viremia as

the disease progresses. The likelihood of staff exposure to blood or other body fluids and the opportunities for virus aerosolization increase with the deterioration of the patient's condition. Fluid-resistant gowns or coveralls, gloves, fluid-resistant masks that filter to 0.03 microns and fit securely, and face shields are highly recommended. A private room is necessary; negative air flow is also strongly recommended whenever possible.

Laboratory specimens should be disposed in routine manner for Level 4 pathogens. All laboratory specimens must be considered infectious and handled in a consistently safe manner from point of collection to disposal. Specimens should be carried by hand to the laboratory for testing. Limit testing to tests critical to the well being of the patient. All tests must be collected and performed in a way that prevents aerosol generation.

c. Disinfection of the environment

VHF viruses are lipid-enveloped RNA viruses and, as such, are inactivated by low-level disinfectants[19]. Low-level disinfectants will be effective for environmental cleaning. Products in this category include quaternary ammonium-based products, phenolic chlorine-based products, and iodophor formulations.

All body secretions, excretions, and fluids should be disinfected or inactivated prior to disposal (i.e., either by a chemical, autoclaving or sterilizing prior to flushing in municipal sewer systems).

Personal protective equipment, including gloves, fluid-resistant masks with face shields, and fluid-resistant gowns, should be worn for cleaning up a spill of blood or other body fluid. (Protective booties and coveralls may be required if the spill is large). Remove excess blood or other body fluid with disposable towels. Discard the towels into a plastic-lined receptacle. After cleaning all the organic material from the surface, decontaminate the area with sodium hypochlorite (5% household bleach) or a low-level disinfectant. Leave the disinfectant in place for at least 10 minutes before rinsing.

d. Isolation of patient during convalescence

Virus may be excreted into the urine for weeks after recovery has begun. Disinfectant (e.g., household bleach) should be added to the toilet bowl prior to urinating or flushing for 6 weeks of convalescence or until patient has a negative culture for the virus. The average toilet contains 4 L of water in the toilet bowl prior to flushing. Place 50 to 100 cc of bleach in the toilet prior to urinating. Wait 5 minutes and then flush.

e. Postmortem

If the patient should die, handling of the body should be minimal. The corpse should be wrapped in a sealed leak-proof material, not embalmed, and then cremated or buried promptly in a sealed casket[7].

If an autopsy is necessary, the Provincial Coordinator should be consulted regarding appropriate precautions.

2. Laboratory Tests and the Collection of Patient Specimens

Upon presentation of a possible case of VHF, it is mandatory that the following tests be performed immediately:

- A thick and thin blood smear to look for malaria parasites — a second smear from a second specimen must be examined if the first does not reveal parasites;
- Two sets of blood cultures from separate venipunctures taken at least 30 minutes apart, with a total volume per set (two vials) of 20 to 30 cc;
- Unless there is an isolated automated system or the specimens have been inactivated (see below), manual white blood cell and differential counts, and either hemoglobin or hematocrit; and
- Urine culture, if urinalysis results suggest an infection.

The following five principles should be observed in the collection of all patient specimens.

1. Only specimens essential for diagnosis or monitoring should be obtained.
2. Specimens should be obtained by staff experienced in the required techniques. The same protective clothing as described for other hospital staff involved in the management of the patient should be worn by those obtaining and testing laboratory specimens.
3. Glass containers should be avoided whenever possible. Disposable sharp objects, such as scalpel blades, should be placed in puncture-proof containers immediately after use and later autoclaved before disposal or incineration.
4. Blood samples must be collected with extreme care to avoid self-inoculation. Universal Precautions should be strictly adhered to; needles must not be bent, broken, removed from disposable syringes, recapped or otherwise handled. After use, venipuncture equipment should be immediately placed in a rigid plastic container filled with disinfectant solution and autoclaved before disposal or incineration.
5. The entire outside surface of each specimen container should be wiped with disinfectant, and a label should be attached bearing the patient's name, hospital identification code, source of the specimen, date of collection, and the nature of the suspected infection. The specimens should then be double-bagged in secure, air-tight and water-tight bags, which have been similarly labelled. Bags containing specimens should be sponged with disinfectant before they are removed from the patient's room.

3. Processing of Laboratory Specimens

The laboratory receiving the specimen should be alerted to the potentially hazardous nature of the material being sent. Each laboratory should have prepared a contingency plan for these situations.

Laboratory staff dealing with specimens from patients with a suspected VHF must take, as a minimum, the same personal precautions as patient-care staff. Disposable gloves, fluid-resistant surgical masks, impermeable gowns, and protective eye wear should be worn. Depending on local conditions, the use of powered air-purifying respirators (PAPRs) and other respirators may be considered. Laboratory tests must be performed in biosafety cabinets. Blood cultures should be prepared in a closed system, if at all possible, and when not possible, all manipulations must occur in a tested and certified biosafety cabinet. Similar attention should be given to the cross matching of blood from patients with these diseases. Centrifuges must have sealed carriers or heads.

Every effort should be made to avoid creating an aerosol or splashing. Routine automated equipment should be used in the usual manner to prevent infections. The Office of Biosafety is available for consultation on biosafety practices and procedures.

Infectivity of serum may be reduced by heating with 0.3% beta-propriolactone for 30 minutes at 37° C, heating serum samples for 60 minutes at 60° C, or by treating the specimen with 2 megarads of gamma irradiation (with the specimen on ice to avoid overheating)[20,21]. Serum separation should be done using sealed centrifuge cups or a sealed centrifuge head. Abundant supplies of disinfectant solutions should be readily available. Use of a PAPR may be appropriate when dealing with specimens that have not been decontaminated.

Recent U.S. recommendations[7] state that serum used in laboratory tests should be pre-treated with polyethylene glycol p-tert-octylphenyl ether (Triton X® -100); treatment with 10µL of 10% Triton X® -100 per 1 mL of serum for 1 hour reduces the titre level of some of the VHFs viruses in serum, although 100% efficacy in inactivating these viruses should not be assumed.

Blood smears (e.g., for malaria) are not infectious following fixation in solvents. Routine procedures can be used for automated analyzers; analyzers should be disinfected as recommended by the manufacturer or with a 500 parts per million solution of sodium hypochlorite (1:100 dilution of household bleach: 1/4 cup to 1 gallon water) after use.

Laboratory personnel accidentally exposed to potentially infected material through spills, splashes, injections, cuts or abrasions should immediately wash the infected part with soap or detergent, apply an antiseptic solution (e.g., chlorhexidine 2%, povidone-iodine 10%, and chlorhexidine 0.5% on alcohol) and notify the employee health office and the Infection Control Unit. Such individuals, as well as those with mucus membrane exposure to biologic fluids or unprotected inhalation of aerosolized material, should then be considered as high-risk contacts and placed under surveillance (see the section entitled "Identification, Surveillance and Management of Patient Contact", p. 9).

Accidental spills of potentially contaminated material should be covered with absorbent paper towels, liberally covered with disinfectant and left to soak for 30 minutes before being wiped up. The area should be evacuated and secured. Following the removal of the initial material, the process should be repeated once again. Individuals attending to this task must wear protective attire. PAPRs or other respirators should be considered for those involved in the clean-up activity. Disposable gloves, impermeable gowns and protective eye wear, which must be removed immediately after completion of the process, should be placed in an autoclave bag and sterilized prior to disposal.

The United States Centers for Disease Control and Prevention (CDC) is evaluating the future of a mobile isolator that can be used as a portable laboratory to safely investigate cases of suspected or confirmed VHF. There is a similar unit in Canada. The U.S. facility is not currently available for use in Canada. The Canadian unit, while not routinely maintained in a state of immediate readiness, could be fully activated within a short time. Further information about the mobile laboratory in Canada can be obtained from the Federal Response Coordinator and/or the Office of Biosafety.

4. Performance of Specific Laboratory Tests

The need to do additional tests for the patient's welfare must be balanced against the possible danger to laboratory personnel. Only tests essential to patient care should be performed.

The diagnosis of VHF is confirmed by isolating the virus, by antigen detection by enzyme-linked immunosorbent assay (ELISA), viral genome detection by polymerase chain reaction (PCR), by demonstrating IgM antibody, or by demonstrating a fourfold rise in IgG antibody in serum. Antibody may not appear in the blood until the second week of illness. Virus is usually recovered from blood, although the Lassa virus may also be isolated from throat secretions or urine. Liver or spleen tissue collected after death may also be a rich source of virus. In hemorrhagic fever with renal syndrome, renal tissue should be obtained, and in cases of hantavirus pulmonary syndrome, lung tissue should be examined.

Designated laboratories for confirmatory diagnostic tests

Generally, it will be advisable to perform serology and attempt viral isolation. For VHF specimens which contain Level 4 agents such as Ebola and Marburg, viral isolation can only be performed at a Class 4 laboratory. At present, no Class 4 laboratory is operational in Canada. The CDC in the United States has a Class 4 facility.

Serology on Level 4 VHF specimens may be performed at the following laboratory:

Special Pathogens Branch
Division of Viral and Rickettsial Diseases
National Center for Infectious Diseases
Centers for Disease Control and Prevention
1600 Clifton Road N.E.
Atlanta, GA 30329-4018
Tel: (404) 639-1115 (from 0900-1700 hours);
(404) 639-2888 after hours
Attention: Dr. C.J. Peters

(The transfer of any material from Canada to facilities in the United States should be closely coordinated with Dr. Harvey Artsob, Acting Chief of the National Laboratory for Special Pathogens, LCDC in Ottawa, Tel: 613-954-0757, and the Office of Biosafety, LCDC in Ottawa, Tel: 613-957-1779. Call 1-800-545-7661 after hours. The transport of potentially pathogenic material across international borders can be a complicated issue administratively.

It should be noted that not all VHFs are caused by Level 4 agents. Dengue hemorrhagic fever, for example, is caused by a virus that is Level 2 and hemorrhagic fever with renal syndrome or hantavirus pulmonary syndrome is caused by hantaviruses that are Level 3 agents. Specimens for these non-Level 4 agents can be adequately dealt with in Canada.

Serology for non-Level 4 VHF specimens may be performed at the following Canadian laboratories:

Zoonotic Diseases

National Laboratory for Special Pathogens
Bureau of Microbiology
Laboratory Centre for Disease Control
Tunney's Pasture, P.L. 1001B
Ottawa, Ontario, K1A 0L2
Ph: (613) 954-0757
Fax: (613) 954-0207
Attention: Dr. Harvey Artsob

Vector-Borne and Special Pathogens Unit

Laboratory Services Branch
Ontario Ministry of Health
81 Resources Road
Etobicoke, Ontario, M9P 3R1
Ph: (416) 235-5725
Fax: (416) 235-6197
Attention: Director

5. Transportation of Specimens for Diagnostic Tests

The shipment of patient specimens must be in compliance with the Transport of Dangerous Goods Regulations. This necessitates an Emergency Response Plan Number, which can only be obtained from Transport Canada (613-991-9396) following the submission of a written response plan. The advice and assistance of the provincial/territorial laboratory should be sought before any specimens are shipped and, preferably, all specimens referred for sending out for testing should be submitted through them. Shipment of specimens must be planned in coordination with the Federal Response Coordinator or the Director, Office of Biosafety, LCDC (Tel: 613-957-1779; Fax: 613-941-0596), and the laboratory to which specimens are being sent. The Emergency Response Plan Number and an emergency phone number must appear on the shipper's declaration form.

As noted, it is advisable to perform serology tests and attempt viral isolation. The essential specimens to be submitted for virus isolation are a sample of venous blood, a mid-stream ("clean-catch") specimen of urine, and a throat swab. If postmortem specimens are available, samples from serum, liver, spleen, lung, and kidney should be sent for culture. The following procedures should be followed:

1. Ten mL of venous whole blood should be collected and submitted as is (i.e., clotted and not separated).

2. Mid-stream urine specimens should be collected by clean catch. Five mL of urine should be put in a plastic screw-cap container with one of the following: rabbit serum albumin diluted to a final concentration of 25%, human serum albumin diluted to a 1% concentration, or bovine serum albumin at a final concentration of 10%. The sample should be buffered.

3. Throat swabs should be placed in plastic screw-cap containers in 1 mL of sterile, phosphate-buffered neutral saline containing 25% rabbit serum, 1% human serum albumin, or 10% bovine serum albumin.

4. Tissue samples for analysis should be placed in plastic screw-cap containers, stored at -70° C until ready for shipment, and then shipped packed in dry ice.

All specimens should be packaged using approved Transport Canada packaging; the most convenient commercially available package is the Saf-T-Pak, catalogue number STP 100, obtained from Saf-T-Pak, Inc., 10450 Mayfield Road, Edmonton, Alberta, T5P 4P4; Telephone (403-486-0211); Fax (403-486-0235). Other commercially available packagings may be obtained from Environmental Packaging Systems Ltd. (902-461-1300). The sender should obtain and forward, by telephone or fax, the waybill number and anticipated time of arrival to facilitate tracing of the package, if required.

When serology alone is to be performed in Canada, only adherence to the following procedure is required.

1. The Saf-T-Pak comes with all necessary labels and instructions for proper packaging.

2. After applying the hazard label to the box, one prints above it "Infectious substances affecting humans UN 2814."

3. Then one completes the "To" and "From" on the top of the box. The "Shipper's declaration for dangerous goods", supplied with the Saf-T-Pak, should be completed.

4. A carrier waybill is supplied by the courrier company. On it one writes, "Dangerous goods as per attached shipper's declaration."

When viral isolation is to be attempted, the package must be placed on dry ice. Therefore, in addition to the above, the Saf-T-Pak is placed in a styrofoam cooler and surrounded with dry ice. On the outside of the cooler, one must affix all the labels and markings that are also on the inner box (e.g., the Saf-T-Pak). In addition, the following markings relevant to the dry ice must be affixed: "Dry ice, UN 1845", the net weight of the dry ice (e.g., 1500 g), and a Class 9 hazard label. The shipper's declaration should be completed.

Specimens for either serology or viral isolation sent to the CDC require an import permit from the American government. These permits must be obtained by telephoning the Office of Biosafety, CDC (404-639-3235). The Office of Biosafety may then fax an import permit to the shipper. As noted above, any shipment of material to the U.S. should be coordinated with the involved provincial laboratory and LCDC.

6. Treatment of the Patient

The supportive care of critically ill VHF patients is the same as that provided to other critically ill patients. Consultation with infectious disease specialists and infection control officials is recommended.

The anti-viral drug ribavirin should be used intravenously to treat all confirmed cases of Lassa VHF. Ribavirin has some effect against the virus that causes Congo-Crimean VHF; its use in patients with confirmed Congo-Crimean VHF should be considered. In addition, there is some evidence to suggest that ribavirin may have some effect against the American hemorrhagic fever viruses such as Junin. Ribavirin does not appear to be indicated for filoviruses (i.e., Marburg and Ebola VHFs). If a non-filovirus VHF is strongly suspected, treatment with ribavirin may begin while confirmation of the diagnosis is pending.

The dose and route of administration are as follows: ribavirin 30 mg/kg loading dose intravenously (IV), then 16 mg/kg IV every 6 hours for 4 days, and then 8 mg/kg IV every 8 hours for 6 days (total treatment time 10 days). Ribavirin for parenteral use is not a licensed preparation in Canada. To obtain this agent as an emergency drug, request authorization from the Emergency Drug Release Program, Bureau of Pharmaceutical Assessment, Drugs Directorate, (613-941-2108) during regular business hours (0830-1630 EST) and (613) 941-3061 after hours. Authorized supplies of ribavirin will be supplied by the National Defence Medical Centre, Ottawa.

Careful fluid management of patients is important to minimize the risks of pulmonary congestion and edema. Central pressure monitoring may be a useful aid in the medical management of these patients but there are serious issues related to the associated risks to medical staff that require consideration.

IDENTIFICATION, SURVEILLANCE AND MANAGEMENT OF PATIENT CONTACTS

A contact is defined as a person who has been exposed to an infected person or to an infected person's secretions, excretions, or tissues within 3 weeks of the patient's onset of illness. Contacts may be subdivided into three levels of risk.

1. **Casual contacts** are persons who have not had close personal contact with the ill patient. These include persons on the same airplane, in the same hotel, visitors to the patient's home, etc. Since the agents associated with VHFs are usually not spread during such contact, no special surveillance is indicated unless the patient had acute respiratory involvement with intense sneezing and coughing. In such situations, exposed persons should be placed under surveillance for "close contacts". In most cases, occupational contacts of suspected patients will fall into this category.

2. **Close contacts** are persons who have had more than casual contact with the patient. They include persons living with the patient, nursing or serving the patient, skin-to-skin contact with or hugging the patient, and handling the patient's laboratory specimens, before the recognition of the nature of the diagnosis. These contact persons should be identified by provincial and local health departments, in collaboration with LCDC, as soon as VHF is considered a likely diagnosis for the index case. Once the diagnosis is confirmed, close contacts should be placed under surveillance. These individuals should record their temperature twice daily and report any temperature $\geq 38.3^{\circ}$ C or any symptom of illness to the public health officer responsible for surveillance. Surveillance should be continued for 3 weeks after the person's last contact with the index patient.

Surveillance is not indicated for routine occupational contact with patients in situations where the diagnosis has been considered and appropriate isolation precautions implemented.

3. **High-risk contacts** are persons who have had mucous membrane contact with the patient, such as kissing or sexual intercourse, or have had a needle stick or other penetrating injury involving contact with the patient's secretions, excretions, blood, tissues, or other body fluids. These individuals should be placed under surveillance as soon as VHF is considered a likely diagnosis in the index case.

Any close or high-risk contact who develops a temperature of ≥ 38.3° C or any other symptoms of illness should be immediately isolated and treated as a VHF patient (see "Management of the Patient", p. 5).

Convalescent patients and their contacts should be warned that some of the causative agents of VHF may continue to be excreted for many weeks in semen, as demonstrated with filoviruses (e.g., Marburg and Ebola) and arenaviruses (e.g., Junin), and in urine, as occurs sometimes with Lassa virus. Collection of both seminal fluid and urine for virus isolation from male patients and urine from female patients in the convalescent period is encouraged (see "Transportation of Specimens for Diagnostic Tests", p. 8). Weekly evaluation for viral excretion is recommended. Convalescent patients must be meticulous about personal hygiene. While data are limited concerning infectivity in the convalescent period, abstinence from sexual intercourse is advised until genital fluids have been shown to be free of the virus. If the patient does engage in sexual intercourse before tests are done, the use of condoms is advised.

Post-exposure Prophylaxis

The use of ribavirin for post-exposure prophylaxis for high-risk contacts of patients with Lassa fever has not been studied. Although experience is more limited, post-exposure prophylaxis with ribavirin may be considered for high-risk contacts of patients with Crimean-Congo hemorrhagic fever. The prophylactic regimen is ribavirin 500 mg by mouth every 6 hours for 7 days. Ribavirin is not licensed for oral use in Canada, and one must request authorization from the Emergency Drug Release Program, Bureau of Pharmaceutical Assessment, Drugs Directorate (613-941-2108) during regular business hours (0830-1630 EST) and (613-941-3061) after hours. Authorized supplies of ribavirin will be supplied by the National Defence Medical Centre, Ottawa.

APPENDIX

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