

VIRAL HEMORRHAGIC FEVERS (VHFs)

CONTINGENCY PLAN – ONTARIO

January 2002

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Listed in Appendix V**

INDEX OF QUICK REFERENCE INFORMATION *(Updated March 2005)*

Physician should contact their local medical officer of health

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Day: (416) 212-3831

FAX: (416) 325-8412

After hours: through Spills Action Centre: (416) 325-3000 or (800) 268-6060

Alternate Provincial Response Coordinator

Public Health Division physician on call

After hours: through Spills Action Centre: (416) 325-3000 or (800) 268-6060

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Federal Response Coordinator

Dr. James Anderson

Director, Office of Public Health Security (OPHS)

Day: (613) 954-3236

QTMH Cellular: (613) 791-1027

(QTMH = Quarantine, Travel and Migration Health)

OPHS Fax: (613) 952-8286

Public Health Agency of Canada: (800) 545-7661 24 Hour Reference Line

Additional Members of the Case Assessment Team:

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Laboratories Branch, MOHLTC

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Day: (416) 235-5841

Pager: (416) 718-0372

Fax: (416) 235-5951

Reference Page

Emergency supplies for obtaining, transporting specimens 6, 9

Laboratory Services Branch - central and regional labs (*Appendix III*)
After hours: (416) 605-3113

Saf-T-Pak (catalogue no. STP 100) ESBE, Markam, Ontario Tel: (905) 475-8232 Fax: (905) 475-5688	Environmental Packaging System Tel: (902) 461-1300 Fax: (902) 466-6889	16
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Emergency Drug Release Program to obtain ribavirin 17

Day: (613) 941-2108, after 16:30 EST: Pager: (613) 941-3061
FAX: (613) 941-3194

Information required:

- name, address, telephone no. of requesting doctor
- initials, age, sex of patient
- name of drug, medical indication
- quantity, dosage form
- drug manufacturer

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Contingency Plan for Viral Hemorrhagic Fevers Ontario

1.0 Introduction

The objective of the Ontario Contingency Plan for Viral Hemorrhagic Fevers is to provide a guide for a co-ordinated response within Ontario to the importation of suspected and confirmed cases of viral hemorrhagic fever (VHF), and to suggest appropriate management of cases and their contacts.

This document replaces any previous contingency plan published by the Ontario government. Although a case of acute VHF has not been confirmed in Ontario, there have been both suspected and confirmed convalescent cases and the potential for importation is an ongoing concern. Circumstances under which the diagnosis of acute VHF should be considered are listed under 4.0, *A Suspected Case of Hemorrhagic Fever*. However, it is important that in all suspected cases, other more common and potentially treatable diseases are eliminated from the differential diagnosis. Evidence about the low transmissibility of Lassa fever by the aerosol route lead to the review of the original recommendations on isolation. Also, the antiviral drug ribavirin is now available for the treatment and possible prophylaxis of Lassa fever, and possibly some other VHFs.

The major differences between this plan and earlier published plans continues to be the following:

1. The use of containment isolator units has been abandoned.
2. Patients with suspected or proven VHF should no longer be transported to a national centre, but should be hospitalized at the closest hospital with a suitable intensive care unit and adequately contained laboratory facilities which include certified level II biosafety cabinet(s).
3. Routine laboratory tests should be performed in the hospital where the patient is admitted. This is important to ensure good patient care and to identify other conditions. Such tests should not result in the aerosolizing of potentially infectious materials or endanger laboratory personnel.
4. Procedures for handling laboratory specimens have been modified.
5. Ribavirin may be used for treatment of and chemoprophylaxis against certain VHFs.
6. Recommendations for terminal disinfection have been changed.

2.0 Rationale

VHFs are not indigenous to Canada. They are diseases associated with a number of geographically restricted viruses characterized by fever and, in most cases, shock and hemorrhage. As well, they are known to have caused outbreaks of disease with person-to-person spread. Among the agents that cause VHF, five have a high case-fatality rate. The management of patients with **Lassa fever, Marburg virus hemorrhagic fever, Ebola virus hemorrhagic fever, Crimean-Congo hemorrhagic fever, Bolivian (Machupo) and Venezuelan hemorrhagic fever (Guanarito)**, requires considerable care to prevent further possible transmission. Although the risk and/or mode of nosocomial transmission differs for each of these viruses, the limited data do not permit clear distinctions. A strongly suspected or proven case of one of these VHFs constitutes a public health emergency and in the rest of this document, VHF refers to one of these six diseases.

Diseases like hantavirus do not pose a risk of person-to-person spread, however, there is a risk to laboratory workers analyzing specimens. This applies also to the Arenaviruses, Junin (Argentinean) and Sabia (Brazilian) which cause viral hemorrhagic fever and are transmitted to humans primarily by inhalation of small particle aerosols derived directly from rodent excreta or saliva containing virus.

The epidemiology and clinical management of VHF and guidelines for their public health management in Canada have been described in *Canadian Contingency Plan for Viral Hemorrhagic Fevers and Other Related Diseases*, CCDR, Vol 23S1, January 1997. In general, the Ontario approach is compatible with that in Canada and in large part information in this document is similar to that in the federal contingency plan.

3.0 Risk of Importation and Transmission within Ontario

Both the speed and volume of international travel have increased the risk that persons incubating any disease, including VHFs, may arrive in Ontario. In North America and Europe several importations from endemic countries have occurred without subsequent disease outbreaks. Indeed, with the exception of Marburg VHF and one case of Ebola, no secondary cases have been identified during importation episodes.

Epidemiological studies of VHF in humans indicate that infection is not transmitted readily from person to person by the airborne route. Airborne transmission involving humans has never been documented and is considered a possibility only in rare instances from persons with advanced stages of disease. The risk for person-to-person transmission of a hemorrhagic fever virus is highest during the later stages of illness, which are characterized by vomiting, diarrhea, shock and often hemorrhage. VHF infection has not been reported in persons whose contact with an infected patient occurred only during the incubation period, i.e., before the patient became febrile.

Although nosocomial transmission has occurred in areas with endemic disease, accumulated evidence shows that transmission of these viruses does not occur through casual contact. Persons at highest risk of secondary infection are those who

are in closest contact with an infected person's body secretions and excretions, blood, semen, and tissue specimens. Such persons include the patient's intimate contacts, those providing direct medical and nursing care, and laboratory workers handling the patient's specimens. The risks associated with various body fluids have not been well defined as most caregivers who acquired infection had multiple contacts with multiple fluids.

4.0 A Suspected Case of Viral Hemorrhagic Fever

The known areas of endemic transmission are exclusively in sub-Saharan Africa for Lassa, Ebola, and Marburg VHF. Crimean-Congo VHF is transmitted throughout Europe, in China, in central Asia, in the Indian subcontinent, in the Middle East and in most of Africa. Bolivian and Argentinean VHFs have occurred in their respective countries of South America. These diseases are acquired almost exclusively in rural areas. This contingency plan applies to individuals who, within 3 weeks before onset of fever, have either:

- travelled in the specific local area of a country where VHF has recently occurred (if exact travel history is unknown, risk assessment should be done through consultation with the case assessment team)
- had direct contact with blood, other body fluids, secretions, or excretions of a person or animal with VHF, or
- worked in a laboratory or animal facility that handles hemorrhagic fever viruses.

The incubation period for these diseases are:

- Lassa - 6 – 21 days
- Ebola - 2 – 21 days
- Marburg - 3 – 9 days
- Crimean Congo - Usually 1 – 3 days with a range of 1 – 12 days
- Bolivian - 7 – 16 days
- Venezuelan - 7 – 16 days

The likelihood of acquiring VHF is considered extremely low in persons who do not meet any of these criteria.

Following an incubation period of 1 to 21 days, depending on the etiology, initial symptoms of all six VHFs are usually systemic and compatible with influenza; fever, myalgia, headache, sore throat, diarrhea and chest pain. At this point, such symptoms in a returning traveller from the above areas would suggest an extensive differential diagnosis, in which the most likely possibilities would be the following infectious diseases:

- Viral: Influenza, mononucleosis, CMV, hepatitis A,B and E, dengue and acute HIV infection
- Rickettsial: Q-fever, typhus and tick-bite fever
- Bacterial: Typhoid, other enteric fevers, pyelonephritis, meningococcal disease, brucellosis and leptospirosis

- Protozoal: Malaria, typanosomiasis, amoebic liver abscess
- Helminthic: Acute schistosomiasis (Katayama syndrome) and strongyloidiasis

Evaluation for and treatment of these other potentially serious infections should not be delayed.

Conjunctivitis, petechiae, or a morbilliform skin rash appear later and are more suggestive of VHF. 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 **thick** blood film for malaria plasmodia. The latter investigation should be undertaken by those experienced in the interpretation of malaria films. 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. However, these signs often appear in the second week of illness.

5.0 Lines of Communication for Suspected or Proven Cases

The management of the presentation and the consequences of a serious infectious disease associated with travel require the coordination of multiple jurisdictional responsibilities.

Local, provincial, national and international action or measures may be indicated. Additionally, the rare nature of VHFs and the complexity of some of the diagnostic investigations call for expedient, efficient and coordinated communication among all those involved.

Reporting to the Medical Officer of Health

If the patient's illness is compatible with or confirmed as VHF, it is the legal responsibility of the attending physician to inform immediately the local medical officer of health. The medical officer of health will in turn contact the Provincial Response Coordinator.

The Ontario Response Coordinator is Dr. Sheela Basrur, Chief Medical Officer of Health for Ontario (see ***Index of Quick Reference Information for contact information or Appendix I***). Alternately, the Public Health Branch physician on call may be contacted through Spills Action Centre, (416) 325-3000 or (800) 268-6060.

Formation of a Case Assessment Team

The Ontario Response Coordinator with Dr. F. Jamieson, Medical Microbiologist, Laboratories Branch and Dr. J. Keystone (or Dr. K. Kain), Centre for Travel and Tropical Medicine, Toronto General Hospital, in collaboration with the local medical officer of health, will form a case assessment team to collaborate on an appropriate course of action.

Appendix I lists the contact numbers of the response coordinators and

assessment team. Appendix II lists contact numbers for local medical officers of health. Appendix V lists Infectious Disease/Travel Medicine Consultants in various locations in Ontario.

The Federal Response Coordinator is Dr. James Anderson, Director, of Public Health Security, Health Canada, Ottawa. 24 Hour Health Canada Reference Line **(800) 545-7661**.

The Provincial Response Coordinator will then notify the Federal Response Coordinator and the laboratory where testing will be performed. The Provincial Response Coordinator will consult with the other members of the case assessment team. Dr. Jay Keystone or Dr. Kevin Kain, tropical disease consultants and Dr. Frances Jamieson, Medical Microbiologist, regarding the potential diagnosis. If the case assessment team and the Federal Response Coordinator agree that a reasonable or strong suspicion of VHF exists, then the procedures described in the rest of this document should be followed.

Cases arising at, or en route to Canadian ports will be reported to the Federal Response Coordinator who will immediately notify the Provincial Response Coordinator. If the two response coordinators concur, the Provincial Response Coordinator will notify the appropriate local medical officer of health.

In the rare instance of a medical evacuation to Canada from overseas of a patient with suspected or proven VHF, the Federal Response Coordinator will notify the Provincial Response Coordinator.

There should be ongoing and close communication between the attending physician(s), the local medical officer of health, the Provincial Response Coordinator, the Central Public Health Laboratory in Toronto and the National Microbiology Laboratory (NML) in Winnipeg, where diagnostic tests for VHF will be done.

6.0 Transport of the Patient to Hospital

If VHF is first suspected by a physician at a hospital without an appropriate isolation room, the physician's office, a residential setting, etc., the local medical officer of health or the Provincial Response Coordinator should arrange with the nearest appropriate hospital to have the patient transported there.

The mode of transport for the patient should be based on the clinical condition and mobility needs of the patient. The decision to use ambulance services for transportation should be based on the clinical condition of the patient after consultation with the local medical officer of health. The patient should **not** travel by public transportation. Where preliminary transportation has been by privately owned vehicle or by ambulance, the same vehicle, if available, should be used for further onward transportation.

Personnel in the transportation vehicle should follow the same precautions as

hospital staff and transport should take place in a manner that minimizes patient contact with other persons (see **Management of the Hospitalized Patient**, p.6). Transport personnel must be informed of the patient's condition prior to moving if the patient is a suspected case at the time. If viral hemorrhagic fever is suspected after admission to hospital, the supervisor of the transport service should be informed immediately.

Because most ill persons undergoing pre-hospital evaluation and transport are in the early stages of disease and would not be expected to have symptoms that increase the likelihood of contact with infectious body fluids (e.g., vomiting, diarrhea, or hemorrhage), universal precautions are generally sufficient. If a patient has respiratory symptoms (e.g., cough or rhinitis), face shields or surgical masks and eye protection (e.g., goggles or eyeglasses with side shields) should be worn by care givers to prevent droplet contact.

A kit containing protective gear for use by personnel obtaining specimens from a suspect or proven case of viral hemorrhagic fever prior to transit is located in the central and regional Laboratories Branch laboratories (see *Appendix III, Ontario Public Health Laboratories*). The kit comprises one Saf-T-Pak for transporting specimens to Laboratory Services Branch, two high efficiency masks (size large, size medium), one face shield, two gowns (size large, size extra large), shoe covers, and two pairs of non-latex gloves (size medium-1 pair, large-1 pair).

The transport vehicle should be promptly decontaminated (see **Terminal Disinfection**, p.17), and it should not be used for other patients or individuals until decontamination has been done.

7.0 Management of the Hospitalized Patient

Patients with VHF are or may become very ill. Appropriate isolation should be instituted immediately upon suspicion of VHF. They should be moved as little as possible, but they must be cared for in a hospital with an isolation unit in which critically ill persons can be cared for and which has adequately contained laboratory facilities including at minimum Class II certified biohazard containment cabinets and aerosol-free centrifuge rotors for analysing the patient's specimens. The director of the hospital laboratory is advised to seek consultation with Dr. Frances Jamieson, Medical Microbiologist, Laboratories Branch on how to handle specimens.

The section below includes the following areas: (7.1) patient isolation and protection of hospital staff; (7.2) collection of laboratory specimens; (7.3) performance of specific laboratory tests; (7.4) processing and transportation of laboratory specimens; (7.5) treatment of the patient; and (7.6) terminal disinfection.

7.1 Patient Isolation and Protection of Hospital Staff

Extensive experience in West Africa has shown that standard blood and body fluid precautions combined with routine barrier nursing effectively prevents Lassa virus transmission in hospitals. This may be true for other VHFs, however, their transmissibility in hospital settings has not been well described.

During the incubation period there is little risk from body fluids other than blood. However, decisions about isolation and precaution techniques should be made in anticipation of the patient's condition worsening. 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. Due to the nature of the situation, the **senior hospital administrator** and the **public affairs department** should be informed as well.

Throughout the course of a VHF illness, nosocomial transmission can occur directly (i.e., droplet infection), 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.

The patient should be isolated in a single room with an adjoining anteroom serving as its only entrance. The anteroom should contain supplies for routine patient care, as well as gloves, gowns, and masks for the staff. Hand washing facilities should be available in the anteroom, as well as containers of disinfectant solutions. A room with negative air pressure is not absolutely required, and the lack of such a room does not constitute a reason for transfer of the patient. However, if a room is available with negative air pressure compared with the anteroom and outside hall, and for which the air is not recirculated, it should be used. If an anteroom is not available, an adjacent room can be used to provide facilities for hand washing and space for supplies and equipment.

Only essential medical and nursing personnel, and immediate family members, should enter the patient's room and anteroom. Isolation signs listing necessary precautions should be posted outside the anteroom. Strict barrier nursing techniques should be enforced; all persons entering the patient's room should wear disposable gloves and gowns. In addition, face shields or surgical masks and eye protection (e.g., goggles or eyeglasses with side shields) should be worn by persons coming within approximately 3 feet of the patient to prevent contact with blood, other body fluids, secretions (including respiratory droplets) or excretions. These should be donned and removed in the anteroom. The need for additional barriers (e.g. leg and shoe coverings) depends on the potential for fluid contact as determined by the procedure to be performed and the presence of clinical symptoms that increase the likelihood of contact with body fluids from the patient. Caregivers and visitors should wash their hands

with an antiseptic solution (e.g., chlorhexidine 2%, providine-iodine 10% and chlorhexidine 0.5% on alcohol) after a patient contact and after leaving the patient's room.

Care should be taken to prevent the inhalation of, or exposure of mucous membranes to the patient's **blood, vomitus, urine or respiratory secretions**. Exposure may occur during procedures such as intubation, respiratory suctioning, insertion of a naso-gastric tube, insertion of an intravenous or intra-arterial line, blood drawing, or any care of a disoriented person. During such procedures protective eyewear should be worn in addition to surgical masks. If surgery is required, surgical staff should wear protective eyewear as well as double gloves. Full-face respirators with HEPA (high efficiency particulate air) filters are not usually necessary. However, full-face respirators, or high efficiency respirator masks that filter to 0.03 microns and fit securely and face shields or safety goggles, are advised in the following situations (As a minimum, disposable fluid shield mask and attached visor type masks are recommended for use):

- possible exposure to airborne particles containing virus (e.g., prominent cough, explosive diarrhea, or hemorrhage)
- Congo hemorrhagic fever is suspected
- where surgery is being carried out
- in cases of seriously ill patients.

If surgical or obstetrical procedures are necessary, the case assessment team should be consulted regarding possible precautions for these procedures (see ***Lines of Communication for Suspected or Proven Cases***, p.4).

There is no evidence of transmission of hemorrhagic fever viruses to humans or animals through exposure to contaminated sewage; the risk of such transmission would be expected to be extremely low with sewage treatment procedures used in Ontario. As an added precaution, however, measures should be taken to eliminate or reduce the infectivity of bulk blood, suctioned fluids, secretions and excretions before disposal. These fluids should be either autoclaved, processed in a chemical toilet, or treated with disinfectant solution (sufficient household bleach to make a dilution of 1:100) for 5 minutes (e.g., in a bedpan or commode) before flushing or disposal in a drain connected to a sanitary sewer. Care should be taken to avoid splashing when disposing of these materials.

All material used for patients, such as disposable linen and pyjamas, should be double-bagged while in the patient's room in clearly labelled, sealed liquid-tight autoclave bags at the site of use and transported directly to the designated area for decontamination in a gravity displacement autoclave or incineration. The outside bags should be sponged with disinfectant solution and later incinerated

or autoclaved. Alternately, linens can be laundered using a normal hot water cycle with bleach if universal precautions to prevent exposures are precisely followed and linens are placed directly into washing machines without sorting. Gowns, gloves and masks should be worn by laundry workers. Disposable items worn by staff, such as gowns, gloves, etc., should be similarly treated. Disposable items used in patient care (suction catheters, dressings, etc.) should be placed in a rigid plastic container with disinfectant solution. The outside of the container should be sponged with disinfectant, and the container should be autoclaved or incinerated.

7.2 Collection of Laboratory Specimens

Before the collection of any specimens, contact should be made with the provincial laboratory response co-ordinator. 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 should be worn by those obtaining and testing laboratory specimens.
3. Wherever possible, glass containers should **not** be used. Disposable sharp objects, such as scalpel blades, should be placed in puncture-resistant containers immediately after use and later autoclaved before disposal or incineration.
4. Blood samples must be collected with extreme care to avoid self-inoculation. Needles should not be bent, broken, removed from disposable syringes, or otherwise handled. After use, blood-taking 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. Clinical laboratory specimens should be placed in plastic bags that are sealed, then transported in durable, leak proof containers directly to the specimen handling area of the laboratory. The outside of these bags should be wiped with a disinfectant solution such as 1:100 dilution of household bleach before leaving the patient's room. Laboratory staff should be alerted to the nature of the specimens, which should remain in the custody of a designated person until testing is done.

7.3 Performance of Specific Laboratory Tests

7.3.1 Preliminary Tests

When a possible case of VHF is suspected, the following tests must be done immediately:

- blood film examination for malaria (thick and thin blood films); a smear from a second specimen must be examined 12 to 24 hours later 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 ml
- white blood cell and differential counts, and either haemoglobin or haematocrit performed manually unless specimens are previously inactivated
- urinalysis; urine culture, if urinalysis suggests infection.
- specimens to be sent to an outside laboratory for testing must be packaged in compliance with TDG regulations (see Pg. 13-15)

7.3.2 Diagnostic Tests for VHF

Diagnostic testing for VHF is carried out at The National Microbiology Laboratory (NML) in Winnipeg. Only limited serological testing is available locally. **Please consult with Dr. Frances Jamieson**, Medical Microbiologist, OMHLTC at telephone (416) 235-5841 or FAX (416) 235-5951 **prior to** submitting any specimens. After hours telephone the Public Health Laboratories emergency number (416) 605-3113.

The National Microbiology Laboratory must be informed prior to the collection or shipping of any specimens for the diagnosis of level 4 agents.

The diagnosis of VHF is confirmed by demonstrating IgM antibody or by demonstrating a fourfold rise in IgG antibody in serum, by isolating the virus, by antigen detection by enzyme-linked immunosorbent assay (ELISA), or viral genome detection by polymerase chain reaction (PCR). Antibody may not appear in blood until the second week of illness. Virus is usually recovered from blood, although Lassa virus may also be isolated from throat secretions or urine.

The essential specimens to be submitted for VHF diagnosis are a sample of venous blood for serology, a sample of venous blood for virus culture/detection, a midstream ("clean catch") specimen of urine, and a throat swab. The following procedures should be followed:

1. **Two red topped tubes** (10 ml.) of venous whole blood should be collected for virus serology, as well as **two tubes of blood in EDTA, heparin or citrate** (for PCR and culture). One set of tubes will be tested by the National Microbiology Laboratory in Winnipeg. The second set will be forwarded to the CDC in Atlanta if required or kept for further diagnostics.
2. Mid-stream **urine** specimens should be collected by clean catch. Five millilitres of urine should be put in a plastic screw-cap container with one of the following solutions: 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%. These solutions should contain penicillin and streptomycin at a concentration of 200 units and 100 mcg/ml respectively. (Contact your local PHL if you do not have these solutions.)
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. These solutions should contain penicillin and streptomycin at a concentration of 200 units and 100 mcg/ml respectively. (Contact your local PHL if you do not have these solutions.)
4. **Tissue** should be placed in sterile screw-cap containers and either frozen (if anticipated delay of more than 24 hours prior to shipping) or refrigerated.

See *Table I: Specimens for Diagnosis of Level 4 Pathogens* for further details.

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.

Post Mortem Diagnosis

Liver, lung, lymph node, brain tissue or spleen collected post mortem may also be a rich source of virus. Also collect renal tissue in cases of hemorrhagic fever with renal syndrome.

Table I: Specimens for Diagnosis of Level 4 Pathogens

Specimen	Test	How to submit*
Blood	Serology	Two red topped tubes (10 ml.)
Blood	Culture Ag detection PCR	Two tubes containing either EDTA or Citrate or Heparin
Urine	Culture	5 ml. (mid-stream urine) in plastic screw cap container with either rabbit serum albumin (final conc. 25%) or human serum albumin (final conc. 1%) or bovine serum albumin (final conc. 10%)
Throat swab	Culture	Place swab in plastic screw cap container with 1 ml. Sterile phosphate-buffered saline with either 25% rabbit serum or 1% human serum albumin or 10% bovine serum albumin Should contain penicillin and streptomycin at conc. Of 200 units and 100 mcg/ml. respectively
Tissue	Culture PCR	Place in sterile screw cap container. Store refrigerated or frozen (if delay of >24 hrs.) prior to transport. Ship with ice pack or on dry ice if specimen frozen

*see Section 7.4.1 for packaging and transportation instructions

Blood, urine and throat swabs should be shipped immediately on wet ice or cool packs. If shipment is expected to take longer than 24 hours it should be shipped on dry ice (never use glass containers on dry ice!). Tissue should be preferentially shipped on dry ice.

7.4 Processing of Specimens in Hospital Laboratories

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

Laboratory staff dealing with specimens from patients with a suspected VHF **must** take the same personal precautions as patient-care staff. Surgical gloves, gowns, shoe covers, masks, head covers and protective eye wear should be worn. Laboratory tests **must** be performed in Class II biosafety cabinets following biosafety level 3 practices (see *Appendix IV: Level 3 Laboratory Biosafety Guidelines*). Blood cultures should be prepared in a closed system if at all possible, and when not, all manipulation should occur in a Class II biosafety cabinet. Similar precautions should be taken when cross matching of blood from patients with suspected VHF. Centrifuges **must** have sealed carriers or heads. Every effort should be made to avoid creating an aerosol or splashing.

If the laboratory director feels that the hospital laboratory is unable to meet these specifications, arrangements should be made to transport the specimens to the nearest appropriate laboratory.

Infectivity of serum may be reduced by heating with 0.3% betapropiolactone 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 specimen on ice to avoid overheating). Serum separation should be done using sealed centrifuge cups or sealed centrifuge head. Abundant supplies of disinfectant solutions should be readily available. Use of a powered air-purifying respirator (PAPR) may be appropriate when dealing with specimens that have not been decontaminated. Serum used in laboratory tests should be pre-treated with polyethylene glycol p-tert-octylphenyl ether (Triton® X-100); treatment with 10 µL of 10% Triton® X-100 per 1 ml of serum for 1 hour reduces the titre of hemorrhagic fever viruses in serum, although 100% efficacy in inactivating these viruses should not be assumed. To date this solution is not available in Canada.

Blood smears, e.g. for malaria, are not infectious after 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: 50 ml to 4.5 L water) after use. Such treatment should not compromise the outcome and interpretation of the laboratory tests to be performed. Where a specimen has not been inactivated and a Class II biohazard containment cabinet is not being used, a full-face respirator should be used during handling of specimens and

additional barrier techniques employed, i.e., gloves, gowns. Serum separation should be done using a safety centrifuge. Abundant supplies of disinfectant solutions should be readily available.

Laboratory personnel accidentally exposed to potentially infected material through a needlestick or cut or abrasion should immediately wash the affected skin surfaces with a soap or detergent. Application of a disinfectant solution or hand washing product (see **Disinfectant Solutions**, p.17) may be considered although the efficacy of this supplemental measure is unknown. Mucous membranes, e.g., conjunctiva should be irrigated with copious amounts of water or eyewash solution. Laboratory personnel should be aware that exposure may also occur through potentially infected aerosol. Exposed persons should notify the infection control consultant and the employee health office. The person should then be considered as a high-risk contact and placed under surveillance (see **Identification, Surveillance and Management of Patient Contacts**, p.18).

Accidental spills of potentially contaminated material should be "encircled" with disinfectant solution such as 1:100 dilution of household bleach, covered with absorbent paper towels, liberally covered with disinfectant and left to soak for 30 minutes before being wiped up. Following the removal of initial material, the process should be repeated once again. Individuals attending to this task **must** wear protective attire. Full face 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 clean up, should be placed in an autoclave bag and sterilized before disposal. If contaminated equipment is to be incinerated, sterilization is not required. After finishing, staff should shower and don clean attire.

7.4.1 Transportation of Specimens for Diagnostic Tests in Ontario

The National Microbiology Laboratory must be informed prior to the collection or shipping of any specimens for the diagnosis of level 4 agents.

The shipment of patients' 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 after submission of a written response plan. Since all provincial public health laboratories already have these numbers, the advice and assistance of the provincial laboratory should be sought before any specimens are shipped, and all specimens referred 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, Health Canada, (613) 957-1779; fax:(613) 941-0596, and the Vector-Borne and Special

Pathogens Unit, LSB, Ontario Ministry of Health. The Emergency Response Plan Number and an emergency phone number **must** appear on the Shipper's declaration form.

All specimens **must** be packaged using approved Transport Canada packaging; the most convenient commercially available package is the "Saf-T-Pak", catalogue number SFO 100 and STP 300 for overpack on dry ice, obtained from ESBE, 80 McPherson Street, Markham, Ontario, L3R 3V6; telephone: (905) 475-8232; fax: (905) 475-5688. The Saf-T-Pak comes with all necessary labels and instructions for proper packaging. Other commercially available packaging may be obtained from Environmental Packaging Systems Ltd., telephone: (902) 461-1300; fax: (902) 466-6889. The sender **must** obtain and forward by telephone or fax, the waybill number and anticipated time of arrival to facilitate tracing of the package.

In the case of an emergency, Saf-T-Paks may be obtained from the central and regional Laboratories Branch laboratories. The duty officer on call may be contacted after working hours at (416) 605-3113.

When serology alone is to be performed, adhere to the following instructions

1. After applying the hazard label to the box, print above it "Infectious substance affecting humans UN 2814".
2. Complete the "To" and "From" on the top of the box.
3. Complete the "Shipper's declaration for dangerous goods" form, supplied with the Saf-T-Pak.
4. A carrier waybill is supplied by the courier company. On it write, "Dangerous goods as per attached shipper's declaration".

When viral isolation is to be attempted and the collected samples have been frozen, they should not be thawed. The package **must** be placed on dry ice for shipping. **(See below)** Where blood and sera are to be used for attempted isolation, and they have not been frozen, they can be shipped refrigerated and on freezer packs (available in local hardware stores).

When shipped frozen, in addition to the directions listed above:

1. Place the Saf-T-Pak in a styrofoam cooler surrounded with dry ice;
2. Affix all the labels and markings that are also on the inner box (the Saf-T-Pak) on the outside of the cooler.
3. Affix the following markings relevant to the dry ice: "Dry ice, UN 1845", the net weight of the dry ice (e.g., 1500 g), and a Class 9 hazard label. Also include a label stating "*Inner packages to comply with prescribed*

specifications” **must** be attached to the outer box to let the courier know if inner package is Transport Canada approved for infectious substances.

4. Complete the shipper's declaration, indicating "Dry ice or ' Carbon dioxide-solid" UN 1845, packing group III.
5. Also include the words "Overpack used" on shipper's declaration. (This will let the courier know that the box inside is OK for "Class 6")

The National Microbiology Laboratory, Health Canada, Winnipeg can be phoned at (204) 789-2066 at any time for further advice on shipping.

7.5 Treatment of the Patient

The supportive care of critically ill VHF patients is the same as that provided to other critically ill patients. The antiviral drug, ribavirin, has some in vitro activity against the virus that causes Crimean-Congo VHF and Lassa Fever; its use in patients with confirmed Lassa Fever and Crimean-Congo VHF may be considered. To be effective in Lassa Fever, it should be used as early as possible and especially in those with high levels of liver enzymes (AST and ALT). Ribavirin shows no in vitro effect against Marburg and Ebola viruses; individual judgement **must** be used to determine if such patients should receive the drug. If VHF is strongly suspected, treatment with ribavirin may begin while confirmation of the diagnosis is pending. Treatment should commence after the collection of blood specimens for viral isolation.

The dose and route of administration are: ribavirin 30 mg/kg intravenously (IV) loading dose, 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 IV is not a licensed drug in Canada. **To obtain as an emergency drug, request authorization from Emergency Drug Release Program, Bureau of Pharmaceutical Assessment, Drugs Directorate, Health Protection Branch, Health Canada, telephone: (613) 941-2108 during regular hours (08:30 - 16:30 EST) and (613) 941-3061 after hours.** The following information should be supplied to the Emergency Drug Release Program: name, address and telephone number of requesting physician, initials, age and sex of patient, name of drug, medical indication for the drug, quantity required, dosage form of the drug and drug manufacturer. Emergency Drug Release Program will forward the request to the pharmacy at the National Defence Medical Centre, telephone: (613) 733-6600, ext. 3963, where ribavirin IV is stockpiled.

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.

7.6 Disinfectant Solutions

VHF viruses, as lipid-enveloped RNA viruses, are readily inactivated by low-level disinfectants. Suitable disinfectant solutions include, quaternary ammonium-based products, phenolic or chlorine-based products (i.e., a 1% (500 parts per million) aqueous solution of sodium hypochlorite (1:100 household bleach solution) and iodophor formulations. Hydrogen peroxide in 3% concentration is a low level disinfectant which is environmentally friendly. Fresh, correctly prepared solutions of glutaraldehyde (2% or as recommended by the manufacturer), may also be used provided occupational exposure to fumes is minimized. Soaps and detergents should be used liberally for washing hands and in body showers

7.7 Terminal Disinfection

(Procedures that should be used following the patient's discharge from hospital)

Disposable items, such as pipette tips, specimen containers, swabs, etc. should be placed in a container filled with disinfectant solution and incinerated. All non-disposable items should be sterilized. Such equipment **must** be cleaned before sterilizing with decontaminating fluids (for example glutaraldehyde or sodium hypochlorite). If cleaning is done by hand, gloves, gown, face shield or surgical facemask and safety glasses **must** be worn. Care should be taken to avoid splashing. Instruments and equipment, e.g., endoscopes that cannot withstand autoclaving should be cleaned and disinfected before being treated with ethylene oxide. Disposable items should be disinfected and bagged for incineration

The patient's bed and other environmental surfaces in the hospital room should be washed with a disinfectant approved for this use (see **Disinfectant Solutions**, p.17). Bed linens should be washed in a disinfectant solution (see **Patient Isolation and Protection of Hospital Staff**, p.7). Transport equipment and exposed surfaces of transport vehicles should be washed and decontaminated with disinfectant solution.

7.8 Handling of Corpses

If the patient dies, handling of the body should be minimal. The corpse should be wrapped in sealed, leak-proof material, not embalmed, and cremated or buried promptly in a coffin of sound construction. Body washing can result in infection of those attending to it and should not be done without the authorization of the medical officer of health. If an autopsy is necessary, the case assessment team (see **Lines of Communication for Suspected or Proven Cases**, p.4) should be consulted regarding an appropriate site and the necessary precautions to be followed by the pathologist.

8.0 Identification, Surveillance and Management of Patient Contacts

8.1 Definition of 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.

8.1.1 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 of VHF are usually not spread by 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".

8.1.2 Close contacts are persons who have had more than casual contact with the patient **before the initiation of isolation procedures**. They include persons living with the patient, nursing or serving the patient when ill, 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 contacts should be identified by local health departments, in collaboration with the case management team and if necessary with the Federal Response Coordinator, 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 of 38.3°C (101°F) or above as well as any symptom of illness to employee health and the infection control consultant and employee health. Surveillance should be continued for 3 weeks after the person's last contact with the index patient.

After isolation procedures have been instituted, surveillance is not indicated for routine occupational contact with patients in situations where the diagnosis was considered and appropriate isolation precautions implemented. But if symptoms develop this should be reported immediately to the infection control consultant.

8.1.3 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 and considered for post-exposure prophylaxis.

Any close or high-risk contact who develops a temperature of 38.3 °C (101°F) or higher or any other symptoms of illness should be immediately isolated and treated as a VHF patient (see ***Management of the Hospitalized Patient***, p.6).

8.2 Post-Exposure Prophylaxis

Ribavirin may be prescribed as post-exposure prophylaxis for high-risk contacts of patients with Lassa fever although to date clear evidence of efficacy for prophylaxis has not been demonstrated. Post-exposure prophylaxis with ribavirin should be considered for high-risk contacts of patients with Crimean-Congo hemorrhagic fever and other hemorrhagic arenaviruses. The prophylactic regimen is: ribavirin 500 mg by mouth every 6 hours for 7 days. Ribavirin for oral use is not licensed in Canada, and one **must** request authorization from Emergency Drug Release Program, Bureau of Pharmaceutical Assessment, Drugs Directorate, Health Protection Branch, Health Canada, telephone: (613) 941-2108 during regular hours (08:30 - 16:30 EST) and (613) 941-3061 after hours. The following information should be supplied to the Emergency Drug Release Program: name, address and telephone number of requesting physician, initials, age and sex of patient, name of drug, medical indication for the drug, quantity required, dosage form of the drug, drug manufacturer. Emergency Drug Release Program will forward the request to Schering Canada, distributor of oral ribavirin.

8.3 Convalescent Patients and their Contacts

Convalescent patients and their contacts should be warned that some of the viruses causing VHF may continue to be excreted for many weeks in semen, as demonstrated with Marburg and Ebola viruses, and in urine, as occurs sometimes with Lassa virus. Collection of seminal fluid and urine for virus isolation from patients in the convalescent period is encouraged (see ***Transportation of Specimens for Diagnostic Tests in Ontario***, p.14). 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 latex condoms is advised.

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 (e.g., the average toilet contains 4 litres of water in the toilet bowl prior to flushing. Place 50-100ml of bleach in the toilet prior to urinating. Wait 5 minutes and then flush.)

APPENDIX I

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Chief Medical Officer of Health, Province of Ontario

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Alternate Provincial Response Coordinator

Public Health Division physician on call

After hours: through Spills Action Centre: (416) 325-3000 or (800) 268-6060

Fax: (416) 327-7439

Federal Response Coordinator

Dr. James Anderson

Director, Office of Public Health Security (OPHS)

Day: (613) 954-3236

QTMH Cellular: (613) 791-1027

(QTMH = Quarantine, Travel and Migration Health)

OPHS Fax: (613) 952-8286

Public Health Agency of Canada: (800) 545-7661 24 Hour Reference Line

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Appendix II

Infectious Disease/Travel Medicine Consultants in Ontario

Appendix V

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APPENDIX III (Updated March 2005)
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APPENDIX IV

LEVEL 3 LABORATORY BIOSAFETY GUIDELINES

<http://www.hc-sc.gc.ca/> *Health Protection Branch – Laboratory Centre for Disease Control*

CONTAINMENT LEVEL 3

Containment Level 3 (CL3) is suitable for work with agents in Risk Group 3. The operational requirements for the Level 3 laboratory are substantially greater than those for Levels 1 and 2 and the laboratory staff must receive specific training in the safe handling and manipulation of the agents used in this laboratory. Because the laboratory is designed to minimize environmental release of hazardous materials and provide enhanced worker protection the containment level 3 laboratory must undergo annual performance, testing and verification (see 7.8).

A Level 3 containment laboratory requires specialized design and construction. Those responsible for biosafety in an institution should maintain close control and seek expert advice and remain in close communication for all phases of design, construction, performance, verification and testing, operation and maintenance, and annual testing.

PHYSICAL REQUIREMENTS

The following are required in addition to the requirements for containment level 1 and containment level 2.

- The laboratory must be located away from general work areas and have controlled access from other areas. This is accomplished by entry through a lockable changing room with self-closing doors. A body shower should be provided within the containment perimeter.

- The laboratory must be held at a negative pressure relative to the surrounding areas at all times such that a directional airflow is created by air ingressing through all entry and exit areas. The laboratory should be provided with a dedicated supply and exhaust system which is sealed. The air discharged from the laboratory cannot be recirculated back into either the air supply system of the laboratory itself or into the building or adjacent buildings. Provided there is a dedicated sealed exhaust system, air may be exhausted from the laboratory to the exterior of the building without HEPA filtration. At the discharge point the exhausted air must be dispersed away from air intake or populated areas.

However, when the air is not exhausted by means of a dedicated exhaust system, it must be passed through a HEPA filtered exhaust before discharging into the main building exhaust air ventilation system. This exhaust housing must be designed to allow in situ decontamination and must pass annual testing and certification by aerosol challenge and scan techniques. A control system must be provided to ensure that the Level 3 laboratory does not become positively pressurized relative to the surrounding area. When the supply air is not provided

by a dedicated system, air-tight back draft dampers or HEPA filters must be installed in the supply system. The supply must be interlocked with the exhaust system.

- Biological safety cabinets must be installed in a manner which does not interfere with the air balance of the cabinet or room. Thimble unit connections are recommended (see Appendix B).
- The laboratory must have a dedicated handwashing sink with foot, knee or automatic controls, located near the exit.
- The laboratory must have a pass-through or stand alone autoclave located in the work zone. Where physical constraints preclude the installation of an autoclave, in an existing level 3, alternative technologies may be used for sterilization of contaminated materials.
- Laboratory furnishings should be kept to a minimum. Work surfaces should be impervious, readily cleanable, and resistant to chemical disinfectants.
- All penetrations for services in the floors, walls, and ceiling of the laboratory must be sealed. The air supply/exhaust system should be provided with manual dampers at the room perimeter that may be closed as required to permit gas decontamination.
- Water supplied to the laboratory must be provided with reduced pressure back flow preventers.
- HEPA filters or equivalent should be provided on all ventlines.
- Dunk tanks may be provided at the containment perimeter.
- Sink and floor drains from this suite should be piped separately to the main building drain and be appropriately labelled. Floor drains are not generally recommended. Infectious materials must never be placed in sinks or floor drains.
- Autoclave condensate drains should have closed connections and go directly to sanitary sewer.
- In animal care facilities for small animals, the disposal of wastes will not differ from other contaminated laboratory materials. Large animals producing quantities of infectious wastes require special facilities which must be designed accordingly.
- Portable vacuum pumps must be fitted with in-line HEPA filters or equivalent equipment. No vacuum lines may exit the containment perimeter.
- Laboratory windows must be sealed and unbreakable.
- Backup power should be provided to critical items such as biological safety cabinets, fume hoods, freezers etc.

OPERATIONAL REQUIREMENTS

The following are required in addition to those stated for CL1 and CL2:

- Laboratory staff must be fully trained in the handling of pathogenic and other hazardous material and in the use of safety equipment, disposal techniques, handling of contaminated waste, and emergency response.
- Staff are required to change into dedicated solid front laboratory clothing on entry to the facility. This laboratory clothing must be removed on completion of work and autoclaved prior to laundering.
- Personal protective clothing, which may include head covers and dedicated shoes or impervious foot covers must be used while in the containment facility and removed on leaving.
- Appropriate respiratory protection should be considered depending on the infectious agents in use.
- Showers may be required depending on infectious agents used and manipulations involved.
- Personal effects may not be taken into or stored in the laboratory.
- Gloves must be worn when handling infective or potentially infective materials, including animals or waste.
- All activities involving infectious materials are conducted in biological safety cabinets or other appropriate combinations of personal protective and physical containment devices.
- Centrifugation must be carried out in closed containers using aerosol proof safety heads or cups which are loaded and unloaded in the biological safety cabinet.

**APPENDIX V (Updated March 2005)
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