V I R A L H A E M O R R H A G I C F E V E R S

INTERIM PHLS GUIDELINES FOR ACTION IN THE EVENT OF A DELIBERATE RELEASE

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Note: these are interim guidelines. Comments are welcome from healthcare, laboratory and public health professionals, and should be sent to DRcomments@phls.org.uk. Since these are interim guidelines, they may be subject to changes as comments are received, so please ensure that you have the latest issue and version, available through the PHLS website at http://www.phls.org.uk/topics_az/deliberate_release/menu.htm

1 BACKGROUND

These guidelines are intended for healthcare, laboratory and public health professionals to guide clinical, laboratory and public health action in the event of a deliberate release of the Haemorrhagic Fever group of viruses.

1.1 Introduction

Viral Haemorrhagic Fevers (VHF) are caused by a diverse group of viruses that cause an array of illnesses from relatively mild to rarely severe and life threatening. Viral survival is dependent on the availability of their natural host and as such they are restricted to where their host species live. Humans are not the natural reservoir for any of these viruses. They become infected when they come into contact with infected hosts or with arthropod vectors. However, with some viruses, if a human is infected, they can transmit it to other humans under specific circumstances (person to person transmission).

1.1.1 Classification of VHF viruses:

Viruses associated with haemorrhagic fever are RNA viruses from 4 distinct virus families. Although a wide range of viruses are involved, they all share some common characteristics. They all have an RNA genome, and are enveloped. They are transmitted in three ways: by mosquitoes, via ticks or as a zoonosis.

1.1.2 Deliberate release of Haemorrhagic Fever Viruses:

In theory, VHF agents can be used as agents of bio-terrorist attacks. However, in. reality, it is very difficult to create a suitable conduit for transmission of these agents in a weaponised form. Laboratory testing on animal models and epidemiology of the Reston outbreak in Phillipino imported monkeys, show that some VHF agents can be spread by the airborne route, however to date this has not been seen in any of the human outbreaks studied.

This document focuses on those VHF agents that are known to be readily capable of person-to-person spread. It assumes that even if aerosolisation does occur, it is the following 4 viruses that, due to their ability for person-to-person spread, will present a risk to public health in the UK.

These agents are: an arenavirus, **Lassa fever**; a bunyavirus, **Crimean/ Congo haemorrhagic fever (CCHF)**; and two members of the filovirus family**, Ebola and Marburg viruses**.

The threat of infection by these pathogens is considered serious because:

- They can cause severe, rapidly fatal infection.
- Secondary cases may arise from contact with primary cases.
- The reputation of these diseases is such that they can induce public anxiety and disrupt everyday life in the population.
- Laboratory testing on animal models shows that some agents may be transmitted by aerosol, although this has not been seen in the human outbreaks studied.

1.2 Epidemiology

Most VHF are endemic in different parts of the world, most notably Africa, parts of South America and some rural parts of the Middle East and Eastern Europe. However, environmental conditions in the UK do not support the natural reservoirs or vectors of any of these viruses and imported cases of VHF are extremely rare in the UK. Between 1997

and 2000, there were only 7 notified cases of suspected VHF (only 2 of which were confirmed) in England and Wales.

Other viruses can cause VHF in humans, but although occasional reports indicate that person-to-person spread has occurred with some of these agents they do not present the same risk to public health.

1.2.1 Person to person transmission

All four viruses are transmitted in the same way. Virus is transmitted through direct contact with virus-infected body fluids such as blood, saliva, vomitus, stools and possibly sweat. Cross infection with partially sterilised needles is associated with a high infection risk and a high fatality rate. Marburg, Ebola and Lassa virus have been shown to be present in the genital secretions of convalescents several weeks after illness; the potential for transmission to sexual contacts in the early convalescence phase has been determined for both Marburg and Lassa fever.

There is no evidence that close personal contact with a non-febrile, non-symptomatic, infected individual during the incubation period or convalescence results in transmission. Previous epidemics in Africa have resulted largely from secondary spread to health care workers and family contacts caring for the ill. Re-use of needles and syringes, inadequate barrier techniques, and unhygienic practices are the major routes for nosocomial transmission among hospital staff and patients. Contact with the body or body fluids of the dead in customary preparation for burial is also a recognised source of infection.

These viruses are not airborne, but maybe transmitted by aerosols of body fluids from infected patients if the aerosols come into contact with mucous membranes.

1.2.2 Infectious dose

The infectious dose of all four infections is unknown.

1.2.3 Incubation period

The incubation period varies between 1 and 21 days. The infectivity period depends on viral type and mode of infection. Table 1 is a summary of the incubation period:

Table 1: Incubation period for VHF viruses

Virus	Disease	Incubation Range
Arenaviridae		
Lassa	Lassa Fever	3-21 days
Bunyaviridae		
Nairovirus	Crimean-Congo HF	1-12 days
Filoviridae		
Ebola Virus	Ebola HF	2-21 days
Marburg Virus	Marburg HF	3-16 days

1.2.4 Period of communicability

Patients who have clinical symptoms are considered infectious. There are reports of late transmission events (92 days for Marburg) and Lassa fever virus can be shed in urine for several weeks or in semen for months after illness has resolved.

1.3 Clinical features:

1.3.1 Lassa fever

The onset of illness is insidious, with fever and shivering accompanied by malaise, headache and generalised aching. A sore throat is a common early symptom. In some cases the tonsils and pharynx may be inflamed with patches of white or yellowish exudate and occasionally small vesicles or shallow ulcers. (Importantly, a similar appearance may be seen in cases of malignant tertian malaria.) As the illness progresses the body temperature may rise to 41ºC with daily fluctuations of 2-3ºC. The duration and severity of fever is very variable. The average duration is 16 days but extremes of 6-30 days have been reported. A feature of severe attacks is lethargy or prostration disproportionate to the fever. During the second week of illness there may be oedema of the head and neck, encephalopathy, pleural effusion and ascites. Vomiting and diarrhoea may aggravate the effects of renal and circulatory failure. In the severest cases bleeding into the skin, mucosae and deeper tissues presages death. In non-fatal cases the fever subsides and the patient's condition improves rapidly although tiredness may persist for several weeks. There is usually a leucopenia although a high polymorphonuclear leucocytosis is encountered occasionally. Another common late complication is sensorineural deafness.

1.3.2 Congo-Crimean Haemorrhagic Fever

The illness begins abruptly with fever, chills, malaise, irritability, headache and severe pains in the limbs and loins, followed by anorexia, nausea, vomiting and abdominal pain. Fever is usually continuous but may be remittent and sometimes biphasic, resolving by crisis after 8 days. The face and neck are flushed and oedematous, the conjunctivae and pharynx are injected, and there is oedema of the soft palate. Patients are often depressed and somnolent. In most cases a fine petechial rash begins on the trunk and then covers the entire body. A haemorrhagic exanthem appears on the soft palate and uvula early in the illness and other bleeding manifestations, including haematemesis and melaena, appear on about the fourth or fifth day in over three-quarters of patients. Leucopenia and severe thrombocytopenia are common. Large ecchymotic areas caused by subcutaneous extravasation of blood occur at times. Severe gastric and nasal haemorrhages often lead to death. The liver is enlarged in about half the cases but the respiratory system is unaffected. Involvement of the central nervous system is seen in 10-25% of patients and usually indicates a poor prognosis; features include neck rigidity, excitation and coma. The mortality rate in outbreaks is often as high as 30-50%. Death is usually due to shock, blood loss or intercurrent infection.

1.3.3 Ebola virus

The disease begins with acute fever, diarrhoea, which can be bloody, and vomiting. Headache, nausea, and abdominal pain are common. Conjunctival infection, dysphagia, hiccups, and haemorrhagic symptoms such as epistaxis, gum haemorrhage, haematemesis, melaena, and purpura may further develop. Some patients may also show a maculopapular rash on the trunk at 3-8 days, which is followed by desquamation. Appearance of haemorrhagic manifestations is an indicator of poor prognosis. Dehydration and significant wasting occur as the disease progresses. At a later stage, there is frequent involvement of the CNS, manifested by somnolence, delirium, or coma. By the second week of illness, the patient will either markedly improve and convalesce or will have multi-organ failure and will die in shock. Autopsies show panencephalitis, cerebral oedema, and serious renal damage. The case fatality rate ranges from 90% in outbreaks caused by Zaire strain, 50% in those caused by Sudan strain and 0% in Reston strain.

1.3.4 Marburg virus

The course of Marburg infection is similar to that of Ebola although Marburg tends to be less severe.

1.4 Mortality

1.4.1 Lassa fever

Approximately 15%-20% of patients hospitalised for Lassa fever die from the illness. However, in endemic countries, only about 1% of patients who become infected through contact with Mastomys rodents, the host species, die from it. The death rates are particularly high for women in the third trimester of pregnancy and their foetuses. The factors affecting disease severity are unknown but there is some suggestion that Nigerian strains cause more severe disease and that route and dose of inoculum may influence pathogenicity.

1.4.2 Congo-Crimean Haemorrhagic Fever

The death rate is often as high as 30-50% in outbreaks.

1.4.3 Ebola virus

Ebola virus outbreaks have shown a wide range of outcomes, from almost 90% mortality in the outbreaks of 1976 and 1995 the in the Democratic Republic of Congo through to 50% in Sudanese outbreaks. The mortality rate is dependent on strain; the Reston strain, identified in imported monkeys from the Philippines, was associated with subclinical infection in the few human cases.

1.4.4 Marburg virus

The one significant Marburg virus outbreak in 1967 had a mortality rate of 28% in primary cases.

1.5 Organism Survival

No specific studies have been undertaken, but these are all RNA viruses with lipid envelopes. This renders them relatively susceptible to detergents as well as to low pH environments. Conversely, they are quite stable at neutral pH, especially in the presence of protein.

1.6 Antiviral sensitivity

Lassa fever can be treated effectively with ribavirin. There is also in vitro evidence that ribavirin is effective against CCHF. There is no evidence to support the use of ribavirin in Ebola or Marburg fevers. Convalescent sera are effective for some arenavirus infections such as Junin (Argentinean Haemorrhagic Fever), but its effectiveness for Lassa fever and Ebola/ Marburg in humans has never been demonstrated.

1.7 Legal issues

Currently, if a person is suspected to have VHF, they should be managed according to the guidelines issued by the Advisory Committee on Dangerous Pathogens (ACDP) on management and control of VHFs. The Health and Safety Executive can prosecute if there is deviation from these guidelines.

In the event of a deliberate release the numbers of patients will exhaust the current capacity to allow adherence to these strict protocols. Other ways of managing these patients may need to be put in place, this may include cohort nursing in a dedicated ward. This interim guideline on bio-terrorism has relied extensively on ACDP protocols and **if there is a deliberate release** of VHF agents it should be used **in conjunction** with the ACDP, VHF guidelines.

2 CLINICAL PROCEDURES

2.1 Diagnosis and Collection of Samples

There are many diseases that have similar presentations to VHF and in case of a deliberate release, high degree of suspicion is needed by the clinicians to consider VHF. The most frequent causes of similar illnesses and their distinguishing features are:

- **Malaria**
  Presents with acute fever, headache and sometimes diarrhoea (children). Blood smears must be examined for malaria parasites. Presence of parasites does NOT exclude concurrent viral infection. Antimalarial drugs must be prescribed in an attempt at therapy.

- **Shigellosis and other bacterial enteric infections**
  A common initial diagnosis of VHF. Presents with diarrhoea, possibly bloody, accompanied by fever, nausea, and sometimes toxaemia, vomiting, cramps, and tenesmus. Stools contain blood and mucous in a typical case. A search for possible sites of bacterial infection, together with cultures and blood smears, should be made. Presence of leucocytosis distinguishes bacterial infections.

- **Typhoid fever**
  Presents with fever, headache, rash, gastrointestinal symptoms, with lymphadenopathy, relative bradycardia, cough and leucopenia and sometimes a sore throat. A therapeutic trial with chloramphenicol or tetracyclines may be indicated. Blood and stool culture can demonstrate causative bacteria.

- **Yellow fever and other Flaviviridae**
  Present with haemorrhagic complications. Epidemiological investigation may reveal a pattern of disease transmission by an insect vector. Virus isolation and serological investigation serves to distinguish these viruses. Confirmed history of previous yellow fever vaccination will rule out yellow fever.

- **Others**
  Systemic Plague, systemic Tularaemia, viral hepatitis, leptospirosis, rheumatic fever, typhus, and mononucleosis produce signs and symptoms that may be confused with VHF in the early stages of infection.

Note that most of the above diseases are not endemic in UK but may occur if there is an appropriate travel history. In the absence of travel history suspicion should be raised.

2.1.1 Precautions for sampling

Blood specimens should be taken by a doctor or nurse experienced in phlebotomy. Urine samples should only be taken by experienced staff (a 20 ml syringe should be used to transfer urine from a bedpan to the specified container).
Protective measures include:

- a protective gown
- a waterproof protective apron
- latex gloves
- particulate filter face mask
- eye protection
- washing hands and exposed skin thoroughly.

The following techniques are recommended when obtaining specimens of blood:

- dry cotton wool balls or gauze swabs (not disposable alcohol swabs) should be used to apply pressure to venepuncture wounds
- use of a vacuum blood sampling system
- specimen tubes should be labelled with patient details before being filled
- use of the most familiar equipment and procedure (unfamiliar procedures are more likely to lead to accidents and spillages).

2.1.2 Samples to be taken from acutely ill humans

The emphasis here is to minimise investigations until a diagnosis is confirmed or excluded. Table 2 identifies specific diagnostic samples needed. This does not include other routine blood samples.

Table 2: Specific Diagnostic Samples needed from acutely ill patients

- **Acute phase whole blood** obtained from a patient within 7 days of onset of illness.
- **Convalescent sera** collected from patients at least 14 days after onset of illness. Paired serum samples are ideal, usually collected 7-20 days apart.

All samples should be identified as "High Risk" according to local protocols. There is no need to separate acute phase sera from blood clots (a procedure that may significantly increase the risk of accidental infection). The use of sealed sterile dry tubes (Vacutainer® type) is recommended.

Ideally, blood samples should be kept in their original tube and stored at 4ºC to allow virus isolation/ PCR. If separate blood samples are collected purely for serological or biochemical purposes, they can be frozen. Each collected blood sample must be coded and dated for easy connection with the corresponding record of the case database. The use of labels prepared in advance for both the collection of clinical samples and case report forms is recommended.

2.1.3 Samples to be taken from the environment

Environmental sampling is unlikely to provide useful information because the organism dies rapidly outside the body. Expert advice will be provided if required.

2.1.4 Transport of samples

Strict procedures should be followed for the transport of samples of to the laboratory. These are outlined in section 3.6.

2.2 Treatment

Specific treatment with ribavirin may be effective for Lassa fever and CCHF. No specific treatments (antiviral drugs, cytokines or vasoactive agents) have been shown to date to influence the course of the other two VHF agents.

Many of deaths attributed to VHF are due to severe dehydration; management of patients should be supportive, with careful maintenance of hydration, and minimal trauma - in

particular, injections and parenteral interventions must be kept to a minimum. Replacement of coagulation factors and of platelets may be of value.

2.3 Infection Control Practice

2.3.1 Isolation of Patients

Patients known or strongly suspected to be suffering from a VHF should be admitted to a designated **High Security Infectious Disease Unit**, or to an intermediate isolation facility after consultation with the physician in charge of the patient. **In the event of a large-scale event, patients may be cohort isolated in a designated ward.**

2.3.2 Cleaning and waste disposal

Normal procedures for standard isolation are appropriate.

2.3.4 Post-mortem

Post-mortem examinations are not allowed if VHF is suspected, if confirmation is needed, a percutaneous liver biopsy would suffice. In the event that a full post-mortem has inadvertently taken place, standard universal precautions (appropriate personal protective clothing, including gloves and gowns) should be supplemented with masks and eye protection.

Bodies can be either buried or preferably cremated. However, Embalming of bodies should be strongly discouraged.

2.4 Prophylactic treatment for persons exposed to VHF

The level of prophylaxis provided depends on the assessment of the situation and ascertainment of the level of risk. Table 3 is a guide to categorising exposed people to various risk groups depending on exposure.

For contacts who fit category 1 description, ribavirin should be administered prophylactically. Also, all those in category 1 or 2 should be actively followed up for development of fever for 21 days; however, those in category 2 do not need prophylactic ribavirin. Contacts in category 3 to 5 need to be identified and made aware of possible signs and symptoms of VHF but no active follow up is needed. The active follow up should be organised locally by the CCDC and co-ordinated by CDSC.

Table 3: Categorisation of contacts:

Category	Description
Category 1	Direct contact (i.e. skin / mucosa with blood / bodily fluids of index case)
Category 2	Direct contact with the patient or specimens from the patient but no direct contact with blood/bodily fluids and appropriate precautions taken
Category 3	Spent time in the same areas as the patient, but no physical contact with the patient / bodily fluids / specimens
Category 4	Shared the same public space as the patient
Category 5	People who were in contact with those in Categories 1 and 2

2.4.1 Immunisation

Currently, there are no vaccines available for the management of pre or post exposure to VHF.

2.4.2 Decontamination of exposed persons

The risk of acquiring infection from contaminated clothing of exposed persons is low. Heavily exposed persons should be instructed to remove outer clothing, which is placed in sealed plastic bags prior to autoclaving or washing according to local infection control policies

2.5 Environmental decontamination

The risk of acquiring infection from contaminated environmental surfaces is extremely low. Drying and exposure to sunlight will kill the organisms. Environmental decontamination is not recommended, except for highly localised contamination like vomitus or blood spillages in the laboratory or the ward. If such a situation rises, standard disinfectants like strong hypochlorite solution containing 2500 ppm of available chlorine should be used according to local policies.

2.6 Protection of frontline workers

This includes all emergency staff involved in management at the scene of a release, and healthcare staff involved in the care of patients.

2.6.1 Protective clothing

Due to the nature of VHF agents, aerosolised spread will cover a distinct area. The area affected by primary aerosolisation depends on the time and place of release. In the event of overt release of VHF agents, this **exposed zone** presents a high risk of infection, and anyone entering it should wear full protective equipment such as Type 3 air filter masks with Class A suits, conferring full biological protection.

Healthcare workers will not normally be asked to enter the exposed zone, but may be called into the exposed zone to treat casualties, for example if an explosive device has accompanied the release of biological agent. In this case full protective clothing should be worn.

Exposed persons will normally be moved from the exposed zone, through decontamination, and into a place of safety (see section 4.3.1) for medical assessment. Frontline workers involved in decontamination, and others who have who have any contact with contaminated clothing and fomites should observe standard Universal Precautions - gloves, gowns and hand washing, and in addition should wear particulate filter masks and eye protection. Healthcare workers who attend exposed persons after decontamination has been completed need observe Universal Precautions only.

For healthcare workers involved in the management of hospitalised patients with all forms of VHF strict protocols in accordance with ACDP publication on management of VHF should be adhered to (reference 9). If such facilities have been exhausted, CDSC Colindale should be contacted for advice on the sufficient level of protection that should be used.

In addition frontline workers involved at the scene of a release, and healthcare workers and mortuary staff involved in the management of VHF cases should be advised to seek urgent medical attention should they develop a febrile illness.

2.7 Other Considerations – patient, visitor and public information

Fact sheets have been prepared for distribution in the event of an incident.

3 LABORATORY PROCEDURES

3.1 Risk assessment

Lassa, Ebola, Marburg and CCHF are hazard group 4 pathogens, and should thus be covered by existing risk assessments for handling such organisms in diagnostic laboratories. These facilities are available at the Central Public Health Laboratory (CPHL) and the Centre for Applied Microbiology and Research (CAMR) where all specimens must be sent for diagnosis.

It is recognised that in the event of a covert deliberate release specimens from the first unsuspected cases might be examined in Regional laboratories before the diagnosis is known. If VHF is not suspected, routine investigation will inevitably be done in local labs. If VHF is suspected, then the level of exposure of the patient should be categorised based on table 4.

Table 4 Categorising risk for VHF

Risk Category	Description
Minimum Risk	Febrile patients who have been in contact with a known or suspected source of VHF but in whom the onset of illness was definitely more than 21 days after their last contact with any potential source of infection
Moderate Risk	Febrile patients who • were adjacent to an exposed zone in the 21 days prior to onset of an illness which has similar signs and symptoms as VHF Or • Lived in or stayed in a house for more than 4 hours where there were ill, feverish persons known or strongly suspected to have a VHF
High Risk	Febrile patients who • Have been in the exposed zone Or • Took part in nursing or caring for ill feverish patients who had or suspected to have VHF Or • Had contact with the body fluids, tissue or the dead body of such patients Or • Were previously categorised as moderate risk, but who have developed organ failure and / or haemorrhage

For minimum risk patients, key investigations such as malaria film can be done in Category 2 laboratories with eye and face protection. For those in moderate risk group, investigations such as malaria can be undertaken in a class 1 Cabinet in Category 3 labs. If VHF cannot be ruled out, any further investigation should be done in a level 4 laboratory.

All investigations for patients in high-risk category should be done in a level 4 laboratory at either CAMR or CPHL. If the capacity of level 4 laboratories for routine investigations (not direct viral investigations) is exhausted, then after appropriate risk assessment and discussion with CPHL automated blood counting machines and chemistry analysers may

have to be used as long as they are designated for this purpose and work in a closed system. (see reference 9 for further details).

In exceptional circumstances such as deliberate release the numbers of cases may quickly exhaust the available facilities. In these situations patients will have to be nursed in cohort isolation in a designated ward and patient support laboratory investigations carried out using closed system blood analysers. If specimen handling for these purposes could produce an aerosol e.g. in blood cross matching then these procedures must be carried out in a category 3 laboratory inside a Class I or Class III cabinet. In no circumstances should any procedures that may lead to propagation of the viruses be carried out, these specimens must be referred to the reference laboratories.

3.1.1 Receipt of samples

Samples should be labelled as 'High Risk' by the submitting staff and discussed with the receiving laboratory. Samples should be handled according to local protocols for such samples. Chain-of-evidence documentation should accompany specimens. In larger incidents, this would only be required for several of the initial cases.

3.2 Isolation and identification

These viruses can be cultured in vero E6 cells but this should only be attempted in a Containment Level 4 laboratory. RT-PCR tests have been described for all four viruses and this is the first line diagnostic test. Identification of virus is on the basis of specific amplification and sequencing.

3.3 Confirmation

Serological confirmation is possible by IF or ELISA but antibodies may not be detectable when the patient first presents. Acute and convalescent sera should be sent to the Reference Laboratory for testing. The laboratory should be warned in advance that sera are being submitted.

3.4 Waste disposal

Waste should be disposed of according to local procedures for Containment Level 4 Laboratory.

3.5 Reference laboratory

Samples should be packed and labelled according to current regulations for Hazard group 4 pathogens and the Reference Laboratory should be notified when samples are despatched.

Specimens, including sera should be sent to:

1. Dr David Brown or Dr Robin Gopa
Viral Zoonosis Unit
Enteric, Respiratory and Neurological Virus Laboratory
Central Public Health Laboratory
61 Colindale Avenue
London. NW9 5HT
Tel: 020 8200 4400 (switchboard)

and

2. Dr Graham Lloyd
Special Pathogens Reference Laboratory
Centre for Applied Microbiology and Research (CAMR),
Porton Down,
Salisbury
Wiltshire. SP4 0JG
Tel: 01980 612100

3.6 Transportation of samples with high suspicion of VHF agents

The following procedures should be adopted for the transport of all specimens. These apply within hospitals and laboratories as well as for specimens sent to the reference laboratory:

- Every effort should be made to avoid external contamination of specimen containers during specimen collection.
- The primary container should be screwed tight, labelled and placed in an intact plastic bag.
- A 'High Risk' label should be affixed to both specimen and request form. The latter should include any other relevant information and include adequate clinical details to indicate level of suspicion.
- Under no circumstances should the request form be placed in the same bag as the specimen.
- The bag should be sealed, using tape or heat sealer. Pins, staples and metal clips should not be used. A separate bag should be used for each specimen.
- Each specimen must then be placed in a leak-proof secondary container with sufficient absorbent material to absorb all the contents should leakage occur.
- Each specimen must be packaged individually - i.e. three specimens, three separate packages.
- The secondary container should be externally disinfected by wiping with hypochlorite (1,000ppm) solution or alcohol wipes.

3.6.1 Samples sent to the reference laboratory

- Secondary containers should be placed within a final outer tertiary packaging.
- This packaging **must** comply with the UN 602 standard packaging for the transport of infectious substances by air, road or rail.
- The package should be certified to this standard and carry the appropriate UN certification numbers on the tertiary packaging along with the following information:
  BIOHAZARD – danger of infection symbol Class UN 6.2.
  Instructions not to open if found.
  Telephone number of a responsible person - e.g. Consultant Microbiologist, Laboratory Manager.
- The container should be transported by an approved courier, without delay, directly to the reference laboratory.

3.6.2 Samples sent within hospitals and laboratories

- Secondary containers should be placed in a good quality box, which is well taped up and clearly labelled "Pathological Specimen – Open only in Laboratory".
- Specimens should be transported by hand by a responsible person using the above packaging. Vacuum-tube systems should **not** be used for transportation of specimens within hospitals or laboratories.
- Extra care should be taken to ensure that laboratory records are kept to a high standard.

4. PUBLIC HEALTH PROCEDURES

4.1 Surveillance and detection of deliberate releases of VHF agents

A deliberate release may be overt and associated with an announcement or covert, where suspicion will not arise until the first cases have been diagnosed.

Even a **single confirmed** case of VHF must be regarded with a high index of suspicion of deliberate release. This suspicion also applies to cases that occur in people who have returned from endemic areas. All infections should be investigated to ascertain that they have not occurred due to deliberate release of VHF agents.

In addition, a deliberate release should be considered in the event of **two or more suspected** cases of VHF that are linked in time and place. Expert advice will be provided in order to confirm the occurrence of a covert release and assist with epidemiological investigations to define an exposed zone in time and space

4.2 Case definition

4.2.1 Suspected cases

Clinicians should be alert to the possibility of cases of VHF. Any previously healthy patient with sudden onset of Pyrexia of Unknown Origin (PUO) and pathognomic signs of facial oedema and haemorrhage should arise suspicion and be immediately reported to the local Consultant in Communicable Disease Control.

In the event of a suspected deliberate release of VHF agents, a higher index of clinical suspicion should be maintained and the diagnosis considered if the symptoms outlined below present at medical services, especially if they arise in people who have been within or in close proximity to the exposed zone. Obviously the level of suspicion depends on clinical symptoms and the circumstances, but if a case is suspected, microbiological investigations should be sent to eliminate or confirm the diagnosis.

VHF syndrome can be described as an acute febrile illness characterised by malaise, prostration, generalised signs of increased vascular permeability and abnormalities of circulatory regulation. Bleeding manifestations often occur, especially in the more severely ill patients. Bleeding is a poor prognostic factor but death may not be due to a massive loss of blood volume.

4.2.2 Confirmed case

A case that clinically fits the criteria for VHF and is supported by laboratory investigations which include culture, PCR or specific serological testing.

4.3 Public Health Action

4.3.1 Procedure for handling exposed persons at the scene of an overt release

Some of them will still be at the scene when emergency services respond to the incident. This group will be decontaminated and then referred to health workers at a nearby **place of safety** for assessment (this is a clinical area just outside the exposed zone and within the cordon that will be established at the scene of the incident). Others will have left the scene before emergency services arrive and will be identified later when they approach GPs

and A+E departments after details of the incident have been made public. Procedures need to ensure that these individuals are identified for monitoring.

4.3.2 Follow up of exposed persons

After an overt release, all exposed persons will be moved to a place of safety. They will be categorised based on the categories used in table 2 and those in category 1 will be offered prophylaxis with ribavirin. Others will either be actively followed up or will be offered advice on the possible symptoms that may develop. The level of involvement by the health professionals depends on the category that the exposed people fit in to.

4.3.3 Case finding

If cases of VHF arise and a covert release is suspected, health services should be contacted to raise awareness of the possibility of the further cases and determine whether any others might already have presented. This should follow the usual chain of command of CCDC, RE and CDSC.

4.4 Epidemiological investigation

If a case is strongly suspected or confirmed, the PHLS/CDSC duty doctor should be notified immediately on 020 8200 4400 (24 hour service).

Epidemiological information may be required for two reasons:

- If cases arise due to a covert release, or following an overt release but in people who have not been present in the exposed zone, epidemiological details will be used to define or redefine the exposed zone and so aid identification of others at risk of infection. This will require details of the movements of cases in time and place during the incubation period in order to identify possible sources of exposure.
- To determine those at risk of infection due to contacts of cases to guide follow up and provide antiviral prophylaxis when appropriate.

4.4.1 Epidemiological sampling

There is no rapid test that can be offered to inform asymptomatic people who suspect they have been exposed whether or not they have been infected.

Collection of acute and convalescent sera from asymptomatic people who have been exposed to a release, or who fit the definition of contacts of VHF cases may provide useful epidemiological data and information about the efficacy of prophylaxis. Obviously the practicalities of this depends on the scale of the incident.

LIST OF NATIONAL SPECIALISTS

Clinical expert advice

Dr B Bannister
Royal free Hospital
Infection Services
10th Floor
Royal Free Hospital
Hampstead
London NW3 2QG

Tel: 020 7830 2606

And

Dr Ed Ong
Newcastle General Hospital,
Infectious Disease Unit,
Ward 25
Westgate Road,
Tyneside NE4 6BE

Tel: 0191 273 8811

Laboratory diagnosis

Dr David Brown or Dr Robin Gopal
Viral Zoonosis Unit
Enteric, Respiratory and Neurological Virus Laboratory
Central Public Health Laboratory
61 Colindale Avenue
London NW9 5HT
Tel: 020 8200 4400 switchboard

and

Dr Graham Lloyd
Special Pathogens Reference Laboratory
Centre for Applied Microbiology and Research (CAMR)
Porton Down
Salisbury
Wiltshire
SP4 0JG
Tel: 01980 612100

Public health

Dr Dilys Morgan **and** Dr Natasha Crowcroft

PHLS Communicable Disease Surveillance Centre
61 Colindale Avenue
London
NW9 5EQ
Tel: (+44) 020 8200 6868
Fax: (+44) 020 8200 7868

E-mail: DMorgan@phls.org.uk E-mail: NCrowcroft@phls.org.uk

Out of hours contact details are held by the 24 hr CDSC on call duty doctor;
Tel: (+44) 020 8200 6868

REFERENCES

1 Enria D, Garcia FS, Ambrosio A, Vallesjos D, et al. Current status of the treatment of Argentine haemorrhagic fever. Med Microbiol Immunol 1986; **175**; 173-76.

2 Cooper CB, Gransden WR, Webster M, et al. A case of Lassa fever: experience at St Thomas' Hospital. BMJ 1982; **285**; 1003-1005.

3 Martini GA, Schmidt HA. Spermatogenic transmission of virus Marburg. Wiener Klinische Wochenschrift; **46**; 398-400.

4 Fischer-Hoch SP, Khan JA, Rehman S, et al. Crimean-Congo Haemorrhagic Fever treated with oral ribavirin. Lancet 1995; **346**; 472-475.

5 McCormick JB, Webb PA, Krebs JW, Johnson KM, Smith ES. A prospective study of the epidemiology and ecology of Lassa fever. J Infect Dis 1987; **155**; 437-444.

6 McCormick JB, King IJ, Webb PA, et al. A case-control study of the clinical diagnosis and course of Lassa fever. J Infect Dis 1987; **155**; 445-455.

7 Fischer-Hoch SP. Stringent precautions are not advisable when caring for patients with viral haemorrhagic fevers. Rev Med Virol 1993; **3**; 7-13.

8 McCormick JB, King IJ, Webb PA, et al. Lassa fever: effective therapy with ribavirin. N Engl J Med 1986; **314**; 20-26.

9 Advisory Committee on Dangerous Pathogens, Management and Control of Viral Haemorrhagic Fevers, HMSO 1996, London.

10 Jahrling PB, Viral Hemorrhagic Fevers in Textbook of Military Medicine (1997), edited by Zajtchuk R and Bellamy RF, Office of the Surgeon General, department of the Army, USA.