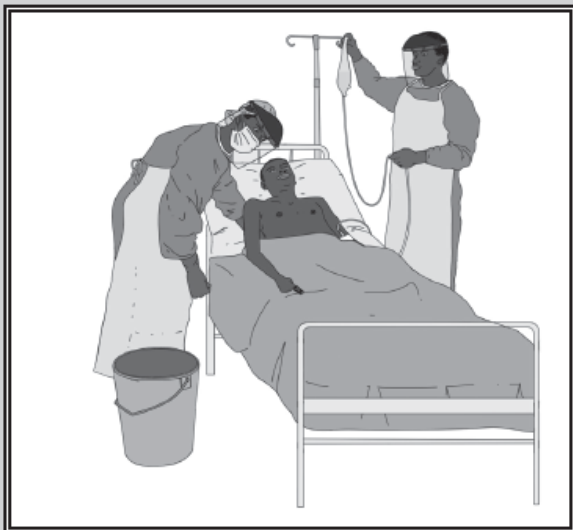


# Clinical Management of Patients with Viral Haemorrhagic Fever:

A Pocket Guide for the Front-line Health Worker

30 MARCH 2014



Interim emergency guidance- generic draft  
for West African adaptation



World Health  
Organization





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## Foreword

[Insert country-specific foreword]

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## Sources

This manual draws heavily on:

- WHO IMAI District Clinician Manual<sup>1</sup>
- WHO Child Pocket Book of Hospital Care for Children<sup>2</sup>
- MSF guidelines for the management of Viral Haemorrhagic Fevers<sup>3</sup>
- WHO Infection Prevention and Control (IPC) guidelines<sup>4</sup>
- Ugandan and MSF experience with running isolation centres and their discharge policies
- Expert review

# 1. Introduction

Viral haemorrhagic fever (VHF) is a general term for a severe illness, sometimes associated with bleeding, that may be caused by a number of viruses.

The term is usually applied to disease caused by:

1. *Arenaviridae* (Lassa, Lujo, Junin, Guanarito, Sabia and Machupo)
2. *Bunyaviridae* (Crimean-Congo Haemorrhagic Fever - CCHF)
3. *Filoviridae* (Ebola and Marburg)
4. *Flaviviridae* (Omsk haemorrhagic fever, Kyasanur forest disease and Alkurma haemorrhagic fever)

This Guide is focused on specific VHFs-- Ebola, Marburg, CCHF, Lassa fever [and Lujo]-- that occur in Africa and have risk of person to person transmission. This Guide does not address the management of other viral infections, such as dengue, Rift Valley Fever and yellow fever, that also have haemorrhagic manifestations, but do not have direct person-to-person transmission.

## Purpose:

The purpose of this pocketbook is to provide clear guidance on current best management practices for VHF across health-care facilities.

## Objectives:

1. To establish a systematic approach to comprehensive clinical management of VHF cases
2. To build capacity in health workers to use current practices in managing VHFs
3. To build confidence in health workers in managing VHFs through training and skills transfer

VHFs are severe and life-threatening viral diseases that are of particular public health importance because they can spread within a hospital setting, have a high case-fatality rate and are difficult to recognize and detect rapidly. There is also a lack of effective and proven treatment options, apart from supportive care, for Ebola and Marburg. Although ribavirin can be used in Lassa fever and CCHF, the case-fatality rate remains high. The death of health workers is often the first sign that a VHF outbreak has begun, and early

recognition and implementation of measures to protect health workers is one of the main objectives of early outbreak management.

- Ebola and Marburg are both Filoviruses with transmission to the index case probably occurring via contact with infected animals, and subsequent transmission via contact with such patient's infected blood and body fluids.
  - The causative agent of CCHF is a Nairovirus, a group of related viruses in the *Bunyaviridae* family. CCHF is transmitted via a tick from infected domestic or wild animals (such as deer, cattle, goats, and sheep etc), but it can also be transmitted by contact with blood or body fluids from infected animals or humans.
- Lassa and Lujo are in the *Arenaviridae* family. Humans become infected by exposure to the excreta of its reservoir *Mastomys natalensis*, also known as the "multimammate rat." Secondary person-to-person transmission of the Lassa virus also occurs through direct contact with infected blood or bodily secretions.

Ebola, Marburg and CCHF outbreaks occur periodically, but unpredictably. Only one small outbreak of Lujo has been reported (in Zambia and South Africa). Unlike most VHF, which are recognized only when outbreaks occur, Lassa fever is endemic in West Africa, with an estimated tens of thousands of cases annually, with highest incidence in the Kenema and Bo districts of Sierra Leone, but also in Nigeria, Guinea, Liberia and other districts in Sierra Leone. In the 2014 epidemic of Ebola in Guinea, Liberia and Sierra Leone, it is necessary to distinguish between Ebola and Lassa fever by laboratory testing, since only the latter should be treated with ribavirin. Other than this specific treatment difference, the clinical management and infection prevention and control efforts in health facilities are the same for Ebola, Marburg, Lassa fever and CCHF.

VHFs can be encountered at any time and require associated preparedness and planning. While VHF outbreaks begin in the community, patients with VHF ultimately present to their local health facility for care and treatment. In the initial stages of an outbreak (before the outbreak has been recognized), patients with VHF present to their local health facility with a constellation of symptoms difficult to differentiate from other

common infections (e.g., malaria, typhoid, bacterial sepsis). Thus, without maintaining standard infection prevention and control precautions at all time, and a high level of suspicion for VHF in the differential diagnosis, health staff and other patients are at risk for acquiring infection.

The provision of medical care to critically ill patients can be challenging in any setting, particularly resource-limited (including health personnel, medical supplies and equipment) remote environments where VHFs tend to occur. During a VHF outbreak, resource limitations along with the inadequate knowledge and skills for minimizing the risks of transmission to the health workers can lead to the de-prioritization of patient care.

Health workers have an obligation to provide the best medical care to improve patient survival, but also to provide symptom relief and palliation when required. In the context of patients with VHF, clinical care must be strengthened whilst minimizing the risk of onwards transmission to others, including health workers. Accordingly, it is critical that health workers improve their understanding of VHF and adhere to best practices of infection control at all times (i.e. during and outside of outbreaks). Importantly, inadequate care for VHF patients may also lead to increased reluctance on the part of individuals from the community to identify and isolate possible patients. This downstream effect makes case finding through community triage difficult and can seriously affect outbreak infection control.

The application of appropriate skills and case management protocols makes the care of a patient with VHF less daunting. The optimal approach depends upon several factors including: a clear understanding of the likely means of transmission in a healthcare environment (and therefore real risks to health workers' trust in the efficacy of protective measures and prudence in their use; and an approach to patient care that minimizes hazard while maximizing worker safety and effectiveness.

The purpose of this pocketbook is to provide clear guidance on current best practices for VHF, including both clinical management and infection control and prevention. Throughout this pocket manual, guidance is provided for the front-line health worker focusing on triage and case definition, early and ongoing case management, infection control and subsequent hospital discharge. Recommendations are drawn predominantly from existing published VHF guidelines (primarily consensus-based), and also draw from algorithms for sepsis management from the WHO Integrated Management

of Adolescent and Adult Illness (IMAI) and Childhood Illness (IMCI) guidelines. The rationale for including these sepsis algorithms is that the suspected pathophysiology and final common pathway of severely ill patients with VHF is often severe sepsis, with manifestations of increased vascular permeability, vasodilatation, multiple organ failure, and shock. In addition, guidance is provided on infection control and common clinical manifestations of VHF to help the front-line health worker increase his or her level of suspicion for VHF, particularly before an epidemic is recognized in the community. Finally, we provide specific contact information for the front-line provider to facilitate the reporting process to the appropriate public health authorities.

Importantly, this document does not cover how to create a VHF treatment unit (i.e. isolation ward), and it also does not address community interventions to control transmission or respond to disease outbreaks. It is hoped that this manual will be a welcome and complementary addition to such guidance and strengthen the overall response to VHF outbreaks in Africa, fulfilling the Integrated Disease Surveillance and Response activities necessary for International Health Regulations compliance.

## 2. Principles of VHF management

### 2.1 Case identification/detection

The diagnosis of VHF is based on 3 components:

1. History of exposure
2. Detailed clinical assessment
3. Laboratory investigations

Health workers should consider VHF in any patient with an unknown etiology as part of the differential diagnosis with more common causes of fever in that setting. Standard case definitions for VHF have been developed to identify 'alert', 'suspect', 'probable' and 'confirmed' cases before and during an outbreak (SEE APPENDIX A1 for Ebola/Marburg). Once 'alert' cases present to the medical personnel, however, the 'alert' label should be discarded and a determination made as to whether the person falls into the category of a 'suspect', 'probable' or 'confirmed' case. These case definitions may need further refinement to reflect clinical and epidemiologic features associated with a particular outbreak.

#### 2.1.1 History of exposure to Ebola/Marburg, Lassa fever, or CCHF

##### Ebola/Marburg:

One of the most important aids in making the diagnosis is eliciting a history of exposure within 2 to 21 days prior to the patient's onset of symptoms – i.e. within the potential incubation period for Ebola and Marburg.

- The most common exposure is to blood or any other body fluid (e.g. excreta, vomit, sweat) from a known or suspected Marburg or Ebola case (dead or alive), usually in providing care or attending a funeral. Prior to an outbreak being identified, the first clue will often be a history of exposure to contacts who have been severely ill or who have died suddenly.
  - People typically most at risk are family members, caretakers, traditional healers, and those participating in traditional burial rituals. Health workers are a recognized high-risk group who should be questioned about recent patient contact and unwell colleagues.

Other exposures are:

- Contact with infected animals, usually apes and bats, alive or dead, e.g. via

handling or consumption of infected bush meat, by going into caves (Marburg), or fields close to fruit trees (Ebola) where infected bats roost.

- ◆ Note: the virus is easy to destroy by heating so well cooked meat is considered virus free.

Being breastfed by a woman with Ebola or Marburg is considered an exposure as Ebola virus has been shown to be present in breast-milk.<sup>5</sup> As it is unclear how long it remains present, being breastfed by a convalescent patient is also considered a risk.

- Being the sexual partner of a known or suspected male case, as the virus remains present in semen up to 3 months after clinical recovery.
- Coming into contact with contaminated items, e.g. medical material, eating utensils, linens from infected patients.<sup>5</sup>
  - ◆ Note: the virus cannot survive very long in non-organic material, but can be present in material contaminated with body fluids (like needles or other medical material that is reused, dirty bed sheets...)
- Receiving healthcare from a provider who is also treating Ebola or Marburg patients and who is not taking appropriate infection control measures.

**Community spread mostly occurs through a social network: when friends and relatives are taking care of a patient or when participating in funeral activities.**

Any acutely ill person arriving with the history of such an exposure should be considered a suspect case (see Appendix A case definitions). Unfortunately an exposure history is not always clear (e.g. poor recollection of interpersonal contacts, reluctance to discuss animal contacts).



## History of exposure to Lassa fever

- ▶ The multimammate rats breed frequently and are a common rodent, most common in rural areas and in dwellings more often than in the countryside<sup>6</sup>. Rats infected with the virus shed virus in their excreta. Humans are infected by contact with rats or their excreta or, in some areas, by eating them. The rodent species which carry the virus are found throughout West Africa, so the actual geographic range of the disease may extend to other countries in the region beyond Sierra Leone, Guinea, Liberia and Nigeria.
- ▶ In Sierra Leone, the highest incidence is documented in the dry season.
- ▶ People of all ages are susceptible. Pregnant women are more likely to develop severe disease, especially in the third trimester.
- ▶ In addition to possible exposure to infected rats at home, other possible modes of exposure include:
  - Close contacts of a Lassa fever patient within 3 weeks of start of their illness. People typically most at risk are family members, caretakers, traditional healers, and those participating in traditional burial rituals.
  - Receiving health care from a provider who is also treating Lassa patients and who is not taking appropriate infection control measures. Health workers are a recognized high risk group who should be questioned about recent patient contact and unwell colleagues. This group includes both those caring for patients and those testing laboratory specimens from patients in the 3 weeks after the onset of illness.
  - Being the sexual partner of a known or suspected male case, as the virus remains present in semen up to 3 months after clinical recovery.
  - Coming into contact with contaminated items, e.g. medical material, eating utensils, linens from infected patients.  
(Note: the virus cannot survive very long in non-organic material, but can be present in material contaminated with body fluids (like needles or other medical material that is reused, dirty bed sheets...))

## History of exposure to CCHF <sup>7, 8</sup>

- ▶ Farmers, abattoir workers, veterinarians, and health workers are included in the occupational risk groups.
- ▶ Transmission of the CCHF virus can occur to humans in several ways:
  - Bite from an infected tick or crushing a tick against the skin. Ixodid (hard) ticks, especially those of the genus, *Hyalomma*, are both a reservoir and a vector for the CCHF virus. Numerous wild and domestic animals, such as cattle, goats, sheep and hares, serve as amplifying hosts for the virus.
  - Contact with the blood of an infected animal. Animal herders, livestock workers, and slaughterhouse workers in endemic areas are at risk of CCHF.
  - Human-to-human transmission through contact with infectious blood or body fluids, in the community or in hospitals.
  - Documented spread of CCHF has also occurred in hospitals due to improper sterilization of medical equipment, re-use of injection needles, and contamination of medical supplies
  - Possible horizontal transmission from a mother to child has been reported. The risk of exposure during breast feeding, however, is unclear<sup>9</sup>

## 2.1.2 Detailed clinical assessment

### Common clinical features of Ebola, Marburg, Lassa fever and CCHF infections

The initial clinical manifestations of Ebola, Marburg, Lassa fever and CCHF infections are non-specific and mimic many common infections making them difficult to diagnose early. Thus, it is important to understand the case definition and expand your differential diagnosis to include other causes of fever and non-specific symptoms (e.g., malaria, typhoid, upper respiratory infections and urinary tract infections). Also, despite being called a viral haemorrhagic fever, the clinical presentation of VHF only includes haemorrhage in less than half of confirmed Ebola/Marburg cases and less than 20% in confirmed Lassa cases. It is critical that health workers make themselves aware of other common signs and symptoms of VHF, to allow early identification of VHF cases that do not include haemorrhage.

In addition, while there is distinction between early and late clinical signs of VHF, it is important to remember that patients may present at different times in the course of their illness. Severity of illness may depend on a number of factors including the body's natural immune response, mode of transmission, duration of exposure, infecting dose, phase of illness of the case, and possibly even the virus strain. Thus, front-line health workers should have a high level of suspicion for VHF in patients who follow the case definitions, even when their clinical presentation is mild.

### Clinical features of Ebola/Marburg <sup>10,11</sup>

The Ebola and Marburg viruses are both part of the family of *Filoviridae*. The incubation period for these viruses (i.e., the period when the patient remains asymptomatic after exposure to a contact) can range from 2 to 21 days. Marburg is typically 5-9 days and Ebola 3-12 days.

Ebola and Marburg virus diseases usually begin with a flu-like syndrome with fever and profound weakness, often accompanied by arthralgia, myalgia, headache, anorexia and hiccups. These are usually followed by gastrointestinal symptoms: nausea, vomiting, and diarrhea.

Patients may also complain of dysphagia. See Table 2.

Despite a common belief that haemorrhage is a defining feature of filovirus disease, visible bleeding is not universal. When present, bleeding is not an early presenting feature, but often only appears in the later stages of filovirus disease. It may

manifest as overt bleeding or a combination of major and minor bleeding signs, but is frequently only minimal and sometimes solely internal (and therefore frequently missed).

### **Clinical features of Lassa fever**

The incubation period is 6-21 days.

Clinical distinction between VHF is difficult, emphasizing the importance of prompt laboratory testing to identify Lassa fever early enough for ribavirin to be effective. Swollen face and neck are classic signs in Lassa fever but only occur in about 10% of cases; these are not seen in Ebola/Marburg. Sore throat occurs in both but exudative pharyngitis and convalescent hearing loss suggest Lassa fever. Tenderness over the liver suggests Ebola/Marburg. Only about 20% of Lassa fever patients develop haemorrhage, as opposed to 50 to 60% of Ebola (depending on the subtype). Lassa fever typically has a more indolent presentation with patients feeling fatigued and "feverish" for a few days, whereas significant illness in Ebola/Marburg begins more abruptly and evolves more rapidly.

Lassa fever is mild or has no observable symptoms in about 80% of people infected and unapparent infection, diagnosed serologically, is common in endemic areas. Because of these frequent mild infections, the overall case fatality rate can be quite low; hospital studies in symptomatic patients report the case fatality rate as 15 to 25%<sup>12,13</sup>. Severe multisystem disease is seen in a subset of patients, however, and in the case of some epidemics, the mortality has been reported as high as 80%. There may be viral strain differences between Lassa fever in Nigeria and Sierra Leone. Moreover, disease seems to be more severe in pregnancy with frequent maternal mortality, particularly in the third trimester, and 80% fetal loss.

The virus is excreted in urine for 3 – 9 weeks after infection and in semen for 3 months<sup>14</sup>. The extent of sexual transmission is unknown.

Clinical stages of severe Lassa fever (adapted from McCarthy 2002 <sup>15</sup> )	
Stage	Symptoms
1 (days 1-3)	General weakness and malaise. High fever, >39°C, constant with peaks of 40-41°C
2 (days 4-7)	Sore throat (with white exudative patches) very common Headache; back, chest, side, or abdominal pain Conjunctivitis Nausea and vomiting Diarrhoea Productive cough Proteinuria Low blood pressure (systolic <100 mm Hg) Anaemia
3 (after 7 days)	Oedema of the face and neck Convulsions Mucosal bleeding (mouth, nose, eyes) Internal bleeding Encephalopathy with confusion or disorientation
4 (after 14 days)	Coma Death

During convalescence, transient alopecia and ataxia may occur. Sensorineural hearing deficit (eighth cranial nerve) is common (29% of confirmed cases compared with none of febrile controls in hospital inpatients)<sup>16</sup>, with no relationship to severity of viral illness. Only about half recover some function.

Laboratory features include early lymphopenia which may be followed by late neutrophilia. Platelet counts are moderately depressed, and platelet function is abnormal. Aspartate amino-transferase (AST) levels above 150 and high viremia are poor prognosis indicators for the patient. Severe disease may be accompanied by albuminuria and hemoconcentration.

### Clinical features of Crimean-Congo Haemorrhagic Fever<sup>17, 18, 19, 20</sup>

For CCHF, the incubation period depends on the mode of acquisition, but is usually 3-7 days. The documented maximum after a tick bite is reported as 9 days and after

contact with infected blood or tissues 13 days. The clinical characteristics of patients with CCHF infection present a wide spectrum of disease severity from mild to fatal outcome (case fatality rate 5–30%).

The onset of CCHF is sudden, with initial signs and symptoms including headache, high fever, back pain, joint pain, abdominal pain, and vomiting. Red eyes, flushed face, red throat, and petechiae (red spots) on the palate are common. Symptoms may also include jaundice, and in severe cases, changes in mood and sensory perception.

The haemorrhagic period is short (usually 2–3 days, but up to 2 weeks), develops rapidly, and usually begins between the third to fifth days of disease. Haemorrhagic manifestations of CCHF are common and range from petechiae to large haematomas appearing on the mucous membranes and skin. The most common bleeding sites are the nose (epistaxis), gastrointestinal system (haematemesis, melena, and intra-abdominal bleeding), uterus (menorrhagia–excessive menstrual bleeding; other vaginal bleeding), urinary tract (haematuria), and the respiratory tract (haemoptysis). Uncontrolled bleeding at injection sites can also be seen and bleeding from other sites, including cerebral haemorrhage have been reported. In approximately 30% of the patients, hepato-splenomegaly can also be found.

Laboratory features of CCHF are thrombocytopenia, leukopenia, elevated liver enzymes, and prolonged bleeding times. Laboratory tests return to normal levels within approximately 5–9 days among surviving patients. Most of the early clinical signs of CCHF are non-specific and can also be seen with Ebola/Marburg and Lassa fever, so differentiation often relies on exposure history and laboratory testing.

**Any acute illness, especially febrile illness, not clearly due to a common pathogen or which is unresponsive to initial empirical therapy, should raise concern for VHF. This is especially true if there is unexplained bleeding or rapid deterioration of the patient's condition.**

TABLE 2

**Early and late clinical features of Ebola/Marburg infection****Early clinical features of Ebola/Marburg<sup>11</sup>**

- |   |   |
|---|---|
| • Intense tiredness, weakness, malaise                | • Conjunctivitis                          |
| • Sudden onset of fever (defined as 38.0°C axillary)* | • Nausea and loss of appetite             |
| • Headache  | • Throat pain and difficulty swallowing   |
| • Myalgia (muscle pain)                               | • Abdominal pain                          |
| • Arthralgia (joint pain)                             | • Diarrhoea (can be bloody or non-bloody) |
| • Hiccups   |   |

Note: There is often an overlap of early and late symptoms. Patients often do not develop all the signs and symptoms.

## Late clinical features

- Confusion and irritability
- Seizures
- Chest pain
- Diarrhoea (watery or bloody)
- Vomiting (sometimes bloody)
- Skin rash
- Internal and/or external bleeding including:
  - oozing from puncture sites
  - rashes suggestive of easy bleeding ecchymoses, petechiae, purpura
  - bleeding from the gums
  - conjunctival haemorrhage (bleeding from the eyes)
  - epistaxis (bleeding from the nose)
  - haematemesis (blood in vomitus) (e.g.,
  - haemoptysis (blood in sputum)
  - dark blood in stool (melena, hematochezia)
  - unexplained vaginal bleeding in women
  - haematuria (blood in urine)
- Miscarriage in pregnant woman\*\*
- Respiratory distress
- Shock (see definition of shock in section 4)

\*Fever may be absent in late stages

\*\* Pregnant patients with VHF often miscarry. However, vaginal bleeding and miscarriage can occur in any pregnancy. During an Ebola/Marburg or CCHF outbreak, fever with miscarriage or abnormal vaginal bleeding (other than normal menstruation) should prompt a PCR test to rule out VHF.



## 2.1.3 Initial response to a suspected or confirmed case of Ebola/Marburg, Lassa fever or CCHF<sup>21</sup>

Initial procedures for evaluation and response to all patients presenting to health centre or hospital in a VHF-prone area

### 1. Screening

- Perform the Quick Check (in adolescents or adults)<sup>1</sup> or ETAT in young children.<sup>2</sup>
- Review the patient history:
  - Any contact with someone in the previous 3 weeks who was ill with fever +/- bleeding or who died from an unexplained illness with fever +/- bleeding?
  - Any contact with other family members who are sick or have died from a disease with similar symptoms and signs?
  - Unexplained death of wild animals in the area?
  - History of contact with blood and body fluids of wild animals (especially monkeys, bats, rats, etc.)?
  - History of visiting/exploring caves or working in mines infested with bats?
  - Received a tick bite or crushed a tick with their bare hands?
  - Home infested with rats?

### 2. If you suspect a case of VHF

- Call for help from doctor within the facility for further evaluation
- After further evaluation, contact the hospital/district surveillance focal person and/or District Health Officer
- Keep the patient in the holding room/area

## 2. Educate the patient if conscious and cooperative

- Educate the patient on what will happen next
- Explain the reasons for the isolation/holding
- Explain the procedures you are following with respect to controlling transmission to the family, health workers and the community
- Educate the patient on respiratory hygiene
- Give the patient a surgical mask and make sure he/she understands how to use it

## 3. Isolate the patient

- Triage rapidly to a separate room /holding area
- The holding area should be:
  - Distant from other crowded areas
  - Well ventilated
  - Have adequate sunlight
  - Known to everyone in the facility

## 4. Notify/Refer the patient

- Make every effort to reduce the waiting time between initially seeing the patient and notification/referral
- Develop a system to move patients quickly and reduce the time that others are exposed

## Summary of what to do when you suspect VHF

- Use standard precautions and use available personal protective equipment before examining the patient(s)
- Isolate the patient
- Notify the district health officer (DHO) immediately using the most urgent available means (telephone, message, etc). The DHO will send the rapid response team to investigate the event further. (Refer to IDSR Guidelines<sup>22</sup> for details)
- Where possible, take off blood samples to diagnose VHF (see Section 2.1.4) and send them to the appropriate laboratory

## 2.1.4 Laboratory investigations & specimen collection

All samples should be considered as highly infectious. Early recognition of VHF depends on a high index of clinical suspicion by the attending health worker. The ability to confirm the diagnosis of VHF also requires highly specialized reference laboratories. In West Africa, these are located in ... [please insert relevant reference labs to send samples for suspected VHF]

Laboratory personnel (technician level or above) who have been trained in shipment of highly infectious biological substances and in safe blood sampling, and also trained on how to put PPE on and off, should ensure the following procedures are followed for investigations:

1. Ensure all specimen collection containers are available (SEE TABLE 4).
2. Collect samples taking necessary protective precautions and ensure samples are appropriately labeled, including unique patient identifiers (name, DOB).
3. Package samples according to standard guidelines.
4. Send the samples immediately to the appropriate reference laboratory marked urgent. There may be a country wide network of laboratories where samples for transportation to the national reference laboratory (or laboratory in a neighboring country) are gathered. Usually the regional centres have means to pick samples from lower health units within their prescribed areas of operation, where they are ultimately picked and dispatched to the appropriate laboratory.
5. If packaging materials are not available keep the sample in a refrigerator or in a freezer at -20° C or colder.

Consider other causes of fever in your differential diagnosis and if available exclude through appropriate investigations. Refer to the IMAI District Clinician Manual differential diagnosis tables for adults<sup>1</sup> and to the Child Pocket Book for children<sup>2</sup>.

TABLE 3

### Interpretation of VHF laboratory results from acute symptomatic patients

Lab confirmation of:	Result
Acute infection	PCR and/or IgM positive
Recent infection (within previous couple of months, i.e. in current outbreak)	IgM and IgG positive
Older infection (within the last couple of years)	High IgG positive only (no IgM)
Past infection (not associated with current outbreak)	Lower IgG positive only (no IgM)

*\*\*\*If a specific diagnosis in addition to VHF is made (e.g. pneumonia), use established principles and guidelines for treating those conditions. It is important that identifying the source of infection should not delay delivery of supportive treatments and empirical antibiotics*

### Malaria testing

Always test for malaria with a rapid diagnostic test (RDT) at the bed side taking necessary precautions. If a RDT or malaria smear is negative, the patient does not have malaria.

- ▶ It is dangerous to attribute fever to malaria when it is not present because the patient does not get the right case management if they are incorrectly diagnosed as having malaria.
- ▶ If the malaria test is positive but the patient is considered to be a suspected case during a Filovirus, Lassa fever or CCHF outbreak, or at any time in a Lassa endemic area, await confirmation from Filovirus, Lassa fever and/or CCHF virus testing (or response to anti-malarial treatment) before discharging the patient from the isolation ward.

TABLE 4

## Specimen collection for viral haemorrhagic fevers

Specimen	<p>For <i>ELISA</i>: Whole blood, serum or plasma  For <i>PCR</i>: Whole blood or blood clot, serum/plasma or tissue  For <i>immunohistochemistry</i>: Skin or tissue specimens from fatal cases.</p>
When and how to collect	<p>Collect specimen from the first suspected case.  If more than one suspected case, collect specimens from every suspected case.  All specimens should be regarded as potentially infectious, and health workers who collect or transport clinical specimens should adhere rigorously to Standard Precautions (SEE SECTION 7) to minimize the possibility of exposure to pathogens.</p>
How to prepare, store, and transport	<p><b>HANDLE AND TRANSPORT SPECIMENS FROM SUSPECTED VHF PATIENTS WITH EXTREME CAUTION. WEAR PROTECTIVE CLOTHING AND USE BARRIER PRECAUTIONS.</b></p> <p><i>For ELISA or PCR:</i>  Refrigerate serum or clot  Freeze (-20° C or colder) tissue specimens for virus isolation</p> <p><i>For immunohistochemistry:</i>  Fix skin snip specimen in formalin. Specimen can be stored up to 6 weeks. The specimen is not infectious once it is in formalin. Store at room temperature. Formalin-fixed specimens may be transported at room temperature.</p> <p><b>NOTE:</b>  <b>ALL SPECIMENS MUST BE PACKAGED USING TRIPLE PACKAGING SYSTEM</b>  <b>SPECIMENS MUST BE APPROPRIATELY LABELLED AND ACCOMPANIED WITH COMPLETE DOCUMENTATION (INCLUDING CASE INVESTIGATION FORM)</b></p>
Results	<p>Diagnostic services for VHF are not routinely available. Advance arrangements are required for VHF diagnostic services. Contact reference laboratory for immediate attention. After the sample arrives, a result will be available within 24 hours</p>

## Other investigations

Due to the potential risk of transmission to laboratory workers, additional blood tests are not to be sent to the routine laboratory until the results of the VHF screen are known and negative. An exception to this is the use of RDT for malaria and other point of care equipment (such as the i-STAT® System) by appropriately trained personnel. The latter, however, is unlikely to be available until an outbreak is declared and additional support is provided.

## Laboratory diagnosis of Ebola/Marburg, Lassa fever or CCHF

Laboratory diagnosis can be difficult depending on the phase/time of presentation, duration of symptoms and previous exposure. The ability to confirm the diagnosis of VHF also requires highly specialized (with high biosafety infrastructure) reference laboratories that are centrally located. If blood tests have been performed, the following laboratory findings (in combination with the clinical presentation) are suggestive of VHF but not conclusive: thrombocytopenia; elevated hematocrit; and marked leukopenia.

To confirm a VHF case, three laboratory tests can be run on blood samples (blood, serum or plasma) collected in patients suspected of having VHF, depending on the time of sample collection relative to the date of disease onset.

- 1) Polymerase chain reaction (PCR) provides evidence of the virus in the blood or tissues during the acute phase of the clinical disease. In certain circumstances, this test can be replaced by an antigen detection ELISA (it is less sensitive and more broadly cross-reactive);
- 2) IgM (antibody showing recent infection) during the early convalescence phase of disease (until approximately 8-12 weeks post onset of disease)
- 3) IgG (antibody showing past infection) persists for several months/ years after the acute phase of the clinical disease. This alone is not suggestive of recent or ongoing infection but can be utilized to confirm acute infection with paired samples showing IgG seroconversion.

The levels of virus increase during the first days of symptoms and this increase correlates with the patient's degree of infectiousness. Viral levels are both dependent on the patient's immune response and the amount of infecting dose. If the patient produces a good immune response to the virus, antibodies (IgM and IgG) will start to be produced

and can be measured. Conversely, a weak immune response to the virus correlates with high levels of virus in the blood and is associated with a high mortality. For patients who have died, immunohistochemistry testing has also been used to detect some VHF (e.g., Ebola or Marburg) from post-mortem skin necropsy. All samples for clinical laboratory tests from patients with possible VHF should be considered very infectious and processed accordingly (i.e. not sent to routine laboratories). Essential investigations should be undertaken and laboratory staff informed.

### **Pitfalls in laboratory results interpretation**

- ▶ Sensitivity is increased by use of paired samples separated by at least 3 days.
- ▶ False negative results are likely to occur in samples taken in early phases of the infection.
- ▶ New VHF strains/virus can occur (e.g., Lujo virus)
- ▶ IgG alone is not diagnostic of acute or recent infection except if evaluating rising titres in paired samples.
- ▶ Cross-reaction of IgG/IgM with other pathogens is possible.

## **2.2 Notification**

Once VHF is suspected, immediate notification to the next level and district should be done using the appropriate and quickest available means, especially telephone and other modalities such as mTRAC. The event also needs documentation using the appropriate reporting form (HMIS 033a). All subsequent suspected cases should be reported and recorded on a line list for further action (refer to the IDSR 2010 guidelines<sup>22</sup> for details).

## **2.3 Isolation**

One of the key guiding principles in the management of VHFs is the triaging of cases and ensuring isolation of suspected and confirmed cases to mitigate further spread of disease. Ideally an isolation area should already be available to admit patients requiring isolation. If an isolation area is not available or if advance preparations have not been done, and VHF is suspected, immediately identify and set aside a single room. This room should have an adjoining toilet or latrine, good ventilation, screened windows and restricted access. Details on how to set up the isolation unit as part of the VHF treatment centre are explained elsewhere.





### 3. Management of suspected and confirmed Ebola, Marburg, Lassa fever or CCHF cases

The clinical management of VHF is predominantly supportive and should focus on early recognition of severe disease and complications, in combination with appropriate symptom management. The level of care and interventions required varies across the spectrum of disease severity, including complex management of septic shock and palliation when indicated. Control of pain and management of anxiety are particularly important and all patients need careful monitoring, as well as psychological support (see **section 6**).

Health workers should pay careful attention to standard precautions and wear PPE (see **section 7**) while providing careful clinical care.

Always start each patient assessment with the Quick Check (in adolescents and adults) or the ETAT (in children) for emergency signs and respond with emergency treatments. The wall charts for these should be posted in the isolation wards. The IMAI District Clinician Manual<sup>1</sup> (IMAI DCM) and the Pocket Book of Hospital Care for Children<sup>2</sup> should be available for consultation for further details on care.

### 3.1 Manage symptoms/signs

TABLE 4

Specific management of signs and symptoms<sup>1,2,3</sup>

Symptom/Sign	Treatment
Fever (>38.0 °C)	<p>Manage fever with paracetamol (see Appendix C for dosing). Avoid diclofenac, ibuprofen or aspirin due to platelet effects.</p> <p><i>Further details in IMAJ DCM Section 10.1; in Child pocket book p. 305</i></p>
Acute significant bleeding/ moderate to severe pallor/ emergency signs of circulatory shock	<p>Transfuse with whole blood</p> <p><i>Further details in IMAJ DCM Section 10.18; in Child pocket book pages 161, 218, 308-312.</i></p>
Pain	<p>Treat pain with paracetamol (if mild) or morphine (if moderate and severe). Avoid diclofenac, ibuprofen or other NSAIDs due to platelet effects.</p> <p><i>Paracetamol and morphine doses are in Appendix C. Further details in IMAJ DCM Section 20; in Child pocket book Section 10.4, p. 306</i></p>
Difficulty breathing/ respiratory distress	<p>Oxygen: titrate to SpO<sub>2</sub> ≥90%</p> <p>If SpO<sub>2</sub> &lt; 90%, start adult on 5 litres/minute (nasal prongs); start child at 1-2 litres/minute (nasal prongs)</p> <p>Evaluate for pneumonia, wheezing, fluid overload, congestive heart failure and manage accordingly. (Do not share nasal prongs - once used by a patient, dispose.)</p> <p><i>Further details in IMAJ DCM: See Section 3.2 for management respiratory distress, CHF, and pneumonia; in Child pocket book Pages 11,82,312-315</i></p>
Diarrhoea, vomiting, signs of dehydration	<p>Provide ORS even if no signs of dehydration. Monitor signs of dehydration. If no, some or severe dehydration, use Fluid Plans A, B and C, respectively (see Appendix B and, for children, see p. 34 below).</p> <p>If severely malnourished child with shock, see p. 35 below.</p> <p>Nausea and vomiting are common- anti-emetic medications may provide some relief and facilitate oral rehydration. For adult, give chlorpromazine 25-50 mg, 4 times daily IM or orally or metoclopramide 10 mg IV/ orally 3 times daily until vomiting stops. For children, give promethazine. Monitor for extrapyramidal signs.</p> <p><i>Further details in IMAJ DCM Sections 10.7c and 10.7d; in Child pocket book Section 5.</i></p>

<b>Specific management of signs and symptoms <i>continued</i></b>	
<b>Dyspepsia</b> (i.e., "heartburn")	In adults and children $\geq 10$ years, give omeprazole 20 mg orally daily or magnesium trisilicate, 2 tabs every 8 hours until symptoms resolved. In children 5-12 years, give magnesium trisilicate: 5-10 mls, 3 times daily  <i>Further details in IMAI DCM: Section 10.7c</i>
<b>Convulsions</b>	Approach: convulsing patients with caution. Give diazepam to abort seizure if prolonged (rectally if there is not an IV already in place- adult 20 mg (4 ml of 10 mg/2ml solution); child 0.5 mg/kg), then control with phenobarbital loading dose (child: 15 mg/kg over 15 minutes- IM or IV); adult: 10 mg/kg.  <i>Further details in IMAI DCM: Quick Check page 42; ETAT page 15</i>
<b>Signs of hypoglycaemia</b>	Test glucose (and monitor regularly)  If low, give IV D50 5 ml/kg in child; 25 to 50 ml of D50 in adult Nutritional support  <i>Further details in IMAI DCM: Quick Check page 42; in Child pocket book page 16</i>
<b>Anxiety</b>	Psychological support (see section 6 of this manual) Diazepam – adults: 5-15 mg/day in 3 divided doses  <i>Further details in IMAI DCM: Section 10.11</i>
<b>Confusion in cooperative patient</b>	Reason with patient in calm and non-aggressive fashion. Keep lighting on at night. Consider diazepam 5 mg at night (adult)
<b>Confusion and aggression in non-cooperative patient</b>	Give sedation-haloperidol 5 mg IM (adult) <i>Further details in IMAI DCM: Quick Check page 60</i>
<b>Shock</b>	See diagnosis and management of septic shock below.  <i>Further details in IMAI DCM: Section 3.1</i>

### 3.2 Specific therapy for Lassa fever and CCHF

Ribavirin can be used to treat patients with Lassa fever and CCHF and also considered for high-risk Lassa fever and CCHF patient contacts. Ribavirin is not used in Ebola or Marburg disease for which it has no activity. Its efficacy in CCHF and Lassa

fever has not been proven by a randomized controlled trial, and there are differences in opinion on its clinical effectiveness in the published literature. Nevertheless, observational data from Lassa fever, for which there has been more experience, suggest that ribavirin is most effective if given in the first 6 days of illness<sup>12,13</sup>.

Ribavirin dose for treatment of Lassa fever and CCHF <sup>13</sup>		
Route	Dose	Interval
IV*	30 mg/kg (maximum 2 grams)**	Loading dose followed by:
IV*	15 mg/kg (maximum 1 gram)**	Every 6 hours for 4 days, followed by:
IV*	7.5 mg/kg (maximum 500 mg)**	Every 8 hours for 6 days.

\* Dilute ribavirin in 150 ml of 0.9% saline and infuse slowly.

\*\* Reduce the dose in persons known to have renal insufficiency (creatinine clearance < 50 ml/minute).

Major adverse effects due to short-term ribavirin therapy are rare but require monitoring. The main side-effect is a dose-dependent, mild-to-moderate haemolytic anaemia that infrequently necessitates transfusion and disappears with cessation of treatment. Rigors may occur when ribavirin is infused too rapidly. Relative contraindications include severe anaemia or haemoglobinopathy, coronary artery disease, renal insufficiency, decompensated liver disease, breast-feeding and known hypersensitivity. Jaundice may develop in patients with Gilbert's syndrome. Haemoglobin/haematocrit and bilirubin levels should be checked at initiation of ribavirin therapy and then every few days, with consideration of transfusion of packed red blood cells if significant anaemia develops. Because of the long terminal half-life (~24 hours) and large volume of distribution, ribavirin may still have effect for hours or even days after cessation, particularly in red blood cells where it accumulates. Although findings of teratogenicity and fetal loss in laboratory animals have rendered ribavirin technically contraindicated in pregnancy, its use must still be considered as a lifesaving measure given the extremely high maternal and fetal mortality associated with Lassa in pregnancy<sup>13</sup>Error! Bookmark not defined.. Patients who have had ribavirin should refrain from unprotected sex for up to 6 months after exposure.

Both progressive hemolytic anemia and hypomagnesemia have been shown to be dose-dependent<sup>23</sup>. Bradycardia has also been reported. Other non-specific complaints associated with ribavirin include headache, fatigue, insomnia, and nausea.

Oral formulations should be restricted to post-exposure prophylaxis for high-risk exposures to Lassa fever and CCHF (see Section 5).

For children, the use of oral or intravenous ribavirin has not been approved.

### 3.3 Special considerations in pregnancy

- Full term deliveries are rare in Ebola/Marburg. Fetal death occurs in 80% of pregnant Lassa fever patients.
- Basic facilities for deliveries and a private area to manage miscarriage and vaginal bleeding should be installed. Extreme caution must be used during management of bleeding to avoid health worker infection.
- There are reports of clinical improvement in pregnant women with Lassa fever after the uterus is evacuated.<sup>24</sup> As uterine evacuation in pregnant patients appears to lower maternal mortality, it should be considered in confirmed cases given the extremely high maternal and fetal mortality. However, this high-risk procedure must be performed with extreme caution, given potential for nosocomial transmission and the risk for inducing maternal haemorrhage<sup>13</sup>.
- Follow clinical guidelines for use of ergometrine in early pregnancy and oxytocin and other interventions post-partum to stop bleeding.

### 3.4 Special considerations in breastfeeding women

- Ebola and Marburg viruses have been found in breast milk. During a Marburg outbreak in Angola in 2005 there was a high number of paediatric cases, and breastfeeding may have been a factor in Marburg virus transmission as indicated by the epidemiology and Marburg virus- positive breast-milk specimens<sup>25</sup>.
- Given the potential risk of transmission through breastfeeding, a woman who has

been admitted as a suspect Ebola, Marburg, Lassa fever or CCHF patient may have already infected her breastfed infant. The infant should also be admitted and isolated.

- Do not send breastfed infants home that may be infected and who could soon be shedding virus.
- Default advice is to STOP breastfeeding, but this should be in context with an individual risk assessment on the likelihood of VHF, and the ability to provide alternative feeding to the infant. If the mother is conscious, help her express her breast milk manually, continue stimulation of milk production, and relieve breast congestion. If she is unconscious, a health worker trained on breastfeeding expression may help the mother extract breast milk. Given the risk of splashes, the person helping with milk expression should use gloves, a gown and face protection.
  - Safely prepared commercial infant formula milk should be given to infants under 6 months. Give training on the safe preparation, storage and use of artificial milk to the staff. If the infant is older than six months, cow's (or other animal) milk and adequate complementary foods are sufficient
  - Discourage wet-nursing; if the baby breastfeeds from another woman, there is a theoretical risk that the baby will transmit infection to this woman, given the close contact during breastfeeding. .
- The mother may require psychological support.

### 3.5 Special considerations for children

- If the child becomes sick and both the mother and child test positive for Ebola or Marburg disease, then the child can be returned to the mother. If the child is negative (and it may be prudent to carry out two tests two days apart), he/she can leave pediatric isolation and be followed closely as a high-risk contact if there is a family member who can care for the child safely at home, while discouraging wet-nursing.

## 4. Manage severe confirmed or suspected cases of Ebola/ Marburg, Lassa fever, or CCHF (with

### 4.1 Shock in VHF patients

General signs of shock (poor perfusion)

- Low BP (SBP <90)
- Fast weak pulse
- Pallor or cold extremities
- Decreased capillary refill
- Dizziness or inability to stand
- Decreased urine output (<30 ml/hour)
- Difficulty breathing
- Impaired consciousness, lethargy, agitation, confusion.

*Note: Assessment of pulse and BP should be taken in the context of the patient's pre-morbid state, pregnancy, age, and medication. Some pregnant women, patients with chronic illness, and others may normally have a SBP <90 mmHg and have normal mental status, capillary refill, and urine output; they do not have shock.*

VHF patients can be in shock from haemorrhage or from septic shock.

- The pathophysiology and the intensive supportive care for VHF are the same for septic shock from a bacterial infection, malaria and other causes of septic shock<sup>26, 27</sup>. Intensive supportive care is the only clinical management that can be provided to these patients and may have a positive impact on disease outcome.
- VHF patients may also have co-infection with bacteria or malaria that can contribute to septic shock.
- It should also be recognized that VHF patients can also develop hypovolaemic shock as a result of haemorrhage.
- The shock in a VHF patient may be a combined picture from haemorrhage, disseminated intravascular coagulation (DIC) and from sepsis.

Call for help from the most experienced clinician available when a VHF patient develops shock.

## 4.2 Manage septic shock in adolescents and adults

**CLINICAL DIAGNOSIS of severe sepsis or septic shock:**

- Suspected infection **plus**
- Hypotension (systolic blood pressure <90 mmHg) **plus**
- One or more of the following:
- Pulse >100 per minute
- Respiratory rate >24 breaths per minute
- Abnormal temperature (<36° C or >38° C).

Use the flowchart on the following pages for specific guidance on the management of septic shock. It is arranged by hours, starting from patient arrival or time septic shock is diagnosed and uses a systematic approach for the recognition of problems, giving oxygen and fluids, and how to monitor, record, and respond to findings. These basic

### General principles of managing patients with septic shock

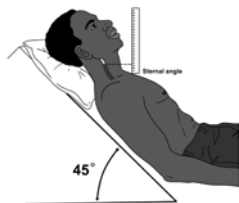
- Manage airway (see Quick Check).
- Give oxygen (see Quick Check).
- Give IV fluid rapidly (see specific fluid recommendations which follow).
- Treat underlying cause.
- Consider vasopressors if SBP <90 and signs of inadequate perfusion after fluid resuscitation.
- Monitor – record – respond.

recommendations provide guidance on intensive supportive care for patients with shock of most aetiologies, including VHF. Below is more detailed information about these basic interventions.



## Give fluids rapidly

- First give an initial 1000 ml LR or NS bolus, continue Ringer's lactate (LR) or Normal saline (NS) at 20 ml/kg/hour, not to exceed a maximum of 60 ml/kg in the first 2 hours (including the initial bolus).
- Monitor systolic blood pressure (SBP) and clinical signs of perfusion (urine output, mental status).
- If SBP remains <90 and signs of poor perfusion continue after fluid resuscitation over the first 2 hours,
  - ▶ Consider adding vasopressors (dopamine or epinephrine) using the instructions in Appendix D (How to give vasopressors).
  - ▶ To avoid fluid overload, decrease the rate of fluids to 5–10 ml/kg/hour.
- At 2–6 hours, if SBP rises above 90, continue fluids at 2 ml/kg/hour. However, if the pulse is still high and there are other signs of poor perfusion, patient may still be volume-depleted and need more fluids.
- Watch carefully for signs of fluid overload (increased jugular venous pressure, increasing crepitations on auscultation). If present, decrease the rate of fluid administration. Call for help from more senior clinician to further evaluate overload and decide fluids.



## Give empirical IV antimicrobials within the first hour.

- Antibiotics: Urgently administer broad spectrum antibiotics by IV. Take blood cultures before antibiotics, but do not delay treatment to get blood cultures.
  - Choice of antibiotics depends on presence of signs of local infection, local disease patterns, and availability of antibiotics. A good choice is ceftriaxone 2 grams daily IV.
  - If community-acquired pneumonia is suspected, refer to your national or institutional guidelines.

# Management of septic shock in adults and adolescents

	Manage Septic Shock: First 2 hours	2-6 hours
Recognize	<p><b>Clinical diagnosis of severe sepsis or septic shock</b></p> <ul style="list-style-type: none"> <li>▶ Suspected infection.</li> <li>▶ Hypotension (systolic blood pressure &lt;90 mmHg) and 1 or more of the following.</li> <li>▶ Pulse &gt;100 beats per minute (bpm).</li> <li>▶ Respiratory rate &gt;24.</li> <li>▶ Abnormal temperature (&lt;36°C or &gt;38°C).</li> </ul>	<p>Reconsider other causes of shock if no change in SBP following fluid boluses.</p> <p>Consider internal haemorrhage.</p> <p>Establish any additional source of infection.</p>
Fix the physiology/ stabilize the patient	<p><b>Oxygen:</b> titrate to SpO<sub>2</sub> 90.</p> <p><b>Fluids:</b> After initial bolus of 1000 ml, continue rapid fluids LR or NS at 20 ml/kg/hour, up to 60 ml/kg within the first 2 hours.</p>	<p><b>Oxygen:</b> Titrate to SpO<sub>2</sub> 90.</p> <p><b>Fluids:</b> If SBP &gt;90, continue fluids at 2 ml/kg/hour.</p> <p>If SBP &lt;90 at 2 hours or later, start vasopressors and continue fluids at 5–10 ml/kg/hour. Only give vasopressor if trained- see Appendix D.</p>
Treat infection	<p><b>Urgent empirical antimicrobials</b></p> <ul style="list-style-type: none"> <li>▶ Antibiotics.</li> <li>▶ Antimalarials (if RDT bedside malaria test positive).</li> <li>▶ Antivirals – consider ribavirin in confirmed Lassa fever or CCHF.</li> </ul> <p><b>Identify any additional source of infection</b></p> <ul style="list-style-type: none"> <li>▶ Use signs or symptoms to consider source.</li> <li>▶ Chest X-ray if portable machine available.</li> <li>▶ AFB smear of sputums, if cough.</li> <li>▶ Chest X-ray, Gram-stain sputum.</li> </ul>	<p>Treat any additional source of infection.</p> <p>Review results of investigations.</p>
Monitor, Record	<p><b>Every 30 minutes until stable; then every 1 hour</b></p> <ul style="list-style-type: none"> <li>▶ SBP, pulse.</li> <li>▶ Respiratory rate.</li> <li>▶ SpO<sub>2</sub>.</li> <li>▶ Mental status (AVPU)</li> <li>▶ JVP, auscultate for crepitations.</li> <li>▶ Check results of emergency laboratory</li> <li>▶ If haemoglobin &lt;7 mg/dl (Hct &lt;20), consider transfusion with fresh whole blood [reference anaemia section]. If glucose &lt;3 mmol/l (54 mg/dl), then give 50% dextrose 25–50 ml (see Quick Check page 19).</li> </ul>	<p><b>Every 30 minutes until stable; then every 1 hour</b></p> <ul style="list-style-type: none"> <li>▶ SBP, pulse.</li> <li>▶ Respiratory rate.</li> <li>▶ SpO<sub>2</sub></li> <li>▶ Mental status (AVPU).</li> <li>▶ JVP, auscultate for crackles (rales).</li> <li>▶ Urine output.</li> </ul>
Respond	<p><b>If respiratory function declining (increasing RR, falling SpO<sub>2</sub>)</b></p> <ul style="list-style-type: none"> <li>▶ Check oxygen supply and fix.</li> <li>▶ If wheezing, give salbutamol.</li> <li>▶ If JVP elevated, increasing crepitations- consider fluid overload</li> <li>▶ If suspect fluid overload, slow rate of fluid administration and start vasopressors if still in shock.</li> <li>▶ If visible secretions and suction is available suction- realizing this may produce an aerosol requiring additional respiratory protection (N95 or equivalent mask)</li> </ul>	<p><b>If respiratory function declining (increasing RR, falling SpO<sub>2</sub>)</b></p> <ul style="list-style-type: none"> <li>▶ Check oxygen supply and increase flow rate if possible</li> <li>▶ If elevated JVP and increasing crackles, consider fluid overload</li> <li>▶ If wheezing, give salbutamol.</li> <li>▶ Check that antimicrobials have been given.</li> <li>▶ Treat other diagnoses or infections; see above.</li> <li>▶ If signs of fluid overload, SBP &gt;100, and shock resolved, stop IV fluids, give furosemide 20 mg IV, and raise head of bed.</li> </ul>

## Manage Septic Shock: 6-24 hours

## Post-resuscitation

Recognize	<p>If no change in SBP following fluid boluses -</p> <ul style="list-style-type: none"> <li>▶ Reconsider the possible diagnoses.</li> <li>▶ Establish source of any additional infection. Could there be a surgical cause that would benefit from drainage?</li> <li>▶ Get a second opinion.</li> </ul>	<p>Perform full reassessment.</p> <p>Review available diagnostic data and treat underlying diagnosis.</p> <p>Evidence of a <u>primary</u> cardiac or pulmonary process? Add its specific management.</p>
Fix the physiology/ stabilize the patient	<p><b>Oxygen:</b> Titrate to SpO<sub>2</sub>: 90.</p> <p><b>Fluids:</b></p> <ul style="list-style-type: none"> <li>▶ When SBP &gt;90, continue fluids at 2 ml/kg/hour.</li> <li>▶ If on vasopressors, reduce rate.</li> <li>▶ If SBP &lt;90, continue or increase vasopressors and continue LR or NS at 2 ml/kg/hour.</li> </ul>	<p><b>Oxygen:</b> Titrate to SpO<sub>2</sub>: &gt;90 and discontinue when 90 on room air.</p> <p><b>Fluids:</b> Reduce to maintenance maximum 2 ml/kg/hour and switch to oral when patient is able to take.</p>
Treat infection	<p><b>Continue empirical antimicrobials – next dose</b></p> <ul style="list-style-type: none"> <li>▶ Antibiotics.</li> <li>▶ Antimalarials (if malaria test positive).</li> <li>▶ Ribavirin, if confirmed Lassa fever or CCHF.</li> </ul>	<p><b>Continue antimicrobials – switch to oral dose</b></p> <ul style="list-style-type: none"> <li>▶ Antibiotics.</li> <li>▶ Antimalarials (give IV antimalarials for at least 24 hours total before switching to oral).</li> <li>▶ Ribavirin, if confirmed Lassa fever or CCHF.</li> </ul>
Nutrition	<p>Add dextrose 50% 25-50 ml every 6 hours to the IV bag.</p>	<p>Procedures to follow once the patient has stabilized, or after 1–2 days:</p> <ul style="list-style-type: none"> <li>▶ Due to risk of aspiration, do not give food orally if patient cannot safely swallow, (due to, e.g. altered mental status, severe shortness of breath, or severely ill with ongoing vomiting).</li> <li>▶ All other patients should be provided with food. Most patients lose their appetite when ill and may find soft foods and fluids easier to tolerate. Small frequent meals often are tolerated better.</li> <li>▶ Consider NG feeding using semisolid (porridge or mashed foods) foods if the patient cannot swallow safely and is not severely ill.</li> <li>▶ Give a small amount initially (e.g. 20–40 ml/hour) and monitor NG aspirates to check for absorption.</li> <li>▶ Increase rate of feeding as tolerated.</li> </ul>
Monitor, Record	<p><b>Every hour if SBP &lt;90 or on vasopressors; otherwise every 2 hours</b></p> <ul style="list-style-type: none"> <li>▶ SBP, pulse.</li> <li>▶ Respiratory rate.</li> <li>▶ SpO<sub>2</sub>.</li> <li>▶ Mental status (AVPU).</li> <li>▶ JVP, auscultate for crackles (rales).</li> </ul> <p><b>Every 6 hours:</b></p> <ul style="list-style-type: none"> <li>▶ Urine output.</li> </ul> <p><b>Every 12 hours:</b></p> <ul style="list-style-type: none"> <li>▶ Repeat glucose and Hb if initial value abnormal.</li> </ul>	<p><b>Every 8 hours (check SBP hourly if weaning off vasopressors); then daily</b></p> <ul style="list-style-type: none"> <li>▶ SBP, pulse</li> <li>▶ Respiratory rate</li> <li>▶ SpO<sub>2</sub></li> <li>▶ Mental status (AVPU)</li> </ul> <p>Respond to changes as indicated earlier.</p>
Respond	<p>Respond to changes as indicated for 2–6 hours on previous page.</p>	<p>Respond to changes as indicated earlier.</p>

ceftriaxone (2 gram daily IV) or ampicillin 2 grams every 6 hours plus gentamicin 1.5 mg/kg IV every 8 hours, plus ciprofloxacin.

- Antimalarials: Do bedside RDT for malaria and if positive start artesunate IV, or if not available, IV quinine (see Appendix C for antimalarial doses)
- Antivirals: Consider ribavirin in confirmed cases of Lassa fever and CCHF only.

In addition to repeated measurement of SBP, pulse, respiratory rate and pulse oximetry, regular clinical examination is important for patients in shock. Pay particular attention to the signs of poor perfusion and signs of fluid overload to help guide on-going management. Use the severely ill patient monitoring form (Appendix D).

- Signs of poor perfusion:
  - decreased urine output
  - altered mental status
- Signs of fluid overload:
  - worsening crepitations on auscultation
  - dyspnoea
  - elevated JVP
  - peripheral oedema

## 4.3 Manage septic shock in children

Children can also be infectious. Use standard precautions (see section 7). Signs of shock in children:

- Cold hands **plus**
- Weak or absent pulse **and either**
- Capillary refill time > 3 seconds **OR**
- AVPU less than Alert

Children in shock who require bolus fluid resuscitation are lethargic and have cold skin, prolonged capillary refill, fast weak pulse and hypotension.

1. Check whether the child's hand is cold. If so, determine whether the child is in shock.
2. Check whether the capillary refill time is longer than 3 seconds. Apply pressure to whiten the nail of the thumb or the big toe for 5 seconds. Determine the time from the moment of release until total recovery of the pink colour.
3. If capillary refill is longer than 3 seconds, check the pulse. Is it weak and fast? If the radial pulse is strong and not obviously fast, the child is not in shock. If you cannot feel the radial pulse of an infant (< 1 year old), feel the brachial pulse or, if the infant is lying down, the femoral pulse. If you cannot feel the radial pulse of a child, feel the carotid. (See the Emergency Triage Assessment and Triage guidelines<sup>2</sup>).

Normal pulse rate and blood pressure in children* <sup>2</sup>		
Age (Years)	Pulse rate (range)	Systolic BP
0-1	100-160	> 60
1-3	90-150	> 70
3-6	80-140	> 75

*\*Note: Normal pulse rates are 10% slower in sleeping children. In infants and children, the presence or absence of a strong central pulse is often a more useful guide to the presence or absence of shock than a blood pressure reading.*

## General principles of managing children with septic shock

- Manage airway (see ETAT).
- Give oxygen through nasal prongs or catheter- start at 1-2 litres/min to aim for oxygen saturation  $\geq 90\%$ .
- Give IV fluid – initial 20 ml/kg LR or NS bolus. See charts below.
- Treat underlying cause:
  - Administer empirical broad spectrum antibiotics (eg ceftriaxone 80 mg/kg once daily (max 2 g)
  - Antimalarials: Bedside RDT for malaria and if positive, start IV artesunate (or quinine if artesunate is not available) (see Appendix C for dosing)
  - Antivirals: Consider ribavirin in confirmed Lassa fever or CCHF
- Consider vasopressors if failure of fluids and blood to raise SBP and if signs of inadequate perfusion persist. Note: the health worker must have been trained to use vasopressors (SEE APPENDIX D)
- Monitor – record – respond.

## Initial intravenous fluid resuscitation for children with shock (and no severe malnutrition)<sup>2</sup>

- Check that the child is not severely malnourished, as the fluid volume and rate are different (see below).
- Insert an IV line (and draw blood for emergency laboratory investigations).
- Attach Ringer's lactate or normal saline; make sure the infusion is running well.
- Infuse 20 ml/kg over 1 hour.

### Urgent Fluid management – Child WITHOUT severe malnutrition<sup>27\*</sup>

Weight kg	Shock, 20 ml/kg Ringer's or Saline immediately	Plan C – Step 1	Plan C – Step 2			Plan B- 75ml/kg
		30 ml/kg Ringer's	70 ml/kg Ringer's or ngt ORS			Oral /ngt ORS
		Age <12 m, 1 hour Age ≥1 yr, ½ hour	Age <12m, over 5 hrs =drops/min**	Volume	Age ≥1yr, over 2 ½ hrs =drops/min**	Over 4 hours
2.00	40	50	10	150	55	150
2.50	50	75	13	200	55	150
3.00	60	100	13	200	66	200
4.00	80	100	20	300	66	300
5.00	100	150	27	400	80	350
6.00	120	150	27	400	80	350
7.00	140	200	33	500	100	750
8.00	160	250	33	500	110	800
9.00	180	250	40	600	110	900
10.00	200	300	50	700	120	950
11.00	220	300	55	800	135	1000
12.00	240	350	55	800	135	1100
13.00	260	400	60	900	150	1200
14.00	280	400	66	1000	160	1300
15.00	300	450	66	1000	160	1300
16.00	320	500	75	1100	180	1400
17.00	340	500	80	1200	180	1400
18.00	360	550	80	1200	190	1500
19.00	380	550	90	1300	190	1500
20.00	400	600	95	1400	190	1500

#### Reassess the child after the appropriate volume has been infused.

Reassess after first infusion

- Can repeat second bolus in second hour. If no response, give blood.
- If whole blood, give 20 ml/kg over 2 to 4 hours.

Reassess after second infusion

If still low BP, consider vasopressors.

## Emergency Fluid management in Severe Malnutrition<sup>28</sup>

### Shock:

Cold hands plus absent, slow (<60 bpm) or weak pulse and either capillary refill >3 seconds or reduced consciousness.

- Give 15 ml/kg in 1 hour of Half Strength Darrows (HSD) in 5% dextrose or Ringers lactate. If HSD in 5% Dextrose not available it can be made by adding 50 ml 50% dextrose to 450 ml HSD (withdraw 50 ml from 500 ml bag first then add 50 ml of 50% dextrose).

Urgent Fluid management – Child WITH severe malnutrition				
	Shock		Oral / ngt Resomal	Emergency Maintenance
	15 ml/kg		10 ml/kg/hr	4 ml/kg/hr
	Half-Strength Darrows in 5% Dextrose		Resomal	HSD in 5% Dextrose
	iv		Oral/ngt	iv
Weight kg	Shock= over 1 hour	Drops/min if 20 drops/ml giving set	10 ml/kg/hr for up to 10 hours	Hourly until transfusion
4.00	60	20	40	15
5.00	75	25	50	20
6.00	90	30	60	25
7.00	105	35	70	30
8.00	120	40	80	30
9.00	135	45	90	35
10.00	150	50	100	40
11.00	165	55	110	44
12.00	180	60	120	46
13.00	200	65	130	48
14.00	220	70	140	50
15.00	240	80	150	52

### If child improves:

- Repeat this bolus over another 1 hour.
- Then switch to oral or ng fluids using ReSoMal at 10 ml/kg/hour for up to 10 hours.
- As soon as conscious introduce F-75 and appropriately reduce amount of ReSoMal given.

### If child does not improve:

- Give maintenance IV fluids at 4 ml/kg/hr.
- Transfuse 10 ml /kg whole blood over 3 hours as soon as it is available.



- Introduce F-75 after transfusion complete.

## Follow fluid guidelines strictly to avoid fluid overload.

### Watch carefully for signs of fluid overload in children

Fluid overload is an important complication of treatment for shock. It can develop due to:

- Excess or too rapid IV fluids
- Incorrect use of hypotonic rather than isotonic crystalloid solutions
- Continuation of IV fluids for too long (once plasma leakage has resolved)
- Use of large volumes of IV fluid in children with severe capillary leakage

#### Early signs:

- fast breathing
- Chest indrawing
- Large pleural effusions
- ascites
- peri-orbital or soft tissue oedema

#### Late signs:

- pulmonary oedema
- cyanosis
- irreversible shock (often a combination of ongoing hypovolaemia and cardiac failure)

## The management of fluid overload varies depending on whether the child is in or out of shock

- ▶ Children who remain in shock and show signs of severe fluid overload are extremely difficult to manage and have a high mortality.
- ▶ Avoid diuretics, as they will cause further intravascular fluid depletion
- ▶ Aspiration of large pleural effusions or ascites can be considered to relieve respiratory symptoms, but the risk of bleeding should be recognized.
- ▶ If shock has resolved but the child has fast breathing and large effusions, consult with pediatric expert to consider giving oral or IV furosemide 1mg/kg once or twice a day for 24 hours (and oxygen therapy)

If shock has resolved and the child is stable, stop IV fluids and keep the child on bed rest for 24-48 hours. The excess fluid will be re-absorbed and lost through urinary diuresis.



## 5. Management of exposed individuals (contacts)

Individuals including health workers with percutaneous or mucocutaneous exposure to blood, body fluids, secretions, or excretions from a patient with suspected VHF should immediately wash the affected skin surfaces with soap and water. Mucous membranes (e.g. conjunctiva) should be irrigated with copious amounts of water or eyewash solution.

Exposed persons should be medically evaluated and receive follow-up care, including fever monitoring, twice daily for 21 days after exposure. In case of temperature above 38.3°C (101°F), hospitalize immediately in strict isolation. The incubation period between exposure and clinical symptoms is a minimum of 48 hours.

Health workers suspected of being infected should be isolated and the same recommendations outlined in this document must be applied until a negative diagnosis is confirmed. Contact tracing and follow-up of family, friends, co-workers, and other patients who may have been exposed to a VHF virus through close contact with the infected health workers is essential.

### Possible use of ribavirin to high-risk contacts of CCHF patients

Post-exposure prophylaxis should be considered for those exposed to Lassa fever or CCHF. This should be limited to high-risk close contacts of the patients and laboratory and health care workers, defined as one of the following:

- (1) Penetration of skin by a contaminated sharp instrument (e.g. needle stick injury);
- (2) Exposure of mucous membranes or broken skin to blood or bodily secretions (e.g. blood splashing in the eyes or mouth);
- (3) Participation in emergency procedures without appropriate personal protective equipment (e.g. resuscitation after cardiac arrest, intubation or suctioning) or
- (4) Prolonged (i.e. hours) and continuous contact in an enclosed space without appropriate personal protective equipment (e.g. a health worker accompanying a patient during medical evacuation in a small airplane)<sup>29</sup>.

In estimating infection risk, note that the most infectious patients are those with severe clinical conditions, usually late in the course of illness. Prophylaxis should not be used when the only exposure was during the incubation period or during convalescence after fever has

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The prophylaxis dose is oral ribavirin 35 mg/kg loading dose (maximum 2.5 g) followed by 15 mg/kg (maximum 1 g) every 8 hours for 10 days **Error! Bookmark not defined.**

If a temperature of 38.3° C or higher develops, treatment with ribavirin can be considered as presumptive treatment of Lassa fever or CCHF.

## 6. Psychological support

Psychological support for the patient and the family are very important in the management of VHF. Anxiety and fear are normal given the high mortality rate for confirmed VHF. It is important to communicate well with the patient and family, explaining the need for isolation and PPE, and to provide psychological support from the beginning of care. Make sure to do a complete mental health assessment in each patient; then look out for mental health problems developing as a result of patient's adjustment to being ill. Depression, associated with feelings of hopelessness and/or suicidal thoughts, may be present. See Section 10.11 (Mental health problems) in the IMAI District Clinician Manual for their management<sup>1</sup>.

Ideally a psychologist or nurse skilled in providing psychological support should be involved from the outset, but providing psychological care in PPE can be uncomfortable and difficult. The PPE is physically exhausting for the psychologist and for the patient it is difficult to see the face of the psychologist (seeing faces helps to establish a good rapport). For mobile patients, an area can be created where the patients can talk over the fence of the high-risk area with the psychologist at sufficient distance to prevent infection<sup>11</sup>. Psychosocial interventions for patients and families are described in Section 10.11 in the IMAI District Clinician Manual<sup>1</sup>. Support groups for family members and for affected patients after discharge may be useful.

Control of pain, abdominal discomfort and nausea, and management of anxiety are important to the patient's well-being (**SEE SECTION 4**). Patients who are terminal need skilled and thoughtful end-of-life care within the isolation facility.

For psychosocial and spiritual support for the patient and support for the bereavement, loss and grief experienced by family members, see also the IMAI-IMCI *Palliative care: symptom management and end-of-life* guideline module<sup>30</sup>.



## 7. Infection Prevention and Control<sup>a</sup>

Infection prevention and control is key to the reduction of spread of infection from patients to health workers, health workers to health workers, and from the patient to the rest of the community. Evidence from outbreaks strongly indicates that the main routes of transmission of VHF infection are direct contact (through broken skin or mucous membrane) with blood or body fluids, and indirect contact with environments contaminated with splashes or droplets of blood or body fluids. Avoiding transmission dictates strict adherence to standard precautions as well as droplet and contact precautions for health care, environmental, and laboratory workers. Moreover, while epidemiology during VHF outbreaks does not suggest airborne transmission, precautions should be taken to avoid procedures or protect health workers, family members and other patients during procedures that might aerosolize virus.<sup>31</sup>

**All health workers (clinical and non-clinical) should use standard precautions in caring for all patients, in all health facilities. These include:**

- Hand hygiene
- Appropriate personal protective equipment (PPE) based on risk assessment at the point of care
- Respiratory hygiene
- Prevention of injuries from needles and other sharp instruments
- Safe waste disposal
- Cleaning and disinfection of the environment
- Safe handling of contaminated linens
- Cleaning and disinfection of patient-care equipment

The systematic application of these precautions should prevent the transmission of viral haemorrhagic fever.

<sup>a</sup> Infection prevention and control recommendations in this document draw heavily on published WHO guidelines.

## 7.1 Recommendations for direct patient care for known or suspected VHF patients

In addition to standard precautions, the following are WHO recommendations for direct patient care for known or suspected viral haemorrhagic fever patients<sup>4, 32</sup>

- Restrict all non-essential staff from patient care areas.
- Maintain a register of all people entering the patient care area.
- Limit the number of visitors allowed access to the patient to include only those necessary for the patient's well-being and care, such as a spouse, child's parent or care-giver.
- Ensure that all visitors use PPE according to the facility guidelines. Prior to entering the isolation area, provide all visitors with instructions on using PPE correctly, and instructions for correct hand hygiene practices- see illustrations on page 44. Make sure they understand and practice the instructions strictly.
- Do not allow other visitors to enter the care area, and ensure that any visitors wishing to observe the patient do so from an adequate distance from the care area (approximately 15 meters).
- Apply infection control precautions to avoid any possible unprotected direct contact with blood and body fluids when providing care to any VHF patient, including suspected cases.
  - Perform hand hygiene before and after direct patient care, after any contact with potentially contaminated surfaces, and after removal of PPE. Neglecting to perform hand hygiene after removing PPE will reduce or negate any benefits of the protective equipment.
  - Wear correctly sized gloves (non-sterile examination gloves or surgical gloves) when entering the patient care area.
  - Wear a disposable, impermeable gown to cover clothing and exposed skin. Wear a waterproof apron over any permeable gown or when undertaking any strenuous activity (e.g. carrying a patient).
  - Wear facial protection to prevent splashes to the nose, mouth, and eyes. Facial protection can be achieved by means of (1) medical mask and eye protection (eye visor or goggles), or (2) with a face shield and medical mask.



- Before exiting the isolation area of a patient with suspected VHF, carefully remove and dispose of protective equipment.
- When removing protective equipment, be careful to avoid any contact between the soiled items (e.g. gloves, gowns) and any area of the face (eyes, nose, or mouth).
- Ensure that clinical and non-clinical personnel are assigned exclusively to VHF patient care areas and that members of staff do not move freely between the isolation areas and other clinical areas during the outbreak.
- Limit the use of needles and other sharp objects as much as possible.
- Limit the use of phlebotomy and laboratory testing to the minimum necessary for essential diagnostic evaluation and patient care.

### **Specify who should wear protective clothing**

- All doctors, nurses, and health workers who provide direct patient care to suspected VHF patients.
- All support staff who clean the isolation room, handle contaminated supplies and equipment, launder re-usable supplies, and collect and dispose of infectious waste from VHF patients.
- All laboratory staff who handle patient specimens and body fluids from suspected VHF cases.
- Laboratory support staff who clean and disinfect laboratory equipment used to test VHF specimens.
- Burial teams who remove bodies of deceased VHF patients and prepare them for burial.
- Family members who care for VHF patients.

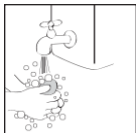
## 7.2 Standard precautions- at all times, for all patients

### Standard Precautions–At All Times, For All Patients

#### Hand hygiene

Ensure availability of hand-washing facilities with clean running water.

Ensure availability of hand hygiene products (clean water, soap, single-use clean towels, and alcohol-based hand rub). Alcohol-based hand rubs should be made available at every point of care and are the standard of care.



When to wash hands with soap and running water:

- when hands are visibly dirty.

When to use alcohol-based hand rub:

- when hands appear clean (i.e. are not visibly soiled).
- Do not wear artificial fingernails or extenders when having direct contact with patients.
- Keep natural nails short (tips less than 0.5 cm long or approximately ¼ inch).
- Keep a healthy skin.
- Avoid using rings, a wrist watch or bracelets.
- Ensure that hands are dry before starting any activity.
- Dry hands with single-use towels.

#### Indications for hand hygiene

Before and after any direct contact between a health worker and a patient and contact between patients, whether or not gloves are worn. Hands should be washed in the following scenarios:

- Before gloves are put on.
- Immediately after gloves are removed.
- Before handling an invasive device.
- After touching blood, body fluids, secretions, excretions, non-intact skin, and contaminated items, even if gloves are worn.

## Standard Precautions—At All Times, For All Patients

- During care, e.g. when moving from a contaminated to a clean body site of the same patient.
- After contact with inanimate objects in the immediate vicinity of the patient.

### Respiratory hygiene

Educate all staff, health workers, patients, and hospital visitors:

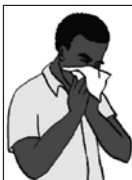
- Cover mouth and nose when coughing or sneezing.
- Hand hygiene after contact with respiratory secretions.
  - Have single-use tissues available in the waiting area or provide a medical mask. Dispose of tissues in no-touch receptacles. Then wash hands.

When tissues, cloths, or face masks are not available, instruct all staff, health workers, patients, and visitors to lift their arm up and cover their nose and mouth with the inner surface of the arm or forearm when they cough or sneeze.

- For persons with respiratory symptoms:
  - (1) source control measures- cover their nose and mouth with a tissue or mask when coughing or sneezing; (2) Spatial separation of at least one metre from persons with acute febrile respiratory symptoms.



Cough or sneeze into your arm.



Use a tissue and then throw away.

## Standard Precautions—At All Times, For All Patients

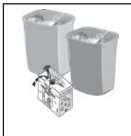
### Prevention of injuries from needles and other sharp instruments

- Use care when handling, using, cleaning, and disposing of needles, scalpels, and other sharps.
- Do not bend, break, or otherwise manipulate used needles, scalpels, or other sharp instruments.
- Do not recap needles.
- Keep a sharps container nearby when giving injections. Discard single-use needles and syringes immediately after use and directly into the sharps container, without recapping and without passing to another person.
- Close, seal, and send sharps containers for incineration before they are completely full.



### Safe waste disposal

- Ensure safe waste management.
- Treat waste contaminated with blood, body fluids, secretions, and excretions, and human tissue and laboratory waste directly associated with specimen, as clinical waste.
- Segregate at the point of generation the 4 categories of waste:
  - sharps
  - non-sharps infectious waste
  - non-sharp non-infectious waste
  - hazardous waste
- Discard single use items properly.



## Standard Precautions—At All Times, For All Patients

### Cleaning and disinfection of the environment

Use adequate procedures for the routine cleaning and disinfection of environmental and other frequently touched surfaces.

- Floors and horizontal work surfaces should be cleaned at least once a day.
- Cleaning should always be carried out from “clean” areas to “dirty” areas, in order to avoid contaminant transfer.
- Dry sweeping with a broom should never be done.



Rags with dust should not be shaken out and surfaces should not be cleaned with dry rags. Cleaning with a moistened cloth helps to avoid contaminating the air with air-borne particles.

- Clean **BEFORE** you disinfect.
- Change cleaning solutions and equipment frequently, as these items will get contaminated quickly (follow your hospital protocols).

### Appropriate handling of contaminated linens

Handle, transport, and process used linen so as to:

- Prevent skin and mucous membrane exposure and contamination of clothing.
- Avoid transfer of pathogens to other patients or the environment:
- Place all used linen and waste in bags or containers that are able to withstand transportation without being damaged.
- Remove any solid matter on soiled linen and flush down a toilet.

### Cleaning and disinfection of patient care equipment

Handle equipment soiled with blood, body fluids, secretions, and excretions in a manner that prevents skin and mucous membrane exposure, contamination of clothing, or transfer of pathogens to other patients or the environment.

Clean, disinfect, sterilize, and reprocess reusable equipment appropriately before use with another patient.

### 7.3 Steps to put on and remove PPE

Viral haemorrhagic fevers can be transmitted person-to-person, usually through direct contact with contaminated blood or body fluids of an infected person, or exposure to objects that have been contaminated with infected secretions. Infection probably occurs most often through oral or mucous membrane exposure (e.g., eyes, mouth, nose) or breaks in the skin. Presently, there is no evidence for human-to-human transmission of VHF through an airborne route.

The following information about proper PPE during a VHF outbreak targets the front line-clinical provider and represents the minimum guidance to achieve appropriate protection for infection prevention and control. Importantly, during an outbreak, the types of PPE available in the field may not be the same across sites and may even differ based on the organization providing them. Thus, it is imperative that the clinical team involved in triage and clinical management of patients assesses the evolving situation during the outbreak to determine whether the minimum requirements can be utilized or additional protective measures are necessary. In any case, it is important for clinicians to weigh the benefits of protecting themselves and patients against the risks of diminishing effective patient care through unnecessary barriers or excessively uncomfortable protective equipment.

Accordingly, the following instructions are an illustration of the steps to put on and remove essential required PPE with some additional measures depending on the conditions occurring during the outbreak:

## 7.3 Steps to put on and remove essential required PPE

### Steps to put on essential required PPE

- 1 Always put on essential required PPE when handling either a suspect, probable or confirmed case of VHF. Gather all the necessary items of the PPE beforehand.
- 2 The dressing and undressing of PPE should be supervised by another trained member of the team. These instructions should be displayed on the wall in the dressing and undressing room.

- 3 Put on the scrub suit in the changing room.



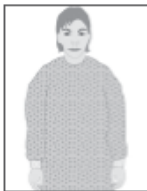
- 4 Put on slip-on shoes with protective covers. If you will be working in wet settings with bodily fluids, water, detergent, waste, etc., use gum boots instead.



OR



- 5 Place the gown over the scrubs.



- 6 Put on face protection:

- 6a Put on a medical mask and goggles. OR



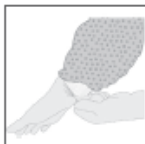
- 6b Put on a face shield (preferred). If the patient has respiratory symptoms or the design of the face shield does not stop you from touching your face (eyes, nose, and mouth), first put on a medical mask and then put the face shield over your face and the medical mask.



**7** If you have any abrasions on your scalp or you have concern for splashing fluids, also place a head cover at this time.



**8** Put on gloves (over cuff).



**9** If gown is permeable or if you expect strenuous activity with an exposed patient, place waterproof plastic apron over gown.



### **Whilst wearing PPE:**

- Avoid touching or adjusting PPE
- Remove gloves if they become torn or damaged
- Change gloves between patients
- Perform hand hygiene before donning new gloves

## **Steps to remove PPE**

**1** Peel off plastic apron and dispose of safely, (if the apron is to be reused, place in a container with disinfectant)



**2** If wearing protective shoe covers, please remove them with your gloves still on. (If wearing gum boots, see step 5).





- 3** Remove gown and gloves and roll inside-out and dispose of safely.



- 4** Perform hand hygiene.



- 5** If wearing gum boots, remove them (ideally using the boot remover) without touching them with your hands. Place the removed boots into a container with disinfectant.



- 6** If wearing a head covering, remove it now (from behind head).



- 7** Remove face protection:

- 7a** Remove face shield or goggles (from behind head). Place eye protection in a separate container for reprocessing. **OR**



- 7b** Remove mask from behind head. When removing a mask, untie the bottom strings first and the top strings next.



- 8** Perform hand hygiene.



- 9** Proceed to the clean area of the isolation facility.

## Perform hand hygiene, Wash hands.



Wet hands with water and apply soap.



Rub hands, palm to palm.



Right palm over left dorsum with interlaced fingers and vice versa.



Palm to palm with fingers interlaced.



Back of fingers to opposing palms with fingers interlocked.



Rotational rubbing of left thumb clasped in right palm and vice versa.



Rinse hands with water.



Dry hands thoroughly with single use towel.

## Apron and boots

Plastic or rubber aprons provide extra protection of the front part of the body. Ideally disposable aprons should be used, but if non-disposable, aprons need to be disinfected by the person wearing it. This should include cleaning to remove gross contamination, disinfection and then hanging to dry outside the changing room in the sun. Boots should also be cleaned to remove gross contamination and then disinfected prior to re-use.

## Goggles or face shields

Goggles must fit comfortably and securely, and person should have his/her own goggles/face shield with their name on them. Goggles or face shields need to be disinfected by the person wearing them, washed with water and then hung outside the changing room to dry. Condensation of the goggles can be a major problem: it impairs the user's vision and is dangerous, but can be minimized by anti-fog spray.

## Protective gloves

The efficacy of gloves in preventing contamination of health workers' hands and helping to reduce transmission of pathogens in health care has been confirmed in several clinical studies. Nevertheless, health workers should be informed that gloves do not provide complete protection against hand contamination.

Pathogens may gain access to the caregivers' hands via small defects in gloves or by contamination of the hands during glove removal. Hand hygiene by rubbing or washing remains the basis to guarantee hand decontamination after glove removal. Medical gloves are also single-use items. Glove decontamination and reprocessing are not recommended and should be avoided, even if it is common practice in many health-care settings with low resources and where glove supply is limited.

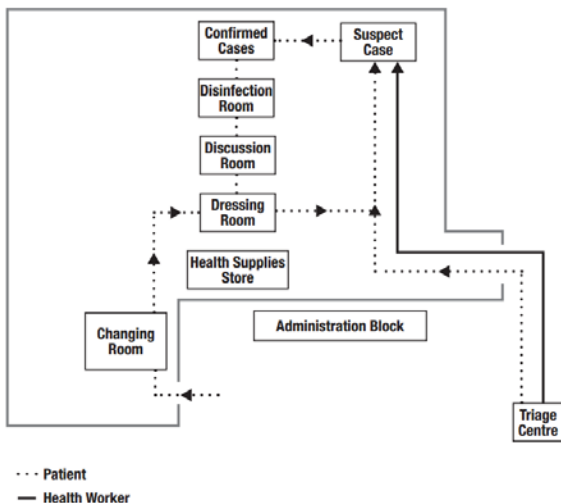
## Disinfection by 'spraying'

Hand-held spraying devices incorporating a chlorine solution have regularly been utilized in VHF outbreaks. This is generally as part of the 'disinfection' process of PPE suspected of being the most heavily contaminated and

to allow its subsequent re-use i.e. gloves, aprons and boots. Although the VHF viruses are susceptible to disinfection with chlorine solutions, generic principles of disinfection in healthcare facilities should be considered and raise doubt to the effectiveness of 'spraying'. The first is that the presence of visible organic matter such as blood or fecal material can interfere with the antimicrobial activity of disinfectants in at least two ways<sup>32, 33</sup>. Most commonly, interference occurs by a chemical reaction between the disinfectant and the organic matter resulting in a complex with less of the active germicide available for attacking the virus. Chlorine and iodine disinfectants, in particular, are prone to such interaction. Organic material also protects the virus from attack by acting as a physical barrier and physical removal is required.

Additionally items must be exposed to the disinfectant for the appropriate minimum contact time. Multiple scientific studies have demonstrated the efficacy of a range of hospital disinfectants against pathogens with a contact time of at least 1 minute<sup>34</sup>. This supports the principle of utilizing disposable equipment in VHF settings when possible, and when PPE is to be re-used it requires physical cleaning followed by disinfection with an adequate contact time.

## 7.4 Flow through the isolation ward, for patients and health workers





## 8. Discharge

Discharge of an alert case is done on the following conditions<sup>35</sup>

- ▶ Patients have been reviewed by the VHF clinical management team and found to not meet the case definition of a suspected case, with no epidemiological link to
- ▶ any suspected or confirmed case.
- ▶ Have a conclusive diagnosis that is not VHF, recognizing that co-infections do occur.
- ▶ Have responded to specific treatment
- ▶ Be in good health condition and able to go back home

Discharge of a VHF-confirmed case or suspected cases is based on the clinical presentation and the correct interpretation of the laboratory findings. Consider discharge when the following criteria are met:

- ▶ Three or more days without fever or any significant symptom<sup>†</sup>
  - ▶ Symptoms that suggest ongoing shedding of virus (e.g. diarrhea, coughing, bleeding) should have completely disappeared.
  - ▶ Viral shedding known to occur in the semen of male patients, and probably in the breast milk of lactating females, need not preclude discharge, but must be taken into consideration when providing instructions to the patient (see below)

AND

- ▶ Significant improvement in clinical condition<sup>†</sup>

AND

- ▶ In a relatively good general condition<sup>†</sup>: independently feeding and to carry out other activities of daily life, like washing and walking, without assistance, taking into account any previous disabilities.

AND, if laboratory testing is available,

- ▶ A negative blood PCR for VHF (regardless of any other serologic tests) on day 3 or later following onset of symptoms.
  - ▶ For patients with previous positive blood PCR tests, this means a subsequent negative test 48 hours from the initial test (regardless of serology).
  - ▶ For previously blood PCR positive mothers, that are breast feeding, it may be safer to delay discharge until PCR on breast milk turns negative as well

(to be discussed with the clinicians and laboratory present).

<sup>1</sup>If a patient continues to suffer symptoms and/or their condition is not improving, but this is not thought to be due to acute filovirus disease, 2 negative blood PCR tests 48 hours apart, with at least one test being done 3 days or more after onset of symptoms, are needed before discharge/ referral to a normal ward for further care.

Discharge package	
<ul style="list-style-type: none"><li>• Mattress (4 inch)</li><li>• Bedsheets</li><li>• Assorted cloth</li><li>• Clothing, if the patient's clothes were destroyed on admission</li><li>• Kitchen wares (saucepan, plastic cup, plastic plate, jerrican, water bucket)</li><li>• Laundry soap</li></ul>	<ul style="list-style-type: none"><li>• Disinfectant -Jik/bleach</li><li>• Tarpaulin</li><li>• Blanket</li><li>• Mosquito net (LLITN)</li><li>• A pair of Shoes</li><li>• Condoms</li><li>• Sanitary pad (for female patients)</li><li>• Food ration</li></ul>



## 9. Follow up

**Discharged convalescent patients:** They may remain weak and suffer persistent symptoms. A system for follow-up care should be set up for these patients. If those patients are discharged back home they often face stigmatization and/or rejection, so discharge should be accompanied by the necessary psychosocial support and community awareness activities.

**Patients that were admitted but turned out not to be cases:** If suffering from another disease, referral to a normal ward is sometimes needed. The normal health care system is often unwilling to accept these patients, or where they are accepted, their care may suffer from neglect. Referral should therefore be followed up closely. If returned home, their community may require assurance from medical authorities before accepting the patient.

### Supportive treatment for all discharged patients

- Provide one-month supply of vitamin supplements.
- Nutritional advice. Identify locally available high-energy foods that are easy to digest, rich in complex carbohydrates and balanced in fat, protein and fiber.
- Provide condoms. Also, provide instructions on using the condoms, and the minimum length of time they should be used (3 months).
- Breastfeeding women should stop breastfeeding until PCR testing of breast milk is negative. Infant feeding counseling and support should be provided according to the infant's age.
- Anticipate that rejection of discharged patients by their communities may occur. Therefore, the patient, his/her family and relatives, and health care personnel (if the patient is transferred) must be counseled to be sure that they understand that the patient does not constitute any danger.

- A medical certificate should be given at discharge to certify that the patient does not constitute any danger to his family and his neighbors.
- Psychological support and follow up should be considered, including advocacy on patients' behalf and interceding with community leaders where necessary.

## APPENDIX A1:

Case definitions for Ebola and Marburg virus disease during an epidemic:

A suspect case is any person:

- Having had contact with a clinical case<sup>1</sup> **AND**
- Presenting with acute fever ( $>38^{\circ}\text{C}$ )

OR

- Having had contact with a clinical case (suspect, probable or confirmed) **AND**
- Presenting with 3 or more of the symptoms below:

OR

- Presenting with acute fever **AND**
- Presenting with 3 or more of the concerning symptoms below:
  - Headache
  - Generalized or articular pain
  - Intense fatigue
  - Nausea or vomiting
  - Loss of appetite
  - Diarrhea
  - Abdominal pain
  - Difficulty in swallowing
  - Difficulty in breathing
  - Hiccups
  - Miscarriage

OR

- Any person with unexplained bleeding<sup>2</sup> or miscarriage

OR

- Any unexplained death.

Cases are confirmed by laboratory testing, e.g. a positive PCR test Ebola or Marburg virus.

The definition of a probable case varies;

2 often used definitions are:

- A suspect case that is known to have had contact with a known case (suspect, probable, or confirmed).

OR

- A patient that is, on clinical and/or epidemiological grounds, very likely to have Ebola or Marburg.

## Case definition for Ebola or Marburg outside of an epidemic:

### An alert case is a patient presenting with:

- Unexplained fever or history of fever (onset less than 3 weeks)

**AND**

- Unexplained bleeding signs:

- Haemorrhagic or purpuric rash
- Blood in stool
- Epistaxis (nose bleed)
- Blood in stool
- Haematemesis (blood in vomit)
- Other haemorrhagic

signs

- Haemoptysis (blood in sputum) **AND**

- No known predisposing factors for haemorrhagic manifestations

**OR**

- A patient presenting with:

- Any fever **OR** 3 more of the following:

- Headache
- Abdominal pain
- Nausea or vomiting
- Generalized or

articular pain

- Loss of appetite
- Difficulty in swallowing
- Diarrhea
- Difficulty in breathing

- Intense fatigue

**AND**

- Possible filovirus exposure:

- Unexplained death(s) in the family or close contacts
- Unexplained (cluster of) serious illness in family or close

contacts

- Provision of care for the seriously ill or handling bodies

(caretakers, health workers, those participating in traditional funerals)

- At risk contact with apes or bats, dead or alive
- When animals in the area, chiefly apes, die unexpectedly
- Handling and/or eating "bush" animals (apes or bats)
- Entry into caves or proximity to fruit trees that host bats

Insert current country case definition

## APPENDIX A2:

### Case definition- suspected case of Lassa fever

Known exposure to a person suspected to have Lassa fever	
Fever $>38^{\circ}\text{C}$ for less than three weeks <b>PLUS</b>	
Absence of signs of local inflammation <b>AND</b>	
Two major signs or one major and two minor signs	
MAJOR SIGNS	MINOR SIGNS
Bleeding	Headache
Swollen neck or face	Sore throat
Conjunctiva or subconjunctival hemorrhage	Vomiting
Spontaneous abortion	Diffuse abdominal pain /tenderness
Petechial or hemorrhagic rash	Chest/retrosternal pain
New onset of tinnitus or altered hearing	Cough
Persistent hypotension	Diarrhea
Absence of clinical response after 48 hrs to antimalarial and/or broad spectrum antibiotic therapy	Generalized myalgia or arthralgia
	Profuse weakness

Insert current country case definition Lassa fever:

## Fluid plans A, B, and C (fluid and food)

**Plan A: Treatment of diarrhoea at home**

- Counsel the patient on the 3 rules of home treatment.
- Drink extra fluid.
- Continue eating.
- Advise the patient when to return to the health facility.

## 1. Drink extra fluid

- Drink extra fluid:
  - as much as the patient will take
  - safe fluid that is clean or has been boiled or disinfected
  - ORS or other fluid (except fluids with high sugar or alcohol)
  - drink at least 200–300 ml after each loose stool
  - continue drinking extra fluid until the diarrhoea stops.

It is especially important to provide ORS for use at home if the patient cannot return to the clinic if the diarrhoea worsens.

If ORS is provided:

- teach the patient how to mix and drink ORS
- give 2 packets to take home.

If the patient is vomiting, they should continue to take small sips.

- Antiemetics are usually not necessary.

## 2. Continue eating

## 3. Return to the health facility when:

- diarrhoea becomes worse
- the patient has persistent diarrhoea or a large volume.



## Plan B: Treatment of patient with some dehydration using ORS

1. Determine amount of ORS to give during first 4 hours.

- The approximate amount of ORS required (in ml) can be calculated by multiplying the patient's weight (in kg) times 75.
- Use the patient's age if you do not know the weight.
- If the patient wants more ORS than shown, give more.
- Give the recommended amount of ORS in the clinic over a 4-hour period.
- If the patient is weak or vomits:
  - give frequent small sips from a cup.

After a vomit, wait 10 minutes then continue, but more slowly.

2. After 4 hours

- Reassess the patient and classify for dehydration.
- Select the appropriate plan to continue treatment.
- Begin feeding the patient in the clinic.

3. If the patient must leave before completing treatment

- Show the patient how to prepare ORS solution at home.
- Show the patient how much ORS is needed to finish a 4-hour treatment at home.
- Give enough ORS packets to complete rehydration.

Give 2 packets as recommended in Plan A.

4. Explain the 3 rules of home treatment

1. Drink extra fluid.
2. Continue eating.
3. Return to the health facility if needed.

## Plan C: Treat severe dehydration quickly

Follow the arrows. If the answer is “yes” go across. If “no”, go down. **START HERE**

<p>Can you give intravenous (IV) fluid immediately? <b>YES→</b> ↓<b>NO</b></p> <p>Is IV treatment available nearby (within 30 minutes) <b>YES↘</b> ↓<b>NO</b></p>	<ul style="list-style-type: none"><li>• Start IV fluid immediately. If the patient can drink, give ORS by mouth while the drip is set up. Give 100 ml/kg Ringer’s lactate solution (or, if not available, normal saline), divided as follows: *Repeat once if radial pulse is very weak or not detectable.</li><li>• Reassess the patient every 1–2 hours. If hydration status is not improving, give the IV drip more rapidly. Also give ORS (about 5 ml/kg/hour) as soon as the patient can drink, usually after 3– 4 hours (infant) or 1–2 hours for children, adolescents, and adults.</li><li>• Reassess an infant for 6 hours and older patient after 3 hours. Classify dehydration. Then choose the appropriate plan (A, B, or C) to continue treatment.</li></ul>
<p>Are you trained to use a naso-gastric (NG) tube for rehydration? <b>YES→</b> ↓<b>NO</b></p>	<p>Refer <b>URGENTLY</b> to hospital for IV treatment.</p> <ul style="list-style-type: none"><li>• If the patient can drink, provide a relative or friend with ORS solution and show how to give frequent sips during the trip.</li></ul>
<p>Can the patient drink? <b>YES→</b> ↓<b>NO</b></p> <p>Refer <b>URGENTLY</b> to hospital for IV or NG treatment.</p>	<ul style="list-style-type: none"><li>• Start rehydration by tube (or mouth) with ORS solution. Give 20 ml/kg/hour for 6 hours (total of 120 ml/kg).</li><li>• Reassess the patient every 1– 2 hours:<ul style="list-style-type: none"><li>◦ if there is repeated vomiting or increasing abdominal distension, give the fluid more slowly;</li><li>◦ if hydration status is not improving after 3 hours, send the patient for IV therapy.</li></ul></li><li>• After 6 hours, reassess the patient. Classify dehydration. Then choose the appropriate plan (A, B or C) to continue treatment.</li></ul>

## Morphine, paracetamol and antimalarial dosing for children and adults

### Paracetamol and morphine In adolescents and adults<sup>1</sup>:

Analgesics	Starting dose in adults	Range	Side-effects and cautions
<b>Paracetamol</b> (also lowers fever)	1 gram every 4–6 hours, but no more than 4 grams in 24 hours	Only 1 tablet may be required in elderly or the very ill, or when combined with an opioid. Mild pain might be controlled with doses every 6 hours.	Do not exceed 4 grams in 24 hours (more can cause serious liver toxicity).
<b>Oral morphine:</b> 5 mg/5 ml or 50 mg/5 ml or 50 mg/5 ml or slow release tablets (10 mg or 30 mg). Give by mouth. If necessary, can be given <b>IV or IM or subcutaneously.</b>	Initially, morphine sulphate 2.5–10 mg every 4 hours, increased by 30%–50% if pain persists. Start with low dose 2.5mg-5mg if patient is very old or frail.	According to Pain  <b>There is NO ceiling dose.</b>	Unless diarrhoea, give laxative to avoid constipation. Excessive dosage can reduce respiratory rate.

## Paracetamol and morphine In children:

Dose according to body weight

Drug	Dosage	Form	3-<6 kg	6-<10 kg	10-<15 kg	15-<20 kg	20-<29 kg
Paracetamol	10–15 mg/kg, up to six times a day	100-mg tablet	-	1	1	2	3
		500-mg tablet	-	¼	¼	½	½
Morphine	Calculate exact dose based on weight of the child. Oral: 0.2–0.4 mg/kg every 4–6 h; increase if necessary for severe pain IM: 0.1–0.2 mg/kg every 4–6 h IV: 0.05–0.1 mg/kg every 4–6 h, or 0.005–0.01 mg/kg per hour by IV infusion						

## Antimalarials: For adolescents and adults<sup>1</sup>:

### How to give emergency antimalarial treatment if falciparum malaria is possible

Preferred treatment is artesunate IV. Use artesunate or artemether rather than quinine, if available. Give artesunate IV in patients in shock, if possible (except for pregnant women in first trimester – give quinine).

Weight	ARTESUNATE IV or IM		ARTEMETHER IM		QUININE IM or IV (Always give glucose with Quinine)			
	For IV, further dilute with 5 ml of 5% dextrose (for 10 mg/ml)	For IM, further dilute with 2 ml of 5% dextrose (for 20 mg/ml)	Initial loading dose: 3.2 mg/kg	Subsequent doses 1.6 mg/kg each day until able to take oral medication	Initial dose: 20 mg/kg IM (divide dose equally in 2 and give 1 in each anterior thigh) or IV by rate-controlled infusion not exceeding 5 mg salt/kg body weight/hour	Subsequent doses 10 mg/kg every 8 hours		
30 kg	7.2 ml	3.6 ml	1.2ml	0.6 ml	4.0 ml	2.0 ml	2.0 ml	0.5 ml
40 kg	9.6 ml	4.8 ml	1.6 ml	0.8 ml	5.4 ml	2.6 ml	2.6 ml	0.7 ml
50 kg	12.0 ml	6.0 ml	2.0 ml	1.0 ml	6.6 ml	3.3 ml	3.3 ml	0.8 ml
60 kg	14.4 ml	7.2 ml	2.4 ml	1.2 ml	8.0 ml	4.0 ml	4.0 ml	1.0 ml
70 kg	16.8 ml	8.4 ml	2.8 ml	1.4 ml	9.3 ml	4.7 ml	4.7 ml	1.2 ml
80 kg	19.2 ml	9.6 ml	3.2 ml	1.6 ml	10.6 ml	5.3 ml	5.3 ml	1.3 ml
90 kg	21.6 ml	10.8 ml	3.6 ml	1.8 ml	12.0 ml	6.0ml	6.0 ml	1.5 ml

## Antimalarials:

### Oral antimalarials (if no signs severe malaria):

Table: First-line antimalarial treatment options for <i>P. falciparum</i> in all adolescent and adult patients except first-trimester pregnant patients*				
Age and weight	Artesunate + amodiaquine daily dose, once daily for 3 days	Artemether/ lumefantrine twice daily for 3 days*		Dihydroartemisinin/ piperazine once daily for 3 days
	Separate tablets: artesunate tablet 50 mg; amodiaquine table 153 mg base	Coformulated tablet: artemether 20 mg + lumefantrine 120 mg		Coformulated tablet: DHP 40 mg + PQP 320 mg
Morning		Evening		
5–7 yrs (19–24 kg)	1+1	2	2	1
8–13 yrs or small or wasted adult (25–50 kg)	2+2	3	3	2
14 yrs + (>50 kg)	4+4	4	4	3

The second dose on the first day should be given any time between 8 and 12 hours after the first dose. Dosage on the second and third days is twice daily (morning and evening). Lumefantrine absorption is enhanced by co-administration with fat. It is essential that patients or caregivers are informed of the need to take this ACT immediately after a fatty meal or drink – particularly on the second and third days of treatment.

## Antimalarials: For children<sup>2</sup>:

Dose according to body weight

Drug	Dosage	Form	3-<6 kg	6-<10 kg	10-<15 kg	15-<20 kg	20-<29 kg
Artemether For severe Malaria	<b>Loading dose:</b> IM: 3.2 mg/kg	40 mg/1-ml ampoule	0.4 ml	0.8 ml	1.2 ml	1.6 ml	2.4 ml
		80 mg/1-ml ampoule	0.2 ml	0.4 ml	0.6 ml	0.8 ml	1.2 ml
	<b>Maintenance dose:</b> IM: 1.6 mg/kg	40 mg/1-ml ampoule	0.2 ml	0.4 ml	0.6 ml	0.8 ml	1.2 ml
		80 mg/1-ml ampoule	0.1 ml	0.2 ml	0.3 ml	0.4 ml	0.6 ml

Give the maintenance dose daily for a minimum of 24 h until the patient can take oral artemisinin-based combination therapy.

Artemether/ Lumefantrine	Oral: 2 mg/kg artemether – 12 mg/kg lumefantrine twice per day	Tablet: 20 mg artemether–120 mg lumefantrine	1	1	1	2	2
Artesunate For severe Malaria	IV or IM: 2.4 mg/kg	60 mg artesunic acid(already dissolved in 0.6 ml of saline and sodium bicarbonate) in 3.4 ml of saline and glucose	0.8 ml	1.4 ml	2.4 ml	3.0 ml	5.0 ml

The IV solution should be prepared just before use. Dilute by dissolving 60 mg artesunic acid (which is already dissolved in 0.6 ml of 5% sodium bicarbonate) in 3.4 ml of 5% glucose. Give a dose at 0, 12 and 24 h and then daily until child is able to take it orally. If the patient is able to swallow, give the recommended full dose of artemisinin-based combination therapy.

Artesunate– Mefloquine	Oral: 4 mg/kg artesunate– 8.3 mg/kg mefloquine once a day	Tablet: 25 mg artesunate–55 mg mefloquine	-	1	2	2	3
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Not recommended for children < 5 months of age owing to limited information

# APPENDIX D1:

## Clinical monitoring tool (first six hours)

Name:	Patient No.:		Birth date: / /		Sex M / F		Admission date		Admission time:							
Diagnosis:			Circle if test sent and record result:		Electrolytes		Malaria		AFB							
					Urine dipstick		Gram stain		CXR							
					Blood culture		Other									
Pregnant:	Yes/No	EDD	Allergies:													
	Time of day		0	30	60 (1 hr)	90	120 (2 hrs)	150	180 (3 hrs)	210 (4 hrs)	240 (4 hrs)	270 (5 hrs)	300 (5 hrs)	330	360 (6 hrs)	390
	Monitoring interval (minutes) from arrival or start															
G30 – 60 min (until normal)	SpO <sub>2</sub>															
	Heart rate															
	Systolic BP															
	Respiratory rate															
	Conscious level															
	(AVPU)															
	Temperature (°C)															
01 – 6 hours, repeat if abnormal	Glucose															
	Urine output*															
	Haemoglobin															
Exam																
Assess																
Response	Fluids (type, rate)															
	Oxygen (method/flow)															
	Salbutamol															
	Vasopressor (type/rate)															





**Clinical monitoring tool (hours 7–24)**

Name:		Patient No.:		Birth date: ____/____/____		Sex: M / F		Admission date:		Admission time:										
Diagnosis:	Pregnant:	Yes/No	EDD:		Urine dipstick		Electrolytes		Urine dipstick											
		Time of day	Monitoring interval (hours)		Malaria		Malaria		Blood culture											
Q 1 hour if SBP < 90 or if on pressors, otherwise Q 2 hours	Q 6 hours	SpO <sub>2</sub>	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24
		Heart rate																		
Q 2 hours (M/PU)	Q 6 hours	Systolic BP																		
		Respiratory rate																		
Q 6 hours	Q 6 hours	Conscious level																		
		Urine output*																		
Repeat if initial value abnormal	Exam	Temperature (°C)																		
		Glucose																		
Access	Response	Haemoglobin																		
		Exam																		
Response	Response	Fluids (l type, rate)																		
		Oxygen (method, flow)																		
Response	Response	Sabutamol																		
		Vasopressor (type, rate)																		
Response	Response	Glucose																		
		Antibiotics																		



## APPENDIX E:

### How to give vasopressors (peripheral epinephrine or dopamine infusion)

#### In adolescents and adults<sup>1</sup>:

**Mechanism:** Vasopressors work by vasoconstriction and increasing the contractility of the heart. Commonly available vasopressor medications include epinephrine (adrenaline) and dopamine.

**Side-effects:** There are many serious side-effects, notably tissue necrosis if the IV infiltrates, arrhythmias, and ischaemia to organs (skin, gut, kidneys).

To minimize these risks, use the minimum dose possible to maintain the blood pressure (target SBP 90) and discontinue as soon the patient improves. Patients who are on a vasopressor infusion will commonly develop tachycardia. The extremities may become cool or cyanotic due to peripheral vasoconstriction.

**Delivery:** Vasopressors must be given carefully by intravenous infusion and are preferably given via a central venous catheter. However, central venous catheters should be placed only by a doctor who is skilled in the correct technique and at a hospital where this type of IV access is used frequently and personnel are familiar with its care. Central venous catheters are associated with significant risks, notably pneumothorax, arterial puncture, and blood infection. See other guidelines for instructions on using a central venous catheter. If central venous access is not possible, it is acceptable to deliver vasopressor medications through a peripheral line with appropriate precautions.

- Use the largest vein possible to deliver a high flow rate.
- Always dilute the medication and give by infusion at a strictly controlled rate.
- Use a burette to limit the volume and control the drip rate.
- Use a metal gate-clamp in the IV rather than the integral roller device, which can become loose.
- Do not use the blood pressure cuff on the same arm through which the medication is infusing.

- Inspect the infusion site regularly to detect any extravasation of the medication into the tissues.

#### Stop the infusion if:

- the drip has infiltrated the tissues (e.g. severe pain and swelling at infusion site)
- the patient develops an arrhythmia (irregular pulse or dangerous tachycardia).

#### How to administer and titrate vasopressors

##### 1. Does the patient have adequate perfusion?

First, check if vasopressors are indicated. If a patient remains in shock and has clinical signs of poor perfusion (low BP, low urine output, altered level of consciousness) after IV fluid resuscitation, consider the use of vasopressor medications to temporarily support the circulation. Some pregnant women, patients with chronic illness, and others may normally have a SBP <90 mmHg but be awake and alert, with normal mental status, normal capillary refill, and normal urine output. These patients may not need vasopressors to support blood pressure since they have no clinical signs of poor perfusion.

##### 2. Choose a vasopressor and prepare the drip for infusion

In most settings the choice of vasopressor is determined by what is available. Become familiar with the dosing and administration of the locally available vasopressor to optimize patient safety and prevent medication errors. For most conditions leading to shock, there is no clear benefit of one vasopressor over the other. In cases of severe malaria, dopamine is preferred. The infusion should be dosed based on the patient's weight.

If the patient cannot be weighed, estimate if the patient is small (50 kg), average (60 kg), large (70 kg). Use the table below to calculate the correct dose. Have a colleague double-check that you are administering the correct medication in the correct dose and to the correct site.

##### 3. Monitor the patient and titrate

Frequent monitoring is required, as changes in pulse and blood pressure can occur very quickly. This may mean reducing or increasing the infusion rate within minutes of starting it. Continuous monitoring is preferred, but

is not available in many district hospitals. For the initial administration, start at the lowest rate and monitor pulse every minute and blood pressure every 2 to 5 minutes. If the SBP is still <90 mm Hg, increase the infusion rate. If the SBP is >90 mm Hg, decrease the infusion rate to the minimum dose necessary to maintain the blood pressure and adequate perfusion. For epinephrine, titrate the dose in 0.05 mcg/kg/minute increments. For dopamine, titrate the dose in 2 mcg/kg/minute increments. If the IV site infiltrates, stop the infusion and start an infusion in a new IV site, preferably in the opposite arm. Monitor the skin. Keep the limb elevated. Patients whose IV line infiltrated while receiving vasopressors may develop skin necrosis and may require surgical debridement several days following the incident.

#### **4. When to stop vasopressors**

Vasopressors are intended for short-term use only, to allow other treatments to take effect. Continue to support the patient with intravenous fluids and blood as needed while the patient is on vasopressors. As the patient's clinical condition improves, titrate the vasopressors down. Discontinue the vasopressor infusion as soon as the patient can maintain an adequate blood pressure, and continue to monitor frequently.

## How to give vasopressor by peripheral infusion

Vasopressor	Peripheral epinephrine infusion		Peripheral dopamine infusion (preferred for shock in severe malaria)			
Commonly available concentrations	1 amp = 1 mg epinephrine (adrenaline) in 1 ml*		1 amp = 200 mg dopamine in 5 ml*			
Target infusion concentration	10 micrograms per ml		1000 micrograms per ml			
Mixing procedure to create target infusion concentration	Use 2 amps in 200 ml normal saline** OR 10 amps in 1000 ml normal saline**		Use 1 amp dopamine in 200 ml normal saline** OR 5 amps dopamine in 1000 ml normal saline**			
	Epinephrine		Dopamine			
Dose rate***	0.05 mcg/ kg/ minute	0.2 mcg/kg/ minute for very hypotensive	10 mcg/ kg/minute	15 mcg/ kg/minute	20 mcg/ kg/minute	
	Infusion rate (ml/hour)****					
Patient weight (kg)	50 kg	15 ml/hour	60 ml/hour	30 ml/hour	45 ml/hour	60 ml/hour
	60 kg	18 ml/hour	72 ml/hour	36 ml/hour	54 ml/hour	72 ml/hour
	70 kg	21 ml/hour	84 ml/hour	42 ml/hour	63 ml/hour	84 ml/hour

\* 1 milligram (mg) is equal to 1000 micrograms (mcg).

\*\* Read ampoule label 3 times to confirm concentration before mixing.

\*\*\* Desired dose rate is weight-based.

\*\*\*\* Infusion rate is commonly presented per hour. Infusion rate = desired dose rate or concentration of the infusion.

## In children<sup>2</sup>:

Dopamine For treatment of shock that is unresponsive to fluids	2–20 µg/kg per min	200 mg/5 ml ampoule Dilute to 250 mg in 250 ml of 0.9% sodium chloride with 5% glucose to 1000 µg/ml	Calculate exact dose based on body weight and required rate of infusion.
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## APPENDIX F:

### INFECTION CONTROL – Non-patient care activities for known or suspected VHF patients

#### Diagnostic laboratory activities

- Activities such as micro-pipetting and centrifugation can mechanically generate fine aerosols that might pose a risk of transmission of infection through inhalation.
- Laboratory personnel handling potential VHF clinical specimens should wear gown, gloves, particulate respirators (e.g., EU FFP2, US NIOSH- certified N951) and eye protection or face shields, or powered air purifying respirators (PAPR) when aliquotting, performing centrifugation or undertaking any other procedure that may generate aerosols.
- When removing protective equipment, avoid any contact between the soiled items (e.g. gloves, gowns) and any area of the face (i.e. eyes, nose or mouth).
- Perform hand hygiene immediately after the removal of protective equipment used during specimen handling and after any contact with potentially contaminated surfaces.
- Place specimens in clearly-labelled, non-glass, leak-proof containers and deliver directly to designated specimen handling areas.
- Disinfect all external surfaces of specimen containers thoroughly (using an effective disinfectant) prior to transport. (Example of effective disinfectant: sodium hypochlorite at 0.05%, 500 ppm available chlorine (i.e. 1:100 dilution of household bleach at initial concentration of 5%).

#### Post-mortem examinations

- Post-mortem examination of VHF-patient remains should be limited to essential evaluations only and should be performed by trained personnel.



- Personnel examining remains should wear eye protection, mask, gloves and gowns as recommended for patient care.
- In addition, personnel performing autopsies of known or suspected VHF patients should wear a particulate respirator and eye protection or face shield, or a powered air purifying respirator (PAPR).
- When removing protective equipment, avoid any contact between soiled gloves or equipment and the face (i.e. eyes, nose or mouth).
- Hand hygiene should be performed immediately following the removal of protective equipment used during post-mortem examination and that may have come into contact with potentially contaminated surfaces.
- Place specimens in clearly-labelled, non-glass, leak-proof containers and deliver directly to designated specimen handling areas.
- All external surfaces of specimen containers should be thoroughly disinfected (using an effective disinfectant) prior to transport.
- Tissue or body fluids for disposal should be carefully placed in clearly marked, sealed containers for incineration.

### **Movement and burial of human remains**

- The handling of human remains should be kept to a minimum. The following recommendations should be adhered to in principle, but may need some adaptation to take account of cultural and religious concerns:
- Remains should not be sprayed, washed or embalmed.
- Only trained personnel should handle remains during the outbreak.
- Personnel handling remains should wear personal protective equipment (gloves, gowns, apron, surgical masks and eye protection) and closed shoes.
- Protective equipment is not required for individuals driving or riding in a vehicle to collect human remains.

- Protective equipment should be put on at the site of collection of human remains and worn during the process of collection and placement in a body bag.
- Protective equipment should be removed immediately after remains have been placed in a body bag and then placed inside a coffin.
- Remains should be wrapped in sealed, leak-proof material and should be buried promptly.

## Cleaning

- Environmental surfaces or objects contaminated with blood, other body fluids, secretions or excretions should be cleaned and disinfected using standard hospital detergents/disinfectants. Application of disinfectant should be preceded by cleaning.
- Do not spray (i.e. fog) occupied or unoccupied clinical areas with disinfectant. This is a potentially dangerous practice that has no proven disease control benefit.
- Wear gloves, gown and closed shoes (e.g. boots) when cleaning the environment and handling infectious waste. Cleaning heavily soiled surfaces (e.g. soiled with vomit or blood) increases the risk of splashes. On these occasions, facial protection should be worn in addition to gloves, gown and closed, fluid-resistant shoes.
- Soiled linen should be placed in clearly-labelled, leak-proof bags or buckets at the site of use and the container surfaces should be disinfected (using an effective disinfectant) before removal from the site.
- Linen should be transported directly to the laundry area and laundered promptly with water and detergent. For low-temperature laundering, wash linen with detergent and water, rinse and then soak in 0.05% chlorine for approximately 30 minutes. Linen should then be dried according to routine standards and procedures.
- Linen that has been used by VHF patients can be heavily contaminated with body fluids (e.g. blood, vomit) and splashes may result during handling. When handling soiled linen from VHF patients, use gloves, gown, closed shoes and facial protection.
- If safe cleaning and disinfection of heavily soiled linen is not possible or reliable, it may be prudent to burn the linen to avoid any unnecessary risks to individuals

handling these items.

### Waste management during VHF outbreaks

- Waste should be triaged to enable appropriate and safe handling.
- Sharp objects (e.g. needles, syringes, glass articles) and tubing that have been in contact with the bloodstream should be placed inside puncture resistant containers. These should be located as close as practical to the area in which the items are used.
- Collect all solid, non-sharp, medical waste using leak-proof waste bags and covered bins.
- Waste should be placed in a designated pit of appropriate depth (e.g. 2 m deep and filled to a depth of 1–1.5 m). After each waste load the waste should be covered with a layer of soil 10–15 cm deep.
- An incinerator may be used for short periods during an outbreak to destroy solid waste. However, it is essential to ensure that total incineration has taken place. Caution is also required when handling flammable material and when wearing gloves due to the risk of burn injuries if gloves are ignited.
- Placenta and anatomical samples should be buried in a separate pit.
- The area designated for the final treatment and disposal of waste should have controlled access to prevent entry by animals, untrained personnel or children.
- Wear gloves, gown and closed shoes (e.g. boots) when handling solid infectious waste.
- Waste, such as faeces, urine and vomit, and liquid waste from washing, can be disposed of in the sanitary sewer or pit latrine. No further treatment is necessary.
- Wear gloves, gown, closed shoes and facial protection, when handling liquid infectious waste (e.g. any secretion or excretion with visible blood even if it originated from a normally sterile body cavity). Avoid splashing when disposing of liquid infectious waste. Goggles provide greater protection than visors from splashes that may come from below when pouring liquid waste from a bucket.

## List of abbreviations, acronyms and definition of some medical terms

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Aerosol	A fine mist or spray that contains minute particles
AFB	Acid-fast bacillus
Antibody	Type of protein in the blood that produces immunity against microorganisms or their toxins
Antigen	A molecule or substance that is recognized by the immune system, which triggers an immune response, such as the release of antibodies
Arthralgia	Joint pain
Asthenia	Severe weakness
AVPU	Alert, responding to voice, responding to pain, unresponsive
BPM	Beats per minute
BUN	Blood urea nitrogen
Case definition	Criteria for deciding whether a person has a particular disease
Carrier	A person or animal that harbors a specific infectious agent without visible symptoms of the disease. A carrier acts as a potential source of infection.
CCHF	Crimean-Congo Haemorrhagic Fever
CDC	Center for Disease Control and Prevention
CPHL	Central Public Health Laboratory
Dysphagia	Painful swallowing
ELISA	Enzyme-Linked-Immunosorbent Assay
F-75	Therapeutic milk (see recipe in the Pocket book of hospital care for children <sup>2</sup> )
g	Grams

Haematemesis	Vomiting of blood
Haemoptysis	Coughing up blood
Host	An organism in which a parasite lives and by which it is nourished.
HR	Heart rate
IgM	Immune globulin M
IgG	Immune globulin G
IM	Intra muscular
IMAI	Integrated Management of Adolescent and Adult Illness
IMCI	Integrated Management of Childhood Illness
Incubation Period	Period that the patient is infected with the virus, but is still asymptomatic and not contagious yet
IPC	Infection Prevention and Control
IV	Intravenous
JVP	Jugular venous pressure
mcg	Microgram
mg	Milligram
ml	Milliliter
MOF	Multiple Organ Failure
MoH	Ministry of Health
MSF	Medecins Sans Frontieres
NGO	Non-governmental organization
Ngt	Nasogastric tube
Nosocomial Infection	An infection acquired at a hospital or other healthcare facility.
NSAID	Non-steroidal anti-inflammatory drug

Oedema	An accumulation of an excessive amount of watery fluid in cells and tissues of the body
ORS	Oral rehydration salt(s)
PAPR	Powered Air Purifying Respirators
Photophobia	Painful oversensitivity to light
PCR	Polymerase Chain Reaction
PPE	Personal Protective Equipment
ReSoMal	Rehydration solution for malnutrition
RDT	Rapid Diagnostic Test
Reservoir	Any person, animal, anthropoid, plant, or substance which can harbor infection and hence act as a source of disease outbreak.
RR	Respiratory rate
SBP	Systolic blood pressure
SpO <sub>2</sub>	Oxygen saturation
Tachypnoea	Fast breathing
UNICEF	United Nations Children's Fund
UVRI	Uganda Viral Research Institute
VHF	Viral Haemorrhagic Fever
WHO	World Health Organization



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