Viral Hemorrhagic Fever (VHF) Protocol

Introduction

Viral hemorrhagic fever (VHF) is a clinical illness associated with fever and bleeding tendency caused by viruses belonging to four distinct families: Filoviridae, Arenaviridae, Bunyaviridae, and Flaviviridae (Table 1). The mode of transmission, clinical course, and mortality of these illnesses vary with the specific virus, but each is capable of causing a VHF syndrome.

This protocol is written to provide management guidelines for VHF in healthcare settings in Saudi Arabia.

Public Health Significance

Viral hemorrhagic fevers are caused by enveloped RNA viruses (Table 1). These viruses are maintained in nature in naturally occurring reservoirs including mosquitoes (yellow fever and dengue); ticks (Crimean-Congo hemorrhagic fever); bats (Marburg and some Ebola strains); rodents (Lassa fever); domestic ruminants (Rift Valley fever); and nonhuman primates (Marburg). VHF are ordinarily restricted to specific geographic areas and are often named for the geographic location where they were first identified. However, cases can be introduced into non-endemic areas by an incubating human host or reservoir species. For Saudi Arabia, the risk is limited to returned travelers or people coming for Hajj and Umrah from the endemic areas. Some diseases have high fatality rates and person-to-person transmission such as Ebola and Marburg. Person-to-person transmission due to poor infection control in healthcare settings could contributes to large outbreaks of Marburg, Ebola, Lassa fever and Crimean-Congo Hemorrhagic fever. For other viruses, (dengue and yellow fever) asymptomatic infection and mosquito transmission are the norm.

Healthcare Provider Responsibilities

1. Remain alert for imported cases of viral hemorrhagic fever (VHF). At this writing, returned travelers and people coming for Hajj and Umrah from Congo (DRC) are at highest risk for Ebola virus disease, from Nigeria, consider Lassa fever, and from Turkey, Iraq, and Iran consider CCHF. ***However, the epidemiology of VHF can change rapidly.*** Consult http://www.who.int/topics/haemorrhagic fevers viral/en/ for information on current outbreaks worldwide.
2. Consider the diagnosis of VHF in :
    a) Returned travelers or person coming for Hajj or Umrah from the endemic areas with clinical

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presentation fulfilling the case definition (see Case Definition).

b) Other risk groups include direct contact with a confirmed or highly suspected VHF case. If there are no risk factors (i.e., no travel history AND no direct contact), then alternative diagnoses should be pursued.

3. For any suspected case of VHF:
    a. Immediately place the suspected case in isolation: *At a minimum*, private room, standard, droplet and contact precautions (gown, gloves, mask, goggles and hand hygiene before donning and after doffing personal protective equipment (PPE)) should be used.
    b. Contact 937 for immediate reporting and notification and enter the case in HESN system.
    c. Immediately inform the infection control team that a case of suspected VHF is in the health care facility.
    d. Immediately inform receiving personnel (including emergency department personnel and emergency medical service workers) if a suspected VHF patient is being transported from one facility to another.
    e. Immediately inform the public health department in the regional health directorate.
    f. Anticipate the need to collaborate with the public l health department on:
        i. Obtaining laboratory confirmation of the diagnosis,
        ii. Obtaining clinical information to confirm the diagnosis, and
        iii. Identifying contacts of the case so that their health can be monitored.

Laboratory Responsibilities

1. Immediately report requests for testing for VHF to the National Health Laboratory (NHL).

Regional CCC Responsibilities

NOTE: A case of viral hemorrhagic fever is potentially a national-level public health emergency.
Regional CCC should be prepared to handle these events with high level of efficiency and professionalism.

1. Prior to the occurrence of a case of VHF:
    a. <u>Protect employee health.</u>

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i. Identify high-risk employees, those who would be expected to cases of VHF
ii. Ensure that high-risk employees are educated about transmission of VHF and personal protective equipment.
iii. Ensure that high-risk employees have access to appropriate personal protective equipment (PPE) (masks such as fit-tested N95 masks or powered air-purifying respirators (PAPR), are trained to properly don and doff PPE, and observe donning and doffing.

b. Identify the Rapid Response Team (RRT) who will be responsible for investigation of a case of VHF.
c. Educate healthcare providers and health facilities about appropriate recognition, isolation and reporting of a VHF case.

2. When a VHF case is reported:
   a. Isolate the case. Immediately assure that the case is under appropriate isolation: *At a minimum*, standard, contact and droplet precautions should be instituted immediately, including *at a minimum*: private room, gowns, gloves, masks, goggles or face shield; with hand hygiene before entry and after/during discarding PPE.
   b. Contact central CCC Immediately .A single case of VHF is considered an outbreak
   c. Consult infectious diseases physician regarding the diagnosis/case status.

Public Health Department (PHD) Responsibilities

a) Conduct contact tracing (for confirmed or highly suspected case).

i. For each confirmed case-patient, identify close contacts. Close contact is defined as:

1. Contact with blood or body fluids of the VHF case-patient
2. Household contact with the VHF case-patient since the onset of illness
3. Visiting the household of the case-patient since the onset of illness
4. All persons who were visited by the case-patient after the onset of illness
5. Direct contact with linens or clothing used by the case-patient after he/she developed symptoms
6. Direct contact with a deceased VHF case-patient
7. Being within 1m of the VHF case-patient for a prolonged period (≥ 1 hour) (not passing by the person in the hallway),
8. Being in the same room with the VHF case-patient for a prolonged period (≥ 1 hour)
9. Skin-to-skin contact, such as shaking hands with the case-patient

b) Arrange direct active daily monitoring and active monitoring of healthcare contacts in collaboration with the employee clinic.

ii. Discuss work, school and travel restrictions with contacts,

iii. Arrange daily monitoring ("direct active monitoring" or "active monitoring") of contacts by public health team

iv. For 'direct active monitoring,' each team should have two well trained members
Team members should be fully vaccinated, including current influenza vaccination to protect monitored persons from developing febrile illness due to exposure to team members.
Teams should be trained to take appropriate precautions during fieldwork and self-monitor for symptoms, including recording their temperature every AM immediately after reporting to work. The purpose of temperature monitoring is two-fold: protection of the monitored persons from exposure to illness in the contact tracer AND early identification of VHF in contact tracers. Fever in contact tracers should be reported to a supervisor immediately.

c) The following safety precautions are recommended for contact tracing:

1. Call ahead to contact residence to determine if the contact has developed symptoms. If the contact has developed symptoms, teams should immediately notify a supervisor and await instructions.
2. Upon arrival at the residence, again inquire if anyone in the household has developed symptoms before entering. Do not enter if anyone in the household has developed symptoms. Contact a supervisor if anyone in the household is symptomatic.
3. In the household, avoid direct physical contact like shaking hands or hugging.
4. Maintain a comfortable distance (> 1m) when interviewing, observing and recording temperatures.
5. Avoid leaning on objects or sitting down.
6. Each contact should have a dedicated quick-read thermometer supplied during the initial interview. During daily monitoring, have the contact take his/her temperature and show the temperature to the contact surveillance team. If the thermometer has been misplaced, give a new thermometer to the contact and leave the thermometer in the household.
7. Do not take the temperature of an obviously symptomatic contact. If you arrive at a contact residence and discover that, a contact has developed symptoms, reassure them that an EMS team will transport them to medical care. Then leave the residence and contact your supervisor to inform him/her that the contact has developed symptoms and needs to be transported to a hospital for evaluation.
8. Notify supervisor immediately if contact is not where they said they would be OR is lost to follow up OR expresses the intention to evade surveillance.
9. Contacts should be checked twice daily – once in person and once by phone.
10. All information should be reported back to the data manager daily and entered into a database so that reports can be compiled for incident command.

v. Educate contacts to:

1. Stay at home as much as possible
2. Restrict close contact with other people
3. Avoid crowded places, social gatherings, and use of public transport

4. Coordinate any necessary travel with the public health department (PHD)
5. Notify the PHD immediately if fever or symptoms develop. Emphasize that early diagnosis and treatment is critical for the best outcome for the contact.
6. Maintain a positive, supportive and empathic attitude.
7. Respond to questions and report concerns to the contact tracing supervisor.

vi. Post-exposure prophylaxis (PEP): there is no PEP for VHF.

vii. Treatment of cases: Arenavirus and Bunyavirus hemorrhagic fever can be treated with ribavirin. Experimental therapies and vaccine are available for EBOLA.

Viral Hemorrhagic Fever Protocol

Disease Prevention Objectives

To prevent disease through education of health care workers and public health workers to: 1) detect index cases and direct contacts rapidly, and 2) use strict adherence to standard precautions, droplet precautions, and contact precautions to minimize exposure to blood and body fluids of living and deceased cases.

Disease Control Objectives

To prevent unnecessary illness and death through rapid identification of populations exposed to VHFs coupled with ***adherence to standard, contact, and droplet precautions***.

To reduce mortality by educating physicians about ribavirin therapy for arenaviruses and bunyaviruses prior to agent confirmation.

Surveillance Objectives

To rapidly detect and confirm a case of VHF if it occurs in KSA

Clinical Description

Because of space and time limitations, clinical description is limited to the most commonly encountered viral hemorrhagic fevers.

Marburg and Ebola

Marburg is named for Marburg, Germany, site of the first recognized Marburg outbreak in 1967, traced back to African green monkeys imported from Uganda. Ebola is named for a small river in what is now Democratic Republic of the Congo.

Onset of illness is acute with fever, headache, myalgia, and extreme fatigue. Early signs also

include conjunctivitis, severe sore throat (with trouble swallowing), nausea, vomiting, abdominal pain and diarrhea. Vital signs may demonstrate bradycardia (low heart rate) and tachypnea (rapid breathing rate). Around the fifth day, a perifollicular (around the hair follicles), nonitching, maculopapular rash may appear on the torso, spreading to the face and limbs. The rash becomes confluent and fades in 3 to 10 days, followed by desquamation (skin peeling). In low-resource areas of Africa, this rash is considered pathognomonic (diagnostic), allowing distinction between malaria and viral hemorrhagic fever. About half of patients have bleeding beginning around day 5-7, including epistaxis (nosebleeds), bleeding gums, hematemesis (vomiting blood), melena (blood in the stool), hematuria (blood in the urine), petechiae, ecchymoses (bruises), and hemorrhages from needle sticks. Internal hemorrhage has been documented in fatal cases. Dehydration, prostration, continued high fever, multi-organ failure (respiratory failure, myocarditis, pancreatitis, renal failure, etc.) and shock could occur. Death occurs 6 to 9 days after onset of symptoms. Infection in pregnancy carries a grave prognosis for mother and child.

Recovery is prolonged, and victims may experience ongoing joint pain, eye inflammation or even blindness, hearing loss, orchitis, hepatitis, and neurological (stroke, personality change, psychosis) complications. Mortality varies with the strain of virus and likely with the quality of available medical care. Ebola Zaire carries a case fatality rate (CFR) of 60-90%; Ebola Sudan has a CFR of 40-60%; Bundibugyo Ebola has a CFR of 25%.

Laboratory findings include leukopenia, lymphopenia and thrombocytopenia early in illness followed by increased neutrophils and atypical lymphocytes. Liver enzymes are elevated (AST > ALT) but alkaline phosphatase and bilirubin levels are usually normal or only slightly elevated. Hypoproteinemia (low protein in the blood) and proteinuria (protein in the urine) may occur. Metabolic disturbances may occur as well as evidence of disseminated intravascular coagulation (DIC).

Because outbreaks of Ebola and Marburg generally occur in resource-poor countries and even a small number of cases can rapidly overwhelm the austere medical services available, the clinical description of these diseases is incomplete and is expected to evolve as we gain more understanding.
Returned travelers would be expected to fall ill within 21 days of last exposure.

Geographic distribution of Ebola and Marburg are posted at:
http://www.who.int/csr/disease/ebola/maps/en/

Lassa fever

Named for Lassa, Nigeria, where it was first identified, Lassa fever is the most commonly diagnosed travel-related VHF.After an incubation period of up to 21 days, the individual may experience gradual onset of low-grade fever, headache, malaise and general weakness.

Eighty percent of Lassa fever infections are subclinical or mild. After a 4-7-day prodrome, the remaining 20% gradually progress to more severe disease including hemorrhage, persistent vomiting, hypotension, edema, pleural and pericardial effusions, shock and respiratory distress. In fatal cases, death from multi-organ failure typically occurs within 2 weeks of onset; however, case-fatality rate is about 2% overall. Disease is more severe in pregnancy. Lassa fever occurs naturally in West Africa. A returned traveler would be expected to fall ill within 21 days of last exposure.

Crimean-Congo Hemorrhagic Fever

Onset is abrupt with fever, headache, myalgia (muscle aches), weakness, rigors (intense chills), nausea, vomiting, diarrhea, abdominal pain, and conjunctival injection. There may be diarrhea, painful eyes and sore throat. After 2-3 days of illness, there may be a brief remission of several hours. During the second phase of illness, hemorrhagic manifestations may occur, including petechiae, epistaxis (nose bleeds), ecchymoses (bruising), bleeding from needle sticks, melena (blood in stool), and hematuria (blood in urine). There may be photophobia, meningismus and mental status changes. The case fatality rate is 25-30%. During the convalescent phase, the patient experiences fatigue and dizziness and may experience sudden onset of deafness.

The returning traveler with Crimean-Congo hemorrhagic fever will present within less than 2 weeks after last exposure.

Rift Valley Fever

Rift Valley fever (RVF) was first identified in an infected sheep in the Rift Valley region of Kenya in 1930. Illness is variable ranging from a self-limited febrile illness to hemorrhagic signs and death. For that reason, outbreaks may not be recognized until sufficient severe cases have occurred. Fever, malaise and headaches are non-specific. Progression to large joint pain (elbows, knees, shoulders), nausea, vomiting, abdominal pain, hepatomegaly, jaundice and delirium helps identify the illness as RVF. Acute renal failure occurs in a majority of hospitalized patients, requiring dialysis. Mortality is 40% among hospitalized patients. Fatal cases often have hemorrhagic manifestations similar to other VHF, hepatic necrosis, encephalitis, renal failure and disseminated intravascular coagulation (DIC). Complications can include long-lasting visual disturbance and neurological impairment.

Mode of Transmission (Table 2)

Transmission occurs by a variety of routes, depending on the type of infection. Infections acquired percutaneously are associated with the shortest incubation period and highest mortality.

Aerosolization of HFVs is also a possible mode of transmission during a bioterrorism (BT) event.

Modes of transmission via naturally occurring routes are discussed below.

Filoviridae: Ebola and Marburg

1. Index cases of Ebola have been associated with exposure to carcasses of nonhuman primates or fruit bats.
2. Once the disease is introduced into human populations, most infections occur through chains of human-to-human transmission. Most cases have occurred after direct contact with blood, secretions, or tissues of infected patients. Cases have followed needle-stick injuries or injections with contaminated needles. Nosocomial spread occurs in underfunded African hospitals unable to take appropriate infection control precautions. This is the primary mode of transmission of Ebola and Marburg during outbreaks.
3. High titers of Ebola virus particles are found in blood and levels are much higher in persons who die from Ebola. Ebola virus has been detected in multiple types of body fluids of acutely ill persons, however data is limited because of small numbers of persons studied.
4. Household contacts who have developed Ebola have had direct contact with the ill person. Household contacts who have not had direct contact with the ill person are protected. This suggests that airborne transmission of Ebola does not occur.
5. Transmission of Ebola and Marburg virus occurs after onset of signs and symptoms.
6. Ebola and Marburg have been isolated from seminal fluid of patients 101 and 82 days after disease onset, respectively. In one case, Marburg may have been sexually transmitted.

Arenaviridae: Lassa fever

1. In nature, Arenaviruses are transmitted to humans via inhalation of aerosols present in rodent urine and feces, by ingestion of food contaminated with rodent excreta, or direct contact of rodent excreta with abraded skin and mucous membranes.

2. Person-to-person transmission occurs predominantly by direct contact with infectious blood and bodily fluids. Nosocomial outbreaks have been described.
3. Person-to-person airborne transmission has been suspected in a few instances for Lassa fever.
4. There are no reports of Arenavirus transmission during the incubation period. However, Lassa fever virus has been detected in semen up to 3 months after acute infection and in urine 32 days after disease onset.

Bunyaviridae: Crimean-Congo Hemorrhagic Fever

1. Humans become infected after a tick bite or after the slaughter of sick domestic animal.
2. Nosocomial outbreaks have been described.

Bunyaviridae: Rift Valley Fever

1. Humans acquire Rift Valley Fever from the bite of an infected mosquito, direct contact with infected animal tissues, or aerosolization of virus from infected animal carcasses. In naturally occurring outbreaks, abortion storms (near simultaneous spontaneous abortions in pregnant ruminants regardless of stage of pregnancy) are a 'classic hallmark' of RVF outbreaks. Exposure to infected tissues or body fluids or aborted materials constitutes the main route of exposure.
2. Ingestion of contaminated raw animal milk has been implicated epidemiologically.
3. There is no evidence of person to person transmission of Rift Valley Fever. However, laboratory technicians are at risk of acquiring the disease by inhalation of infectious aerosols generated from specimens.
4. If Rift Valley Fever were used as a bioterrorist weapon, susceptible livestock could also be infected which could lead to further mosquito transmission to humans and other animals.

Flaviviridae: Yellow fever

1. Humans acquire yellow fever from the bite of an infected mosquito.

2. There are no reported cases of person to person transmission or nosocomial spread of flaviviruses.
3. Infection of laboratory personnel via inhalation of aerosols during cultivation of these viruses has been reported.

Incubation Period

Table 3: Incubation Period in Days for Viral Hemorrhagic Fevers

Virus	Incubation period (days)
Ebola	2-21
Marburg	2-21
Lassa F.	6-21
Rift Valley F.	2-6
Yellow F.	3-6

Infectious Period

There is no person-to-person transmission prior to onset of symptoms with Filoviruses (Ebola and Marburg) and Arenaviruses. There is no person-to-person transmission with Flavivruses (e.g., Yellow Fever) or for Rift Valley Fever (Bunyaviruses).

Because some of the HF viruses may remain in bodily fluids for a long time following clinical recovery, convalescent patients continue to pose a risk of disease transmission. Therefore

patients convalescing from a Filovirus or an Arenavirus infection should refrain from sexual activity for 3 months after clinical recovery. Viruses have been found in seminal fluid of patients or sexually transmitted after 82 and 101 days after symptom onset for Ebola, 83 days for Marburg, 3 months for Lassa Fever. Virus can be shed in urine for 3-9 weeks after infection with Lassa fever.

Outbreak Recognition

One case of VHF constitutes an outbreak.

Case Definition

Clinical Criteria

An illness with acute onset with the following clinical findings:

- A fever >38.6°C
- One or more of the following clinical findings:
  - Severe headache
  - Muscle pain
  - Erythematous maculopapular rash on the trunk with fine desquamation 3–4 days after rash onset
  - Vomiting
  - Diarrhea

- Pharyngitis (arenavirus only)
- Abdominal pain
- Bleeding not related to injury
- Retrosternal chest pain (arenavirus only)
- Proteinuria (arenavirus only)
- Thrombocytopenia

Plus Epidemiologic Linkage

One or more of the following exposures within the last 21 days before onset of symptoms:

- Contact with blood or other body fluids of a patient with VHF
- Residence in—or travel to—a VHF endemic area
- Work in a laboratory that handles VHF specimens
- Work in a laboratory that handles bats, rodents, or primates from endemic areas

Laboratory Criteria for Diagnosis

One or more of the following laboratory findings:

- Detection of viral hemorrhagic fever (VHF) viral antigens in blood by enzyme-linked Immunosorbent Assay (ELISA) antigen detection
- VHF viral isolation in cell culture for blood or tissues
- Detection of VHF-specific genetic sequence by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) from blood or tissues
- Detection of VHF viral antigens in tissues by immunohistochemistry

Case Classification

Suspected

Case meets the clinical and epidemiologic linkage criteria.

Confirmed

Case meets the clinical and laboratory criteria.

Infection control procedures:

Direct patient care (for suspected or confirmed patient with VHF)

a) Patient placement, staff allocation and visitors

- Put suspected or confirmed cases in single isolation rooms with an adjoining dedicated toilet and sink equipped with running water, soap and single-use towels, alcohol-based handrub dispensers, stocks of personal protective equipment (PPE), stocks of medicines, good ventilation, screened windows, doors closed and restricted access.
- if isolation rooms are unavailable, cohort these patients in specific confined areas while rigorously keeping suspected and confirmed cases separate and ensure the items listed here for isolation rooms are readily available. Make sure that there is at least 1 meter distance between patient beds.
- 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 VHF isolation areas and other clinical areas during the outbreak.
- Restrict all non-essential staff from VHF patient care areas.
- Stopping visitor access to the patient is preferred, but if this is not possible, limit their number to include only those necessary for the patient's well-being and care, such as a child's parent.
- Do not allow other visitors to enter the isolation rooms/areas and ensure that any visitors wishing to observe the patient do so from an adequate distance (approximately 3 meters).
- Before allowing visitors to VHF patients to enter the healthcare facility, screen them for signs and symptoms of VHF.
- Ensure that all visitors use PPE and perform hand hygiene as recommended by infection control team and are prior to entry into the isolation room/area.
- Ensure that all health workers wear PPE before entering the isolation rooms/areas and having contacts with the patients and/or the environment as recommended by infection control team.(see Annex 1)
- Personal clothing should not be worn for working in the patient areas. Scrub or medical suits should be worn.

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Treatment

The mainstay of treatment for VHF is supportive, with careful maintenance of fluid and electrolyte balance, circulatory volume, and blood pressure. There are no antiviral drugs or vaccines for post exposure prophylaxis for VHFs.

Drug Therapy

Ribavirin has some in vitro and in vivo activity against Arenaviruses and Bunyaviruses but no utility against Filoviruses or Flaviviruses.

New investigational therapieutics are available for Ebola.

Vaccine

With the exception of Yellow fever live attenuated 17D vaccine, which is highly effective when administered to travelers to endemic areas, there is no licensed vaccine for any of the VHFs.
The Yellow fever vaccine is not useful in preventing disease if given in the postexposure setting.
New vaccine for Ebola has been used recently for vaccinating contacts during the 2018 outbreak in DRC.

References

http://www.cdc.gov/vhf/ebola/index.html

http://www.who.int/csr/disease/ebola/en/

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Table 1 Selected Viruses Causing Viral Hemorrhagic Fever

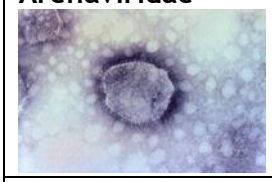
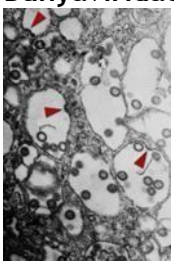
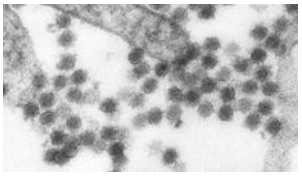
Virus Families (Public Health Image Library)	Characteristics of the family (Principles and Practice of Infectious Diseases)	Selected Examples associated with hemorrhagic fever (WHO)
Arenaviridae 	• Round, oval or pleomorphic RNA viruses that form their membranes by budding from the host membrane	• Lassa fever • Junin • Machupo
Bunyaviridae 	• Spherical, lipid membrane-enclosed RNA viruses with glycosylated envelope proteins • Photograph (Rift Valley fever) shows virus budding from cell membranes; however virions from some other viruses in this family mature by budding from intracellular structures • Also includes California encephalitis (La Crosse)	• Rift Valley Fever • Crimean-Congo hemorrhagic fever • Hantaan hemorrhagic fever
Filoviridae 	• Elongated, filamentous RNA virus with membrane formed as the virus buds from the host cell. • Photograph shows viruses budding from a cell in tissue culture	• Marburg virus • Ebola virus
Flaviviridae 	• More than 60 species • 30 are known to cause human disease • Icosahedral RNA viruses with a lipid envelope studded with glycoproteins • Unstable in the environment and sensitive to heat, ultraviolet radiation, disinfectants (including alcohol and iodine), and acid pH • Also includes West Nile virus (photograph), St. Louis encephalitis,	• Dengue fever • Yellow fever • Omsk fever • Kyasanur forest disease • AlKhumrah

Table 2 : Transmission of VHF

Family	Genus	Virus*	Disease	Vector/Reservoir in Nature	Nosocomial Spread
Filoviridae	Filovirus	**Ebola**	Ebola HF	Fruit bat reservoir for some strains (Zaire). Primates (Reston, Côte d'Ivorie) and pigs (Reston) have been infected with some strains of Ebola	Nosocomial spread; spread from direct contact with deceased Ebola patients
		Marburg	Marburg HF	Fruit bat reservoir; primates may be a source for index case infection	Nosocomial spread
Arenaviridae**	Arenavirus	**Lassa**	Lassa F.	Rodent reservoir; humans infected by inhalation, ingestion, inoculation with rodent feces	Frequent nosocomial transmission
Bunyaviridae	Nairovirus	Crimean-Congo HF	CC HV	Tick–mammal—tick cycle; humans infected from tick bite or contact with slaughtered ruminants	Nosocomial outbreaks
	Phlebovirus	**Rift Valley Fever**	Rift Valley HF	Mosquito transmission with amplification through cattle and sheep; humans are infected through mosquito bite or exposure to infected tissues of sheep, goats and cattle	no
	Hantavirus	HF with renal syndrome	HF with renal syn.	Rodent reservoir; human infection through aerosolized rodent urine	no
Flaviviridae	Flavivirus	Dengue	Dengue fever, Dengue HF	*Aedes aegypti* – human cycle	no
		Yellow Fever	Yellow fever	Mosquito–human or mosquito–nonhuman primate cycles	no

Annex 1: donning and doffing PPE

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Steps recommended to put on PPE including gown	Steps recommended to remove PPE including gown
1. Remove all personal items (jewellery, watch, cell phones, pens, etc.). 2. Put on the scrub suit and rubber boots* in the changing room. 3. Move to the clean area at the entrance of the isolation unit. 4. By visual inspection, ensure that all sizes of the PPE set are correct and the quality is appropriate. 5. Undertake the procedure of putting on PPE under the guidance and supervision of a trained observer (colleague/buddy). 6. Perform hand hygiene. 7. Put on gloves (examination, nitrile gloves). 8. Put on disposable gown made of fabric that is tested for resistance to penetration by blood or body fluids OR to blood-borne pathogens. 9. Put on face mask. 10. Put on face shield OR goggles. 11. Put on head and neck covering: surgical bonnet covering neck and sides of the head (preferable with face shield) OR hood. 12. Put on disposable waterproof apron (if not available, use heavy duty, reusable waterproof apron). 13. Put on a second pair of (preferably long cuff) gloves over the cuff of the gown. **If not available, use closed shoes (slip-ons without shoelaces and fully covering the dorsum of the foot and ankles) and shoe covers (nonslip and preferably impermeable).*	1. Always remove PPE under the guidance and supervision of a trained observer (colleague). Ensure that infectious waste containers are available in the doffing area for safe disposal of PPE. Separate containers should be made available for reusable items. 2. Perform hand hygiene on gloved hands.[4] 3. Remove apron leaning forward and taking care to avoid contaminating your hands. When removing the disposable apron, tear it off at the neck and roll it down without touching the front area. Then untie the back and roll the apron forward. 4. Perform hand hygiene on gloved hands. 5. Remove outer pair of gloves and dispose of them safely. 6. Perform hand hygiene on gloved hands. 7. Remove head and neck covering taking care to avoid contaminating your face, by starting from the bottom of the hood at the back and rolling from back to front and from inside to outside, and dispose of safely. 8. Perform hand hygiene on gloved hands. 9. Remove the gown by untying the knot first, then pulling from back to front rolling it from inside to outside and dispose of it safely. 10. Perform hand hygiene on gloved hands. 11. Remove eye protection by pulling the string from behind the head and dispose of safely. 12. Perform hand hygiene on gloved hands. 13. Remove the mask from behind the head, by first untying the bottom string above the head and leaving it hanging in front; and then the top string next, from behind the head, and dispose of safely. 14. Perform hand hygiene on gloved hands. 15. Remove rubber boots without touching them (or overshoes if wearing these). If the same boots are to be used outside of the high-risk zone, keep them on but clean and decontaminate appropriately before leaving the doffing area*.[5] 16. Perform hand hygiene on gloved hands. 17. Remove gloves carefully with appropriate technique and dispose of safely. 18. Perform hand hygiene.

Annex 2 : **implementation of IPC best practices during direct patient care and related activities**

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What?	How?	Who is responsible?
Create isolation rooms or areas	• Identify single rooms and prioritise these for patients with known or suspected Ebola virus. • Refer to guidance on setting up an isolation area.[2]	• Coordinator or infection prevention and control (IPC) staff to identify areas/rooms for patient placement. • Health workers to adhere to recommendations and report to the coordinator when a patient is not placed in an isolation room/area.
Restrict all non-essential staff from HF patient care rooms/areas	• Ensure that clinical and nonclinical personnel are assigned exclusively to patient care areas and that members of staff do not move freely between these areas and other clinical areas during the outbreak. • Cohort staff between areas with suspected and those with confirmed haemorrhagic fever (HF) patients. • Use signage to alert restrictions of staff. • Maintain a log of persons entering the room.	• Coordinator and/or IPC staff
Limit the number of visitors allowed access to the patient.	• Use signage and other communications to alert restrictions of visitors. Make simple messages understandable for the public but also be careful to avoid stigmatization. • Maintain a log of persons entering the room.	• Coordinator and/or IPC staff • Involve patient or community representatives, if available. • Health workers to adhere to recommendations and report to the coordinator when they are not followed.
Ensure that all staff and visitors correctly use and remove recommended personal protective equipment (PPE).	• Ensure the equipment is always available at the entry of the isolation rooms/areas. • Provide staff and visitors with instructions on the use and correct removal of PPE through training and reminder posters.	• Coordinator and/or IPC staff • Involve patient or community representatives, if available. • Health workers to adhere to recommendations and report to the coordinator when they are not followed. • Another staff member should be assigned to supervise the sequence of putting on and removing PPE by his/her colleague.

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Ensure that all staff and visitors perform hand hygiene according to the above recommendations. These hand hygiene actions should be performed when recommended even if PPE is worn.	• Provide staff and visitors with instructions on the importance of hand hygiene best practices through training and reminder posters. • Ensure continuous availability of alcohol-based handrub and soap, water and single-use towels at the isolation room/areas entry and at the point of care.	• Coordinator and/or IPC staff. • Involve patient or community representatives, if available. • Health workers to adhere to recommendations and report to the coordinator when they are not followed.
Limit the use of needles and other sharp objects as much as possible. If this cannot be avoided see instructions in the text.	• Provide staff and carers with instructions on the essential use of needles and sharps through training and reminder posters. • Ensure the equipment is available to do this.	• Health workers to adhere to recommendations.
Dispose of needles and other sharp objects safely.	• Provide staff and carers with instructions on the safe disposal of sharps through training and reminder posters. • Ensure the equipment is available to do this.	• Health workers to adhere to recommendations and report to the coordinator when they are not followed.
Create system of safe management of waste and linen.	• Provide staff and visitors/carers with instructions on the safe management and disposal of waste and linen through training and reminder posters. • Ensure the equipment is available to do this.	• Health workers to adhere to recommendations and report to the coordinator when they are not followed.
Limit the use of phlebotomy and laboratory testing to the minimum necessary for essential diagnostic evaluation and patient care.	• Provide staff with training and visual instructions on the need for essential phlebotomy and laboratory testing.	• Health workers to adhere to recommendations.
Only take a patient out of their room/care area if they are free of virus, or for essential, life-saving tests.	• Provide staff with training and visual instructions on the appropriate times to take the patient from their care area and on precautions to take.	• Health workers to adhere to recommendations and report to the coordinator when they are not followed.
Undertake cleaning of the environment and patient care equipment safely following recommendations in the text.	• Provide staff and visitors/carers with instructions on cleaning through training and reminder posters. • Ensure the equipment is available to undertake recommended cleaning.	• Health workers to adhere to recommendations and report to the coordinator when they are not followed.