Viral Hemorrhagic Fevers

CASE AUTHORS: Steven J. Durning, MD, Maj, USAF, MC
Michael J. Roy, MD, MPH, FACP, LTC, MC

ACCREDITATION & DESIGNATION STATEMENT

Rush University Medical Center is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians.

Rush University Medical Center designates this educational activity for a maximum of 1 credit of category 1 credit toward the AMA Physician's Recognition Award. Each physician should claim only those credits that he/she actually spent in the activity.

This CME activity was planned and produced in accordance with the ACCME Essentials.

CME credits are available free of charge through March 2007.

DISCLAIMER

This project was funded by the Metropolitan Chicago Healthcare Council (MCHC) through a grant from the Health Resources and Services Administration (HRSA).

The opinions or assertions contained herein are the private views of the authors and are not to be construed as official or as representing the opinion of Rush University Medical Center, the Department of the Army, Department of the Navy, Department of the Air Force, Department of Defense, MCHC or HRSA.

FDA Approved Drug and Devices Assurance Statement

In accordance with requirements of the FDA, the audience is advised that information presented in this continuing medical education activity may contain references to unlabeled or unapproved uses of drugs or devices. Please refer to the FDA approved package insert for each drug/device for full prescribing/utilization information.

INSTRUCTIONS

The questions that appear throughout this case are intended as a self-assessment tool. For each question, select or provide the answer that you think is most appropriate and compare your answers to the key at the back of this booklet. The correct answer and a discussion of the answer choices are included in the answer key.

Note: These self-assessment questions are not intended for CME credit. To apply for CME credit, you must complete the CME Test at the back of this booklet and submit it according to the directions provided.

In addition, a sign is provided in the back of this booklet for posting in your office or clinic. Complete the sign by adding your local health department's phone number.

Viral Hemorrhagic Fevers

CASE AUTHORS: Steven J. Durning, MD, Maj, USAF, MC
Michael J. Roy, MD, MPH, FACP, LTC, MC

INTENDED AUDIENCE

Internal medicine, family medicine, and emergency medicine physicians, and other clinicians who will provide evaluation and care in the aftermath of a terrorist attack or other public health disaster

EDUCATIONAL OBJECTIVES

Upon completion of this case, participants will be able to:

- Describe the natural and intentional sources of transmission and spread of viral hemorrhagic fevers (VHF), including use as a biologic weapon.
- Discuss the initial presentation and clinical manifestations of VHF, including methods for confirming this diagnosis.
- Outline important strategies for infection control for healthcare workers caring for patients with cases of suspected VHF.
- Describe processes for communication with public health authorities and media about VHF.
- Describe the current recommended therapy for patients with VHF.

CASE HISTORY

A 32-year-old newspaper reporter with no significant past medical history presents to your office complaining of a 2-day history of fevers, diffuse myalgias, and severe pharyngitis. He also complains of vomiting and bloody diarrhea that began this morning. On physical examination, his vitals are T=102.8°F, BP=100/80, HR=80, RR=15. He has marked edema of the posterior pharynx, as well as a nonpruritic maculopapular eruption over his chest and back. He has not had recent travel overseas, exposure to pets, or recent outdoor recreational activities. He received an influenza vaccination earlier this year. He states that two of his coworkers have been absent from work and had been referred by the *Tribune*'s health insurance provider to your office for evaluation.

Two of your practice partners confirm that recently they each have seen a worker from the *Tribune* who presented with fevers, diffuse myalgias, and pharyngitis. One patient was a 40-year-old editor with a history of diabetes. Her most prominent findings on presentation were conjunctivitis, facial flushing, and new onset of nondependent edema. Initially, she was sent home with close follow-up. The other

patient was a 24-year-old photographer whose examination was remarkable for hypotension, relative bradycardia, somnolence, oropharyngeal bleeding, and petechiae over his chest and abdomen. He was transferred to a nearby hospital immediately. Like your patient, neither of these 2 people reported other sick contacts, overseas travel, exposure to unusual pets, or recent outdoor recreational activities. They also all reported receiving their annual influenza vaccination.

QUESTION 1

You are called to the emergency room to evaluate a patient with suspected Ebola virus infection. The presence of which of the following should raise concern regarding a potential bioterrorism-related outbreak?

a. **No history of travel to Africa**
b. **News of an outbreak of pharyngitis among local children on a school trip**
c. **Temporal cluster of patients presenting with fever and increased vascular permeability on examination**
d. **Abrupt onset of fever and signs of increased vascular permeability on exam**
e. **a and c only**

Reminder: You can find the Answer Key & Discussion on page 9.

COMMENT: This case vividly illustrates the varying typical presentations of Ebola or Marburg hemorrhagic fever syndrome, two of the several etiologies of VHF. The VHF agents are a diverse group of RNA viruses that present with common clinical characteristics known as the VHF syndrome. The Ebola and Marburg viruses are specific etiologies of VHF in humans (see Table 1).

VHF syndrome can manifest as an acute febrile illness similar to influenza (characterized by prominent nonspecific findings such as malaise, myalgias, and prostration), but patients with VHF are also at risk for virus-induced endothelial damage that increases vascular permeability. Early signs of this process may include conjunctival injection, flushing, and petechiae or ecchymoses; later signs of vascular permeability include hypotension, shock, or disseminated intravascular coagulation (DIC). VHF should be suspected in any patient presenting with a febrile illness accompanied by evidence of vascular involvement (ie, flushing, nondependent edema, hypotension, petechiae, and/or hemorrhagic diathesis), who has traveled to an area where a hemorrhagic fever virus is known to circulate (see Table 1) and/or where evidence suggests a possible bioterrorism-related outbreak. In this case, the near simultaneous presentation of 3 individuals who work in close proximity and lack other likely etiologies for their symptoms should immediately raise the possibility of a bioterrorism-induced outbreak. This concern should be further heightened given their work in the media environment, which was targeted in the anthrax attacks in the fall of 2001.

The Filovirus hemorrhagic fevers, Marburg and Ebola, share similar pathologic and clinical features and have specific findings that facilitate their differentiation from other forms of VHF. Ebola virus, named after a small river in northwest Zaire, is morphologically similar to, but antigenically distinct from, Marburg virus, which is named after the city in Germany where it was first identified. These two viruses cause necrosis of parenchymal cells in the liver, spleen, lung, kidney, skin, testes and other organs. Highly suggestive findings of Filovirus hemorrhagic fever include severe posterior pharyngeal edema that can cause dysphagia or dyspnea, and an evanescent nonpruritic maculopapular rash that is followed by desquamation of the affected skin.[2] Previous case reports and experiments in primates have shown that neutrophilia, lymphopenia, and abnormalities of platelet number (thrombocytopenia) and function often occur early in the illness.[5,6] Evidence suggests that lymphopenia is due to early virus-induced apoptosis, while thrombocytopenia is often a manifestation of DIC that can occur with Ebola

and Marburg hemorrhagic fever. Anemia may also be seen in the setting of DIC, however, the hemoglobin is usually normal on presentation; hemoglobin may alternatively be increased in the presence of concurrent dehydration. Elevated liver transaminase levels, with AST greater than ALT, are common.[5] Proteinuria has also been reported with these agents and typically occurs early in the course of disease. Several subtypes of Ebola virus have been identified, and all but one have originated in Africa and been highly pathogenic to humans (case lethality rates up to 88%). Devastating outbreaks of Ebola were documented in central Africa in 1976. A U.S. Army SWAT team was called in to quell a 1989 outbreak in a laboratory in Reston, Virginia that was traced to monkeys imported from the Philippines for research purposes — an event that was described so compellingly by Richard Preston in his book, The Hot Zone.[7] There have been numerous cases of Ebola in Gabon and the Republic of Congo in recent years, attributed to handling infected gorilla, chimpanzee, or duiker carcasses.[8] The initial Marburg virus outbreak was traced to monkeys imported from Uganda. Marburg hemorrhagic fever has subsequently been reported in South Africa and Kenya. The natural reservoirs of Ebola and Marburg viruses have not been determined.[8]

The differential diagnosis of VHF is quite extensive and includes other infections associated with fever, rash, and hemorrhage such as falciparum malaria, acute African trypanosomiasis, typhoid fever, leptospirosis, pneumonic plague, and bacterial septicemia.

You obtain the following lab results for your patient:

Complete blood count: WBC=2,000/mm^3, hemoglobin=15.1gm/dL, platelets=100,000/mm^3.

Serum chemistries: Sodium=141mEq/L, potassium=4.0mEq/L, chloride=100mEq/L, bicarbonate=20mEq/L, BUN=22mg/dL, creatinine=1.1mg/dL.

Liver panel: AST=80U/L, ALT=60U/L, albumin=4.1mg/dL, total bilirubin=1.5mg/dL Alkaline phosphatase=100U/L.

Urinalysis: 1+ protein with 0 RBCs, 0 WBCs, and no sediment findings.

Similar laboratory findings were present in his two coworkers, and the one who was sent to the hospital also had schistocytes on his peripheral blood smear, indicative of DIC.

QUESTION 2

Given these laboratory findings, what is the most appropriate next step?

a. Send the patient home and advise him to drink plenty of fluids.

b. Contact local public health officers due to concern for a potential bioterrorism-induced outbreak, and admit to hospital.

c. Arrange for immediate air transport to a nearest tertiary care hospital and contact local public health officers.

d. Administer an empiric course of doxycycline.

Table 1. Recognized Causes of VHF in Humans*

Virus Genera	Disease	Natural Distribution	Vector/Exposure	Incubation Period (days)
Arenavirus	Lassa fever	Africa	Rodent‡	5-16
	Argentine HF†	South America	Rodent	7-14
	Bolivian HF	South America	Rodent	9-15
	Brazilian HF	South America	Rodent	7-14
	Venezuelen HF	South America	Rodent	7-14
Phlebovirus	Rift Valley fever	Africa	Mosquito§	2-5
Nairovirus	Crimean-Congo HF	Europe, Asia, Africa	Tick||	3-12
Hantavirus syndrome	Hantavirus Renal	Asia, Europe, likely worldwide	Rodent	9-35
	Hantavirus Pulmonary Syndrome	North & South America	Rodent	3-28
Filovirus	Marburg	Africa	Unknown¶	3-16
	Ebola	Africa	Unknown¶ Exposure to Carcasses#	2-21
Flavivirus	Yellow fever	Africa, South America	Mosquito	3-6
	Dengue HF	Asia, Americas, Africa	Mosquito	Unknown
	Kyasanur Forest disease	India	Tick	3-8
	Omsk HF	States of the former Soviet Union	Tick**	3-8

* Data from Jahrling[1], Isaacson[2], Rigquelme[3], and Peters[4].
† HF = Hemorrhagic Fever
‡ Nosocomial transmission is a less likely source of human infection than the listed vector.
§ Domestic animal slaughter is a less likely source of human infection than the listed vector.
|| Domestic animal slaughter and nosocomial transmission are less likely sources of human infection than the listed vector.
¶ Nosocomial transmission is uncommon.
# Gorilla, chimpanzee, or duiker carcasses
**Muskrat contaminated water is a less likely source of human infection than the listed vector.

The local health department instructs you to place the patient in isolation while waiting for a mobile laboratory that will be sent from the Centers for Disease Control and Prevention (CDC) to assist with handling of blood and body fluid specimens from the patient.

QUESTION 3

Which of the following is *not* an accepted means to confirm the diagnosis of Ebola or Marburg virus?

a. Demonstrating IgM or a 4-fold rise in IgG antibodies titers for the virus

b. Electron microscopy

c. Viral isolation

d. Reverse transcriptase polymerase chain reaction (RT-PCR) assay

e. Toxin isolation

COMMENT: Biosafety Level 4 (BSL-4) is required for laboratory work with dangerous and exotic agents of VHF, such as Ebola, Marburg, Rift Valley Fever, and hantavirus, because these viruses pose a high individual risk of aerosol-transmitted laboratory infections and life-threatening disease. Laboratory personnel should be verbally notified that VHF is a diagnostic consideration, and specimens should remain in the custody of a designated individual until testing is completed. Laboratory staff that work under this Biosafety Level have specific and thorough training in handling extremely hazardous infectious agents; they also understand the primary and secondary containment functions of the standard and special practices, the containment equipment, and the laboratory design characteristics. BSL-4 laboratories are typically located within a dedicated, specially structured building, or in the instance of a laboratory building that is used for other investigations, within a controlled area which is completely isolated from all other areas of the building. Entry into a BSL-4 area is through an airlock fitted with airtight doors. Personnel who enter a BSL-4 area wear a one-piece positive pressure suit that is ventilated by a life-support system protected by HEPA filtration. A chemical shower is provided to decontaminate the surface of the suit before the worker leaves the area.

All suspected cases of infection with VHF should be reported immediately to local and state health departments and to the CDC. The CDC can be contacted 24 hours a day by calling the emergency response hotline at 770-488-7100. Specimens for virus-specific diagnostic testing should be sent to the CDC as rapidly as possible, following CDC instructions. Given the potential for spread with contact with blood, laboratory testing should be kept to the minimum required for the immediate care of the patient until a mobile CDC laboratory arrives. Further, all specimens submitted to the laboratory should be labeled as biohazardous material.

QUESTION 4

Given your high clinical suspicion of Filovirus hemorrhagic fever, you place the patient in isolation as instructed by the local public health official and the CDC. Which of the following isolation precautions should be instituted?

a. **Place the patient in a private room; universal precautions for hospital personnel**

b. **Place the patient in a private room with negative pressure; barrier precautions for hospital personnel**

c. **Place the patient in a private room with negative pressure; Biosafety Level 4 for hospital personnel**

d. **Transfer the patient to the CDC mobile unit as soon as possible; Biosafety Level 4 for all contacts**

COMMENT: As the Filovirus hemorrhagic fevers are lipid containing RNA viruses, they are readily inactivated by disinfectant solutions to include 0.5% sodium hypochlorite, glutaraldehyde, and phenolic disinfectants. Likewise, soaps and detergents also induce viral inactivation and thus should be used liberally. Further, patients with Filovirus hemorrhagic fever should use a chemical toilet, by autoclaving or treating with several ounces of bleach for more than 5 minutes,[5] before flushing or disposing in a drain connected to a sanitary sewer.

Disinfectant solution should also be copiously applied to the outer surface of airtight bags for all materials used by the patient (such as disposable linen and pajamas), disposable items worn by caretakers, and the outside and inside of containers in the patient's room, such as disposable sharps containers. If available, an anteroom for putting on and removing protective clothing is useful.[5]

If an individual is exposed to potentially infected material (eg, through an injection or a cut on the hand) the individual should immediately wash the affected area of the skin, apply a disinfectant solution, and notify the VHF patient's physician. These individuals should be considered high-risk contacts and placed on surveillance.

Spills of potentially contaminated fluids should be liberally covered with disinfectant and left to soak for a minimum of 30 minutes.[5] The contaminated area should then be wiped up with an absorbent material that is likewise soaked in disinfectant.

INFECTION CONTROL PRECAUTIONS WITH SYMPTOMATIC VHF PATIENTS

- Patient placed in private negative pressure room (with an anteroom, if available)
- Caretakers of patient use barrier precautions: gloves, gowns, N-95 masks, eye protection, leg covers, shoe covers
- Disinfectant solution applied to outer surface of airtight bags for all materials used by the patient, disposable items worn by caretakers, and the outside and inside of containers in the patient's room
- Mark all patient blood and/or other body fluid specimens as biohazards
- Face shields or masks with eye protection should be worn to prevent contact with blood, body fluids, or respiratory secretions that may be rendered airborne by coughing or sneezing

QUESTION 5

Your patient expresses concern for his family. He has a 10-year-old son and his wife is 20 weeks pregnant. He reports that they are both feeling well, with no symptoms of illness. What should you do regarding his family's care?

a. Isolate both his wife and 10-year-old son

b. Isolate his wife

c. Conduct daily medical surveillance of family members without isolating them

d. Admit his wife and son to the hospital

COMMENT: The levels of contact risk are summarized in Table 2, and details on the definitions of contact risk are as follows:

1. Casual contacts

Persons who have remote contact with the suspected case of VHF. Individuals in this category include people who sat next to the suspected case of VHF on the bus or metro, stayed in the same hotel as the suspected case, or shopped in the same mall as the suspected case. Since the agents of VHF are not spread by such casual contact, no special surveillance is indicated.

2. Close contacts

Persons who have more than casual contact with the patient. Close contacts include persons living with the patient, those caring for the patient (eg, nurses, physicians), and/or those who have shook hands with or hugged the patient. State and local health departments should identify close contacts as soon as VHF is considered to be a likely diagnosis.

Once the diagnosis of VHF is *confirmed*, close contacts should be placed under *surveillance*. This requires close contacts to record their temperature twice daily and report any temperature over 101°F or any symptom of illness. Surveillance should be continued for 3 weeks after the person's last contact with the index case. If a fever ≥101°F and/or symptoms of illness develop, the patient should be immediately placed in *isolation* and treated as a VHF patient.[5]

3. High-risk contacts

High-risk contacts are individuals who have had mucous membrane contact with the patient, such as kissing or sexual intercourse, or have had a needlestick or other penetrating injury involving contact with the patient's blood and/or other body fluids. These patients should be placed under *surveillance* as soon as VHF is *considered* a likely diagnosis in the index case. Again, if a high-risk contact develops fever ≥101°F and/or other symptoms of illness, the patient should be immediately placed in *isolation* and treated as a VHF patient.[5]

MANAGING PUBLIC FEAR

It is important to clearly convey risk categories to the lay press once an outbreak is identified due to the heightened concern and possible fear that can be connected with the identification of VHF. It is also important to discuss these categories to educate the public regarding risk and to prevent rumors. The media can also be used to provide emergency information about personal protection or evacuation. Ongoing communication with the media is necessary. Establishing and maintaining good relations with the media and identifying internal media liaisons should be part of hospital and public health center disaster preparedness plans.

Table 2. Risk Categories for Contacts of Patients With VHF*

Risk Category	Description	Surveillance†
Casual contacts	Remote contact with index case, eg, stayed in same hotel	VHF not spread by casual contact, no special surveillance required
Close contacts	More than casual contact, eg, living with contact caretaker, shook hands with contact	Place under surveillance once index case is confirmed
High-risk contacts	Mucous membrane contact, eg, kissing, or penetrating injury involving contract with index case's blood (needlestick)	Place under surveillance as soon as consider diagnosis of VHF in index case

*CDC Update: Management of patients with suspected viral hemorrhagic fever—United States[5]
†Surveillance should be continued for 3 weeks after the person's last contact with the index case. If a fever > 101°F and/or symptoms of illness develop, the patient should be immediately placed in *isolation* and treated as a VHF patient.

QUESTION 6

The CDC mobile laboratory calls you because they have confirmed a diagnosis of Ebola virus. Which of the following statements best describes the current therapy for Ebola virus?

a. Supportive care only
b. Supportive care + ribavirin
c. Supportive care + immunoglobulin
d. Supportive care + vaccine

COMMENT: Treatment of Ebola virus is supportive, as there is currently no definitive treatment for Ebola virus. Aspirin and other antiplatelet agents or anti-clotting factor drugs should be avoided, as they may potentiate hemorrhage. Secondary bacterial infections are relatively common and should be aggressively sought and treated. Intravenous lines, catheters, and other invasive techniques should be avoided unless clearly indicated given the concern of diffuse hemorrhage. The diffuse nature of vascular involvement often leads to multi-system organ failure.

The management of bleeding in VHF patients is controversial. Uncontrolled observations support administration of fresh frozen plasma, clotting factor concentrates, and platelets. Corticosteroids may be helpful, but remain an untested modality for treating shock due to Ebola virus.[1] Patients with hypotension and shock, due to advanced capillary leak syndrome, often respond poorly to fluid resuscitation and develop pulmonary edema. Judicious use of saline solution and consideration of dopamine may be helpful for persistent hypotension. Alpha-adrenergic agents have not been shown to be helpful except in rare cases when emergent intervention to treat refractory hypotension is needed.

Ribavirin is ineffective against the Filoviruses. Immunoglobulin therapy for experimental animals infected with Ebola virus has been disappointing. In a small, uncontrolled trial, transfusion of blood from patients convalescing from Ebola virus infection resulted in a markedly lower case fatality rate (13%) among 8 transfused patients in comparison with the overall case fatality rate of 80% during a 1995 epidemic; however these patients were transfused late in the course of their illness, when they may well have survived without the transfusion.

There are no current vaccines available against Ebola virus, however two recent vaccine candidates raise great hope. The first is a DNA-based vaccine, and the second is a harmless Ebola virus-like particle (VLP); they have been shown to evoke good humoral and cellular response, and are now in Phase 3 human studies.[9,10]

Yellow fever virus is the only VHF for which vaccine is available. Yellow fever is endemic in Africa and South America and vaccination should be considered before traveling to these regions. A vaccine has been licensed in the Republic of Korea for Korean Hemorrhagic Fever, and investigational vaccines are being studied for other VHF.

CASE CONCLUSION

The 3 patients described in this case scenario survived with aggressive supportive care. They had no physical long-term sequelae due to their illness.

ANSWER KEY & DISCUSSION

QUESTION 1

You are called to the emergency room to evaluate a patient with suspected Ebola virus infection. The presence of which of the following should raise concern regarding a potential bioterrorism-related outbreak?

a. **No history of travel to Africa**
b. **News of an outbreak of pharyngitis among local children on a school trip**
c. **Cluster of patients presenting with fever and increased vascular permeability on examination**
d. **Abrupt onset of fever and signs of increased vascular permeability on exam**
e. **a and c only**

ANSWER: The correct answer is e. Given the fact that this patient has not traveled to a region where the Ebola virus is endemic, and that there is a cluster of people presenting with similar symptoms, the possibility of a bioterrorism attack should be considered and the local health department should be notified immediately according to your emergency preparedness and disaster plan.

QUESTION 2

Given these laboratory findings, what is the most appropriate next step?

a. **Send the patient home and advise him to drink plenty of fluids**
b. **Contact local public health officers due to concern for a potential bioterrorism-induced outbreak, and admit to hospital**
c. **Arrange for immediate air transport to a nearest tertiary care hospital and contact local public health officers**
d. **Administer an empiric course of doxycycline**

ANSWER: The correct answer is b. As previously discussed, this patient's presentation is consistent with VHF syndrome. You also have reasonable evidence that 2 close contacts may have the same illness. Given that this patient and his coworkers have neither a history of travel to an area endemic for VHF or exposure to exotic animals, you should be very concerned that this may represent the deliberate dissemination of VHF. Given the prominent rash and pharyngeal findings on physical examination, you should be particularly concerned about an Ebola or Marburg virus or Lassa fever outbreak. Therefore, you should contact local public health officials immediately.

VHF agents are characteristically stable viruses that are highly infectious fine-particle aerosols. Sending the patient home may lead to further spread of VHF to close contacts. Unnecessary transport should be avoided in patients where the diagnosis of VHF is suspected. In particular, air transport should be avoided since changes in ambient pressure with flight can further damage fragile capillary beds, resulting in pulmonary hemorrhage. Doxycycline is **not** effective therapy for VHF and may exacerbate the alterations in liver function tests.

QUESTION 3

Which of the following is *not* an accepted means to confirm the diagnosis of Ebola or Marburg virus?

a. **Demonstrating IgM or a 4-fold rise in IgG antibodies titers for the virus**
b. **Electron microscopy**
c. **Viral isolation**
d. **Reverse transcriptase polymerase chain reaction (RT-PCR) assay**
e. **Toxin isolation**

ANSWER: The correct answer is e. Scientists have not developed an assay to detect toxin proteins in Ebola or Marburg virus infections to date. Choices a-d are all acceptable means for making a diagnosis of Marburg or Ebola virus, and each of these tests will discriminate between the two Filovirus hemorrhagic fevers. Appropriate precautions should be observed in collection, handling, shipping, and processing of blood and/or other body fluid diagnostic samples. Due to the potential risks associated with handling these infectious materials, laboratory testing should be the minimum necessary for diagnostic evaluation and patient care. Clinical laboratory specimens should be placed in plastic bags that are sealed, and then transported in clearly labeled (as biohazardous material) durable, leakproof containers directly to the specimen handling area of the laboratory. Care should be taken not to contaminate the external surfaces of the container.[5] Viral isolation should not be attempted without maximum Biosafety Level (BSL-4) containment. RT-PCR identification of VHF agents may grow in use due to the need of maximum biosafety with viral isolation, time lag with IgM assay (need acute and convalescent sera) and equipment, as well as technical expertise needed with electron microscopy.

QUESTION 4

Given your high clinical suspicion of Filovirus hemorrhagic fever, you place the patient in isolation as instructed by the local public health official and the CDC. Which of the following isolation precautions should be instituted?

a. **Place the patient in a private room; universal precautions for hospital personnel.**
b. **Place the patient in a private room with negative pressure; barrier precautions for hospital personnel.**
c. **Place the patient in a private room with negative pressure; Biosafety Level 4 for hospital personnel.**
d. **Transfer the patient to the CDC mobile unit as soon as possible; Biosafety Level 4 for all contacts.**

ANSWER: The correct answer is b. The patient was vomiting. Patients with symptoms such as prominent cough, vomiting, diarrhea, as well as hemorrhage, should be placed in a negative-pressure room, given the potential for aerosolization of the virus and possibility of infecting other individuals. This being said, the available evidence indicates that the majority of reported nosocomial VHF cases, including Filovirus hemorrhagic fever, have been acquired by inoculation with virus-contaminated instruments or by direct contact with blood or body fluids from infected patients.

In addition to isolation in a negative pressure room, the caretakers of symptomatic patients should use barrier precautions to prevent skin or mucous membrane exposure to blood, other body fluids, or secretions. All persons entering a VHF patient's room should wear gloves and gowns to prevent contact with surfaces that may be contaminated. Further, face shields or masks with eye protection should be worn to prevent contact with blood, body fluids, or respiratory secretions that may be rendered airborne by coughing or sneezing. Leg and shoe covers should also be worn to minimize the risk of transmission outside of the room.

Patients with suspected VHF who do not have a prominent cough, vomiting, diarrhea, or hemorrhage can be placed in a private room with institution of universal precautions.[5] Individuals attempting virus isolation or cultivation must institute Biosafety Level 4 (BSL-4) precautions. Specimens in clinical laboratories should be handled in a class II biological safety cabinet following BSL-3 practices. Routine procedures can be used for automated analyzers and should be disinfected per manufacturer's recommendations. Serum used in laboratory tests should be pre-treated, though 100% inactivation of virus should not be assumed.[5]

QUESTION 5

Your patient expresses concern for his family. He has a 10-year-old son and his wife is 20 weeks pregnant. He reports that they are both feeling well with no symptoms of illness. What should you do regarding his family's care?

a. Isolate both his wife and 10-year-old son
b. Isolate his wife
c. Conduct daily medical surveillance of family members without isolating them
d. Admit his wife and son to the hospital

ANSWER: The correct answer is c. A contact is an individual who has been exposed to an infected person or to an infected person's secretions, excretions, or tissue within 3 weeks (conservative incubation period) of the patient's onset of illness. Contacts can be divided into 3 levels of risk: casual contacts, close contacts, and high-risk contacts. The patient's wife and son are high-risk contacts. The patient's wife and son should be placed under surveillance, given the clinical suspicion of VHF.

QUESTION 6

The CDC mobile laboratory calls you because they have confirmed a diagnosis of Ebola virus. Which of the following statements best describes the current therapy for Ebola virus?

a. Supportive care only
b. Supportive care + ribavirin
c. Supportive care + immunoglobulin
d. Supportive care + vaccine

ANSWER: The correct answer is a. The only current treatment of Ebola is supportive care. Aspirin and other antiplatelet agents or anti-clotting factor drugs should be avoided, as they may potentiate hemorrhage. Secondary bacterial infections are relatively common and should be aggressively sought and treated. Intravenous lines, catheters, and other invasive techniques should be avoided unless clearly indicated given the concern of diffuse hemorrhage. The diffuse nature of vascular involvement often leads to multi-system organ failure.

Ribavirin is ineffective against the Filoviruses. Immunoglobulin therapy for experimental animals infected with Ebola virus has been disappointing. There are no current vaccines for Ebola virus.

REFERENCES

1. Jahrling PB. Viral Hemorrhagic Fevers. In: Sidell FR, Takafuji ET, Franz DR, eds. *Textbook of Military Medicine: Medical Aspects of Chemical and Biologic Warfare*. Washington, DC: Borden Institute; 1997:592-601.
2. Isaacson M. Viral Hemorrhagic Fever hazards for travelers in Africa. *CID*. 2001;33:1701-1712.
3. Riquelme R, Riquelme M, Torres A, et al. Hantavirus Pulmonary Syndrome, Southern Chile. *EID*. 2003:1438-1443.
4. Peters CJ. California Encephalitis, Hantavirus Pulmonary Syndrome, and Bunyavirid Hemorrhagic Fevers. In Mandell GL, Bennett JE, Dolin R, eds. *Mandell, Douglas and Bennett's Principles and Practice of Infectious Diseases*. Edinburgh, UK: Churchill Livingstone; 2000:1850-1855.
5. CDC Update: Management of patients with suspected viral hemorrhagic fever—United States. *MMWR*. 1995;44:475-479.
6. Fisher-Hoch SP, Platt GS, Neild GH, et al. Pathophysiology of shock and hemorrhage in a fulminating viral infection (Ebola). *J Infect Dis*. 1985;152:887-894.
7. Preston R. *The Hot Zone: A Terrifying True Story*. New York, NY: Random House; 1995.
8. Leroy EM, Rouquet P, Formenty P, et al. Multiple Ebola Virus transmission events and rapid decline of central African wildlife. *Science*. 2003;303:387-397.
9. Balter M. On the trail of Ebola and Marburg Viruses. *Science*. 2003;290:923-925.
10. Vastag B. Ebola vaccines tested in humans, monkeys. *JAMA*. 2004;291:549-550.

SUGGESTED READING

1. CDC Update: Outbreak of Ebola Hemorrhagic Fever—Uganda, August 2000-January 2001. *MMWR*. 2001;50:73-76.
2. CDC Update: Filovirus infection associated with contact with nonhuman primates or their tissues. *MMWR*. 1990;39:404-405.
3. Geisbert TW, Marty A, Jahrling B. Viral Hemorrhagic Fevers. In: Roy MJ, ed. *Physician's Guide to Terrorist Attack*. Totowa, NJ: Humana Press; 2003:221-242.
4. Dieter Klenk H, Feldman H. Symposium on Marburg and Ebola Viruses. *Virus Res*. 2001;80:117-123.
5. Thacker PD. An Ebola epidemic simmers in Africa. *JAMA*. 2003;290:317-319.