Expedited Review

Rift Valley Fever

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ABSTRACT

Rift Valley fever is a viral disease that affects domestic animals and humans. In humans, Rift Valley fever causes a flu-like disease but occasionally leads to high morbidity and mortality. The disease is generally known in the African continent. However, cases started to appear in Saudi Arabia and Yemen. The objective of this review is to give a general briefing about the epidemiology, ecology and management of the disease.

Keywords: Rift valley, fever, hemorrhagic, outbreaks, viral, disease.

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Rift Valley fever (RVF) is an acute febrile viral disease that effects domestic animals (cattle, buffalo, sheep, goats and camels), as well as, humans.[1-3] Rift Valley fever may cause abortions of pregnant animals and high mortality rate in young livestock.[4,5] In humans, it usually causes an influenza-like disease but occasionally leads to more serious complications leading to high morbidity and mortality.[1-3] The agricultural and medical costs of controlling RVF outbreaks may lead to considerable economic loss.

Geographic location and geologic features of the Rift Valley. Africa's Great Rift Valley is a 6,000 mile crack in the earth's crust, stretching from Lebanon to Mozambique. One of its most dramatic sections slices through East Africa dividing Kenya into 2 segments, Geologists know that the Rift Valley was formed by violent subterranean forces that tore apart the earth's crust. These factors caused huge chunks of the crust to sink between parallel fault lines forcing up molten rock in volcanic eruptions.[6] Kenya's Rift Valley has a geologic feature called dambos.[6] These are shallow depressions located often near rivers filled with water during the rainy season. A dambo can be a kilometer in length and several hundreds of meters in width. Due to the frequent presence of water, tall papyrus and several other grasses grow around their edges. These dambos are breeding grounds for mosquitoes, even in the dry season, as they remain greener than other areas.

History of infection. Rift Valley fever, at least in Kenya, has been well known for over 60 years. As early as 1913, a disease fitting the description of RVF was blamed for the loss of sheep in the Rift Valley of Kenya.[6] In July 1930, Kenya was hit with very heavy rains that substantially increased the wetlands where mosquitoes bred, at the same time, occurrences of the disease increased.[3,4,6] However, it was not until scientists studied an outbreak of the disease in 1931 that a virus was isolated from the blood of a newborn lamb and later from the blood of sheep and cattle that was shown to cause the disease. In the 1930s, one of the carriers for the disease was found to be the mosquito. Those studying the disease made the connection between increased rains, wetlands, mosquitoes and disease and were eventually able to identify the associated virus. Since that time, major outbreaks have been noted throughout sub-Saharan Africa, with occasional outbreaks in other parts of the continent.[1-3,6]

Rift Valley fever outbreaks. Rift Valley fever outbreaks are often associated with periods of heavy rain after which the mosquito population flourishes. Outbreaks have been reported in Kenya, Sudan, Egypt, Cameroon, Central African Republic, Mali, Mauritania, Madagascar, Nigeria, Senegal, Somalia,

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South Africa, Tanzania, Zambia and Zimbabwe.[2,3,6-14] It is the first time for the disease to cross the boundaries of the African continent into Saudi Arabia and Yemen. Table 1 shows dates and regions of the outbreaks in the last half century.[2,3,6-14] One of the earliest reported outbreaks occurred in 1950-51 in Kenya resulting in the death of 100,000 sheep imported from Europe and especially susceptible to RVF. The 1977 Egypt outbreak was thought to be caused by an unexplained spread from Sudan possibly from the wind, imported camels or sheep, or by mosquitoes. The epizootic affected 25-50% of all sheep and cattle and ended in 1980. Among 200,000 humans fell ill, 18,000 clinical cases were confirmed with 598 deaths from hemorrhagic fevers. Human infection rates ran as high as 35%. In 1987, RVF broke out in Mauritania following the opening of Diama Dam at the mouth of the Senegal River, in an area where the virus was present but not generally recognised and resulted in more than 200 human deaths. The 1993 Egypt outbreak followed the opening of the Aswan Dam, started in that region and spread to other governorates all over the country. The 1997 outbreaks in Kenya and Somalia have been associated with periods of heavy rain, when standing floodwaters became available as breeding groups for the RVF mosquito vectors and resulted in large losses of domestic animals, as well as, more than 300 human deaths.

Situation in Saudi Arabia and Yemen. An internet search, on the Saudi Arabia Information Resource and the Press release issued by WHO, has revealed that the first suspected cases of RVF in Saudi Arabia (Jizan province) and the near borders in Northern Yemen (Wadi Mawr, El-Zuhrah district in Al-Hodeidah Governorate) were reported on the 10th of September 2000. As shown in Table 2, on the 17th of September, the Ministry of Health of Saudi Arabia reported deaths of 14 men and 2 women from Rift Valley fever. Laboratory analysis at the United States' Centers for Disease Control (CDC) in Atlanta confirmed the diagnosis of RFV in Saudi Arabia. On the 23rd of the same month, 96 males and 17 females were reported. Giving the breakdown of figures by region, 98 cases were reported in Jizan, 9 in Asir and 5 in Al-Qunfuda and one case in Najran. Two days later, the number of cases rose and from the newly reported cases, 2 were detected in Riyadh coming from Jizan, one case in Jeddah, 3 cases in Asir and one in Najran. Among the new cases, reported by the 1st of October there was one more case in Riyadh and one in Asir. In Yemen, the Ministry of Health has reported 113 human cases including 30 deaths of RVF on the 26th of September 2000. Also, 266 animal deaths have been reported mainly of sheep and goats but some cattle and camels have been affected. On September 29th, 134 suspected cases of RVF including 31 human deaths were reported. On October 9th, a total of 321 cases of RVF with 32 deaths and case fatality rate of 10% were reported. The latest figures reported for Yemen up to 25th of October showed a total of 653 suspected cases including 80 deaths.

Table 1 - Rift Valley fever outbreaks in the last half century.

Year	Country
1950-1951	Kenya
1967-1970	Nigeria
1969	Central African Republic
1976-1977	Sudan
1977-1980	Egypt
1987	Mauritania
1990-1991	Madagascar
1993	Egypt - Senegal
1997	Kenya - Somalia
1999	South Africa
2000	Yemen - Saudi Arabia

Table 2 - Cumulative incidence of Rift Valley fever outbreak in Saudi Arabia.

	Suspected cases	Deaths	Recovery
17/09/2000	38	16	-
23/09/2000	113	24	19
25/09/2000	129	27	22
29/09/2000	160	33	-
01/10/2000	233	52	62
08/10/2000	291	64	104
10/10/2000	316	64	106
19/10/2000	409	80	188
23/10/2000	443	85	-
02/11/2000	546	93	353
09/11/2000	611	100	443

Causative agent.[15-18] The RVF virus belongs to the family bunyaviridae. The bunyaviruses were at one time placed together with other groups in the large taxonomic group known as arboviruses. However, sufficient information about this group has since been obtained to give it the status of a family called the Bunyaviridae. The prefix 'bunya' refers to a place in Africa (Bunyamwera) were the family prototype (Bunyamwera virus) was first isolated. At

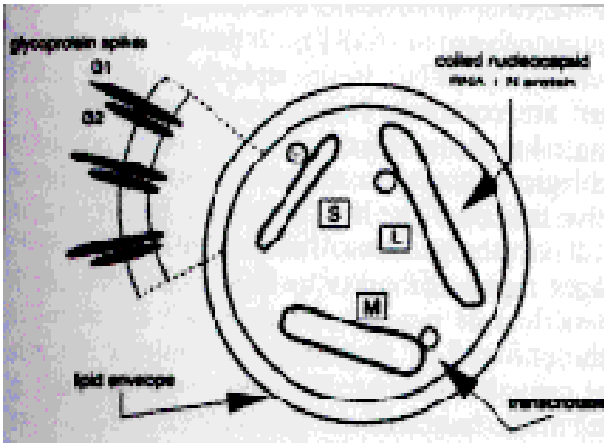

Figure 1 - Diagram representing the structure of Rift Valley virus. RNA- Ribonucleic acid; S - small, L - large, and M - medium.

present the family contains more than 250 viruses and is divided into 5 genera: Bunyavirus, Hantavirus, Phlebovirus, Uukuvirus and Nairovirus. Rift Valley fever virus belongs to the genus Phlebovirus. The viruses in this family inhabit arthropods (mosquitoes and other blood sucking insects) and vertebrates including humans. Structurally, the RVF virus (Figure 1) possess a helical nucleocapsid (viral nucleic acid is closely associated with the protein capsid forming a coiled shape) and 3 single-stranded, negative sense (and ambisense) ribonucleic acids (RNAs). The viruses are lipid-enveloped spherical structures, 80 nm to 120 nm in diameter and contain 5 nm to 10 nm surface projections (spikes). The virus lipid envelope contains 20-30% lipids totally derived from the host cell membrane and is acquired during the final stages of replication. The virion spikes are made up of 2 surface glycoproteins (G1 and G2). The Gl or G2 proteins mediate the attachment of the virus to the host cell receptors (to initiate the entrance of the virus into the cell), serve as hemagglutinin (attach to receptors on red blood cells causing these cells to agglutinate) and are the targets for the host's neutralising antibodies. The viral capsid protects the enclosed nucleic acid and facilitates assembly and package of viral genetic information. The virion core contains a single nucleocapsid protein; termed N. The capsid protein is the target for the host's neutralising antibodies. The virus also encodes a virion-associated polymerase that is liberated after the virus is uncoated and is responsible for initiating the early steps of virus replication. The 3 negative-strand RNA genomic segments are termed large (L), medium (M), and small (S). The Phleboviruses exhibit a remarkable variation, in that the S RNA segment contains both negative (3' half) and positive sense (5' half) information. This unique arrangement of genetic information is termed ambisense. The L RNA segment likely encodes the virion-associated RNA polymerase. The M RNA segment has been shown to encode a polyprotein that is processed in infected cells to form the G1 and G2 glycoproteins, as well as, a nonstructural protein, designated NS_M. The S RNA segment has been shown to encode the N protein and a nonstructural protein NS_S. The virus replicates in the cytoplasm of the host cell. Following attachment and adsorption of the virus to specific receptors on the surface of the cell, penetration occurs as either the host cell engulfs the virus or the viral envelope fuses with the host envelope (endocytosis). Then the uncoated virion is delivered in the cytoplasm of the cell and the viral nucleic acid is released. Following infection, the negative sense, 3' half of this virion RNA segment is transcribed by the virion associated polymerase into positive-sense mRNA that are translated on host ribosomes. The positive-sense portion (5' half) of the viral genome is not translated directly. However, following transcription (replication) of the entire segment to form a complementary strand, selective transcription occurs to provide a mRNA encoding the non-structural protein NS_S. This is followed by translation of mRNA into viral proteins, assembly and package of virus that is liberated by budding during which it gains the lipid envelope.

The RVF virus can survive several months at 4°C but is inactivated in serum by 56°C for 120 minutes. The virus is resistant to alkaline pH but inactivated by pH less than 6.8. Also, the virus can be inactivated by ether, chloroform and strong solutions of sodium or calcium hypochlorite (residual chlorine should exceed 5000ppm). The RVF virus survives in dried discharges and can survive contact with 0.5% phenol at 4°C for 6 months and can multiply in some arthropod vectors.

Vector and mode of transmission.[1-3,5,7,19-24] Rift Valley fever virus primarily spreads among animals and humans by the bite of infected mosquitoes. A wide variety of mosquito species (Aedes, Culex, Mansonia, Anopheles, Entremapodites, etc.) act as the vector for transmission of RVF virus; in different regions different species of mosquito may prove to be the predominant vector. Uninfected mosquitoes feed on infected viremic animals or humans and transmit the infection to another host in their subsequent feed. Also, Aedes mosquitoes are capable of transovarial transmission to offspring via eggs, so new generations of infected mosquitoes may hatch from their eggs. This provides a durable mechanism for maintaining the virus in nature, as the eggs of these mosquitoes may survive for periods of up to several years in dry conditions. During periods of inundation or rainfall, eggs hatch and the infected mosquito population flourishes and transmits the virus to the host. Rift Valley fever virus was isolated from both male and female mosquitoes. Possibly other blood sucking insects, such as sandfly and culicoides, could act as vectors but their role appears to be limited in biological and mechanical transmission. Also, transmission through direct handling of infected animals or meat and contact

with blood and other body fluids of infected animals were documented. This exposure can result from the slaughtering or handling of infected animals or touching contaminated meat during the preparation of food. Consumption of raw milk of infected animals could be a possible mode of transmission but consumption of meat of infected animals does not appear to be a common means of transmission. Person-to person transmission has not been reported in persons whose contact with an infected patient occurred during the incubation period. However, contact with blood and other body fluids of infected humans especially during the later stages of illness which are characterized by vomiting or hemorrhage could spread the infection. Airborne transmission during work with virus cultures or laboratory samples containing the virus was also reported among laboratory workers. Inoculation through broken skin or wound could be another means of transmission.

Mechanism of organ involvement.[15-18] Rift Valley fever virus is cytopathic, it replicates to high titre and tends to target the liver (focal necrosis), red blood cells (hemagglutination) and brain (necrotic encephalitis). It is thought that after infection, the virus moves from the skin to draining lymph nodes, where it replicates. Efferent lymphatics spread the virus throughout the body. As the liver is rapidly invaded, hepatocytes become involved. The virus may also cross the blood-brain barrier and infect neurons and glia. Meningoencephalitis and retinitis develop.

Non-human host.[2-5,7] Many types of animals may be infected with RVF virus and disease may be severe in many domestic animals including cattle, sheep, goats and camels. Sheep appear to be more susceptible than cattle and goats are less susceptible. Exotic breeds introduced into an endemic area appear to be more susceptible than breeds adapted to local conditions. Clinical signs in animals vary considerably and disease progression and severity are generally inversely proportional to age. Adult cattle and sheep may suffer mortality rates of 10-30% or higher, depending on the nutritional state of the animal; but in animals fewer than 7 days old, fatality rates may approach 100%. The disease in animals is characterized by a short incubation period, fever, hepatitis, abortion, and death. Widespread abortion, infertility, and rapidly fatal neonatal disease are typical of outbreaks among cattle and sheep. Other overt signs are inconsistent, but include congestion of mucous membranes, injected conjunctiva, hyperemia of the oral mucosa, mucopurulent nasal discharge, salivation, vomiting, anorexia, general weakness, an unsteady gait, fetid diarrhoea, and a rapid decrease in milk production. A definite leukopenia, most severe in younger animals, which corresponds to maximal viremia and temperature response, is seen, often followed by leukocytosis in later stages of the disease. Elevated serum aspartate aminotransferase (AST), gamma glutamyl transferace (GGT), lactic dehydrogenase (LDH) values are common. No long-term carrier state in animals has been identified. The most consistent pathologic changes in all animal species affected involve the liver. The liver appears to be the primary site of virus replication. Initial mild hepatocellular changes rapidly progress to final massive necrosis. Hepatic lesions in adult ruminants are not as severe as those found in neonates, but multiple necrotic areas may be present. Coagulated blood may be found in the lumen of the gallbladder in those cases with marked hemorrhage in the liver. Hemorrhages are seen infrequently in the intestinal tract.

Human host. The incubation period varies from 2 to 6 days. Some people show no symptoms. Others show an influenza-like illness with sudden onset of fever of more than 38°C for more than 48 hours (possibly with a biphasic course), headache, weakness, nausea, myalgia, backache, as well as, abdominal pain, diarrhoea and photophobia. The symptoms last for 2 to 7 days after which the immune response to infection becomes detectable with the appearance of IgM and IgG and the patient recovers. While most human cases are relatively mild, a small proportion of patients develop a much more severe disease. These complications are in the form of ocular lesions, meningioencephalitis and hemorrhagic fever.[1-3,8,9] The most common complications are the ocular lesions (0.5-2% of cases) that ranged from blurred vision syndrome to macular exudate like lesions, retinal detachment and retinitis.[11,25,26] The onset of eye disease is usually one to 3 weeks after the onset of first symptoms. The patient presents with severe localized pain, blurring or loss of vision. When the lesions are in the macula, some degree of permanent visual loss may result in 1-10% of patients with ocular lesions. Death in patients with ocular disease is uncommon. Meningoencephalitis appears in less than 1% of cases, one to 3 weeks after the first symptoms appear.[1-4,7] The patient develops severe headache, vertigo, seizures or coma. Still deaths in patients with meningoencephalitis is uncommon. Rift Valley fever may also manifest itself as hemorrhagic fever in less than 1% of cases.[1-4,7,27] Two to 4 days after the onset of illness, the patient shows evidence of acute fulminant hepatitis with hepatic failure and hepatorenal syndrome, disseminated intravascular coagulation (DIC) and hemolytic anemia with hemoglobin less than 3gm/dL. The patient presents with hemorrhagic phenomenon as hematemesis, melena, purpuric rash and bleeding gums. Jaundice was also reported but in a low percentage of patients. Most patients with severe disease have elevated creatinine phosphokinase enzyme (CPK). Despite the marked elevation of liver enzymes AST and alanine aminotransferase (ALT) more than triple fold,

bilirubin level remains normal or slightly elevated and alkaline phosphatase (ALP) remain normal. The lesion in the liver appears in the form of focal or generalized hepatic necrosis (white necrotic foci of about 1 mm in diameter) with hepatic congestion, enlargement and discoloration accompanied by subcapsular hemorrhages. Patients with hemorrhagic fever may remain viremic for up to 10 days and case-fatality rate is as high as 50%. Thus most fatalities occur in patients with hemorrhagic fever. The total case fatality rate has varied widely in various documented epidemics but, overall, is less than 1%.

High risk groups.[1-3,22,23] This group comprises people who sleep outdoors at night in areas where outbreaks occur, animal herdsmen, slaughterhouse workers, veterinarians, butchers and others who handle tissues of infected animals in areas where the virus is present, health professionals in contact with patients during late stages of disease, laboratory technicians working with infected samples and international travelers visiting areas during period of epidemic.

Laboratory diagnosis.[1-3,22-24,27] 1. Procedures: Several approaches may be used in the diagnosis of RVF either to identify the virus itself or the presence of specific antibodies to the virus. a) Identification of the agent includes (i) virus isolation by inoculation of mice or hamsters, inoculation of 1-2-day-old lambs, inoculation of embryonated chicken eggs, tissue culture inoculation (Vero, CER, BHK-21, mosquito line cells or primary calf, lamb and goat kidney and testis cells) in combination with immunofluorescence, viral antigen identification by immunofluorescence in cryostat sections or in impression smears of liver, spleen and brain. Also by complement fixation and immunodiffusion on tissue suspensions. (ii) Antigen detection in blood by immunodiffusion or enzyme immunoassay. (iii) Polymerase chain reaction (PCR), a molecular method for detecting the viral genome, may be used to detect the virus itself in blood during the viremic phase of illness or postmortem tissues. b) Serological tests such as (i) enzyme-linked immunosorbent assay (ELISA or EIA methods), (ii) virus neutralisation, (iii) fluorescent antibody test, (iv) hemagglutination inhibition, (v) plaque reduction neutralization, (vi) complement fixation, (vii) immunodiffusion. 2. Samples such as a) heparinized or clotted blood b) plasma or serum, c) tissue samples of liver, spleen, kidney, lymph node, brain from aborted fetus. Specimens should be submitted preserved in 10% buffered formalin and in glycol/saline and transported at 4°C.

Prevention and control.[1-7,21,22,27,28] There are several measures suggested to prevent and control RVF epidemic. These measures target animals, mosquitoes and humans. Healthy animals can be protected by applying a sustained program of animal vaccination. Both live attenuated and killed vaccines have been developed for veterinary use. The live vaccine Smithburn strain requires only one dose, was supposed to produce long-lasting immunity but proved to confer immunity for 3 years. However, the presently available vaccine may cause abortion or birth defects if given to pregnant animals. The killed vaccines do not cause these effects but require 2 inoculations and annual revaccination to produce protective immunity. A live attenuated vaccine (MP-12) has shown to be safe and efficacious against virulent virus challenge and is safe in pregnant and neonatal livestock but is still under investigation. Prohibiting use of common needles for vaccination, disallowing the movement of non-vaccinated animals from affected areas, spraying of animals by using safe insecticides to eradicate blood sucking insects., performing periodic surveillance of susceptible animals to assess immune status of vaccinated animals after vaccination campaigns and applying quarantine measures for regular testing of imported animals are other preventive measures to be considered. For infected animals, notification of any sick or dead animal, as well as, rapid burial of dead animals should be performed. Measures to combat mosquitoes should be adopted such as removal of stagnant water and or any water collection to prevent mosquitoes from laying their eggs, weekly treatment of any water collection with insecticides (Tampos) in appropriate concentration to avoid maturation of mosquito larvae, application of insecticide (Icon) every other day, half an hour before sunrise in all gardens to reduce the number of mosquitoes, removal of any stagnant water and possible water collection containers as discarded tires, barrels and old buckets as they can act as water collection sites. Moreover, measures to protect humans include a) Individual measures such as sleeping indoors, using bed nets during sleep, putting screens on windows, wearing clothes that protect the whole body such as long pants, socks, long sleeved blouses, long shirts and trousers to avoid mosquito bites, applying mosquito repellent containing DEET (N, N-diethylmetatoluamide) to exposed areas of the body to reduce the number of bites especially in children, using spray on clothing and skin except face, avoid peaks of mosquitoes activities at sun-down and sun-rise, avoid sitting near vegetation during evening hours where mosquitoes reside, avoiding contact with animals, if not possible wearing gloves, masks and gowns for such contacts particularly with sick animals or their tissues, washing hands well after contact with animals, avoid buying meat imported from East Africa or local meat especially from Southern Saudi Arabia and avoid drinking unboiled milk. b) Community measures which include health education to increase public awareness about the disease and the preventive measure, implementation of descriptive and analytic epidemiologic research programs to learn more about the magnitude,

distribution and determinants of the disease, implementation of active disease surveillance, as well as, seroprevalence outside the area of active virus transmission and development of check measures at air, sea and land entry points to test national and international travelers from epidemic areas. c) Prevention of occupational hazards. For the present, there is no vaccine available but the inactivated vaccine (MP-12) has been developed for human use. This vaccine is not licensed and is not commercially available but has been used experimentally to protect veterinary and laboratory personnel at high risk of exposure to RVF. All persons in contact with infected animals, their tissue, blood or other body fluids should wear masks, gloves and gowns. Health professionals caring for infected humans especially in late stages should wear gloves and gowns. In addition, face shields or surgical masks and eye protection should be worn by persons coming with approximately 3 feet of the patient. The need for other barriers, such as leg and shoe coverings, depends on the potential for fluid contact, the clinical symptoms and the procedure performed. After leaving patients' rooms, all protective barriers used should be removed and disinfected. Laboratory investigations for suspected cases should be handled by trained staff and processed in suitably equipped laboratories. Laboratory staff should be aware of the nature of the sample and wear gloves, masks and other protective clothing. Persons with percutaneous or mucocutaneous exposure to blood or other body fluids from a patient should immediately wash the affected skin surfaces with soap and water. Application of an antiseptic solution or handwashing product may be considered also, although the efficacy of this supplemental measures is unknown. Mucous membranes (e.g. conjunctiva) should be irrigated with copious amounts of water or eye wash solution. Exposed persons should receive medical evaluation and follow-up management. d) Travelers' measures. Travelers can reduce their risk of exposure by avoiding contact with livestock, minimizing exposure to arthropod bites and following the general preventive measures.

Management of suspected cases.[1-7,20-28] Include 1) General Measures: notification of suspected cases., ascertainment of cases using diagnostic tests and identification, screening and surveillance among contacts. 2) Recommended investigations for suspected cases include complete blood count, urea, creatinine, AST, ALT, ALP, bilirubin, albumin, prothrombin time (PT), partial prothrombin time (PTT), LDH and CPK. Hepatitis A IgM and IgG, hepatitis B surface antigen (HBsAg), hepatits B core antibody (HBcAB), hepatitis C antibody (HCV-Ab), RFV serology & viral culture. 3) Management of un-hospitalized patients includes Isolation at home, contacts should wear masks, gloves and protective clothes when in contact with patients, safe disposal of patients linens and clothes, close follow-up for 6 weeks as outpatient in general clinic and ophthalmology clinic and use of general supportive measures. 4) Indications for admission to hospital are: shock (systolic blood pressure (SBP) <90 mmHg or diastolic (DBP) <60mmHg), decreased urine output, AST & ALT > 200U/mL, bilirubin > 100 mol/L, thrombocytopenia < 100,000/mm^3, anemia < 8gm/dL, confusion or other central nervous system (CNS) manifestations, creatinine > 150mol/L, evidence of DIC (increased PTT with thrombocytopenia). 5) Management of hospitalized patients. Currently there is no specific treatment for RVF and the mainstay is general supportive therapy especially of severe cases. Ribavirin has shown some promise as an antiviral. Other treatments which also show promising effect are interferon, immune modulators and convalescent phase plasma. Patients should be placed in single rooms preferably with negative airway pressure compared to the outside (or suction fans) and with separate exhaust system to prevent possible airborne infection. Soiled linens should be placed in clearly labelled leak-proof bags and transported to decontamination area. Linens can be decontaminated in a gravity displacement autoclave or incinerated. Alternatively linens can be laundered using normal hot water cycle with bleach and placed directly into washing machines. There is no evidence for transmission of infection through sewage; however, measures should be taken to reduce the infectivity of bulky blood or other body fluids. These fluids should be either autoclaved, processed in a chemical toilet or treated with several ounces of household bleach for at least 5 minutes before flushing or disposal in a drain connected to a sanitary sewer. Solid medical wastes such as contaminated needles, syringes and tubing should be either incinerated or decontaminated by autoclaving or immersion in a suitable chemical germicide. Patients are introduced to the intensive care unit in case of shock, hepatic failure, hepatorenal syndrome, disseminated intravascular coagulation, respiratory failure, coma or seizures. Hemodialysis is indicated in patients with volume overload, hyperkalemia, metabolic acidosis, uremic encephalopathy or uremic pericarditis. If the patient dies, handling of the body should be minimal, the corpse wrapped in leak-proof material and buried. 6) Hospital discharge is allowed in cases of improvement in general status, declining liver symptoms, recovery of mental functions, stable renal functions for 2 consecutive days, recover from disseminated intravascular coagulation, hemoglobin level > 6 gm/dL for 2 consecutive days, platelets level > 50,000mm^3 for 2 consecutive days. Patients should be followed for up to 6 weeks in the medical or general clinic, as well as, in the ophthalmology clinic.

In conclusion, RVF that was previously confined to the African continent has spread to the east of the Red Sea. The disease in humans is often mild but occasionally leads to severe morbidity and mortality.

Currently there is no vaccine to prevent the disease and no specific treatment of infected cases. Many questions regarding the disease epidemiology and ecology remain unanswered. A number of challenges remain for the prevention and control of RVF outbreaks.

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