

Rift Valley Fever

*Infectious Enzootic
Hepatitis of Sheep and Cattle*

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Importance

Rift Valley fever (RVF) is a zoonotic, arthropod-borne viral disease important in domestic ruminants. This disease is characterized by high mortality rates in young animals and abortions in pregnant ruminants. Rift Valley fever is endemic in sub-Saharan Africa. Epidemics occur in this region when heavy rainfalls cause infected mosquito eggs to hatch, and large numbers of susceptible animals are present. Rift Valley fever first appeared outside Africa in 2000, when outbreaks were reported in Saudi Arabia and Yemen.

Rift Valley fever epizootics are often accompanied by human disease. Many human cases are caused by occupational exposure to blood and tissues from infected animals, but mosquito-borne transmission can cause epidemics. The most common form of the disease is a self-limiting, flu-like illness; however, ocular disease and rare cases of fatal hemorrhagic fever also occur.

Etiology

Rift Valley fever results from infection by the Rift Valley fever virus, an RNA virus in the genus *Phlebovirus* (family Bunyaviridae).

Geographic Distribution

The Rift Valley fever virus is found throughout most of Africa. The disease is endemic in southern and eastern Africa, where outbreaks occur at irregular intervals. Epidemics have also been reported in Egypt, Saudi Arabia and Yemen.

Transmission

Rift Valley fever is transmitted by mosquitoes and is usually amplified in ruminant hosts. In endemic regions, cases can occur sporadically or in epidemics. The virus appears to survive in the dried eggs of *Aedes* mosquitoes; epidemics are associated with the hatching of these mosquitoes during years of heavy rainfall and localized flooding. In Africa, outbreaks typically occur in savannah grasslands every 5 to 15 years, and in semi-arid regions every 25 to 35 years. Once it has been amplified in animals, the RVF virus can also be transmitted by other vectors, including many mosquito species and possibly other biting insects such as ticks and midges. The virus can be transmitted *in utero* to the fetus. It has also been found in semen and raw milk.

Humans do not seem to be infected by casual contact with live hosts, but can be infected by aerosols or direct contact with tissues during parturition, necropsy, slaughter, laboratory procedures or meat preparation for cooking. *In utero* transmission to a human infant was first reported in 2006.

Both animals and humans theoretically have the potential to introduce Rift Valley fever into new areas by infecting mosquitoes.

Disinfection

Under optimal conditions, the Rift Valley fever virus remains viable in aerosols for more than an hour at 25°C (77 °F). In a neutral or alkaline pH, mixed with serum or other proteins, the virus can survive for as long as four months at 4°C (40 °F) and eight years below 0° C. It is quickly destroyed by pH changes in decomposing carcasses.

The Rift Valley fever virus is susceptible to low pH (≤ 6.2), lipid solvents and detergents, and solutions of sodium or calcium hypochlorite with residual chlorine content greater than 5000 ppm.

Infections in Humans

Incubation Period

In humans, the incubation period is 2 to 6 days.

Clinical Signs

Infection with the Rift Valley fever virus usually results in an asymptomatic infection or a mild to moderate, non-fatal, flu-like illness with fever and liver abnormalities. The

symptoms of uncomplicated infections may include fever, headache, generalized weakness, dizziness, weight loss, myalgia and back pain. Some patients also have stiffness of the neck, photophobia and vomiting. Most people recover spontaneously within two days to a week.

Complications including hemorrhagic fever, meningoencephalitis or ocular disease occur in a small percentage of patients. Hemorrhagic fever usually develops two to four days after the initial symptoms. The symptoms may include jaundice, hematemesis, melena, a purpuric rash, petechiae and bleeding from the gums. Hemorrhagic fever frequently progresses to frank hemorrhages, shock and death.

Ocular disease and meningoencephalitis are usually seen one to three weeks after the initial symptoms. The ocular form is characterized by retinal lesions and may result in some degree of permanent visual impairment. Death is rare in cases of ocular disease or meningoencephalitis.

Communicability

Virus titers in infected humans are theoretically high enough to infect mosquitoes and introduce Rift Valley fever into new areas. The virus can be found in the blood and tissues.

Diagnostic Tests

The Rift Valley fever virus can be isolated from the blood, brain, liver or other tissues; in living hosts, viremia usually occurs only during the first three days of fever. The virus can be grown in numerous cell lines including baby hamster kidney cells, monkey kidney (Vero) cells, chicken embryo reticulum, and primary cultures from cattle or sheep. Hamsters, adult or suckling mice, embryonated chicken eggs or 2-day-old lambs can also be used.

Viral antigens and RNA can be detected in blood and tissue samples by various antigen detection tests and reverse transcription polymerase chain reaction (RT-PCR) assays. Enzyme-linked immunoassay (ELISA) and other serologic tests can detect specific IgM or rising titers.

Treatment

No specific treatment, other than supportive care, is available; however, ribavirin has been promising in animal studies. Interferon, immune modulators and convalescent-phase plasma may also prove to be helpful. Most cases of Rift Valley fever are relatively mild, brief illnesses and may not require treatment.

Prevention

Mosquito repellents, long shirts and trousers, bednets, and other arthropod control measures should be used to prevent transmission by mosquitoes and other potential insect vectors. Outdoor activities should be avoided, if possible, during periods of peak mosquito activity. Insecticides may be helpful. During epidemics, vaccination of susceptible animals can prevent amplification of the virus and protect people as well as animals.

Barrier precautions should be used whenever contact may occur with infectious tissues or blood from animals; recommended measures include personal protective equipment such as protective clothing, gloves and goggles. Diagnostic tissue samples should be processed by trained staff in appropriately equipped laboratories. Universal precautions are recommended for healthcare workers who care for patients with confirmed or suspected Rift Valley fever. Barrier techniques are recommended when nursing hospitalized patients.

A human vaccine has been developed, but has limited availability. Additional vaccines are under investigation.

Morbidity and Mortality

Humans are highly susceptible to Rift Valley fever. Most cases develop in veterinarians, abattoir workers and others who work closely with blood and tissue samples from animals. During outbreaks in animals, mosquitoes may spread the virus to humans and cause epidemics.

Most people with Rift Valley fever recover spontaneously within a week. Ocular disease is seen in approximately 0.5% to 2% of cases, and meningoencephalitis and hemorrhagic fever in less than 1%. The case fatality rate for hemorrhagic fever is approximately 50%. Deaths rarely occur in people with eye disease or meningoencephalitis, but 1% to 10% of patients with ocular disease have some permanent visual impairment. The overall case fatality rate for all patients with Rift Valley fever is less than 1%.

Infections in Animals

Species Affected

Rift Valley fever can affect many species of animals including sheep, cattle, goats, buffalo, camels, and monkeys, as well as gray squirrels and other rodents. The primary amplifying hosts are sheep and cattle. Viremia without severe disease may be seen in adult cats, dogs, horses and some monkeys, but severe disease can occur in newborn puppies and kittens. Rabbits, pigs, guinea pigs, chickens and hedgehogs do not become viremic.

Incubation Period

The incubation period can be as long as 3 days in sheep, cattle, goats and dogs. In newborn lambs, it is 12 to 36 hours. Experimental infections usually become evident after 12 hours in newborn lambs, calves, kids and puppies.

Clinical Signs

The clinical signs vary with the age, species and breed of the animal. In endemic regions, epidemics of Rift Valley fever can be recognized by high mortality rates in newborn animals and abortions in adults.

Rift Valley fever is usually most severe in young animals. In lambs, a biphasic fever, anorexia and lymphadenopathy may be followed by weakness and death within 36 hours. Hemorrhagic diarrhea or abdominal pain can also be seen. The youngest animals are most severely affected; in

neonates, the mortality rate may reach 90% to 100%. Similar symptoms occur in young calves: fever, anorexia and depression are typical, with mortality rates of 10% to 70%.

Abortions are the most characteristic sign in adult sheep and cattle. Other symptoms that may occur in adult sheep include fever, weakness, a mucopurulent nasal discharge (sometimes bloodstained), melena, hemorrhagic or foul-smelling diarrhea, and vomiting. In adult cattle, fever, anorexia, weakness, excessive salivation, fetid diarrhea and decreased milk production have been reported. Icterus may also be seen, particularly in cattle.

Similar but milder infections occur in goats. Adult camels do not develop symptoms other than abortion, but young animals may have more severe disease. Viremia without severe disease may be seen in adult cats, dogs, horses and some monkeys, but severe disease can occur in newborn puppies and kittens.

Post Mortem Lesions [Click to view images](#)

The most consistent lesion is hepatic necrosis; the necrosis is more extensive and severe in younger animals. In aborted fetuses and newborn lambs, the liver may be very large, yellowish-brown to dark reddish-brown, soft and friable, with irregular patches of congestion. Multiple gray to white necrotic foci are usually present, but may only be visible microscopically. The liver lesions are usually less severe in adult animals and may consist of numerous pinpoint reddish to grayish-white necrotic foci.

Additional lesions may include jaundice, widespread cutaneous hemorrhages and fluid in the body cavities. The peripheral lymph nodes and spleen are typically enlarged and edematous, and often contain petechiae. The walls of the gallbladder are often edematous, with visible hemorrhages. A variable degree of inflammation or hemorrhagic enteritis can sometimes be found in the intestines. In lambs, numerous small hemorrhages typically occur in the abomasal mucosa, and the small intestine and abomasum may contain dark chocolate-brown contents with partially digested blood. In addition, petechial and ecchymotic hemorrhages may be seen on the surface of other internal organs. Microscopically, hepatic necrosis is the most prominent lesion.

Communicability

Infections are typically transmitted by mosquitoes and not by direct contact; however, during parturition, necropsy or slaughter, viruses in the tissues can become aerosolized or enter the skin through abrasions. The Rift Valley fever virus has also been found in raw milk and may be present in semen.

Diagnostic Tests

Rift Valley fever can be diagnosed by isolation of the virus from the blood of febrile animals. The RVF virus can also be recovered from the tissues of dead animals and aborted fetuses; the liver, spleen and brain are generally used. This virus can be grown in numerous cell lines including baby hamster kidney cells, monkey kidney (Vero) cells, chicken embryo reticulum and primary cultures from cattle or sheep.

Hamsters, adult or suckling mice, embryonated chicken eggs or two-day-old lambs can also be used.

Viral titers in tissues are often high, and a rapid diagnosis can sometimes be made with complement fixation, neutralization or agar gel diffusion tests on tissue suspensions. Viral antigens can also be detected by immunofluorescent staining of impression smears from the liver, spleen or brain. Enzyme immunoassays and immunodiffusion tests can identify virus in the blood. RT-PCR testing can detect viral RNA.

Commonly used serologic tests include virus neutralization, ELISA and hemagglutination inhibition tests. Immunofluorescence, complement fixation, radioimmunoassay and immunodiffusion are used less frequently. Cross-reactions with other phleboviruses can occur in serologic tests other than virus neutralization.

Treatment

No specific treatment, other than supportive care, is available.

Prevention

Vaccines are generally used to protect animals from Rift Valley fever in endemic regions. During epidemics, vaccination of susceptible animals can prevent amplification of the virus and protect people as well as animals. Attenuated and inactivated Rift Valley fever vaccines are both available. Attenuated vaccines produce better immunity; however, abortions and birth defects can occur in pregnant animals. Subunit vaccines are in development.

Additional, less commonly used, preventative measures include vector controls, movement of stock to higher altitudes, and the confinement of stock in insect-proof stables. These control methods are often impractical, or are ineffective because they are instituted too late. The movement of animals from endemic areas to RVF-free regions can result in epidemics.

Morbidity and Mortality

Epidemics of Rift Valley fever tend to occur at intervals, when heavy rainfalls cause infected mosquito eggs to hatch and a susceptible animal population is present. Outbreaks are characterized by large numbers of abortions and high mortality in neonates. Indigenous cattle may have asymptomatic infections, while more severe disease is seen in exotic species.

The mortality rate can be very high in young animals including neonatal ruminants, puppies and kittens, with fatalities decreasing in older age groups. The mortality rate in newborn lambs is 90% to 100%, while the mortality rates in adult sheep can vary from 5% to almost 100% in different epidemics and on different farms. Deaths are most common in pregnant ewes that abort. The estimated mortality rate in calves varies from 10% to 70%, but fewer than 10% of infections in adult cattle are usually fatal.

Abortion rates vary from 5% to almost 100% in ewes. Although up to 85% of cattle have aborted in some out-

breaks, the abortion rate is typically less than 10% in this species. Abortion rates in camels can be as high as in cattle.

Internet Resources

- Centers for Disease Control and Prevention (CDC) Health Topics. <http://www.cdc.gov/az.do>
- Manual for the Recognition of Exotic Diseases of Livestock <http://www.spc.int/rahs/>
- Medical Microbiology <http://www.gsbs.utmb.edu/microbook>
- OIE International Animal Health Code http://www.oie.int/eng/normes/mcode/A_summry.htm
- Preparation of Rift Valley Fever Contingency Plans. FAO Animal Health Manual No. 15 <http://www.fao.org/DOCREP/005/Y4140E/y4140e00.htm#TopOfPage>
- The Merck Veterinary Manual. <http://www.merckvetmanual.com/mvm/index.jsp>
- United States Animal Health Association. Foreign Animal Diseases. http://www.vet.uga.edu/vpp/gray_book02/fad/index.php
- World Health Organization (WHO). Rift Valley Fever Fact Sheet <http://www.who.int/inf-fs/en/fact207.html>
- World Organization for Animal Health (OIE). Manual of Diagnostic Tests and Vaccines for Terrestrial Animals http://www.oie.int/eng/normes/mmanual/a_summry.htm

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