

Rift Valley fever

Overview

Rift Valley Fever (RVF) is a viral zoonosis that primarily affects animals but also has the capacity to infect humans. Infection can cause severe disease in both animals and humans, leading to high rates of disease and death. The disease also results in significant economic losses due to death and abortion among RVF-infected livestock.

RVF virus is a member of the Phlebovirus genus, one of the five genera in the family Bunyaviridae. The virus was first identified in 1931 during an investigation into an epidemic among sheep on a farm in the Rift Valley of Kenya. Since then, outbreaks have been reported in sub-Saharan and North Africa. In 1997-98, a major outbreak occurred in Kenya, Somalia and Tanzania and in September 2000, RVF cases were confirmed in Saudi Arabia and Yemen, marking the first reported occurrence of the disease outside the African continent and raising concerns that it could extend to other parts of Asia and Europe.

TRANSMISSION TO HUMANS

- The vast majority of human infections result from direct or indirect contact with the blood or organs of infected animals. The virus can be transmitted to humans through the handling of animal tissue during slaughtering or butchering, assisting with animal births, conducting veterinary procedures, or from the disposal of carcasses or fetuses. Certain occupational groups such as herders, farmers, slaughterhouse workers and veterinarians are therefore at higher risk of infection. The virus infects humans through inoculation, for example via a wound from an infected knife or through contact with broken skin, or through inhalation of aerosols produced during the slaughter of infected animals. The aerosol mode of transmission has also led to infection in laboratory workers.
- There is some evidence that humans may also become infected with RVF by ingesting the unpasteurized or uncooked milk of infected animals.
- Human infections have also resulted from the bites of infected mosquitoes, most commonly the *Aedes* mosquito.
- Transmission of RVF virus by hematophagous (blood-feeding) flies is also possible.
- To date, no human-to-human transmission of RVF has been documented, and no transmission of RVF to health care workers has been reported when standard infection control precautions have been put in place.
- There has been no evidence of outbreaks of RVF in urban areas.

CLINICAL FEATURES IN HUMANS

Mild form of RVF in humans

- The incubation period (interval from infection to onset of symptoms) for RVF varies from two to six days.
- Those infected either experience no detectable symptoms or develop a mild form of the disease characterized by a feverish syndrome with sudden onset of flu-like fever, muscle pain, joint pain and headache.
- Some patients develop neck stiffness, sensitivity to light, loss of appetite and vomiting; in these patients the disease, in its early stages, may be mistaken for meningitis.
- The symptoms of RVF usually last from four to seven days, after which time the immune response becomes detectable with the appearance of antibodies and the virus gradually disappears from the blood.

Severe form of RVF in humans

- While most human cases are relatively mild, a small percentage of patients develop a much more severe form of the disease. This usually appears as one or more of three distinct syndromes: ocular (eye) disease (0.5-2% of patients), meningoencephalitis (less than 1%) or haemorrhagic fever (less than 1%).
 - Ocular form: In this form of the disease, the usual symptoms associated with the mild form of the disease are accompanied by retinal lesions. The onset of the lesions in the eyes is usually one to three weeks after appearance of the first symptoms. Patients usually report blurred or decreased vision. The disease may resolve itself with no lasting effects within 10 to 12 weeks. However, when the lesions occur in the macula, 50% of patients will experience a permanent loss of vision. Death in patients with only the ocular form of the disease is uncommon.
 - Meningoencephalitis form: The onset of the meningoencephalitis form of the disease usually occurs one to four weeks after the first symptoms of RVF appear. Clinical features include intense headache, loss of memory, hallucinations, confusion, disorientation, vertigo, convulsions, lethargy and coma. Neurological complications can appear later (> 60 days). The death rate in patients who experience only this form of the disease is low, although residual neurological deficit, which may be severe, is common.
 - Haemorrhagic fever form: The symptoms of this form of the disease appear two to four days after the onset of illness, and begin with evidence of severe liver impairment, such as jaundice. Subsequently signs of haemorrhage then appear such as vomiting blood, passing blood in the faeces, a purpuric rash or ecchymoses (caused by bleeding in the skin), bleeding from the nose or gums, menorrhagia and bleeding from venepuncture sites. The case-fatality ratio for patients developing the haemorrhagic form of the disease is high at approximately 50%. Death usually occurs three to six days after the onset of symptoms. The virus may be detectable in the blood for up to 10 days, in patients with the hemorrhagic icterus form of RVF.

The total case fatality rate has varied widely between different epidemics but, overall, has been less than 1% in those documented. Most fatalities occur in patients who develop the haemorrhagic icterus form.

DIAGNOSIS

- Acute RVF can be diagnosed using several different methods. Serological tests such as enzyme-linked immunoassay (the "ELISA" or "EIA" methods) may confirm the presence of specific IgM antibodies to the virus. The virus itself may be detected in blood during the early phase of illness or in post-mortem tissue using a variety of techniques including virus propagation (in cell cultures or inoculated animals), antigen detection tests and RT-PCR.

TREATMENT AND VACCINE

- As most human cases of RVF are relatively mild and of short duration, no specific treatment is required for these patients. For the more severe cases, the predominant treatment is general supportive therapy.
- An inactivated vaccine has been developed for human use. However, this vaccine is not licensed and is not commercially available. It has been used experimentally to protect veterinary and laboratory personnel at high risk of exposure to RVF. Other candidate vaccines are under investigation.

RVF VIRUS IN ANIMAL HOSTS

- RVF is able to infect many species of animals causing severe disease in domesticated animals including cattle, sheep, camels and goats. Sheep appear to be more susceptible than cattle or camels.
- Age has also been shown to be a significant factor in the animal's susceptibility to the severe form of the disease: over 90% of lambs infected with RVF die, whereas mortality among adult sheep can be as low as 10%.
- The rate of abortion among pregnant infected ewes is almost 100%. An outbreak of RVF in animals frequently manifests itself as a wave of unexplained abortions among livestock and may signal the start of an epidemic.

RVF VECTORS

- Several different species of mosquito are able to act as vectors for transmission of the RVF virus. The dominant vector species varies between different regions and different species can play different roles in sustaining the transmission of the virus.
- Among animals, the RVF virus is spread primarily by the bite of infected mosquitoes, mainly the *Aedes* species, which can acquire the virus from feeding on infected animals. The female mosquito is also capable of transmitting the virus directly to her offspring via eggs leading to new generations of infected mosquitoes hatching from eggs. This accounts for the continued presence of the RVF virus in enzootic foci and provides the virus with a sustainable mechanism of existence as the eggs of these mosquitoes can survive for several years in dry conditions. During periods of heavy rainfall, larval habitats frequently become flooded enabling the eggs to hatch and the mosquito population to rapidly increase, spreading the virus to the animals on which they feed.
- There is also a potential for epizootics and associated human epidemics to spread to areas that were previously unaffected. This has occurred when infected animals have introduced the virus into areas where vectors were present and is a particular concern. When uninfected *Aedes* and other species of mosquitoes feed on infected animals, a small outbreak can quickly be amplified through the transmission of the virus to other animals on which they subsequently feed.

PREVENTION AND CONTROL

Controlling RVF in animals

- Outbreaks of RVF in animals can be prevented by a sustained programme of animal vaccination. Both modified live attenuated virus and inactivated virus vaccines have been developed for veterinary use. Only one dose of the live vaccine is required to provide long-term immunity but the vaccine that is currently in use may result in spontaneous abortion if given to pregnant animals. The inactivated virus vaccine does not have this side effect, but multiple doses are required in order to provide protection which may prove problematic in endemic areas.
- Animal immunization must be implemented prior to an outbreak if an epizootic is to be prevented. Once an outbreak has occurred animal vaccination should NOT be implemented because there is a high risk of intensifying the outbreak. During mass animal vaccination campaigns, animal health workers may, inadvertently, transmit the virus through the use of multi-dose vials and the re-use of

needles and syringes. If some of the animals in the herd are already infected and viraemic (although not yet displaying obvious signs of illness), the virus will be transmitted among the herd, and the outbreak will be amplified.

- Restricting or banning the movement of livestock may be effective in slowing the expansion of the virus from infected to uninfected areas.
- As outbreaks of RVF in animals precede human cases, the establishment of an active animal health surveillance system to detect new cases is essential in providing early warning for veterinary and human public health authorities.

Public health education and risk reduction

- During an outbreak of RVF, close contact with animals, particularly with their body fluids, either directly or via aerosols, has been identified as the most significant risk factor for RVF virus infection. In the absence of specific treatment and an effective human vaccine, raising awareness of the risk factors of RVF infection as well as the protective measures individuals can take to prevent mosquito bites, is the only way to reduce human infection and deaths.
- Public health messages for risk reduction should focus on:
 - reducing the risk of animal-to-human transmission as a result of unsafe animal husbandry and slaughtering practices. Gloves and other appropriate protective clothing should be worn and care taken when handling sick animals or their tissues or when slaughtering animals.
 - reducing the risk of animal-to-human transmission arising from the unsafe consumption of fresh blood, raw milk or animal tissue. In the epizootic regions, all animal products (blood, meat and milk) should be thoroughly cooked before eating.
 - the importance of personal and community protection against mosquito bites through the use of impregnated mosquito nets, personal insect repellent if available, by wearing light coloured clothing (long-sleeved shirts and trousers) and by avoiding outdoor activity at peak biting times of the vector species.

Infection control in health care settings

- Although no human-to-human transmission of RVF has been demonstrated, there is still a theoretical risk of transmission of the virus from infected patients to healthcare workers through contact with infected blood or tissues. Healthcare workers caring for patients with suspected or confirmed RVF should implement Standard Precautions when handling specimens from patients.
- Standard Precautions define the work practices that are required to ensure a basic level of infection control. Standard Precautions are recommended in the care and treatment of all patients regardless of their perceived or confirmed infectious status. They cover the handling of blood (including dried blood), all other body fluids, secretions and excretions (excluding sweat), regardless of whether they contain visible blood, and contact with non-intact skin and mucous membranes. A WHO Aide-memoire on Standard Precautions in health care is available at: <http://www.who.int/csr/resources/publications/standardprecautions/en/index.html>
- As noted above, laboratory workers are also at risk. Samples taken from suspected human and animal cases of RVF for diagnosis should be handled by trained staff and processed in suitably equipped laboratories.

Vector control

- Other ways in which to control the spread of RVF involve control of the vector and protection against their bites.
- Larviciding measures at mosquito breeding sites are the most effective form of vector control if breeding sites can be clearly identified and are limited in size and extent. During periods of flooding,

however, the number and extent of breeding sites is usually too high for larviciding measures to be feasible.

RVF FORECASTING AND CLIMATIC MODELS

Forecasting can predict climatic conditions that are frequently associated with an increased risk of outbreaks, and may improve disease control. In Africa, Saudi Arabia and Yemen RVF outbreaks are closely associated with periods of above-average rainfall. The response of vegetation to increased levels of rainfall can be easily measured and monitored by Remote Sensing Satellite Imagery. In addition RVF outbreaks in East Africa are closely associated with the heavy rainfall that occurs during the warm phase of the El Niño/Southern Oscillation (ENSO) phenomenon.

These findings have enabled the successful development of forecasting models and early warning systems for RVF using satellite images and weather/climate forecasting data. Early warning systems, such as these, could be used to detect animal cases at an early stage of an outbreak enabling authorities to implement measures to avert impending epidemics.

Within the framework of the new International Health Regulations (2005), the forecasting and early detection of RVF outbreaks, together with a comprehensive assessment of the risk of diffusion to new areas, are essential to enable effective and timely control measures to be implemented.

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