RIFT VALLEY FEVER (RVF)
**Definition:**

Rift Valley fever (RVF) is one of the most serious transboundary animal diseases. RVF is an acute mosquito-borne viral disease mainly affecting ruminant animals and humans. It can cause abortions in pregnant animals and a high mortality in young animals. RVF is also an important zoonosis and one of the significant acute haemorrhagic fevers affecting human beings. Until recently it had only been recognized in the African continent, but in 2000 it occurred in the Arabian Peninsula. RVF is designated as a List of multiple species disease by the Office International des Epizooties (OIE). OIE-Listed diseases, infections and infestations in force in 2014. The Disease of this List are, ‘Communicable diseases which have the potential for serious and rapid spread, irrespective of national borders; which are of serious socioeconomic or public health importance and which are of major importance in the international trade of animals and animal products’.

**Aetiology:**

The RVF virus is a member of the Phlebovirus genus of the family Bunyaviridae. It is a single-stranded RNA virus with three segments. The Zinga and Lunya viruses first isolated, respectively, in the Central African Republic in 1969 and in Uganda in 1955, are identical.

The RVF virus is serologically related to other phleboviruses, but can be differentiated from these by virus-serum neutralization tests. There is only one serotype of RVF virus. The virus is inactivated by lipid solvents (e.g. ether) and by strong solutions of sodium or calcium hypochlorite (residual chlorine should exceed 5 000 ppm).

**Epidemiological features:**

RVF was first identified in an outbreak of abortions and deaths in exotic wool sheep and illness in humans that occurred in the Rift Valley of Kenya after heavy rainfall in 1930-31. In 1973, RVF outbreaks occurred in irrigation areas of the Sudan. In 1977 the disease was recognized in Egypt and caused an estimated 600 human deaths as well as heavy losses in sheep, goats, cattle, buffaloes and camels along the Nile Valley and Delta. RVF outbreaks again occurred in Egypt in 1993. Until recently RVF was thought to be restricted to Africa. However, it was reported in the Tihama region of both Saudi Arabia and Yemen in September 2000.
Although many mammalian species are susceptible to RVF infection, birds are not. Of the livestock species, sheep are the most susceptible, followed in order by goats, cattle, camels and water buffaloes.

For epidemics to occur, three factors must be present:

- The pre-existence or introduction of the virus in the area.
- The presence of large populations of susceptible ruminants;
- Climatic or environmental conditions that encourage a massive build-up in vector mosquito population. The latter usually occurs when there are warm conditions and unusually heavy and persistent rainfalls that cause surface flooding and lead to the hatching of infected Aedes spp. mosquito eggs and large numbers of vector mosquitoes. Alternatively, it may occur in the absence of rainfall, where there is a great deal of surface water, as in a river floodplain, originating from heavy rainfall in river basins that may be hundreds of kilometres away in the mountains, or from irrigation (as was the case in the Gezira area of the Sudan and in Egypt).
Infected mosquitoes may be transported for long distances in low-level wind or air currents, which may lead to the rapid spread of the virus from region to region or even internationally. This may have been a factor in the spread to and within Egypt in 1977 and 1993. Humans can become infected from mosquito bites but the majority of human cases are thought to result from handling the blood, tissues, secretions or excretions of infected animals, notably after abortion. This may be through handling, milking, slaughtering, butchering or autopsying such animals. RVFV has also caused serious infections in laboratory workers and must be handled with biosafety and biocontainment measures. It is recommended that laboratory workers be vaccinated if possible.

**Clinical Signs:**

In Camels, although infection is generally subclinical in mature animals, pregnant camels may abort at any stage of pregnancy and neonatal deaths can occur. Abortion rates of 70 percent of those pregnant have occurred with many deaths in camel calves up to 3-4 months of age.

Sheep is more severely affected with 100% morbidity and 95% mortality in young lambs. In per-acute cases, sheep are either found dead or suddenly weaken and collapse when driven. In acute cases, there is a very short incubation period - less than 24 hours - followed by fever, rapid pulse, weakness, unsteady gait, vomiting, mucopurulent nasal discharge and death in 24-72 hours. Other signs often observed are lymphadenitis, colic, haemorrhagic diarrhoea and petechial or ecchymotic haemorrhages in visible mucous membranes.
RVF in goats and cattle is similar to that in sheep but is usually not quite so severe. Abortion is an almost inevitable consequence of infection of pregnant animals of all species, and may occur in either the acute or convalescent stages of the disease.

In humans, Uncomplicated RVF is characteristically manifests as an acute influenza-like illness with transient fever, rigor (shivering), headache, severe muscle and joint pain, photophobia and anorexia sometimes with a petechial rash, nausea, vomiting and epistaxis. The course is 4 to 7 days leading to full recovery in 2 weeks. The most frequent complication is retinitis, usually bilateral; there may be permanent unilateral or bilateral blindness. In a proportion of RVF cases a biphasic fever is seen with encephalitis developing during the second febrile phase. Patients suffer confusion, hallucinations, vertigo and choreiform movements sometimes leading to coma. The case mortality rate is generally low but full recovery may be protracted and long-term neurological complications have been reported. The most severe RVF syndrome is Hemorrhagic RVF: an acute fever of 2–4 days duration is followed by jaundice and hemorrhage; in the following 3–6 days either death occurs or the patient begins to recover slowly.

**Diagnosis:**

**Field diagnosis**

RVF epidemics should always be strongly suspected when there is a sudden onset of large numbers of abortions in sheep, goats, cattle or camels and deaths in lambs, kids or calves. This is specially the case if there is surface flooding in savannah or semi-arid areas following prolonged rains (or in irrigated areas); if the mosquito populations are high; and if there is concurrent illness in human populations. The disease in domestic animals may only be noticed after the illness in people has been identified as RVF.

**Laboratory Diagnosis**

**Collection and transport of diagnostic specimens.** Whole blood, liver, lymph nodes and spleen are the tissues of choice for isolation of the virus. Blood samples should be collected from febrile animals into ethylene-diamine-tetra-acetic acid (EDTA) or heparin to which antibiotics have been added as preservatives (penicillin 200 units and streptomycin 200 µg/ml, final concentration). Samples of liver and spleen should be collected aseptically both from freshly dead animals at autopsy and from aborted fetuses, if available, and placed in sterile containers. Duplicate tissue specimens should be collected in neutral buffered formalin for histopathology.
Blood samples, about 20 ml each, should be collected from animals in the acute and convalescent phases of the disease, for serum.

**Histopathology.** The finding of characteristic histological lesions with pan-necrosis in the liver of young animals or foetuses is suggestive of RVF.

**Virus isolation.** The RVF virus can be isolated from whole blood or homogenates of fresh tissues by intracerebral injection of suckling mice or intraperitoneal injection of adult mice or hamsters. It can also be readily isolated in various primary cell cultures (e.g. primary lamb and calf kidney or testis) or cell lines (e.g. BHK-21 and Vero). The identity of the isolated virus is confirmed by polymerase chain reaction (PCR), enzyme linked immunosorbent assay (ELISA), fluorescent antibody staining or virus-serum neutralization tests.

**Antigen detection.** The RVF antigen may be detected by direct or indirect immunofluorescence tests on impressions smears or cryostat sections of liver, spleen and brain. A rapid diagnosis can sometimes be made by agar gel immunodiffusion (AGID) tests on fresh tissues. Immunocapture-ELISA and histochemical staining of cryostat sections or formalin fixed tissues and PCR are now much more widely used for RVF.

**Antibody detection.** The ELISA test has now replaced the older inhibition of haemagglutination (IHA), immunofluorescence assay (IFA) and serum neutralization tests as the test of choice. ELISA systems are available to test for the presence of IgM and IgG, which are extremely valuable in epidemiological investigations. The virus serum neutralization test in microtitre tissue culture systems is still the definitive test system. It is highly specific with little or no cross-neutralization with other phleboviruses. It can be used to detect antibodies in all animal species. However, as it requires the use of live virus, it is not recommended for use outside endemic countries unless a high level of biocontainment is available in laboratories.

Other serological tests are less specific, but still have a very useful role.

The indirect ELISA test is a reliable and sensitive test and can provide results within hours. There are tests for both IgM and IgG antibodies. In an index case in an outbreak situation the low-level serological cross-reactions with other members of the *Phlebovirus* genus may cause problems. Doubtful results should therefore be interpreted with caution and may need to be confirmed by serum neutralization (SN) tests at a reference laboratory.
Detection of viral genetic material. A reverse transcriptase PCR test is now available for detection of viral genetic material. Sequencing of the NS (S) protein-coding region of the genome may be used for phylogenetic analysis (genetic fingerprinting) of virus isolates.

Control:

The limits of an area for control activities may be determined by prior knowledge of the distribution of RVF in earlier epidemics in the country and of potential vector species.

Theoretically, measures taken could include, inter alia:

- chemical control of vectors by, for example, ultra-low volume spraying of insecticides and application of systemic insecticides to target species
- movement of stock from low-lying areas to well-drained and wind-swept pastures at higher altitudes
- the confinement of livestock to mosquito-proof stables
- control of livestock movements
- slaughter and disposal of all infected livestock

However, such measures are usually impractical, instituted too late and at best palliative in the face of a RVF epidemic. Immunisation remains the only effective means of protecting livestock. All ruminants in herds within the infected area should be vaccinated immediately with an inactivated RVF vaccine and revaccinated after 2 to 4 weeks. The use of live attenuated vaccines should only be considered if RVF spreads outside the initial area affected.

References.