RIFT VALLEY FEVER

AETIOLOGY

Classification of the causative agent

Rift Valley fever (RVF) virus is a negative-sense, single-stranded RNA virus of the family Bunyaviridae within the genus *Phlebovirus*. Only one serotype is recognised but strains exist of variable virulence.

Resistance to physical and chemical action

Temperature:	Virus recoverable from serum after several months at 4°C or 120 minutes at 56°C.
pH:	Resistant in alkaline environments but inactivated at pH <6.8.
Chemicals/Disinfectants:	Inactivated by lipid solvents (i.e. ether, chloroform, sodium deoxycholate), low concentrations of formalin and by strong solutions of sodium or calcium hypochlorite (residual chlorine should exceed 5000 ppm).
Survival:	Survives in freeze dried form and aerosols at 23°C and 50–85% humidity. Virus maintained in the eggs of certain arthropod vectors during inter-epidemic periods. Can survive contact with 0.5% phenol at 4°C for 6 months

EPIDEMIOLOGY

RVF is a vector-borne disease of sheep, cattle and goats; susceptibility of different breeds to RVF varies considerably. The disease usually presents in an epizootic form over large areas of a country following heavy rains and sustained flooding, and is characterised by high rates of abortion and neonatal mortality, primarily in sheep, goats and cattle.

Hosts

- Cattle, sheep, goats, dromedaries, several rodents
- Wild ruminants, buffaloes, antelopes, wildebeest, etc.
- Humans are very susceptible (major zoonosis)
- African monkeys and domestic carnivores present a transitory viraemia

Transmission

- RVF virus regularly circulates in endemic areas between wild ruminants and haematophagous mosquitoes; disease is usually inapparent
- Certain *Aedes* species act as reservoirs for RVF virus during inter-epidemic periods and increased precipitation in dry areas leads to an explosive hatching of mosquito eggs; many of which harbour RVF virus
- Precipitation cycles of 5–25 years produce RVF-inmuno-naïve animal populations and when combined with introduction of virus, explosive outbreaks of the disease occur
    - satellite imaging has been used to confirm historic importance of precipitation in RVF outbreaks and in forecasting high-risk areas for future outbreaks
- Infected *Aedes* feed preferentially on domestic ruminants which act as an amplifier of RVF
    - broad vector range of mosquitoes (*Aedes*, *Anopheles, Culex, Eretmapodites, Mansonia,* etc.) coupled with increased circulating virus leads to expansion of disease
    - extrinsic incubation also occurs in vectors.
- Sylvatic cycle and inter-epidemic maintenance also occurs in some areas
- Direct contamination: occurs in humans when handling infected animals and meat
- Mechanical transmission by various vectors has been demonstrated in laboratory studies

Sources of virus

- For animals: wild fauna and vectors
- For humans: nasal discharge, blood, vaginal secretions after abortion in animals, mosquitoes, and infected meat; also by aerosols and possibly consumption of raw milk

Occurrence

RVF is endemic in tropical regions of eastern and southern Africa. Epizootic outbreaks in Africa among peri-endemic countries have been associated with above average rain fall and climatic conditions favourable for competent vectors. Important outbreaks of RVF have been recorded in Egypt (1977–78 and 1993), Mauritania (1987), Madagascar (1990–91), Kenya and Somalia (1997). RVF was recognised for the first time outside of the African continent in 2000 with outbreaks reported in Saudi Arabia and Yemen. The disease has not established itself in the Arabian Peninsula but sero-positive animals have been detected. RVF activity was recorded from 2002 to 2004 at various locations in Senegal, Mauritania and Gambia. Madagascar and Swaziland have most recently reported RVF in 2008 and later that year also South Africa.

For more recent, detailed information on the occurrence of this disease worldwide, see the *OIE World Animal Health Information Database* (WAHID) interface [http://www.oie.int/wahis/public.php?page=home] or refer to the latest issues of the *World Animal Health* and the OIE *Bulletin*.

DIAGNOSIS

Incubation period varies from 1 to 6 days; 12–36 hours in lambs. For the purposes of the Terrestrial Code, the infective period for RVF is considered 30 days.

Clinical diagnosis

Severity of clinical disease varies by species: lambs, kids, puppies, kittens, mice and hamsters are considered “extremely susceptible” with mortalities of 70–100%; sheep and calves are categorised as “highly susceptible” with mortality rates between 20–70%; in the “moderately susceptible” category are cattle, goats, African buffalo, domestic buffalo, Asian monkeys and humans with mortalities less than 10%; and camels, equids, pigs, dogs, cats, African monkeys, baboons, rabbits, and guinea pigs are considered “resistant” with infection being inapparent. Birds, reptiles and amphibians are not susceptible to RVF. Signs of the disease tend to be non-specific; however, the presentation of numerous abortions and mortalities among young animals, together with influenza-like disease in humans, is indicative.

Cattle

- Calves (highly susceptible)
  - fever (40–41°C)
  - inappetence
  - weakness and depression
  - bloody or fetid diarrhoea
  - more icterus than in lambs
- Adults (moderately susceptible):
  - often inapparent infection but some acute disease
  - fever lasting 24–96 hours
  - dry and/or dull coat
  - lachrymation, nasal discharge and excessive salivation
  - anorexia
  - weakness
  - bloody/fetid diarrhoea
  - fall in milk yield
  - abortion rate may reach 85% in the herd

Sheep

- Newborn lambs or under 2 week of age (extremely susceptible):
  - biphasic fever (40–42°C); fever subsides just prior to death

    - anorexia; in part due to disinclination to move
    - weakness, listless
    - abdominal pain
    - rapid, abdominal respiration prior to death
    - death within 24–36 hours
- Lambs over 2 weeks of age (highly susceptible) and adult sheep
    - peracute disease: sudden death with no appreciable signs
    - acute disease more often in adult sheep
    - fever (41–42°C) lasting 24–96 hours
    - anorexia
    - weakness, listlessness and depression
    - increased respiratory rate
    - vomiting
    - bloody/fetid diarrhoea
    - mucopurulent nasal discharge
    - icterus may be evident in a few animals
    - in pregnant ewes, 'Abortion storms' with a rates approaching 100%

Goat

- Similar to adult sheep (see above)

Humans

- Influenza-like syndrome: fever (37.8–40°C), headache, muscular pain, weakness, nausea and epigastric discomfort, photophobiae
- Recovery occurs within 4–7 days
- Complications: retinopathy, blindness, meningo-encephalitis, haemorrhagic syndrome with jaundice, petechiae and death

Lesions

- Focal or generalised hepatic necrosis (white necrotic foci of about 1 mm in diameter)
- Congestion, enlargement, and discoloration of liver with subcapsular haemorrhages
- Brown-yellowish colour of liver in aborted fetuses
- Widespread cutaneous haemorrhages, petechial to ecchymotic haemorrhages on parietal and visceral serosal membranes
- Enlargement, oedema, haemorrhages and necrosis of lymph nodes
- Congestion and cortical haemorrhages of kidneys and gallbladder
- Haemorrhagic enteritis
- Icterus (low percentage except in calves)

Differential diagnosis

- Bluetongue
- Wesselsbron disease
- Enterotoxemia of sheep
- Ephemeral fever
- Brucellosis
- Vibriosis
- Trichomonosis
- Nairobi sheep disease
- Heartwater
- Ovine enzootic abortion
- Toxic plants
- Bacterial septicaemias
- Rinderpest and Peste des petits ruminants
- Anthrax

Laboratory diagnosis

Samples

- Heparinised or clotted blood
- Plasma or serum
- Tissue samples of liver, spleen, kidney, lymph node, heart blood and brain from dead animals or aborted fetuses
    - specimens should be submitted preserved in 10% buffered formalin and in glycerol/saline and transported at 4°C
    - liver or other tissue for histological examination may be placed in formol saline in the field for diagnostic purposes; facilitates handling and transport in remote areas

Procedures

Identification of the agent

- Culture – primary isolation is usually performed in hamsters, infant or adult mice, or on cell cultures of various types
    - virus may also be detected by immunofluorescence carried out on impression smears of liver, spleen and brain
- Agar gel immunodiffusion – useful in laboratories without tissue-culture facilities
- Polymerase chain reaction
    - used for rapid diagnosis
    - for antigen detection and used to detect RVF virus in mosquito pools
    - RT-PCR followed by sequencing of the NS(S) protein-coding region has been used in phylogenetic analysis
- Histopathology – examination of the liver of affected animals will reveal characteristic cytopathology, and immunostaining will allow the specific identification of the RVF viral antigen in infected cells

Serological tests

- Virus neutralisation (the prescribed test for international trade) – microneutralisation, plaque reduction neutralisation (PRN) and neutralisation in mice
    - cannot differentiate presence of antibodies of naturally infected animals from animals vaccinated with RVF vaccine; detects antibodies against RVF virus in the serum of a variety of species
    - highly specific and will record the earliest response
    - these tests can only be performed with live virus; thus not recommended for use outside endemic areas or in laboratories without appropriate biosecurity facilities and vaccinated personnel
- Enzyme-linked immunosorbent assay
    - can be performed with inactivated antigen and can therefore be used in RVF-free countries
    - cross-reactions may occur between RVF virus and other phleboviruses
    - use of inactivated whole virus or mouse liver antigens has recently been replaced by recombinant nucleocapsid (N) protein as antigen
    - commercially available kits
    - indirect ELISA with pre-coated plates using a nucleocapsid protein (NC) recombinant antigen and Protein G peroxidase conjugate is described in OIE Terrestrial Manual
    - IgM-capture ELISA allows diagnosis of a recent infection
- Haemagglutination inhibition
    - can be performed with inactivated antigen and can therefore be used in RVF-free countries
    - employed with great confidence in non-endemic areas
    - Note: sera from individuals that have had previous infections with phleboviruses other than RVF may result positive

For more detailed information regarding laboratory diagnostic methodologies, please refer to Chapter 2.1.14 Rift Valley fever in the latest edition of the OIE *Manual of Diagnostic Tests and Vaccines for Terrestrial Animals* under the heading "Diagnostic Techniques".

PREVENTION AND CONTROL

- There is no specific treatment for RVF.

Sanitary prophylaxis

- Control of animal movements (extension of disease)
- Controls at slaughterhouses (exposure to disease)
- Draining of standing water to eliminate or reduce vectors
    - Disinfestations of low depression accumulations of water where mosquitoes may reproduce (in Africa known as 'dambos')
        - use of methoprene spraying or controlled burning
- Hygiene and vector control may have limited effect during widespread outbreaks

Medical prophylaxis

- Attenuated virus vaccine (Smithburn strain)
    - one inoculation confers immunity lasting 3 years
    - residual pathogenicity for pregnant ewes (abortion)
    - pathogenic for humans
- Inactivated virus vaccine
    - requires two inoculations and annual revaccination
- Live-attenuated mutant vaccine - MV P12 Vaccine
    - safe and efficacious for use in pregnant or lactating bovids; non-pathogenic in young lambs
    - colostrum from vaccinated ewes induces temporary protective immunity

For more detailed information regarding vaccines, please refer to Chapter 2.1.14 Rift Valley fever in the latest edition of the OIE *Manual of Diagnostic Tests and Vaccines for Terrestrial Animals* under the heading "Requirements for Vaccines".

For more detailed information regarding safe international trade in terrestrial animals and their products, please refer to the latest edition of the OIE *Terrestrial Animal Health Code*.

REFERENCES AND OTHER INFORMATION

- Brès P. (1981). - Prevention of the spread of Rift Valley fever from the African continent. Contributions to Epidemiology and Biostatics, 3:178-190.
- Brown C. & Torres A., Eds. (2008). - USAHA Foreign Animal Diseases, Seventh Edition. Committee of Foreign and Emerging Diseases of the US Animal Health Association. Boca Publications Group, Inc.
- Coetzer J.A.W. & Tustin R.C. Eds. (2004). - Infectious Diseases of Livestock, 2nd Edition. Oxford University Press.
- Fauquet C., Fauquet M., & Mayo M.A. (2005). - Virus Taxonomy: VIII Report of the International Committee on Taxonomy of Viruses. Academic Press.
- Kahn C.M., Ed. (2005). - Merck Veterinary Manual. Merck & Co. Inc. and Merial Ltd.
- Spickler A.R. & Roth J.A. (2006). - Emerging and Exotic Diseases of Animals. Iowa State University, College of Veterinary Medicine, Ames, Iowa.
- World Organisation for Animal Health (2009). - Terrestrial Animal Health Code. OIE, Paris.
- World Organisation for Animal Health (2008). - Manual of Diagnostic Tests and Vaccines for Terrestrial Animals. OIE, Paris.

*

* *

The OIE will periodically update the OIE Technical Disease Cards. Please send relevant new references and proposed modifications to the OIE Scientific and Technical Department (scientific.dept@oie.int). Last updated October 2009.