Rift Valley fever affects humans as well as animals. It is a serious zoonosis.

In addition to the bites of mosquitoes, humans can be infected by contact with blood or body fluids from infected animals which may occur during slaughtering of animals or handling of aborted foetuses and animal tissues. NECROPSY PROCEDURES AND HANDLING OF TISSUES FOR LABORATORY DIAGNOSTIC PURPOSES HAVE RESULTED IN MANY INFECTIONS OF DIAGNOSTICIANS AND LABORATORY PERSONNEL, SOMETIMES WITH MOST SERIOUS CONSEQUENCES. GREAT CARE SHOULD BE EXERCISED IN HANDLING SUCH MATERIALS. LABORATORY CONFIRMATION OF RIFT VALLEY FEVER AND OTHER DIAGNOSTIC TESTS ON MATERIAL DERIVED FROM ANIMALS WHICH COULD BE INFECTED WITH RIFT VALLEY FEVER REQUIRE BIOLOGICAL CONTAINMENT FACILITIES.

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NATURE OF THE DISEASE

The first indication of development of an epidemic is frequently the abortion of sheep. Index cases and sporadic cases (see Epidemiological features) are usually misdiagnosed. Signs of the disease in animals tend to be non-specific, making it difficult to recognise individual cases of RVF. The simultaneous occurrence of numerous cases of abortion and disease in ruminants, together with disease of humans, following heavy and prolonged rainfall, is characteristic of Rift Valley fever (RVF).

Aetiology

RVF is a peracute or acute insect-borne disease of man and animals caused by a member of the Phlebovirus genus of the family Bunyaviridae. Zinga virus, originally isolated in the Central African Republic in 1969, and Lunyo virus isolated in Uganda in 1955 are both indistinguishable from RVF virus. Strains of the virus differ in virulence.
Species affected

Clinical disease has been observed in sheep, goats, cattle, domesticated Asian buffaloes, camels and humans. The susceptibility of wild antelopes to disease has not been established fully but it is believed that at least some species suffer mortality and abortion. Some breeds of sheep and goats appear to be relatively resistant to the disease.

World distribution and occurrence

RVF appears to be restricted to Africa. It was recognised first in the Rift Valley of Kenya at the turn of this century but the agent was not isolated until 1930. The disease was first observed in southern Africa in 1950. Most epidemics have occurred in eastern and southern Africa and, until 1977, the furthest north that the disease was known to have occurred was the Sudan. During 1977 and 1978, a major epidemic occurred in the Nile delta and valley in Egypt. A severe epidemic affected the Senegal River basin in Mauritania and Senegal in 1987 and again in Egypt in 1993. [The periodicity of major epidemics is discussed below in Epidemiological features.]

The epidemics in Egypt indicate that the potential exists for spread to other regions of the world outside the African continent.

Clinical appearance

In humans

Uncomplicated RVF in man 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, occurring 1 to 3 weeks after the primary febrile illness. Permanent loss of central vision is suffered by some 50 per cent of those affected; there may be permanent unilateral or bilateral blindness. Other, often fatal, complications have been more prominent in the epidemics in West Africa and Egypt. 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. A haemorrhagic diathesis with hepatitis is a relatively new form of the disease, first described in 1975 in South Africa. It is an acute febrile illness of 2 to 4 days duration followed by jaundice and widespread haemorrhages in mucosae and subcutaneously. Bleeding occurs at needle puncture sites, from the gums and nose and there may be haematemesis and diarrhoea with melaena. Death usually occurs within another 3 to 6 days and a few patients recover after a long slow convalescence.

In animals
Infection is more common than severe disease, it is often mild or sub-clinical.

Most, if not all, infected pregnant sheep, goats, cattle (and most likely domesticated Asian buffaloes) and camels abort affected fetuses at any stage of gestation, usually undergoing autolysis.

The most severe reactions occur in newborn lambs and kids which die within hours of infection, rarely surviving more than 36 hours. Onset is marked by high fever which subsides sharply before death. Affected animals are listless, disinclined to move or feed and respiration is rapid. Mortality reaches 90 per cent or more in animals less than one week of age.

Older lambs and kids and mature sheep and goats may develop inapparent, peracute or acute disease. In peracute disease death occurs before the development of notable signs. Acute disease is characterised by high fever for 1 to 3 days, anorexia, weakness, listlessness and rapid respiration. Some animals regurgitate ruminal contents and exhibit blood-stained nasal discharge, fetid diarrhoea and melaena. Jaundice may be evident. Death occurs after about three days of illness. The mortality rate is lower than in week-old lambs but can still reach 50 per cent or more.

The disease in calves resembles that in lambs - essentially fever, weakness, inappetance and diarrhoea, which may be blood-stained - but jaundice is more frequent. Death occurs in from 2 to 8 days and the mortality rate is generally low at around 20 per cent.

Adult cattle exhibit clinical signs of disease infrequently but some may develop acute disease with fever for 2 to 3 days, anorexia, lachrymation, hypersalivation, nasal discharge, dysgalactia and diarrhoea which may be blood-stained. Frequently abortion is the only manifestation in this species. The mortality rate does not usually exceed 10 per cent but can be higher. A prolonged course of 10 to 20 days with marked jaundice has been described in the Sudan.

Asian water buffaloes are known to be susceptible from the Egyptian epidemics. Abortion and deaths occur.

Antibodies to RVF virus have been detected in camels and RVF virus has been isolated from them during epidemics.Deaths and abortions almost certainly occur but the disease has been little studied in this species.

Antibody surveys and experimental infection studies have demonstrated that many species of wild ruminants (African buffaloes and numerous antelope species) sustain infection, yet, the results of that infection have not been clearly described. It is highly likely that both abortions and mortalities occur in at least some wildlife species during epidemics.

**Pathology**

The pathogenesis of RVF results from the spread of virus from the site of introduction to the body and initial replication sites to critical organs such as the spleen, liver and brain. These are either directly damaged by the effects of the virus or by immunopathological mechanisms.

Even in benign infections of livestock there is a marked leukopenia during the first 3 to 4 days of infection, corresponding with the peak fever and viraemia. At the same time there are marked increases
in the serum concentrations of some enzymes indicative of liver cell damage.

The most severe lesions are found in aborted sheep fetuses and newborn lambs. The liver is usually enlarged, soft, friable and yellowish-brown to dark reddish-brown in colour. Irregular congested patches and haemorrhages of varying size are often present in the substance of the liver together with pale foci. Jaundice is seen in only a relatively small proportion of lambs because of the short time to death. In older sheep, the hepatic lesions are generally not so severe but jaundice may be more marked. Pale areas of cell necrosis combined with large haemorrhages give a mottled appearance to the liver. Haemorrhages and oedema of the gall bladder are common and the bile may contain blood. Elsewhere, in newborn lambs, petechial and ecchymotic haemorrhages are found in the abomasal mucosa and the contents are often dark brown from the presence of partly-digested blood; the contents of the small intestine may be similar. Most mature sheep have haemorrhages and oedema in the abomasal folds and sometimes free blood in the intestinal lumen.

Aborted cattle fetuses, calves and older cattle show lesions essentially similar to those in sheep fetuses, lambs and older sheep.

In all animals the peripheral and visceral lymph nodes are enlarged, oedematous and may contain petechial haemorrhages and, in most, the spleen is enlarged with haemorrhages in the capsule.

Hepatic necrosis of varying degree is the most striking microscopic lesion in all animals. Many animals have lung congestion, oedema, haemorrhage and emphysema.

Laboratory diagnostic confirmation

The clinical diagnosis can be confirmed by a number of tests amongst which are:

- histopathology performed on formalin-fixed sections of liver; lesions are distinctive but immunoperoxidase staining of viral antigen adds specificity;
- virus isolation in cell culture or by intraperitoneal or intracerebral inoculation of weanling mice or hamsters confirmed by immunofluorescent or immunoperoxidase staining;
- detection of viral antigen by immunofluorescent or immunoperoxidase staining of frozen sections, immunodiffusion, complement fixation and ELISA;
- detection of viral RNA by reverse transcriptase polymerase chain reaction (RT-PCR);
- detection of antibodies by virus neutralisation and ELISA (not the haemagglutination-inhibition test which is non-specific); these are used mainly retrospectively to determine the extent of an epidemic. For diagnostic confirmation, recent or current infection must be distinguished from pre-existing immunity. Paired samples collected during the acute phase and again 2 to 3 weeks later provide evidence of recent infection. IgM-capture ELISA allows diagnosis of recent infection to be made on a single serum sample.

Specimens required include heparinised and clotted peripheral blood, heart blood, tissue samples (liver, spleen, kidney and lymph nodes), collected preferably at the height of fever, and serum. Samples from aborted fetuses should include brain. Where delay is anticipated in samples reaching a laboratory or where samples have to be transported at ambient temperature, tissue samples can be preserved in glycerol-saline solution (50:50).
Differential diagnosis

Wesselsbron disease tends to occur under the same climatic conditions as RVF. Both cause mortality in lambs, kids and calves and abortion in ewes, but RVF is associated with much higher mortality and abortion rates. Wesselsbron disease is usually inapparent in adult animals and is limited to southern Africa, although evidence of the virus infection is present in most of sub-Saharan Africa. RVF could also be confused with Nairobi sheep disease (transmitted by Rhipicephalus and Amblyomma sp. ticks) of sheep and goats because of abortion, mortality and jaundice. Intoxication by poisonous plants can cause mortality associated with hepatic lesions, haemorrhages and jaundice superficially resembling RVF as can bacterial septicaemias, such as pasteurellosis, salmonellosis and anthrax. Conditions of high rainfall and humidity favour the occurrence of leptospirosis (L. grippotyphosa, L. icterohaemorrhagiae and other serovars) which can mimic many of the clinical signs of RVF.

It should be noted that the conditions which precipitate an epidemic of RVF (inter alia, heavy and prolonged rainfall leading to flooding) are also those predisposing to the occurrence of other major disease epidemics which can occur simultaneously. In pastoral areas, the movement of humans and their livestock away from flooded areas and their congregation on higher land favours the transmission of other disease agents including foot-and-mouth disease, contagious bovine pleuropneumonia, contagious caprine pleuropneumonia, capripox and morbillivirus infections (rinderpest and peste des petits ruminants).

Following rain, there is a lag phase before tick populations increase, generating epidemics of tick-borne diseases. Ephemeral fever and lumpy skin disease also occur at this time, favoured by vector multiplication. Orbivirus infections, such as bluetongue and epizootic haemorrhagic disease, may also increase in incidence but bluetongue disease will only be seen clinically in imported sheep and their crosses, for example, wool and Dorper sheep.

Epidemiological features

Outbreaks of RVF occur generally when particularly heavy, prolonged and, often, unseasonal rainfall favours the breeding of mosquito vectors. Epidemics in most of eastern and southern Africa occur in 5 to 20 year cycles, but, in the dry semi-arid zones of eastern Africa the periodicity is 15 to 30 years.

The generation of epidemics and inter-epidemic persistence of RVF infection

Recurrent viral activity occurs in localised areas in southern and eastern Africa where transmission of RVF virus to ruminants occurs during most years. This provides one of the keys to understanding virus survival during inter-epidemic periods. The other key to virus persistence lies in the biology of certain floodwater-breeding aedine mosquitoes. These aedine mosquitoes endure dry periods as eggs which can survive for long periods, possibly several seasons, in dried mud. Indeed, it is obligatory for these eggs to be subjected to a period of drying before they can hatch. RVF virus is transmitted transovarially in certain Aedes species mosquitoes and infection persists for their life. Ideal conditions for the breeding of aedine mosquitoes (and other mosquito species) are found in low-lying shallow depressions, termed dambos, which flood when abnormally heavy rainfall raises the water table sufficiently. An explosive increase in the aedine mosquito vector populations follows with increased transmission of RVF virus.
mainly to cattle, on which they feed selectively. Amplification of the virus in cattle then provides infection for a range of secondary or epidemic mosquito vectors, such as culicine and anopheline mosquitoes, which transmit infection to many susceptible ruminant species and humans.

Floodwater-breeding aedine mosquitoes are absent from Egypt; Culex pipiens was the main vector during the epidemics experienced there.

Thus, the generation of epidemics seems generally to be associated with the simultaneous intensification of vector and viral activity over large areas within which the virus is already present in some sites, rather than lateral spread from cryptic endemic foci. After prolonged droughts during which dambos remain dry for many years, it is possible that aedine mosquito populations could decline to a point where they and RVF virus entirely disappear from large areas. Considerable virus amplification would then have to occur before the disease again became evident or it would need to be reintroduced through long range dispersal of viraemic animals or infected vectors. There is no carrier state known in any species.

Flooding and humid weather conditions favour the breeding not only of mosquitoes but also of other biting insects which are potential mechanical transmitters of RVF virus. Eggs of species which breed in water, other than those of aedine mosquitoes, cannot survive dry conditions and these insects recolonise flooded dambos from nearby rivers or dams. A succession of vector species become available once flooding occurs. Mechanical transmission of infection by mosquitoes, midges, phlebotomids, stomoxids, simulids and other biting flies appears to play a significant role in epidemics. It has been suggested that Hyalomma species ticks on cattle could have spread RVF infection to West Africa and Egypt but this is now considered unlikely. Ticks appear to play no part in the epidemiology of RVF.

**Non-vector transmission of RVF**

Unlike in humans, non-vector transmission of RVF virus is not considered to be important in livestock. The risk of human-to-human infection through direct contact appears also to be very low. However, in addition to mosquito transmission, humans are easily infected by contact with the body fluids of infected animals through contact with abraded skin, wounds or mucous membranes or by inhalation of aerosols generated. Thus, the slaughter of infected animals, necropsy procedures and laboratory manipulation of tissues and isolated viruses are activities carrying a high risk of disease transmission.

RVF outbreaks have not been seen in urban consumer populations suggesting that the fall in pH of meat with maturation inactivates the virus.

Low concentrations of RVF virus are found in the milk of infected animals and the connection has been made between human infection and the consumption of raw milk. Clearly this could be a significant factor in pastoral communities where milk is a major component of the diet.

It is suspected, and it is highly likely given the high concentration of RVF virus in the blood of affected animals, that infection can be transferred between animals when they are vaccinated or blood sampled in succession with the same needle during an epidemic.

**Potential for long range spread - events in Egypt**

The means by which RVF reached Egypt in, or shortly before, 1977 have never been established definitively. Factors which appear to merit serious consideration include:

- the arrival in Egypt of viraemic people;
● transport of infected (viraemic) livestock on the Nile - humans slaughtering or handling tissues could have become infected and served as amplification hosts for the infection of mosquitoes;

● transport of infected mosquitoes by plane;

● wind-borne movement of infected mosquitoes from the Sudan - high altitude movement of mosquitoes by strong winds is known to occur over long distances and suitable conditions existed between the Sudan and Egypt just prior to occurrence of the outbreak. It is some 500 km from the Sudan to the Aswan Dam area of Egypt where agricultural development had provided irrigation channels highly suitable for the breeding of mosquito species.

These mechanisms represent those most likely to result in the introduction of RVF into new regions.

Wind-borne dispersal of infected mosquitoes on a north-south axis in association with the inter-tropical convergence zone could provide a mechanism for the extension of RVF outbreaks in sub-Saharan Africa.

Immunity

Natural

As animals mature their susceptibility to RVF disease decreases. Innate immunity varies between breeds and some breeds of sheep and goat appear to be relatively resistant. Herd immunity levels are high after epidemics; the immunity appears to be life-long. Immune dams transfer immunity to their offspring via colostrum and this affords some protection for up to 5 months in lambs.

Vaccines

The mouse-adapted Smithburn strain of RVF virus is used to produce live vaccines. They are highly immunogenic and induce durable, probably life-long, immunity within 7 days after a single inoculation, although cattle may not be fully protected. Large quantities can be produced readily and inexpensively. However, the virus is only partially attenuated and can cause abortion or fetal damage and prolonged gestation in a proportion of pregnant animals. It is also conceivable that the virus could be transmitted between animals by mosquitoes and revert to full virulence. The use of such vaccines is therefore inadvisable in countries where the presence of the virus has not been proven.

Vaccines prepared by the inactivation of wild strains of RVF virus with formalin or J-propriolactone give low antibody responses. Repeated inoculation after an initial double vaccination with an interval of 2 to 4 weeks is required to maintain immunity which is short-lived. They are safe in pregnant animals but are expensive to produce. Sheep are protected better than cattle whilst colostral immunity is inadequate.

Other experimental vaccines are undergoing assessment.

RVF virus survival in the environment

The survival of RVF virus in the environment is limited and it is susceptible to low pH (acid). Areas contaminated with blood spillage can be decontaminated with 2 per cent acetic acid or 5 per cent sodium
hypochlorite. Blood, even dried blood, may remain contaminated and infectious for humans for some months at ambient temperature. Pasteurisation renders milk safe. Chilled or frozen meat is probably safe to eat after storage and cooking. Hides and skins, bones and manure are rendered safe if sun-dried.

**PRINCIPLES OF CONTROL**

**Introduction**

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.

Vaccination in the face of established RVF epidemics has usually been applied too late to avert them or prevent considerable losses from occurring. Nevertheless, vaccination of large numbers of animals could ultimately have contributed to the abatement of epidemics and have been beneficial in reducing losses through their impact on herd immunity.

The facts that epidemics of RVF occur at long, irregular intervals of many years and that outbreaks tend to occur simultaneously across an extensive area makes it difficult to advocate, and justify the expense of, repeated prophylactic vaccination of susceptible livestock species during the long inter-epidemic periods. A promising approach to resolving this dilemma is the prediction of RVF epidemics. Monitoring of meteorological and remote sensing data, inter alia, Cold Cloud Duration (CCD - a measure of rainfall) and Normalized Difference Vegetation Index (NDVI - a measure of vegetation density/soil moisture), within a geographic information system can indicate when conditions suitable for high vector multiplication are developing and sero-monitoring of livestock can indicate periods of increased viral activity. Prophylactic immunisation of livestock could then, conceivably, be applied in time to avert the most serious consequences.

**Control and elimination of outbreaks in newly-infected countries**

Activities undertaken should attempt to contain the virus at the site of introduction (by movement controls) and then eliminate it (destruction of infected and potentially infected livestock). It is very
important that the timing and sequence of operations give the greatest chance of eliminating the virus before it becomes widespread in an insect vector or animal populations, including wildlife.

Quarantine and movement controls

Immediately on suspicion of the disease, an infected area should be designated extending at least 10 km from known infected animals. The area at risk is also determined with respect to geographical features, prevailing winds, the presence of possible vectors and the density of prospective hosts. Movements in and out of the area are prohibited.

After introduction of RVF to a new area, effective quarantine and movement controls are essential to reduce spread, even if the virus has become established in an insect vector population. Initially stringent, these controls can be relaxed a little in favour of zonal restrictions, centred on the infected area, once the extent of infection has been assessed.

Slaughter of clinical cases and contacts

The slaughter of all animals on the premises is likely to be used only on an index farm or herd when it is believed that the virus has not been widely disseminated. The availability of compensation will largely determine its feasibility. Clinical cases should be slaughtered first (by shooting preferably), followed by animals in direct contact and then the remaining susceptible animals. It is not necessary to slaughter healthy animals outside the affected herd. Care must be taken not to generate aerosols and expose animals and people to infection. Disposal by burial is preferable.

Surveillance and tracing

Infected humans can play an important role in the transmission of RVF and it will be necessary to trace both animal and human movements. Close collaboration between human and medical staff is called for to trace both the source of infection and possible secondary cases. Surveillance involves clinical examination of livestock at risk and serological monitoring of a statistically significant sample at short intervals to determine if virus transmission is occurring. Vector studies may also be needed. Vector and serological surveillance will need to be continued for at least one year to start to demonstrate freedom from infection. The actual or potential role of wild ruminants must be assessed early.

Vaccination

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.
Vector control

A realistic assessment of the feasibility of vector control must be made at the earliest possible time in discussion with locust and other plant pest control personnel. Aerial or ground ultra low volume application of insecticides or thermal fogs or mists generated on the ground could be considered. Treatment of livestock with a systemic insecticide (e.g. an avermectin) or a topical insecticide (e.g. a synthetic pyrethroid) over a wide area could assist in reducing the populations of potential vectors. Biological control systems using Bacillus thuringiensis or hormones suppressing larval development are more acceptable alternatives.

Public awareness

Public awareness programmes are essential to keep the public fully and accurately informed, not only to reduce concern but also to assist in recognition of disease cases. An informed press statement should be released immediately the disease diagnosis is confirmed.

SOURCES OF ASSISTANCE

- RVF is one of the foci of strategic planning and tactical responses by FAO's Emergency Prevention System for Transboundary Animal and Plant Pests and Diseases - EMPRES. Any country experiencing problems or requiring advice is invited to contact EMPRES staff either directly in Rome or through any FAO Office.

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Advice on diagnostic procedures and possible assistance could be available from the WHO RVF Collaborating Centre:

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