RIFT VALLEY FEVER
STANDARD OPERATING PROCEDURES:
1. OVERVIEW OF ETIOLOGY AND ECOLOGY

FAD PReP

Foreign Animal Disease
Preparedness & Response Plan

USDA

United States
Department of
Agriculture

United States Department of Agriculture • Animal and Plant Health Inspection Service • Veterinary Services

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The Foreign Animal Disease Preparedness and Response Plan (FAD PReP) Standard Operating Procedures (SOPs) provide operational guidance for responding to an animal health emergency in the United States.

These draft SOPs are under ongoing review. This document was last updated in **October 2013.** Please send questions or comments to:

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FAD PReP
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Rift Valley Fever (RVF)

Etiology and Ecology Quick Summary

Disease

Rift Valley fever, Enzootic Hepatitis, Slenkdalkoors (Afrik.).

Mortality and Morbidity

High morbidity. Mortality varies by species, very high in young animals.

Susceptible Species

Cattle, sheep, goats, dromedaries, wild ruminants, dogs, cats, some rodents, horses, non-human primates, humans.

Zoonotic Potential?

Yes. Humans are very susceptible. Typically causes undifferentiated febrile illness.

Reservoir

Thought to be *Aedes* mosquitoes.

Transmission

Predominantly vector-borne. Aerosol transmission is possible.

Persistence in the Environment

RVF degrades in the environment. Inactivated by lipid solvents, detergents, and acidic pH.

Animal Products and By-Products

Virus is inactivated by pasteurization and quickly destroyed by pH changes in decomposing carcasses. Little is known about persistence in skins, wool, bones, and other products.

1.1 Introduction

Rift Valley fever (RVF) is an acute arthropod-borne viral disease important in domestic ruminants (cattle, sheep, and goats) and humans. Though RVF is endemic in many areas of Africa, it does not currently exist in the United States. RVF is a World Organization for Animal Health (OIE) notifiable disease in 2013; RVF virus is a select agent regulated by both the U.S. Department of Agriculture (USDA) and U.S. Department of Health and Human Services.[1] Having no prior exposure to the RVF virus, both animal and human populations in the United States would be highly susceptible if RVF was introduced.

RVF in ruminants causes abortions in adult cattle, sheep, and goats and high mortality in young animals. Humans are very susceptible to RVF infection, which is usually associated with a self-limiting mild influenza-like disease, with spontaneous recovery within a week. However in a small percentage (approximately 1-2 percent) of cases, infection progresses to more serious disease such as acute hepatic necrosis or hepatitis, meningoencephalitis, retinitis, and rarely, to the most severe, fatal, hemorrhagic fever form.[2]

This document is intended to be an overview. Additional resources on RVF are listed in Attachment 1.A. Foreign Animal Disease Preparedness and Response Plan (FAD PReP) documents are available on the APHIS public website (http://www.aphis.usda.gov/animal_health/emergency_management/) or on the APHIS Intranet (http://inside.aphis.usda.gov/vs/em/fadprep.shtml, for APHIS employees).

1.1.1 Preparedness Goal

The USDA Animal and Plant Health Inspection Service (APHIS) will provide etiology and ecology summaries for RVF, and update these summaries at regular intervals.

1.1.2 Response Goal

Unified Command and stakeholders will have a common set of etiology and ecology definitions and descriptions, to ensure proper understanding of RVF when establishing or revising goals, objectives, strategies, and procedures.

1.2 Purpose

The purpose of this document is to provide responders and stakeholders with a common understanding of the disease agent.

1.3 Etiology

1.3.1 Name

Rift Valley fever, Enzootic Hepatitis, Slenkdalkoors (Afrik.). RVF was first reported in 1931 by Daubney, Hudson, and Garnham as an outbreak of enzootic hepatitis observed in the Rift Valley

[1] Agricultural Bioterrorism Protection Act of 2002. 7 CFR Part 331 and 9 CFR Part 121.

[2] Center for Food Security and Public Health (CFSPH), Iowa State University, College of Veterinary Medicine. 2007. "Rift Valley Fever." http://cfsph.iastate.edu/Factsheets/pdfs/rift_valley_fever.pdf.

of Africa (hence, its name).[3,4]

1.3.2 Virus Characteristics

According to the International Committee on Taxonomy of Viruses, this disease has the following characteristics:[5]

- Family: Bunyaviridae
- Genera: Phlebovirus
- Type species: Rift Valley fever virus (RVFV)
- Baltimore Classification: Group V (-) ssRNA (the small segment is ambisense, RNA is ribonucleic acid).

1.3.3 Morphology

RVFV forms enveloped, spherical virions with diameters of 90–110 nm and contains no matrix proteins. It has a tripartite genome consisting of large (L), medium (M), and small (S) RNA segments. These RNA segments are single-stranded and exist in a helical formation within the virion. The L segment codes for the viral polymerase in the negative sense, the M segment codes for the enveloped glycoproteins G1 and G2, and the S segment codes for the N nucleoprotein. There is only one serological and immunological type of RVFV. Virus strains are classified into three lineages: Egyptian, West African, and Central-East African. [6]

1.4 Ecology

1.4.1 General Overview

RVF is a peracute or acute febrile disease of sheep, cattle, and goats. The disease in these species is characterized by high abortion rates and high mortality in neonates. After death, pathology typically finds hepatic necrosis, splenomegaly, and gastrointestinal hemorrhage. Humans usually present with acute febrile disease, which in a small percentage of cases may progress to retinal, hepatic, or encephalitic lesions.[7,8]

The historic distribution of RVF is the African continent, Madagascar, and the Arabian Peninsula. It is especially prevalent in sub-Saharan areas. Major epizootics have occurred at intervals of 5–20 years in southern and eastern Africa. Significant outbreaks occurred in Egypt in 1977–78 and 1993. More recently there have been outbreaks in Central African Republic (1997), Kenya (1997–98), Mauritania (1998), Mozambique (1997), Tanzania (1998), Zambia (1997),

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[3] R. Daubney, J.R. Hudson, and P.C. Garnham. 1931. "Enzootic hepatitis or Rift Valley fever: an undescribed disease of sheep, cattle, and man from East Africa. *Journal of Pathology and Bacteriology*, 34, 545-579.

[4] Also see Findlay, G.M. 1932. "Rift Valley fever or enzootic hepatitis." *Transac Royal Soc Trop Med Hyg*. 25(4), 229-265.

[5] International Committee on Taxonomy of Viruses. 2008. *Universal Database of the International Committee on Taxonomy of Viruses*. http://www.ictvdb.org/Ictv/ICTVindex.htm.

[6] United States Animal Health Association (USAHA). 2008. *Foreign Animal Diseases*. 7th Ed. Boca Raton, FL: Boca Publications Group, pp.369-375.

[7] United States Animal Health Association (USAHA). 2008. *Foreign Animal Diseases.* 7th Ed. Boca Raton, FL: Boca Publications Group, pp.369-375.

[8] World Organization for Animal Health (OIE). 2008. *OIE Manual of Diagnostic Tests and Vaccines for Terrestrial Animals*. "Section 2.1.14 Rift Valley Fever." http://www.oie.int/fileadmin/Home/eng/Health_standards/tahm/2.01.14_RVF.pdf.

Zimbabwe (1998), and South Africa (1999). In 2000, the disease was first reported off the African continent in Saudi Arabia and Yemen. Recent outbreaks in Kenya (2006–07), and in South Africa and Somalia (2010), were also reported in the Morbidity and Mortality Weekly Report (MMWR).[9,10] In 2011-2012, there were additional reports of infection in Mauritania, Senegal, Namibia, and South Africa.[11]

Outbreaks outside the recorded historic disease pattern of RVFV demonstrate the ecological flexibility of the virus and cause for vigilance.

1.4.2 Susceptible Species

RVF infects a wide range of vertebrate hosts, including

- cattle, sheep, goats
- dromedaries
- wild ruminants, buffaloes, waterbucks
- humans
- horses
- dogs, cats, bats, several rodents, and
- nonhuman primates.

Susceptibility varies amongst these species: younger animals, including lambs, kids, puppies, and kittens are extremely or highly susceptible. Cattle, buffalo, humans, and Asian monkeys are moderately susceptible. Camels, horses, and pigs are less susceptible, and develop a mild form of disease and viremia. Birds, reptiles, and amphibians are not susceptible to RVF.[12]

Key species susceptible to RVF in the United States include sheep, cattle, goats, and buffalo. Disease outbreaks can affect up to 90 percent of susceptible animals. In adult sheep, mortality rates are between 15–30 percent; the abortion rate is nearly 100 percent in pregnant ewes. A 95 percent mortality rate is observed in lambs less than 1-week old. In pregnant cows, the abortion rate can reach 85 percent, and the mortality rate in calves ranges from 10–70 percent.[13,14] Typically, RVF is recognized by the sudden onset of abortion storms after heavy rainfall.[15] In young animals, fever, anorexia, and weakness are common symptoms. There is a significant variation in the susceptibility of animals depending on the specific RVF genotype.

[9] Centers for Disease Control and Prevention (CDC). 2007. "Outbreak of Rift Valley Fever—Kenya, November–January 2007." *Morbidity and Mortality Weekly Report (MMWR),* 56(04), 73-76.

[10] Food and Agriculture Organization of the United Nations (FAO). 2002. "*Preparation of Rift Valley Fever Contingency Plans*." *FAO Animal Health Manual No.15.* Rome: FAO. http://www.fao.org/DOCREP/005/Y4140E/y4140e00.htm.

[11] World Organization for Animal Health (OIE). 2013. World Animal Health Information Database (WAHID). http://www.oie.int.

[12] World Organization for Animal Health (OIE). 2009. Rift Valley Fever Technical Disease Card. Available at http://www.oie.int/animal-health-in-the-world/technical-disease-cards/.

[13] Center for Food Security and Public Health (CFSPH), Iowa State University, College of Veterinary Medicine. 2007. "Rift Valley Fever." http://cfsph.iastate.edu/Factsheets/pdfs/rift_valley_fever.pdf.

[14] World Organization for Animal Health (OIE). 2009. *Rift Valley Fever Technical Disease Card.* Available at http://www.oie.int/animal-health-in-the-world/technical-disease-cards/.

[15] Bird, B.H., Kstazek, T.G., Nichol, S.T., MacLachlan, N.J. 2009. "Rift Valley fever virus." *JAVMA,* 234(7), 883-93.

1.4.3 Reservoirs

There is evidence that *Aedes mcintoshi* mosquitoes are capable of vertical transmission and are thought to be the primary reservoir for RVFV. However, an animal reservoir has not been ruled out and an inter-epidemic cycle is thought to exist in Egypt and sub-Saharan Africa. In Africa, RVF circulates in widespread outbreaks occurring at 5- to 15-year intervals in dry areas of the continent, after periods of heavy rainfall.[16] This allows the development of a susceptible population and requires a viral reservoir during the inter-epidemic period. Inter-epizootic periods may last for several decades in arid areas, and during this time, the prevalence of infection in humans, animals, and mosquitoes may be difficult to detect.[17]

1.4.4 Introduction and Epizootic Cycle of RVF

RVF is predominantly a vector-borne disease. The major vectors are specific species of mosquitoes, although biting midges and ticks have been implicated in some research. A wide range of vertebrate hoses are susceptible, but ruminants are the amplifying hosts. Humans are also highly susceptible and amplifying hosts; they are typically infected by mosquitoes, though human infections have also occurred with exposure to infected carcasses. Of susceptible animal species, 85–95 percent of all those exposed will become sick rapidly, typically in 1–3 days.[18]

RVF circulates in both epizootic and inter-epizootic cycles. This occurs particularly in high rainfall forest zones in coastal and central Africa, though epizootics have occurred in Saudi Arabia, Egypt, and Yemen. Epizootics of RVF occur in infected areas after unusually heavy rainfall and flooding;[19] climatic conditions that favor the mosquito vector populations, such as high rainfall and localized flooding, are being used to predict ideal conditions for an RVF outbreak.[20] During an epizootic, the virus circulates among infected vector and mammalian hosts. Cattle and sheep are the most significant livestock amplifiers of RVFV.

1.4.4.1 Rainfall and the Epizootic Cycle

RVFV is maintained in a cyclical pattern in Africa, resulting in significant epizootics of the disease during favorable climatic conditions. In southern Africa, outbreaks are usually associated with above average rainfall during the wet season. This leads to flooding of the dambos and subsequent hatching of the floodwater *Aedes* (see section on “Reservoirs”), which have been vertically infected. This can lead to the rapid spread of RVF as mosquitoes with an existing infection at adult emergence can transmit the virus with the first blood meal without the need to encounter a viremic host, followed by the incubation period for virus multiplication and dissemination. Heavy rainfall also provides breeding sites for the mosquito genera such as *Culex, Anopheles*, and *Mansonia.*

In northern Africa, outbreaks have appeared mainly along irrigation areas of the Nile River. In

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[16] World Organization for Animal Health (OIE). 2013. Terrestrial Animal Health Code. Chapter 8.12, Rift Valley Fever. http://www.oie.int.

[17] Gordon, S.W., R.F. Tammariello, K.J. Linthicum, D.J. Dohm et al. 1992. “Arbovirus isolations from mosquitoes collected during 1988 in the Senegal River Basin.” *Am J. Trop. Med. Hyg.* 47(6), 742-8.

[18] Bird, B.H., Kstazek, T.G., Nichol, S.T., MacLachlan, N.J. 2009. “Rift Valley fever virus.” *JAVMA,* 234(7), 883-93.

[19] World Organization for Animal Health (OIE). 2013. Terrestrial Animal Health Code. Chapter 8.12, Rift Valley Fever. http://www.oie.int.

[20] Center for Food Security and Public Health (CFSPH), Iowa State University, College of Veterinary Medicine. 2007. “Rift Valley Fever.” http://cfsph.iastate.edu/Factsheets/pdfs/rift_valley_fever.pdf.

eastern Africa, the virus may survive inter-epidemic periods through vertical transmission in *Aedes* belonging to the subgenera *Neomelaniconion* and possibly *Aedimorphus*. Field isolates of virus from *Ae. mcintoshi* males and females collected as immatures are suggestive evidence for the inter-epizootic survival of RVFV by vertical transmission of the virus in floodwater *Aedes* mosquitoes. RVFV is present in dormant eggs of the mosquito *Ae. Mcintoshi*, located in the soil of grassland depressions known as dambos. When these depressions fill with water, the eggs hatch, and infected mosquitoes develop. These mosquitoes infect an amplifying host (ruminant), which serves as a source of infection for many other genera of mosquitoes that rapidly spread the disease. If the area of infected mosquitoes extends into areas of susceptible animals, many clinical cases may arise.

1.4.5 Transmission of RVF

Transmission of RVFV is associated with the *Aedes* species of mosquitoes (particularly *Aedimorphus* and *Neomelaniconion*) in east and south Africa.[21] In west Africa, other *Aedes* species, commonly *Aedes vexans*, typically transmit RVFV, though *Culex poicilipes* has also been associated with RVFV transmission in this region.[22,23,24] In north Africa, during the 1977–1978 epizootic in Egypt, *Culex pipiens* played an important role.[25] The epidemiology of RVF in east Africa (e.g., vector: *Ae mcintoshi* with vertical transmission), as described above, may differ from that in western Africa, where vertical transmission has not been observed. However, there is currently not evidence suggesting the presence or absence of vertical transmission in most mosquito species.

Other vectors are also likely to transmit RVFV, including other species of *Aedes* (particularly *Ae. cumminsii*, *Ae. circumluteolus*, and *Ae. mcintoshi*), Anopheles, *Culex, Eretmapodites,* and *Mansonia*. In addition, it is important to note that variation in vector competence has been demonstrated for mosquitoes of the same species from different geographical regions.[26] RVFV can also be transmitted through direct and indirect (fomite) contact. The following sections provide an overview of these various transmission pathways.

1.4.5.1 Vectors

1.4.5.1.1 Vertical Transmission

RVFV may be transmitted vertically between generations of mosquitoes without cycling through a vertebrate host. Epizootics are the most notable manifestation of RVF, but persistence of the virus in the environment likely depends on vertical transmission in certain *Aedes spp*, subgenera

[21] Fontenille, D., M. Traore-Lamizana, M. Diallo, J. Thonnon, J.P. Digoutte, and H.G. Zeller. 1998. "New Vectors of Rift Valley Fever in West Africa." *Emerging Infectious Diseases,* 4(2).

[22] Fontenille, D., M. Traore-Lamizana, M. Diallo, J. Thonnon, J.P. Digoutte, and H.G. Zeller. 1998. "New Vectors of Rift Valley Fever in West Africa." *Emerging Infectious Diseases,* 4(2).

[23] Diallo, M., Nabeth, P., Ba, K. et al. 2005. Mosquito vectors of the 1998-1999 outbreak of Rift Valley Fever and other arboviruses (Bagaza, Sanar, Wesselsbron, and West Nile) in Mauritania and Senegal." *Med Vet Entomol.* 19(2), 199-26.

[24] Diallo, M., L. Lochouarn, K. Ba, A.A. Sall, et al.2000. "First isolation of the Rift Valley fever virus from *Culex poicilipes* (Diptera: Cuclicidae) in Nature. *Am. J. Trop. Med. Hyg.* 62(6), 702-4.

[25] Meegan, J.M., G.M. Khalil, H. Hoogstraal, F.K. Adham. 1980. "Experimental transmission and field isolation studies implicating Culex pipiens as a vector of Rift Valley fever virus in Egypt." *Am. J. Trop. Med. Hyg.* 29(6): 1405-1410.

[26] Turell, M.J., K.E. Bennett, and W.C. Wilson. 2010. "Potential for North American mosquitoes (Diptera: Culicidae) to transmit Rift Valley fever virus."*J Med Ent, 4*7(5), 884-9.

Neomelaniconion and possibly *Aedimorphus*.[27] These mosquitoes, the "floodwater *Aedes*" mentioned previously, have drought-resistant eggs that survive for several years without hatching. [28] This vertical transmission allows RVFV to survive in the environment. These mosquitoes lay eggs in which the first stage larvae develop but then enter a resting phase until heavy rainfall and subsequent flooding stimulates adult emergence. Egg hatching is also staggered, which is a survival adaptation of the species of mosquito and beneficial to RVFV.[29] There is no evidence suggesting how long RVFV can survive in mosquito eggs.

1.4.5.1.2 Biological Transmission

Aedes mosquitoes are thought to serve as the major reservoir and vector. However, other species are key secondary vectors capable of biological transmission.[30] Biological vectors are the *Aedes*, *Culex*, *Eretmopodites*, and *Mansonia* mosquito species. The virus has been isolated in 40 mosquito species in 8 genera in the field, and experimentally more than 30 species have shown the ability to transmit the virus biologically.[31,32] The virus has also been isolated in Culicoides (biting midges) and Simulids (black flies), as well as in two tick species (*Amblyomma variegatum* and *Rhipicephalus appendiculatus*).[33] However, isolation does not necessarily demonstrate that a species is a competent biological vector.[34]

1.4.5.1.3 Mechanical Transmission

Biting midges (species of Culicoides) and sand flies could also play less significant roles in RVFV transmission.[35] RVFV can be mechanically transmitted by biting flies such as Culicoides, Phlebotomids, *Stomoxys calcitrans* (stable fly), Simulids, and other biting insects.[36, 37] Research has also demonstrated that mosquito species can transmit RVFV mechanically.[38] Though livestock are primarily infected by biological vectors, midges, and other biting insects play a role in mechanical dissemination of the disease once virus amplification has occurred in an animal host.

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[27] For example, see K.J. Linthicum, F.G. Davies, A. Kairo, and C.L. Bailey. 1985. "Rift Valley fever virus (family Bunyaviridae, genus *Phlebovirus).* Isolations from Diptera collected during an inter-epizootic period in Kenya." *Journal of Hygiene.* 95, 197-209.

[28] Bird, B.H., Kstazek, T.G., Nichol, S.T., MacLachlan, N.J. 2009. "Rift Valley fever virus." *JAVMA,* 234(7), 883-93.

[29] Mondet, B., A. Diaïté, J.A. Ndione, A.G. Fall et al. "Rainfall patterns and population dynamics of *Aedes (Aedimorphus) vexans arabiensis,* Patton 1905 (Diptera: Culicidae), a potential vector of Rift Valley Fever virus in Senegal." *J. Vector Ecology.* 30(1), 102-6.

[30] Bird, B.H., Kstazek, T.G., Nichol, S.T., MacLachlan, N.J. 2009. "Rift Valley fever virus." *JAVMA,* 234(7), 883-93.

[31] Turell, M.J., K.J. Linthicum, L.A. Patrican, F.G. Davies et al. 2008. "Vector Competence of Selected African Mosquito (Diptera: Culicidae) Species for Rift Valley Fever Virus." *J Med Ent* 45(1): 102-108.

[32] Fontenille, D., M. Traore-Lamizana, M. Diallo, J. Thonnon, J.P. Digoutte, and H.G. Zeller. 1998. "New Vectors of Rift Valley Fever in West Africa." *Emerging Infectious Diseases,* 4(2).

[33] Pepin, M. Bouloy, M., Bird, B., et al. 2010. "Rift Valley fever virus (*Bunyaviridae: Phlebovirus)*: an update on pathogenesis, molecular epidemiology, vectors, diagnostics and prevention." *Veterinary Research.* 41(61).

[34] Gerdes, G.H. 2004. "Rift Valley fever." *Rev. Sci. tech. Off. Int. Epiz.,* 23(2): 613-623.

[35] Jennings, M., G.S. Platt, and E.T. Bowen. 1982. "The susceptibility of Culicoides variipennis Coq. (Diptera: Ceratopogonidae) to laboratory infection with Rift Valley Fever virus." Trans. R. Soc. Trop. Med. Hyg. 76(5), 587-9.

[36] United States Animal Health Association (USAHA). 2008. Foreign Animal Diseases. 7th Ed. Boca Raton, FL: Boca Publications Group, pp.369-375.

[37] Turell, M.J., Dohm, D.J., Geden, C.J. et al. 2010. "Potential for Stable Flies and House Flies (Diptera: Muscidae) to Transmit Rift Valley Fever Virus." *Journal of the American Mosquito Control Association,* 26(4), 445-448.

[38] Hoch, A.L., T.P. Gargan, and C.L. Bailey. 1985. "Mechanical transmission of Rift Valley fever virus by hematophagous Diptera." *Am. J. Trop. Med. Hyg*. 34(1), 188-93.

1.4.5.1.4 Live Animals

There is no evidence that direct contact transmission plays a significant role in the transmission of RVF. However, in susceptible species, the virus can be transmitted in *utero* to the fetus.[39] RVFV has also been found in semen.[40] Because transmission can occur through direct contact with blood and other body fluids, it is hypothetically possible that animals could become infected through contact with an aborted fetus or placental membranes which do contain virus, though the relative importance of this transmission mechanism is not well understood.[41]

1.4.5.1.5 Animal Products and Byproducts

RVFV can be transmitted by physical contact with infected tissues, particularly during parturition, necropsy, slaughter, laboratory procedures, or meat preparation.[42] For humans, exposure to blood and tissue during slaughter poses the greatest risk for infection. Meat should be cooked thoroughly before eating; meat has not been implicated as a vehicle for human infection.[43]

Epidemiological evidence suggests RVFV can be transmitted through raw, unpasteurized milk.[44,45] The use of fresh, unpasteurized milk in RVF outbreaks should be avoided.

Little or no information is available on the role of wool, bones, skins, or other animal fibres in virus transmission. The OIE considers hides, skins, wool, and fiber to be "safe commodities," and recommends not requiring any specific cleaning, disinfection, or treatment of these commodities from countries with RVF.[46]

1.4.5.2 Fomites

Fomites that are contaminated with blood or other fluids need to be cleaned and disinfected to prevent the transmission of RVFV. In addition, reusing hypodermic needles for vaccination can transmit the virus from an infected to an uninfected animal.

1.4.5.3 Personnel

In addition to direct contact with infected animals and animal products, aerosol transmission has been documented in people involved with slaughter, post-mortem examinations, and laboratory

[39] Bird, B.H., Kstazek, T.G., Nichol, S.T., MacLachlan, N.J. 2009. "Rift Valley fever virus." *JAVMA,* 234(7), 883-93.

[40] Center for Food Security and Public Health (CFSPH), Iowa State University, College of Veterinary Medicine. 2007. "Rift Valley Fever." http://cfsph.iastate.edu/Factsheets/pdfs/rift_valley_fever.pdf

[41] Pepin, M. Bouloy, M., Bird, B., et al. 2010. "Rift Valley fever virus (*Bunyaviridae: Phlebovirus)*: an update on pathogenesis, molecular epidemiology, vectors, diagnostics and prevention." *Veterinary Research.* 41(61).

[42] Center for Food Security and Public Health (CFSPH), Iowa State University, College of Veterinary Medicine. 2007. "Rift Valley Fever." http://cfsph.iastate.edu/Factsheets/pdfs/rift_valley_fever.pdf.

[43] Peters, C.J. and K.J. Linthicum. 1994. "Rift Valley Fever." In G. Beran (ed.) *Handbook of Zoonoses*. Boca Raton, FL: CRC Press.

[44] Borio, L., T. Inglesby, C.J. Peters et al. 2002. "Hemorrhagic fever viruses as biological weapons: medical and public health management." *JAMA*, 287(18), 2391-405.

[45] United States Animal Health Association (USAHA). 2008. Foreign Animal Diseases. 7th Ed. Boca Raton, FL: Boca Publications Group, pp.369-375.

[46] World Organization for Animal Health (OIE). 2013. Terrestrial Animal Health Code. Rift Valley Fever, Chapter 8.12. Available at http://www.oie.int.

handling of tissues from infected animals.[47,48] Aerosol transmission is a potential pathway.[49] In addition, the first *in utero* transmission of RVFV in a newborn was reported in 2006.[50]

1.4.5.3.1 Incubation Period and Symptoms

In humans, infection with RVFV typically causes an asymptomatic infection or a mild to moderate, non-fatal, flu-like illness with fever and liver abnormalities after a 2–6 day period. In uncomplicated RVF infections, symptoms include fever, headache, generalized weakness, myalgia, and back pain. In addition, neck stiffness, vomiting, and photophobia are also observed in some patients.[51]

While most people recover spontaneously from RVF within approximately two days to a week, a few patients develop ocular disease and meningoencephalitis; these clinical signs are typically observed one to three weeks after the initial symptoms.[52] 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 meningoencphalitis.

In an even smaller percentage of patients, complications—including hemorrhagic fever—occur.[53] Hemorrhagic fever usually develops two to four days after initial symptoms, which may include jaundice, hematemesis, melena, a purpuric rash, petechiae, bleeding from the gums, and can progress to frank hemorrhages. Hemorrhagic fever appears to be the major cause of death in RVFV infection.[54]

1.4.5.4 Factors Influencing Transmission

Infection rates of biological vectors are directly proportional to the titer of the virus in the circulating blood of the host. The high titers that occur in vertebrate hoses, including RVFV infected humans, are conducive to high infection rates in a range of vectors.[55] High titers of circulating virus are also required for mechanical transmission.

There is evidence that *Culex pipiens* mosquitoes infected with RVF are adversely affected by the virus.[56] The infected mosquitoes are less able to engorge with blood, which leads to an increase in probing and an increase in attempted feedings on a greater number of hosts. Both of these

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[47] Smithburn, K.C., A.F. Mahaffy, A.J. Haddow, et al. 1949. "Rift Valley Fever: Accidental Infections Among Laboratory Workers." J. *Immun*. 62, 213-27.

[48] Bird, B.H., Kstazek, T.G., Nichol, S.T., MacLachlan, N.J. 2009. "Rift Valley fever virus." *JAVMA*, 234(7), 883-93.

[49] Borio, L., T. Inglesby, C.J. Peters et al. 2002. "Hemorrhagic fever viruses as biological weapons: medical and public health management." *JAMA,* 287(18), 2391-405.

[50] Arishi, H.M., A.Y. Ageel, and M.N. Hazmi. 2006. "Vertical transmission of fatal Rift Valley fever in a newborn." *Ann Trop Paediatr*. 26(3), 251,-3

[51] Center for Food Security and Public Health (CFSPH), Iowa State University, College of Veterinary Medicine. 2007. "Rift Valley Fever." http://cfsph.iastate.edu/Factsheets/pdfs/rift_valley_fever.pdf.

[52] Center for Food Security and Public Health (CFSPH), Iowa State University, College of Veterinary Medicine. 2007. "Rift Valley Fever." http://cfsph.iastate.edu/Factsheets/pdfs/rift_valley_fever.pdf.

[53] Bird, B.H., Kstazek, T.G., Nichol, S.T., MacLachlan, N.J. 2009. "Rift Valley fever virus." *JAVMA,* 234(7), 883-93.

[54] Center for Food Security and Public Health (CFSPH), Iowa State University, College of Veterinary Medicine. 2007. "Rift Valley Fever." http://cfsph.iastate.edu/Factsheets/pdfs/rift_valley_fever.pdf.

[55] Center for Food Security and Public Health (CFSPH), Iowa State University, College of Veterinary Medicine. 2007. "Rift Valley Fever." http://cfsph.iastate.edu/Factsheets/pdfs/rift_valley_fever.pdf.

[56] For example, Gad, A.M., A.N. Hassan, A.I. Merdan. 1989. "Transmission of Rift Valley feer virus by different geographic strains of Culex pipiens Egypt." *J Egypt Public Health Assoc.* 64(5-6): 363-79.

behavioral changes are likely to increase the transmission rate of the virus. Temperature also impacts the susceptibility of *Culex pipiens* to RVFV; at lower temperatures, fewer mosquitoes have virus that is detectable (13°C in comparison to 26°C).[57]

Mosquito survival is governed by a range of factors, such as temperature, wind, rainfall, and host availability. These factors impact how long adult mosquitoes may be able to survive and maintain RVFV.[58] Adult mosquitoes that become infected with RVFV usually remain infected for life. At least one species of mosquito has been shown capable of transmitting RVFV 36 days after oral infection. In general, the likelihood of survival of RVFV in mosquitoes in excess of approximately 4 weeks is very low.

1.5 Risk of Introduction

It is possible that RVF could be introduced to North America and the United States. With increasing travel and trade, there are many pathways for the entry of RVFV such as the importation of infected animals, people, and vectors.[59] Intentional introduction may also be a concern: RVFV has been considered as a potential biological weapon.[60,61] The United States has millions of susceptible animals, including over 5 million sheep and 90 million cows.

Few studies have thoroughly explored vector competency, but preliminary results suggest that several species of North American mosquitoes are capable of transmitting RVFV effectively.[62] Studies have demonstrated that multiple species of North American mosquitoes could be potential vectors, including multiple species of *Aedes* and *Culex* mosquitoes.[63,64] One study, published in 2008, collected selected mosquito species from the southeastern United States to assess their ability to serve as potential vectors for RVFV. Mosquitoes were transported to research facility and fed on adult hamsters that had been inoculated one day prior with RVFV. These mosquitoes were tested for infection and ability to transmit RVFV after incubation at 26ºC for 7–21 days. None of the species tested (*Ae. taeniorhynchus, Ae. vexans, Cx. erraticus, Cx. nigripalpus, Cx. quinquefasciatus, and Cx. salinarius*) were efficient vectors after they fed on hamsters with viremias ranging from 104.1 to 106.9 plaque-forming units (PFU)/ml. However, *Ae. taeniorhynchus, Ae. vexans, and Cx. erraticus* all developed disseminated infections after they fed on hamsters with viremias between 108.5 and 1010.2 PFU/ml, and both *Ae. vexans* and *Cx. erraticus* transmitted RVFV by bite.[65]

[57] Brubaker, J.F. and M.J. Turell. 1998. "Effect of environmental temperature on the susceptibility of Culex pipiens (Diptera: Culicidae) to Rift Valley fever virus." *J Med Entomol*. 35(6), 918-21

[58] Brubaker, J.F. and M.J. Turell. 1998. "Effect of environmental temperature on the susceptibility of Culex pipiens (Diptera: Culicidae) to Rift Valley fever virus." *J Med Entomol.* 35(6), 918-21

[59] Kasari, T.R., D.A. Carr, T.V. Lynn, J.T. Weaver. 2008. "Evaluation of pathways for release of Rift Valley fever virus into domestic ruminant livestock, ruminant wildlife, and human populations in the continental United States. *JAVMA*, 232(4): 514-29.

[60] Borio, L., T. Inglesby, C.J. Peters et al. 2002. "Hemorrhagic fever viruses as biological weapons: medical and public health management." *JAMA,* 287(18), 2391-405.

[61] Bird, B.H., Kstazek, T.G., Nichol, S.T., MacLachlan, N.J. 2009. "Rift Valley fever virus." *JAVMA,* 234(7), 883-93.

[62] House, J.A., M.J. Turell, and C.A. Mebus. 1992. "Rift Valley fever: present status and risk to the Western Hemisphere." *Journal of Med Ent*. 35(2): 132-5.

[63] Gargan, T.P., G.G. Clark, D.J. Dohm, M.J. Turrell, and C.L. Bailey. 1988. "Vector Potential of Selected North American Mosquito Species for Rift Valley Fever Virus." *Am. J. Trop. Med. Hyg.* 38(2), 440-6.

[64] Bird, B.H., Kstazek, T.G., Nichol, S.T., MacLachlan, N.J. 2009. "Rift Valley fever virus." *JAVMA,* 234(7), 883-93.

[65] Turell, M.J., D.J. Dohm, C.N. Mores, L. Terracina, et al. 2008. "Potential for North American Mosquitoes to Transmit Rift Valley Fever Virus." *Journal of the American Mosquito Control Association,* 24(4): 502-507.

An additional study evaluated the ability of: *Cx. erraticus, Cx. erythrothorax, Cx. nigripalpus, Cx. pipiens, Cx. quinquefasciatus, Cx. tarsalis, Ae. dorsalis, Ae. vexans, An. quadrimaculatus, and Culicoides sonorensis* from the Western, Midwestern, and Southern United States to transmit RVFV. *Cx. tarsalis*, a principal vector of West Nile virus, was found to be a competent vector of RVFV with an estimated transmission rate of 52 percent. Lower estimated transmission rates were reported for *Cx. erythrothorax, Cx. pipiens, Cx. erraticus*, and *Ae. dorsalis* from 2-10 percent and for the remaining species were <1 percent. *An. quadrimaculatus and C. sonorensis* were found to not be compent vector species of RVFV.[66]

Further vector competence and ecology studies are needed to determine the potential role of North American mosquito species and the factors such as temperature dependence, seasonality and longevity that would affect the potential role of these species in RVFV transmission. However, the introduction of RVFV to the United States is definitely a concern.

1.5.1 Vector Competence and Transmission

Table 1-1 lists selected species of mosquitoes, their primary geographic location, whether any evidence has suggested that they may be a competent RVFV vector, and whether they are capable of vertical transmission.[67,68]

[66] Turell, M.J., K.E. Bennett, and W.C. Wilson. 2010. “Potential for North American mosquitoes (Diptera: Culicidae) to transmit Rift Valley fever virus.”*J Med Ent, 4*7(5), 884-9.

[67] Adapted from National Veterinary Stockpile. 2006. National Veterinary Stockpile Countermeasures Working Group Report: Rift Valley Fever. Water Reed Biosystematics Unit, 2010.

[68] Also see the following references:

- Turell, M.J., C.L. Bailey, J.R. Beaman, 1988. “Vector competence of a Houston, Texas strain of Aedes Albopictus for Rift Valley Fever Virus. J. American Mosquito Control Assoc. 4(1), 94-6.;
- Turell, M.J., S.M. Presley, A.M. Gad, S.E. Cope et al. 1996. “Vector Competence of Egyptian Mosquitoes for Rift Valley Fever Virus.” Am. J. Trop. Med. Hyg. 54(2): 136-139.;
- Turell, M.J., K.E. Bennett, and W.C. Wilson. 2010. “Potential for North American mosquitoes (Diptera: Culicidae) to transmit Rift Valley fever virus.”J Med Ent, 47(5), 884-9.;
- Gargan, T.P., G.G. Clark, D.J. Dohm, M.J. Turrell, and C.L. Bailey. 1988. “Vector Potential of Selected North American Mosquito Species for Rift Valley Fever Virus.” Am. J. Trop. Med. Hyg. 38(2), 440-6.;
- Turell, M.J., K.E. Bennett, and W.C. Wilson. 2010. “Potential for North American mosquitoes (Diptera: Culicidae) to transmit Rift Valley fever virus.”J Med Ent, 47(5), 884-9.;
- Diallo, M., Nabeth, P., Ba, K. et al. 2005. Mosquito vectors of the 1998-1999 outbreak of Rift Valley Fever and other arboviruses (Bagaza, Sanar, Wesselsbron, and West Nile) in Mauritania and Senegal.” Med Vet Entomol. 19(2), 199-26.;
- Brubaker, J.F. and M.J. Turell. 1998. “Effect of environmental temperature on the susceptibility of Culex pipiens (Diptera: Culicidae) to Rift Valley fever virus.” J Med Entomol. 35(6), 918-21.
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- Turell, M.J., K.J. Linthicum, L.A. Patrican, F.G. Davies et al. 2008. “Vector Competence of Selected African Mosquito (Diptera: Culicidae) Species for Rift Valley Fever Virus.” J Med Ent 45(1): 102-108.

Table 1-1. Sample Mosquito Species Vector Competence and Transmission[69]

Selected Mosquito Vectors	Primary Geographical Location of Mosquito[a]	RVFV Vector Competence	Vertical Transmission
Aedes aegypti	Worldwide	Yes[b]	Unknown
Aedes albopictus	Worldwide	Yes[b]	Unknown
Aedes caballus	Africa, Middle East	Yes	Unknown
Aedes calceatus	Africa	Yes[b]	Unknown
Aedes canadensis	N. America	Yes[b]	Unknown
Aedes caspius	Africa, Europe, Middle East	Yes	Unknown
Aedes circumluteolus	Africa	Yes	Unknown
Aedes dorsalis	N. America, Europe, Asia	Yes	Unknown
Aedes excrucians	N. America, Europe, Asia	Yes[b]	Unknown
Aedes mcintoshi	Africa, Australia	Yes	Suspected
Aedes palpalis	Africa, Australia	Yes	Unknown
Aedes sollicitans	N. America	Yes	Unknown
Aedes taeniorhynchus	Americas	Yes	Unknown
Aedes triseriatus	N. America	Yes[b]	Unknown
Aedes vexans	Worldwide except South America	Yes	Unknown
Anopheles species	N. America, Africa (Tested, Anopheles exist worldwide)	No	Unknown
Culex antennatus	Africa, Middle East	Yes	Unknown
Culex erraticus	Americas	Yes	Unknown
Culex erythrothorax	N. America	Yes	Unknown
Culex neavei	Africa	Yes	Unknown
Culex nigripalpus	Americas	No	Unknown
Culex perexiguus	Africa, Middle East	Yes	Unknown
Culex pipiens	Worldwide	Yes	Unknown
Culex poicilipes	Africa	Yes	Unknown
Culex quinquefasciatus	Worldwide	Inefficient	Unknown
Culex salinarius	N. America	Yes[b]	Unknown
Culex tarsalis	N. America	Yes	Unknown
Culex territans	Europe, Africa, North America	Yes[b]	Unknown
Culex theileri	Africa, Middle East, Asia	Yes	Unknown
Culex tritaeniorhynchus	Africa, Asia, Middle East	Yes	Unknown
Culex univittatus	Africa	Yes	Unknown
Culex zombaensis	Africa	Yes	Unknown
Eretmapodites chrysogaster	Africa	Yes	Unknown

[69] For a good source of mosquito information, see Walter Reed Biosystematics Unit. 2010. Systematic Catalog of Culicidae. Available at: http://www.mosquitocatalog.org/default.aspx.

Selected Mosquito Vectors	Primary Geographical Location of Mosquito[a]	RVFV Vector Competence	Vertical Transmission
Eretmapodites quinquevittatus	Africa	Yes	Unknown
Eretmapodites species (other)	Africa	Suspected	Unknown
Mansonia species	Africa	Suspected	Unknown
Psorophora columbiae	Americas	Unknown	Unknown

[a] This is the geographic distribution of the mosquitoes. However, there is variation in vector competence based on geographic location even in mosquitoes of the same species. See Turell et al. 2010 for more information.

[b] Probably of lower importance.

Table 1-2 lists selected non-mosquito vectors, their primary geographical location, and whether they can transmit RVF.

Table 1-2. Other Selected Vectors

Vector	Primary Geographical Location	Type of Transmission
Culicoides species	Europe, Africa	Mechanical, unknown biological
Phlebotomus species	Europe, Africa	Mechanical, some spp. also biological
Simulium species	Worldwide	Mechanical, unknown biological
Stomoxys species	N. America	Mechanical

1.6 Environmental Persistence of RVF Viruses

RVFV degrades in the environment. The virus is inactivated by lipid solvents, detergents, and low pH.[70] At neutral or alkaline pH, particularly in the presence of protein material, such as serum, the virus can remain viable for up to 4 months at 4 °C and for several days at ambient room temperature. The virus is destroyed by strong sunlight, and can survive in dried blood for up to 3 months.[71]

Aerosolized RVFV increases in stability as the relative humidity decreases. An aerosol has a half-life of 77 minutes at 24 °C and 30 percent relative humidity.[72] Disinfectants containing strong solutions of sodium or calcium hypochlorite are effective for inactivating the virus on clean surfaces; potassium peroxymonosulfate and sodium chloride (Virkon-S) is also very effective.[73]

[70] National Veterinary Stockpile. 2006. National Veterinary Stockpile Countermeasures Working Group Report: Rift Valley Fever.

[71] Food and Agriculture Organization of the United Nations (FAO). Manual on procedures for disease eradication by stamping out. Part 3: Decontamination Procedures. Available at http://www.fao.org/docrep/004/y0660e/Y0660E03.htm.

[72] Brown, J.L., J.W. Dominik, and E.W. Larson. 1982. “Airborne Survival of Rift Valley Fever Virus.” *DTIC*. USAMRIID.

[73] Center for Food Safety and Public Health (CFSPH). 2006. “Rift Valley Fever: Prevention Practices.” Available at http://www.cfsph.iastate.edu/BRMForProducers/English/FADs/RVF_response_package.pdf.

The OIE states the following about the resistance of RVF to physical and chemical action:[74]

- *Temperature*: Virus is 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 parts per million).
- *Survival*: Survives in freeze dried form and aerosols at 23°C and 50-85 percent humidity. Virus is maintained in the eggs of certain arthropod vectors during inter-epidemic periods. Can survive contact with 0.5 percent phenol at 4°C for 6 months.

1.6.1 In Animals, Products, and By-Products

The virus can persist in animals. For example, the OIE recommends, for ruminants from infected countries or zones with disease, that animals show no evidence of RVF on the day of shipment, and that the animals were vaccinated against RVF at least 21 days prior to shipment with a modified live virus vaccine, OR that animals "were held in a mosquito-proof quarantine station for at least 30 days prior to shipment during which the animals showed no clinical sign of RVF and were protected from mosquito attacks between quarantine and the place of shipment as well as at the place of shipment." Further requirements for animals and animal products are listed in the OIE Terrestrial Animal Health Code (2013).[75]

The virus content in meat decreases rapidly following slaughter, the pH dropping as the meat is stored. RVFV is quickly destroyed by pH changes in decomposing carcasses. RVFV can persist in milk, but is inactivated by pasteurization or treatment with acid. The OIE recommends pasteurization, or a combination of control measures with performance equivalent to those described in the Codex Alimentarius Code of Hygienic Practice for Milk and Milk Products.[76] Little is known about the persistence of the virus in skins, wool, bones, manure, and other fibers. Because some of these products may contain blood, the virus may persist. Appropriate cleaning and disinfection measures should be taken with products that may contain RVF.

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[74] World Organization for Animal Health (OIE). 2009. Rift Valley Fever Technical Disease Card. Available at http://www.oie.int/fileadmin/Home/eng/Animal_Health_in_the_World/docs/pdf/RIFT_VALLEY_FEVER_FINAL.pdf.

[75] World Organization for Animal Health (OIE). 2013. *Terrestrial Animal Health Code*. Rift Valley Fever, Chapter 8.12. Available at http://www.oie.int.

[76] World Organization for Animal Health (OIE). 2013. *Terrestrial Animal Health Code*. Rift Valley Fever, Chapter 8.12. Available at http://www.oie.int.

Attachment 1.A References and Resources

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Attachment 1.B Abbreviations

APHIS	Animal and Plant Health Inspection Service
FAD PReP	Foreign Animal Disease Preparedness and Response Plan
MMWR	Morbidity and Mortality Weekly Report
OIE	World Organization for Animal Health
PFU	plaque-forming units
RNA	ribonucleic acid
RVF	Rift Valley fever
RVFV	Rift Valley fever virus
SOP	standard operating procedure
USDA	United States Department of Agriculture