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Journal of Chemical and Pharmaceutical Research

J. Chem. Pharm. Res., 2010, 2(1): 228-239

ISSN No: 0975-7384

Rift Valley Fever: A Review

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Abstract

Rift Valley Fever is mosquito-borne viral infection affecting animals and humans. It is an acute viral disease that affects domestic animals such as cattle, buffalo, sheep, goats, and camels and primarily domestic livestock, but can be passed to humans causing fever. Serious complications like jaundice, haemorrhage, renal failure may occur in chronic cases. Spread is by the bite of infected mosquitoes, typically the Aedes or Culex genera. Humans are also readily infected through aerosols from infected animals when humidity is high, or by exposure to infected animal tissues, aborted fetuses, mosquito bites, and laboratory procedures. ELISA test confirms diagnosis along with careful symptomatic observation.

Keywords: Aedes, Culex, mosquito-borne viral infection

Introduction

Rift Valley Fever(RVF) is Mosquito-borne viral infection affecting animals and humans. It is an acute, fever-causing viral disease that affects domestic animals (such as cattle, buffalo, sheep, goats, and camels) and humans. RVF is most commonly associated with mosquito-borne epidemics during years of heavy rainfall. RVF is a viral zoonosis (affects primarily domestic livestock, but can be passed to humans) causing fever. [1] It is spread by the bite of infected mosquitoes, typically the Aedes or Culex genera. The disease is caused by the RVF virus, a

member of the genus *Phlebovirus* (family *Bunyaviridae*). Rift Valley fever (RVF) is a peracute or acute zoonotic disease of domestic ruminants in Africa and, recently, the Arabian Peninsula. Signs of the disease tend to be nonspecific, rendering it difficult to recognize individual cases [2]. During epidemics, the occurrence of numerous abortions and deaths among young animals, together with an influenza-like disease in humans, tends to disease was first reported among livestock by veterinary officers in Kenya in the early 1900s.Humans usually get RVF through bites from infected mosquitoes and possibly other biting insects . The disease is caused by the RVF virus member of the genus have virus-contaminated mouthparts. Humans can also get the disease if they are exposed to the blood, body fluids, or tissues of infected animals. Direct exposure to infected animals can occur during slaughter or through veterinary and obstetric procedures. Infection through aerosol transmission of RVF virus has occurred in the laboratory environment. Until recently it had only been recognized in the African continent, but in 2000 it occurred in the Arabian Peninsula. Major epidemics have occurred at irregular intervals of 10-30 years in the eastern half of Africa, from South Africa to Egypt. As well as its severe socio-economic and public health consequences, it is a major constraint to international livestock trade. Rift Valley fever (RVF) is a peracute or acute zoonotic disease of domestic ruminants in Africa and, recently, the Arabian Peninsula. Signs of the disease tend to be nonspecific, rendering it difficult to recognize individual cases. During epidemics, the occurrence of numerous abortions and deaths among young animals, together with an influenza-like disease in humans, tends to be characteristic. [3]

History [4, 5, 6]

Table 1: History of Rift Valley Fever

Year	Disease History
1910-12	Disease Compatible With Rvf Described In Lambs [European Breed] In Rift Valley Kenya
1930	Virus First isolated indiseas Rift valley disease outbreaks in Kenya
1944	Isolation of rvf virus in semliki forest Uganda [no livestock or humans in vicinity] hence rvf assumed to be endemic in forests with spread to grasslands after heavy rains
1950-51	Large outbreak in south Africa – associated with pans & vleis [dambos] – ocular lesions recognized
1976	Large outbreak in south Africa- fatal human disease Recognized for first time
1977-78	Appearance of rvf beyond sub- Saharan Africa – in Egypt- 200,000 human infections -598 deaths
1979	Recognition of rvf in Madagascar
1987	Large outbreaks in Mauritania/Senegal-many human deaths
1997-98	Large outbreak kenya/somalta/Tanzania 300 human deaths
1999	Large outbreak in south Africa, 3 giraffes and 1 waterbuck were found dead &infection to human also.
2000-1	Appearance of rvf beyond African region in Saudi Arabia and Yemen 200 deaths
2003	Egypt-45 cases; 17 deaths; All cases were Egyptian farmers.

2006	32 cases and 19 deaths of Rift Valley Fever virus in Garissa district & **in** Kenya has reported 12 cases with 11 deaths of Rift Valley Fever in the North Eastern province in Kenya.
2006-07	In Tanzania and Somalia over 1000 cases 300 deaths.
2007	211 deaths In Sudan. & a total of 264 cases including 109 deaths of Rift Valley fever in Tanzania. Total of 114 cases including 51 deaths of Rift Valley Fever were reported in Somalia. A total of 684 cases including 155 deaths by rvf in Kenya.
2008	406 cases and 148 deaths in Sudan.

Epidemiology

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 [7]

RVF has been recognized exclusively in African countries, with an underlying association with high rainfall and dense populations of vector mosquitoes. The only epizootic outbreaks of RVF outside sub-Saharan Africa were recorded in animals and humans in Egypt in 1977-78, Mauritania in 1987 and again in Egypt in 1993. Laboratory infections have been recorded in other parts of the world For detailed information on occurrence, see recent issues of *World Animal Health* and the OIE *Bulletin*RVF virus belongs to the genus *Phlebovirus* , and is a typical Bunyavirus. It has a 3-segmented, single-stranded, negative-sense RNA genome with a molecular weight of 4-6 × 10^6, and each of the segments, L (large), M (medium), and S (small), is contained in a separate nucleocapsid within the virion. No significant antigenic differences have been demonstrated between RVF isolates from many countries, but differences in pathogenicity are seen.[8] The disease is endemic in tropical regions of mainly eastern and southern Africa, although an epidemic was reported in 2000 in Saudi Arabia and Yemen. Cyclic epidemics have occurred at 5- to 20-yr intervals in drier areas. The cycles are normally associated with periods of abnormally heavy rainfall. In the periods between epidemics, the virus is believed to be dormant in eggs of the mosquito *Aedes mcintoshi (linneatopennis)* in the dry soil of grassland depressions (dambos). Although transovarial transmission is believed to be the most important interepidemic survival strategy of the virus, inapparent cycling of disease may occur at forest edge habitats. RVF may spread by windborne mosquitos or introduction of viremic animals. With adequate rainfall, the infected maintenance mosquitos develop and infect ruminants, which amplify the virus. The virus is spread epidemically by many species of mosquitos or mechanically by other insect's characteristic of different regions. The incidence of RVF peaks in late summer. After the first frost, both the disease and vectors may disappear. In warmer climates where insect vectors are present continuously, seasonality is usually not seen. Humans are also readily infected through aerosols from infected animals when humidity is high, or by exposure to infected animal tissues, aborted fetuses, mosquito bites, and laboratory procedures, and have the potential to introduce the disease (via mosquitoes) to animals in uninfected area.[9]

Global Scenario: [10, 11, 12, 13]

Table 2: Global Scenario of Rift Valley Fever

Kenya	1900's	First recognized in sheep
	1930	Agent isolated
Africa	1950-51	500,000 sheep abortions
	1965	100,000 sheep deaths
Egypt	1977-1978	Humans 18,000 cases, 598 deaths

Other Important Outbreaks:

1987: Senegal, Africa

- Differed from other outbreaks
- Not associated with rainfall

1997-98: Kenya, Africa

- Largest outbreak reported
- 89,000 human's cases - 478 deaths

2000-01: Saudi Arabia and Yemen

- First outbreak outside of Africa
- 2003: Egypt -45 cases; 17 deaths; All cases were

Saudi Arabia and Yemen- 2000-2001

- 683 humans hospitalized
- 95 deaths (13.9% mortality)
- 82.7% male
- Median age: 50 years
- Youngest patient 14 yrs. old
- 76% had close contact with animals

Rift Valley Fever Distribution Map

Figure 1: Geographical Distribution of Rift Valley Fever

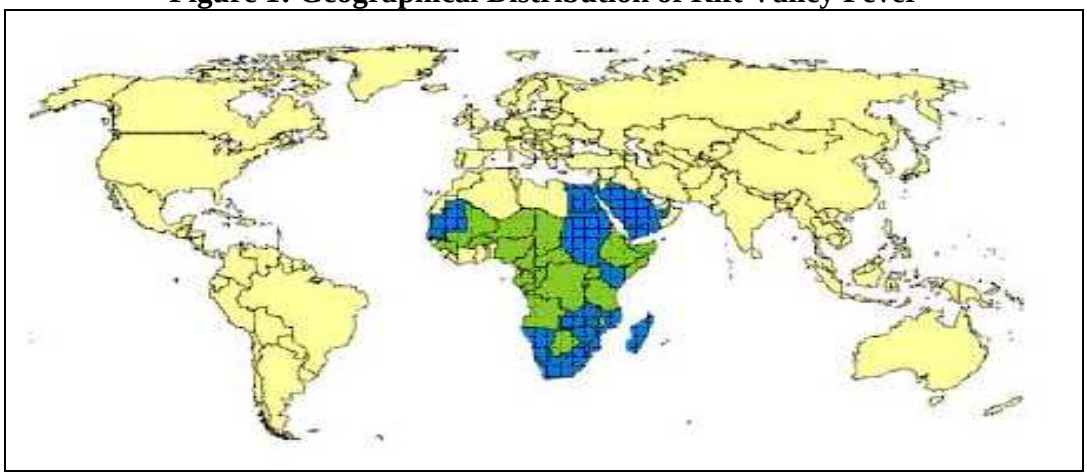
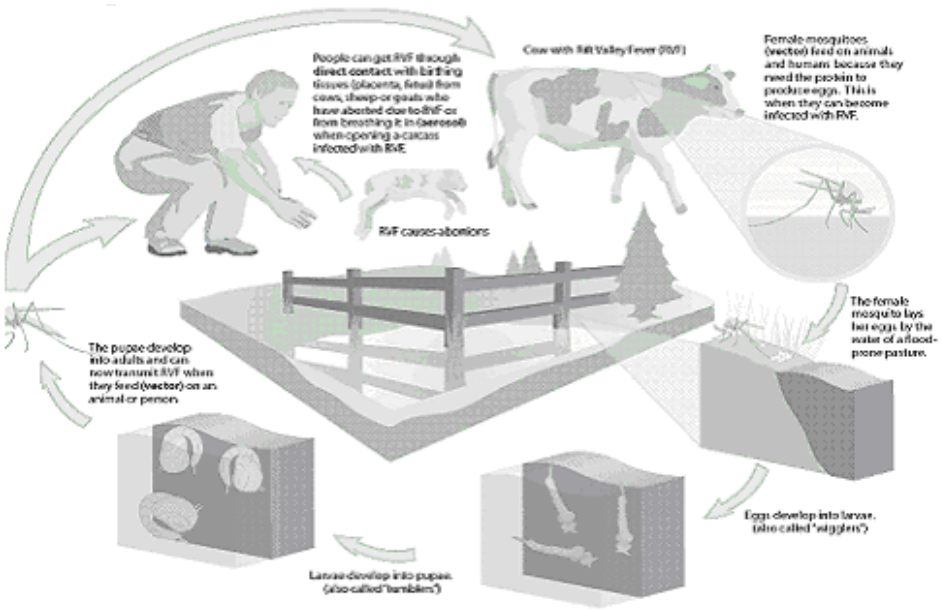


Table 3: Geographical Distribution of Rift Valley Fever

	Countries with endemic disease and substantial outbreaks of RVF	Gambia, Senegal, Mauritania, Namibia, South Africa, Mozambique, Zimbabwe, Zambia, Kenya, Sudan, Egypt, Madagascar, Saudi Arabia, Yemen
	Countries known to have some cases, periodic isolation of virus, or serologic evidence of RVF	Botswana, Angola, Democratic Republic of the Congo, Congo, Gabon, Cameroon, Nigeria, Central African Republic, Chad, Niger, Burkina Faso, Mali, Guinea, Tanzania, Malawi, Uganda, Ethiopia, Somalia

Life Cycle: [14, 15]

Figure 2: Life Cycle of Rift Valley Fever



Transmission : [16, 17, 18, 19]

- Arthropod vector
  - Mosquitoes
  - *Aedes*
  - *Anopheles*
  - *Culex*
  - Others Reservoir

•Mosquitoes – *Aedes* species

➢ Transovarial transmission

➢ Eggs dormant in soil for long periods

➢ Heavy rainfall, eggs hatch

•Ruminant amplifying host

•Secondary vectors can be infected

- *Culex* and *Anopheles* mosquito species
- Biting flies: midges, phlebotomids, stomoxids, simulids

Hosts-RVF virus can affect a variety of livestock species as well as wild animals. Predominant animal hosts include

- Cattle
- Sheep
- Goats
- Camels
- African buffalo
- Dromedaries
- White rhinoceroses
- Waterbucks
- Bats and several rodent species, such as the Namaqua rock mouse
- Wild ruminants
- Dogs
- Humans

Other Modes of Transmission

- Mosquito species in the U.S. could serve as vectors
- Biting flies possible vectors
- Direct contact or Aerosol
- Tissue or body fluids of infected animals
- Aborted fetuses, slaughter, necropsy
- High levels of virus in blood
- Aerosol
- Amplify virus
- Infect other mosquitoes
- Establish disease in environment
- May lead to large outbreaks
- No person-to-person transmission
- Human's possible source of virus for mosquitoes
- Rift Valley Fever (RVF) is a viral disease spread by mosquitoes

That affects:

- Cats & dogs
- Horses
- Rodents

RVF is a mosquito-borne disease. *Aedes* mosquitoes serve as the major reservoir and vector. Transovarial transmission occurs within *Aedes* mosquitoes; infected eggs lie dormant for years until flooding occurs, allowing them to hatch and spread the virus to the livestock on which they feed. Other mosquito species, 10 of which are native to North America, and other biting insects, such as sandflies, also can serve as vectors. They become infected after feeding on infected animals, further

Pathophysiology: [20, 21, 22, 23]

•Phlebovirus (Bunyaviridae)

•Stable at

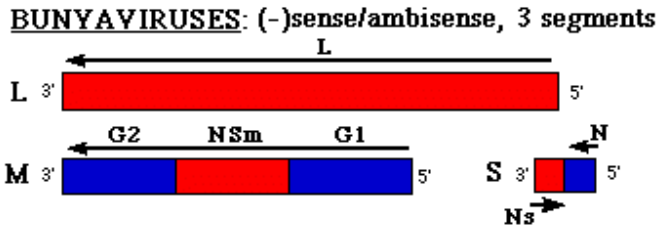
- -60^{o}C to 23°C
- 50-85% relative humidity

•Inactivated

- Lipid solvents
- Detergents
- Low pH
-

Genomic Structure: [24, 25]

Figure 3: Genomic Structure of Bunya viruses



- Virions enveloped, slightly pleomorphic, and 80 to 120 nm in diameter
- Genome contains single-stranded negative-sense RNA with three segments
- Segments are named S (small), M (medium), and L (large).
- Each segment is enclosed in a separate nucleocapsid within the virion.

Signs And Symptoms: [26, 27, 28, 29]

Table 4: Signs And Symptoms of Rift Valley Fever

SIGNS OF ILLNESS IN HUMAN	Back pain; Dizziness; Fever; Liver abnormalities; Weakness; and Weight loss. encephalitis (inflammation of the brain); Disease affecting the eyes; or Haemorrhagic fever.
Rvf in human-usually uncomplicated	Heoatocellular failure Acute renal failure Hemorrhagic manifestation

acute febrile illness	Retinitis meningoencephalitis Death association with hepatorenal failure, shock severe anemia
In animal	ortion the most important sign Dystocia,some teratology,hydrops amnii orexia, sgalactia,nasal and lachrymal discharges livation ,vomiting, lymphadenitis -colic, jaundice, haemorrhagic enteritis

Prevention: [30, 31, 32, 33, 34]
You can reduce the chances of becoming infected with Rift Valley fever by taking measures to decrease mosquito exposure such as using mosquito repellent and foggers and avoiding the outdoors when mosquitoes are most active. When assisting animals with the delivery of newborn animals or if handling animal tissues, wear gloves, a mask and other protective clothing. Always wash your hands after touching animals. Person's chances of becoming infected can be reduced by taking measures to decrease contact with mosquitoes and other bloodsucking insects through the use of mosquito repellents and bednets. Avoiding exposure to blood or tissues of animals that may potentially be infected is an important protective measure.

Table 5: Preventive action- disinfectant for rift valley fever virus

Product	**Dilution**	**Mixing instruction**	**Comment**
Sodium hypochlorite 5.25%(NaoCl)	3%	2 gallon of bleach to 3gallon of water mix thouroughly	Not effective when area / object are not clean unstable in warm ,sunny condition
Calcium hypochlorite (ca(ocl)2)	3%	30 g/liter	Not effective when area / object are not clean unstable in warm ,sunny condition
Potassiumperoxy monosulphate & sodium chloride	2-3%	Follow label direction	e.g virkon -s
Hydrochloric acid	2%	10molar conc.dilute 1 part acid to 50 part water .always pour acid into water	Use only when better disinfectant is not available damages many metal and concrete.
Citric acid	0.2%	1ounce powder to 4gallon of water	Safe for cloth,body decontamination.

Sanitary prophylaxis: [35]
Hygiene and vector control have had little effect

Medical prophylaxis: [36, 37, 38]

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 The Canadian Food Inspection Agency (CFIA) imposes strict regulations on the import of animals and animal products from countries where RVF is known to occur. These regulations are enforced through port-of-entry inspections done either by the Canada Border Services Agency or the CFIA Inactivated vaccines also have been developed for use in both animals and humans. Respiratory masks and rubber gloves reduce contact with infectious aerosols and fluids. Taken together, these precautions can help slow the spread of the disease

- Vaccination of ruminants
  - May cause birth defects and abortions
  - Not approved for use in the U.S.
- Avoid and control vectors
- Personal protective equipment
  - Aborted fetuses, necropsy
- Avoid contact with infected tissues and blood
- Restrict movement of animals
- Precautions when traveling
- Do not slaughter sick animals
  - Bury or burn carcasses during an outbreak
- Personal protective equipment
  - Gloves, coveralls, boots, eyewear, mask
- Avoid contact with infected tissues and blood
  - Aborted fetuses, necropsy
- Greatest risk to travelers Clean animal housing areas
- Wear personal protective equipment
- Remove all organic material from surface (manure, feed, animal tissue)
- Use soap or detergent with warm water
- Let dry
- Disinfect animal housing areas
- 1 part bleach:10 parts water
- Virkon-S

Diagnosis and Treatment: [39, 40, 41, 42]

- Diagnosis
  - ELISA, human blood
  - Demonstration of viral antigen
- Treatment
  - Symptomatic and supportive therapy
  - Replacement of coagulation factors
  - Ribavirin may be helpful.

There is no established course of treatment for patients infected with RVF virus. However, studies in monkeys and other animals have shown promise for Ribavirin, an antiviral drug, for future use in humans. Additional studies suggest that interferon, immune modulators, and convalescent-phase plasma may also help in the treatment of patients with RVF.

Vaccination: [43, 44, 45, 46]

This is the most effective means to control RVF. Early warning of high-risk periods for the disease is possible and this information should drive strategic vaccination campaigns. The most effective vaccine is the modified live Smithburn neurotropic strain (SNS). This vaccine is immunogenic but has the disadvantage that it can cause foetal pathology and abortion in pregnant sheep of susceptible genotypes. Up to 30 percent of such animals may be affected by abortion or foetal abnormalities. Inactivated vaccines have been prepared but are often poorly immunogenic. Onderstepoort Biological Products in South Africa produce an inactivated vaccine that is based on a bovine virulent RVF isolate, adapted and produced in cell culture. The vaccine is then inactivated and mixed with aluminium hydroxide gel as adjuvant. It has the advantage of being suitable for use in pregnant ewes. Given the poor antibody response in cattle, the inactivated vaccine is recommended even in cows so that they can confer colostral immunity to their offspring. A booster three to six months after initial vaccination is required, followed by annual boosters. Routine vaccination when animals are not pregnant is recommended. The SNS vaccine is perfectly safe and protective in cattle. Vaccination is NOT recommended once evidence of epizootic virus activity has been confirmed. Apart from being too late, needle propagation of the virus is a real danger.

Vaccine development

Other modified live virus and molecular derived RVF antigens are being developed, but are not currently available for field use. The MP 12 strain was developed by mutagen induced changes in the ZH 548 strain of the RVF virus and Clone-13 is a cloned population, obtained from a field strain isolated from a mild human case in the Central African Republic. Both have been shown to be good immunogens in mice, and produce antibodies detectable by ELISA and plaque reduction neutralization assays. The Protective Dose (50 percent) (PD 50) for Clone 13 was 100.1 TCID50 and for MP 12 were 103. The S segment of the RVF virus determines virulence/loss of virulence and the NSs deletion results in attenuation. The role of NSs has been elucidated: it is an antagonist of type I interferon production. Indeed, infection of mice with strains that possess efficient NSs does not lead to any production of interferon, whereas high levels of interferon were observed in mice infected with the NSs defective Clone 13 virus. Clone 13 is of interest because of the low risk of reversion in this virulence/attenuation marker. However, the L and M segments do not contain markers for attenuation. If animals are vaccinated when virulent strains are circulating, there is a possibility that reassortment may occur; in this case Clone 13 would induce a viraemia (which is not observed in mice). The majority of reassortants could become virulent. An R566 strain has been derived from Clone 13 and MP 12 by reassortment in Vero cells: it contains the S segment of Clone 13 and the L and M segments of MP12, which contain seven and nine point mutations compared with their virulent parent. Some of them induce attenuation and thermo sensitivity. Thus R566 is safe, because of its attenuation in the three segments of the genome. R566 has been shown to protect mice in the laboratory.

Conclusion

Rift Valley Fever is mosquito-borne viral infection affecting usually animals and then transmitted to humans through various ways including mosquito bite. Although disease is not severe in early days, it may show serious complications if not treated. Prophylaxis needs using mosquito repellent and foggers and avoiding the outdoors when mosquitoes are most active. Careful animal handling is must to prevent zoonotic spread. Attenuated virus vaccine offers immunity upto few years. Ribavirin, may be a promising antiviral drug for future use in humans. Apart from that interferon, immune modulators, and convalescent-phase plasma may also show synergistic effect in the treatment of patients with RVF.

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