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Rift Valley Fever

Updated Nov 2007

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Overview

- Organism
- History
- Epidemiology
- Transmission
- Disease in Humans
- Disease in Animals
- Prevention and Control



In today's presentation we will cover information regarding the organism that causes Rift Valley Fever and its epidemiology. We will also talk about the history of the disease, how it is transmitted, species that it affects (including humans), and clinical and necropsy signs observed. Finally, we will address prevention and control measures for Rift Valley Fever virus.

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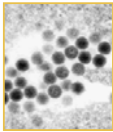

The Organism

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Agent

- Phlebovirus (Bunyaviridae)
- Stable at
 - -60°C to 23°C
 - 50-85% relative humidity
- Inactivated
 - Lipid solvents
 - Detergents
 - Low pH


Rift Valley Fever (RVF) is caused by a Phlebovirus (Family Bunyaviridae). It is a three stranded RNA virus and requires a mosquito vector. The virus is very stable at temperatures from -60 to 23 °C and at 50-85% relative humidity. It is inactivated by lipid solvents, detergents and low pH. The photo is an electron micrograph of the Rift Valley Fever virus (RVFV) from the CDC website.

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Rift Valley Fever Overview

- Acute febrile disease
 - Sheep, cattle, goats
 - High abortion rates and death in young
- Can affect humans
- Heavy rainfalls
- Arthropod vector
 - Most commonly mosquito
- OIE List A Disease



Rift Valley fever is an acute febrile disease that severely affects sheep, cattle and goats, especially young animals. There is a very high rate of abortion and death in neonates. RVF can also affect humans. Typically cases have mild, flu-like signs that are self-limiting, but severe disease can occur. Rift Valley fever is associated with heavy rainfalls and is transmitted by an arthropod-vector, usually mosquitoes. However, contact with contaminated tissue from infected animal, especially aborted fetuses, can transmit the virus to humans. Currently, RVF is one of the OIE List A Exotic Diseases.

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History

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Rift Valley - Kenya, Africa

- 1900's: First recognized in sheep
- 1930: Agent isolated
- Intermittent outbreaks in Kenya
 - 1950-51, major epizootic
 - 500,000 sheep abortions
 - 100,000 sheep deaths




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Rift Valley Fever was first recognized as a disease in sheep in Rift Valley, Kenya, Africa around 1900. The virus was not actually isolated until 1930. Since then there have been intermittent outbreaks throughout Kenya. A major epizootic occurred in 1950-51 which resulted in 500,000 sheep abortions and 100,000 sheep deaths. This map depicts the area in Africa where this disease was first recognized- Kenya.

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Egypt: 1977-1978

- Humans
 - 18,000 cases
 - 598 deaths
 - Encephalitis and hemorrhagic fever
 - Case-fatality less than 1%
- Ruminants
 - Abortions and deaths
 - Sheep, cattle, goats
 - Water buffalo, and camels



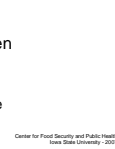
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In 1977-78, a outbreak of RVF occurred along the Nile in Egypt. This was the first epidemic out of sub-Saharan Africa. This outbreak resulted in an estimated 18,000 human cases. There were 598 human deaths which occurred from encephalitis and hemorrhagic fever. The case-fatality rate was reported as less than 1%. Many abortions and deaths were reported in sheep, goats, cattle, water buffalo and camels. This map depicts the location of the 1977-1978 outbreak in Africa- Egypt.

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Other Important Outbreaks

- 1987: Senegal, Africa
 - Differed from other outbreaks
 - Not associated with rainfall
- 1997-98: Kenya, Africa
 - Largest outbreak reported
 - 89,000 humans cases - 478 deaths
- 2000-01: Saudi Arabia and Yemen
 - First outbreak outside of Africa
- 2003: Egypt
 - 45 cases; 17 deaths; All cases were Egyptian farmers



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In 1987, an outbreak of RVF occurred in the Senegal river basin (West Africa). This epizootic differed from prior outbreaks in that it was not associated with the typical heavy rainfall. Mosquito breeding occurred in large rivers and dams. The largest outbreak of RVF reported occurred in Kenya, Africa in 1997-1998. An estimated 89,000 humans were infected with 478 deaths. The most recent outbreak of RVF occurred in Saudi Arabia from August 2000 to September 2001. This epidemic was the first confirmed outbreak of RVF outside of Africa. This outbreak illustrated the potential for the spread of this disease to other regions of the world. An outbreak of Rift Valley Fever occurred in Egypt in August of 2003. Forty-five cases of RVF were diagnosed with 17 deaths. The outbreak occurred in a rural region 150 kilometers north of Cairo and all cases were Egyptian farmers.

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Outbreak 2006-2007

- Began in Kenya
- Spread to U.R. Tanzania and Somalia
- By May 2007
 - Over 1000 cases
 - 300 deaths
 - Case-fatality 23-45%

FIGURE 3. Number of reported Rift Valley fever cases in > 300, by date of disease onset — Kenya November 2006–January 2007.

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In November, an outbreak of Rift Valley Fever began in Kenya. It soon spread to the surrounding countries of United Republic of Tanzania and Somalia. As of May 2007, over 1000 human case were reported with case-fatality varying between the countries from 23-45%. Animal movement and slaughter restrictions were implemented as has vaccination efforts for livestock in affected areas.

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Epidemiology

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Epidemiology

- Endemic in tropical Africa
 - Cyclic epidemics every 5-20 years
 - Susceptible animal populations
 - Abnormally heavy rainfalls
 - Peaks in late summer
- Outbreaks
 - Saudi Arabia, Yemen, and Egypt

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Currently RVF is endemic throughout most of Africa. Outbreaks tend to occur in a cyclic pattern every 5-20 years and is usually associated with abnormally heavy rainfalls. The long intervals between outbreaks allows for development of a susceptible animal population that is consequently severely affected by the following outbreak. Recent outbreaks have occurred in Saudi Arabia, Yemen, and Egypt. Photo of Egyptian delta farm from http://www.4egypt.info/images/delta_farm.gif

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Distribution of Rift Valley Fever

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This map is from the CDC web site (Rift Valley Fever). The blue areas indicate African countries with endemic disease and substantial outbreaks of RVF. The green areas are countries know to have some cases, periodic isolation or serological evidence of RVF.

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**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

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During the outbreak of RVF in Saudi Arabia and Yemen in 2000-2001, 683 humans were hospitalized with severe disease. Of those cases, 95 died (13.9% mortality). The median age of the patients was 50 years old with the youngest confirmed patient being 14 years old. Males were attributed to 82.7 percent of cases. The mean duration from disease onset to hospitalization was 3.3 days. The average time from disease onset to death was 6.3 days. Seventy-six percent of the patients reported having close contact with sheep and goats.

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Reservoir

- Mosquitoes – *Aedes* species
 - Transovarial transmission
 - Eggs dormant 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, simuliids



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The reservoir for RVF is mosquitoes, particularly *Aedes* species. In the African outbreaks, *Aedes lineatopinnus* was the primary reservoir. The virus is transovarially transmitted to the eggs of the mosquito. These eggs lay dormant for many years in the dry soil of grassland areas. Following heavy rainfalls, the pooling water gives the eggs a proper environment to hatch. These newly hatched infected mosquitoes then seek an feeding source (human or animal). Once a ruminant is infected, it serves as an amplifying host. Secondary arthropod vectors can become infected from the ruminant and rapidly spread the disease. Other species of *Culex* and *Anopheles* mosquitoes can serve as secondary vectors. Biting flies such as midges, phlebotomids, stomoxids and simuliids may serve as mechanical transmitters of the virus, however this is thought to be minimal route of infection.

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Amplifying Hosts

- Infected livestock
- High levels of viremia
- Amplifying
 - Sufficient to infect mosquito vectors
 - Establishes disease in environment
 - Leads to large epizootic epidemics
- Humans
 - Viremia enough to amplify

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Infected livestock (sheep, cattle, goats) can have high levels of viremia which is sufficient to infect various mosquito vectors. These amplifying hosts help the disease become established in the environment and can lead to large epizootic epidemics. Humans also develop a high enough viremia to be a source of infection for mosquitoes.

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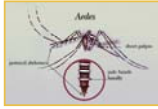
Transmission

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Transmission

- Arthropod vector
 - Mosquitoes
 - *Aedes*
 - *Anopheles*
 - *Culex*
 - Others
- Mosquito species in the U.S. could serve as vectors
- Biting flies possible vectors



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RVF is transmitted by an arthropod vector, typically a mosquito. RVF virus has been isolated from several species of *Aedes*, *Anopheles*, *Culex*, and other species of mosquitoes. Several of these species of mosquitoes are found in the United States and could potentially contribute to the spread of RVF in this country. Since the virus is transmitted via hematogenous routes, biting flies (midges, phlebotomids, stomoxids, and simuliids) may also serve as mechanical transmitters, but this has not been documented to date. Currently, investigation of the potential of hematophagous flies is being explored.

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Other Modes of Transmission

- 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
 - Humans possible source of virus for mosquitoes

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Rift Valley Fever can also be transmitted from the tissue or body fluids of infected animals. This can be either direct contact with the tissue or aerosolization of body fluids (i.e., blood, parturient material). Exposure can occur from aborted fetuses or during slaughter or necropsy. To date, no person-to-person transmission has been documented. Infected cattle, sheep and goats may have high levels of virus in their blood which is enough to infect mosquitoes. These animals may serve as a source of infection by boosting the amount of virus (amplify) for many other mosquitoes that may then rapidly spread the disease. These animals may help the disease become established in the environment and may lead to large outbreaks. Humans also develop a high level of virus and may be a source of infection for mosquitoes.

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Disease in Humans

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Human Disease

- Incubation period: 2-6 days
 - Inapparent or flu-like signs
 - Fever, headache, myalgia, nausea, vomiting
 - Recovery in 4-7 days
 - Retinopathy
 - Hemorrhagic fever
 - Encephalitis
- Overall mortality ~1%

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The incubation time in humans has been reported to be anywhere from 2 to 12 days. The average is 2-6 days. Typically humans are asymptomatic or have self-limiting flu-like signs. These signs include fever, headache, muscle and joint pain, and possible nausea and vomiting. Recovery is usually in 4-7 days. In less than 1% of humans infected, severe disease can occur. This can include retinitis, hemorrhagic fever or encephalitis.

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Human Disease

- Retinopathy (1-10%)
 - 1-3 weeks after onset of symptoms
 - Conjunctivitis
 - Photophobia
 - Can lead to permanent vision loss
 - Death is uncommon

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Of the 1% of cases developing into severe syndromes, 1-10% of these cases will develop retinopathy. Clinical signs seen include conjunctivitis and photophobia. Damage from this complication can lead to permanent vision loss. Death from this syndrome is uncommon.

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Human Disease

- Hemorrhagic fever
 - 2-4 days after fever
 - Melena, hematemesis, petechia, jaundice, shock, coma
 - Death
 - Case-fatality is ~50%
- Encephalitis
 - 1-3 weeks after onset of symptoms
 - Can occur with hemorrhagic fever

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Other possible complications from RVF include hemorrhagic fever or encephalitis. People demonstrating the hemorrhagic fever syndrome will have fever, melena, hematemesis, petechia and subcutaneous bleeding. Additionally, deep jaundice is present. The syndrome quickly progresses to shock and coma followed by death. The case-fatality rate for persons with this syndrome is approximately 50%. The encephalitic syndrome typically occurs 1-3 weeks after the onset of symptoms. It can occur concurrently with the hemorrhagic fever. Both of these syndromes occur in only about 1% of human cases.

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Diagnosis and Treatment

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



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Diagnosis in humans consists of an ELISA test on human blood or demonstration of the viral antigen via various methods. Treatment is symptomatic and supportive therapy. With the hemorrhagic syndrome, blood transfusions may be needed to replace coagulation factors. The anti-viral medication, ribavirin, may prove helpful. Testing is still being done. Image: cataloging samples for testing.

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Animals and Rift Valley Fever

RVF has been found to infect many species of animals, however the most commonly affected are sheep, goats and cattle. This table is revised from the Foreign Animal Disease Grey Book. Animals can serve as a sentinel species for this disease. Sheep, cattle and goats are the primary host and amplifiers. Dogs are also highly susceptible. Horses and pigs are resistant to the virus. RVF causes an acute disease in domestic ruminants. Sheep, goats and cattle have a high mortality of newborn animals and high rate of abortion in pregnant animals. The disease causes necrotic hepatitis and a hemorrhagic state. There is a great economic impact from this disease due to the large losses of young animals.

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Animal Disease

Mortality 100%	Severe Illness Abortion Mortality	Severe Illness Viremia Abortion	Infection Viremia	Refractive to Infection
Lambs Calves Kids Puppies Kittens Some rodents	Sheep Cattle Goats Humans	Monkeys Camels Rats Squirrels	Horses Cats Dogs Monkeys	Rodents Rabbits Birds

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RVF has been found to infect many species of animals, however the most commonly affected are sheep, goats and cattle. This table is revised from the Foreign Animal Disease Grey Book. Animals can serve as a sentinel species for this disease. Sheep, cattle and goats are the primary host and amplifiers. Dogs are also highly susceptible. Horses and pigs are resistant to the virus. RVF causes an acute disease in domestic ruminants. Sheep, goats and cattle have a high mortality of newborn animals and high rate of abortion in pregnant animals. The disease causes necrotic hepatitis and a hemorrhagic state. There is a great economic impact from this disease due to the large losses of young animals.

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Sheep and Goats

- Incubation period: less than 3 days
 - High rate of abortion (5-100%)
 - Any stage of gestation
 - Asymptomatic
 - Foul diarrhea, icterus, mucopurulent nasal discharge
 - Acute death (20-30%)

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Abortion in adult sheep and goats is the most common sign of RVF. It can occur at any state of gestation. The fetus will have an autolysed appearance. Abortion rates are very high – in some cases as high as 100%. **Remember parturient material can contain RVF virus.** Adult sheep can have inapparent infection. Clinical signs most commonly seen include fever, mucopurulent nasal discharge and possibly vomiting. Mortality in adults, especially those that have aborted, can be 20-30%; however, abortion may be the only sign seen.

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Lambs and Kids

- Incubation period: 12-36 hrs
- Newborn deaths
 - High fever, listless, anorexia
 - Death - 12 hours to 2 days
 - Less than 1 week old
 - Mortality >90%
- Lambs and kids over 2 weeks old
 - Mortality over 20%



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The incubation period in lambs and kids is 12-36 hours. As previously mentioned, aborted fetuses are the most common sign. Newborns are highly susceptible. Signs include high fever (105.8 °F), listlessness, and anorexia. Most lambs die within 2 days, but can occur in as short as 12 hours. Mortality can be over 90% for young less than 1 week old. Lambs and kids over 2 weeks old have a mortality rate over 20%.

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Cattle

- Adults
 - Fever, weakness, anorexia, ptyalism, diarrhea, icterus
 - Death - Mortality 10%
 - Abortion can be up to 100%
- Calves
 - Similar signs to lambs and kids
 - Mortality 10-70%



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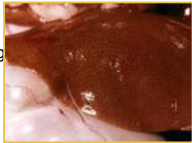
Cattle are also affected by RVF. Adults usually have inapparent disease. Clinical signs seen include fever, weakness, anorexia, excessive salivation and fetid diarrhea. Icterus is also commonly seen. Death in adult cattle can be 10%. Abortions also occur in cattle and can be as high as 100%. Calves show similar signs as lambs and kids - fever, depression and acute death. Mortality in calves can be from 10-70%.

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Post Mortem Lesions

- Hepatic necrosis
 - Liver enlarged, yellow, friable
 - Petechial hemorrhages prominent
 - Cutaneous
 - Serosal



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Post mortem lesions found in sheep, cattle and goats indicate hepatic necrosis. This can be quite extensive in younger animals and fetuses. The liver is greatly enlarged, yellow and friable. Petechial hemorrhages may be very prominent and found on cutaneous or serosal surfaces.

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Other Species

- Dogs
 - Abortion up to 100%
 - Severe disease and death in puppies
- Cats: Death in kittens
- Horses: Viremia but resistant
- Pigs: Resistant
- Birds: Refractory

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Other species can be infected by RVF, but such cases are less common. Dogs can have abortion rates as high as 100%. Puppies are severely affected and typically die. Kittens have also been reported to be highly susceptible to RVF virus. Horses have been experimentally shown to have a low grade viremia; however, to date there have been no equine cases. Pigs have been reported to either be very resistant to the virus or have inapparent infections. Birds have been found to be refractory to the virus.

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Prevention and Control

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Prevention

- 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

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Immunization of sheep, goats and cattle is the most effective method of controlling the disease. The current vaccine can be abortigenic and teratogenic but is usually less than the effect of the disease. Current research is being conducted to develop a safer vaccine. Avoid and control mosquito vectors by using repellants and destroying breeding places. Wear personal protective equipment (gloves, coveralls and boots) when handling aborted fetuses or performing necropsies. If possible, avoid contact with infected tissues and blood. If RVF is suspected, the state or federal veterinarian should be contacted immediately and movement of animals should be restricted. Currently the greatest risk for RVF is for travelers to endemic African countries. If travel to this area is expected, protect yourself from mosquito vectors. Use insect repellents, such as DEET, and wear long sleeved shirts and long pants. Avoid being out during prime mosquito biting times (dusk, early evening and dawn).

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Control

- 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

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Although humans may contract RVF through the bite of an infected mosquito, they may also inhale the virus when handling infected animal tissues. This is why sick animals should not be slaughtered during a RVF outbreak. Bury or burn carcasses. Wear personal protective equipment such as gloves, coveralls, boots, protective eyewear and a respirator when handling aborted fetuses or performing necropsies. If possible, avoid contact with infected tissues and blood. Currently the greatest risk for RVF is for travelers to endemic African countries.

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Control

- 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®

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The RVF virus is easily destroyed by disinfectants. However, some disinfectants are easily inactivated by organic material (manure, feed, animal tissues, etc.). Therefore, cleaning is the first important step when treating an area that has become contaminated with RVF virus. When cleaning and disinfecting, it is important to wear personal protective equipment (gloves, coveralls, boots, protective eyewear and a respirator) since the virus may become airborne. Cleaning begins by removing all organic material from the surface. Next, use soap or a detergent with warm water and let the surface dry. Then apply the disinfectant. One part bleach diluted with 10 parts water or using the product Virkon-S® by DuPont will destroy the RVF virus.

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Control and Prevention

- Who to call
 - State veterinarian
 - Federal (APHIS) veterinarian
 - State public health veterinarian



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If RVF is suspected, contact your state veterinarian or federal (APHIS) veterinarian immediately. If human illnesses are noted, contact your state public health veterinarian.

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Rift Valley as a Biological Weapon

- Aerosol or droplets
 - 1 km downwind
 - 35,000 humans incapacitated
 - 400 deaths (1% mortality)
- Human introduction
- Animals as sentinels

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The use of the RVF virus as a bioterrorism agent would most likely be via virus-laden aerosol or droplets. It has been hypothesized that if RVF virus were disseminated by an airplane, 50 kg of the agent would have a 1 km downwind reach with 35,000 humans incapacitated and 400 deaths (1% mortality). It may be possible for a human to introduce RVF as well. A unsuspecting traveler from Africa may be incubating the disease. Upon arriving in the U.S., if he is bitten by a mosquito, the mosquito then becomes infective. The virus can then be transmitted to an animal which serves as an amplifying host. Currently the U.S. has several species of mosquitoes capable of transmitting RVFV. Since disease in animals typically occurs before that in humans, animals may serve as sentinel species for this disease.

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Additional Resources

- CDC – Special Pathogens Branch
 - www.cdc.gov/ncidod/dvrd/spb/mnpages/dispages/rvf.htm
- WHO Fact Sheet
 - www.who.int/inf-fs/en/fact207.htm

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Acknowledgments

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