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Rift Valley Fever

Infectious Enzootic Hepatitis of Sheep and Cattle

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Overview

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

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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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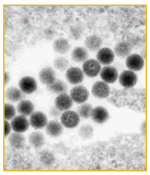
The Virus

- *Phlebovirus*, Bunyaviridae
- Stable at
  - -60ºC to 23°C
  - 50 to 85% relative humidity
- Inactivated by:
  - Lipid solvents
  - Detergents
  - Low pH



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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^{o}C and at 50 to 85% relative humidity. It is inactivated by lipid solvents, detergents and low pH.

Photo: Electron micrograph of the Rift Valley fever virus (RVFV), CDC.

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Disease Overview

- Acute febrile disease
  - Sheep, cattle, goats
  - High abortion rates and death in young
- Zoonotic
- Heavy rainfalls
- Arthropod vector
  - Most commonly mosquito
- OIE Listed disease

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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 animals, especially aborted fetuses, can transmit the virus to humans. Currently, RVF is an OIE-listed disease.

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HISTORY

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History

- 1900s: First recognized in sheep
- 1930: Agent isolated
- Major outbreaks
  - 1950-51: Kenya
    - 500,000 sheep abortions
    - 100,000 sheep deaths
  - 1977-78: Egypt
    - 18,000 human cases
    - 598 human deaths

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Rift Valley fever was first recognized as a disease in sheep in Rift Valley, Kenya around 1900. The virus was not 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. 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. Many abortions and deaths were reported in sheep, goats, cattle, water buffalo and camels.

Image: This map depicts the locations of Kenya and Egypt. Map from www.worldatlas.com.

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Important Outbreaks

- 1987: Senegal
  - Not associated with rainfall
- 1997-98: Kenya
  - 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. An RVF outbreak occurred in Saudi Arabia from August 2000 to September 2001; it 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 RFV 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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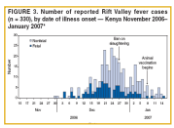
Important Outbreaks

- 2006-7: Kenya
  - Spread to surrounding areas
  - 1000+ human cases
    - 300 deaths
- 2010: South Africa
  - Over 14,000 animal cases
    - 489 separate outbreaks
  - Abnormally high rainfall



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In 2006, an outbreak of Rift Valley fever began in Kenya. It soon spread to the surrounding countries of United Republic of Tanzania and Somalia. Over 1000 human case were reported with case-fatality varying between the countries from 23 to 45%. Animal movement and slaughter restrictions were implemented as has vaccination efforts for livestock in affected areas. In 2010, South Africa had over 14,000 cases of RVF; 489 separate outbreaks were observed. Abnormally high rainfall likely contributed to these outbreaks.

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EPIDEMIOLOGY

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Epidemiology

- Endemic in tropical Africa
  - Cyclic epidemics
    - 5 to 15 years in savannah grasslands
    - 25 to 25 years in semi-arid regions
  - Susceptible animal populations develop between epidemics
  - Associated with heavy rainfalls
  - Peaks in late summer

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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 are usually associated with abnormally heavy rainfalls. The long intervals between outbreaks allow for development of a susceptible animal population that is severely affected by the following outbreak.

Photo: Egyptian delta farm, http://www.4egypt.info/images/delta_farm.gif

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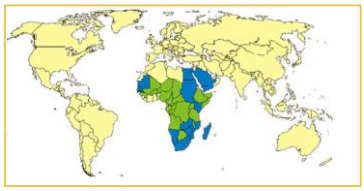
Distribution



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This map shows the distribution of RVF. The blue areas indicate African countries with endemic disease and substantial outbreaks of RVF. They include: Gambia, Senegal, Mauritania, Namibia, South Africa, Mozambique, Zimbabwe, Zambia, Kenya, Sudan, Egypt, Madagascar, Saudi Arabia, and Yemen. The green areas are countries know to have some cases, periodic isolation or serological evidence of RVF. They include: Botswana, Angola, Democratic Republic of the Congo, Congo, Gabon, Cameroon, Nigeria, Central African Republic, Chad, Niger, Burkina Faso, Mali, Guinea, Tanzania, Malawi, Uganda, Ethiopia, and Somalia. Image from Centers for Disease Control and Prevention. http://www.cdc.gov/ncidod/dvrd/spb/mnpages/dispages/rvfmap.htm

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TRANSMISSION

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Transmission

- Mosquitoes
  - *Aedes* species
  - Transovarial
  - Virus survives in dried eggs
  - Hatching associated with heavy rainfall, flooding
- Ruminants are amplifying hosts
  - Highly viremic
  - Source of infection for other vectors

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Rift Valley fever is transmitted by mosquitoes, particularly *Aedes* species. 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. Infected livestock can have be highly viremic and cause infection other mosquitoes. Humans also develop a high enough viremia to be a source of infection for mosquitoes. [Photo shows *Aedes aegypti* mosquito. From the CDC Public Health Image Library]

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Transmission

- Secondary arthropod vectors
  - Rapidly spread disease
  - *Culex* and *Anopheles* mosquito species
  - Biting flies
    - Midges, phlebotomids, stomoxids, simulids

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Secondary arthropod vectors can become infected from the ruminant and rapidly spread the disease. *Culex* and *Anopheles* mosquitoes can serve as secondary vectors. Several of these species of mosquitoes are found in the United States and could potentially contribute to the spread of RVF in this country. Biting flies such as midges, phlebotomids, stomoxids and simulids may serve as mechanical transmitters of the virus, however this is thought to be minimal route of infection.

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Additional Modes of Transmission

- Secondary arthropod vectors
  - Rapidly spread disease
  - *Culex* and *Anopheles* mosquito species
  - Biting flies (mechanical)
    - Midges, phlebotomids, stomoxids, simulids
- Animals
  - *In utero*
  - Semen, raw milk

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Secondary arthropod vectors can become infected from the ruminant and rapidly spread the disease. *Culex* and *Anopheles* mosquitoes can serve as secondary vectors. Biting flies such as midges, phlebotomids, stomoxids and simulids may serve as mechanical transmitters of the virus, however this is thought to be minimal route of infection. The virus can also be transmitted *in utero* to the fetus. It has also been found in semen and raw milk.

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Additional Modes of Transmission

- Humans
  - Direct contact or aerosol
  - Tissue or body fluids of infected animals
    - Aborted fetuses, slaughter, necropsy
  - *In utero*

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Humans do not seem to be infected by casual contact with live hosts, but can be infected by aerosols or direct contact with tissues during parturition, necropsy, slaughter, laboratory procedures or meat preparation for cooking. In utero transmission to a human infant was first reported in 2006.

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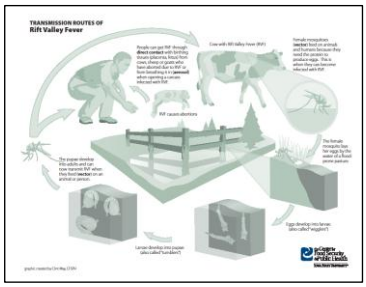

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This diagram depicts the various transmission routes of Rift Valley fever.
[Graphic illustration by Clint May, Center for Food Security and Public Health]

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DISEASE IN HUMANS

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Human Disease

- Incubation period: 2 to 6 days
  - Often asymptomatic
  - Influenza-like illness
    - Fever, headache, myalgia, vomiting
    - Recovery in 2 to 7 days
  - Rarely
    - Retinopathy
    - Hemorrhagic fever
    - Encephalitis

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The incubation time in humans has been reported to be anywhere from 2 to 12 days. The average is 2 to 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 2 to 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 to 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 to 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 to 4 days after fever
  - Melena, hematemesis, petechia, jaundice, shock, coma
  - Death
  - Case-fatality is ~50%
- Encephalitis
  - 1 to 3 weeks after onset of symptoms
  - Can occur with hemorrhagic fever

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Other possible complications from RVF include hemorrhagic fever and encephalitis. People demonstrating 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 to 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
  - Virus isolation
  - Antigen detection
  - RT-PCR
  - Serology
- Treatment
  - Symptomatic and supportive therapy
  - Replacement of coagulation factors
  - Ribavirin may be helpful

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Viral antigens and RNA can be detected in blood and tissue samples by various antigen detection tests and reverse transcription polymerase chain reaction (RT-PCR) assays. Enzyme-linked immunoassay (ELISA) and other serologic tests can detect specific IgM or rising titers. 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.

Photo: Cataloging samples for testing.

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DISEASE IN ANIMALS

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RVF in Animals

- Sheep and cattle
- Goats, buffalo, camel, other ruminants
- Cats, dogs,
- Some rodents
- Horses, some monkeys
- Pigs, birds, others resistant

RVF can affect many species of animals. Sheep and cattle are most severely affected and they are the primary amplifying hosts for the virus. Adult sheep and cattle may develop clinical disease and abortions can reach 100%. In kids and calves clinical disease is severe and mortalities are high. Other ruminants are also affected. Generally, the adults do not show clinical disease but abortion and disease of young animals can be severe. The same is true for dogs and cats. Some rodents are susceptible and others are resistant. Neutralizing antibody has been reported in a small percentage of horses and some monkeys in areas where the disease is endemic. Pigs, birds, rabbits, guinea pigs, and others appear to be resistant to the virus.

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Sheep and Goats

- Incubation period: less than 3 days
  - High rate of abortion (5 to 100%)
    - Any stage of gestation
  - Asymptomatic
  - Fever, weakness, foul diarrhea, icterus, mucopurulent nasal discharge, vomiting
  - Acute death (20 to 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 to 30%; however, abortion may be the only sign seen.

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Lambs and Kids

- Incubation period: 12 to 36 hrs
- Newborn deaths
  - High fever, listless, anorexia
  - Death in 12 hours to 2 days
- Mortality age-dependent
  - Less than 1 week old
    - Mortality >90%
  - Over 2 weeks old
    - Mortality 20%

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The incubation period in lambs and kids is 12 to 36 hours. As previously mentioned, aborted fetuses are the most common sign. Newborns are highly susceptible. Signs include high fever (105.8 ^{o}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
  - Usually asymptomatic
  - Abortion: up to 100% affected
  - Fever, weakness, anorexia, diarrhea,
  - Mortality: 10%
- Calves
  - Similar to lambs, kids
  - Mortality 10 to 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 to 70%. [Photo from Plum Island Animal Disease Center]

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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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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. [Photo shows a sheep liver that is pale, swollen and contains multiple foci of hemorrhage. Photo from Armed Forces Institute of pathology (AFIP)]

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PREVENTION AND CONTROL

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Recommended Actions

- Notification of Authorities
  - Federal Area Veterinarian in Charge (AVIC) http://www.aphis.usda.gov/animal_health/area_offices/
  - State Veterinarians www.usaha.org/stateanimalhealthofficials.aspx
- Quarantine

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State and federal veterinarians should be notified immediately of any suspicious cases of RVF. While waiting for the authorities or a confirmed diagnosis, all suspect animals should be quarantined.

Photo from Dr. Katie Steneroden, ISU.

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Prevention

- Vaccination
  - Common in endemic areas
  - May be used in outbreaks
  - Two forms: attenuated and inactivated
    - Attenuated
      - Better immunity but may cause abortion and birth defects in pregnant animals
- Vector control
- Keep livestock at high altitudes
- Animal housing controls

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Vaccines are generally used to protect animals from Rift Valley fever in endemic regions. During epidemics, vaccination of susceptible animals can prevent amplification of the virus and protect people as well as animals. Attenuated and inactivated Rift Valley fever vaccines are both available. Attenuated vaccines produce better immunity; however, abortions and birth defects can occur in pregnant animals. Subunit vaccines are in development. Additional, less commonly used, preventative measures include vector controls, movement of stock to higher altitudes, and the confinement of stock in insect-proof stables. These control methods are often impractical, or are ineffective because they are instituted too late. The movement of animals from endemic areas to RVF-free regions can result in epidemics.

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Prevention

- Vector control
  - Mosquito repellents, long shirts and pants, bed nets
- Barrier precautions
  - During exposure to infectious tissues or blood
  - Wear personal protective equipment
- Human vaccine
  - Limited availability

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Mosquito repellents, long shirts and trousers, bednets, and other arthropod control measures should be used to pre-vent transmission by mosquitoes and other potential insect vectors. Outdoor activities should be avoided, if possible, during periods of peak mosquito activity. Insecticides may be helpful. During epidemics, vaccination of susceptible animals can prevent amplification of the virus and protect people as well as animals. Barrier precautions should be used whenever contact may occur with infectious tissues or blood from animals; recommended measures include personal protective equip-ment such as protective clothing, gloves and goggles. Diagnostic tissue samples

should be processed by trained staff in appropriately equipped laboratories. Universal precautions are recommended for healthcare workers who care for patients with confirmed or suspected Rift Valley fever. Barrier techniques are recommended when nursing hospitalized patients. A human vaccine has been developed, but has limited availability. Additional vaccines are under investigation.

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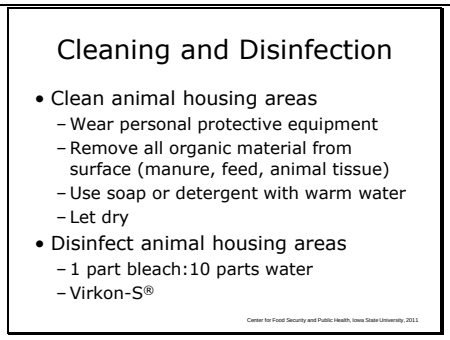

The RVF virus is easily destroyed by disinfectants. However, some disinfectants are easily inactivated by organic material (manure, feed, animal tissues, etc.). Therefore, cleaning is the first important step when treating an area that has become contaminated with RVF virus. When cleaning and disinfecting, 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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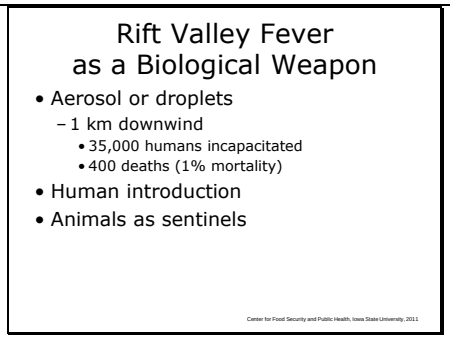

The use of the RVF virus as a bioterrorism agent would most likely be via virus-laden aerosol or droplets. It has been hypothesized that if RVF virus were disseminated by an airplane, 50 kg of the agent would have a 1 km downwind reach with 35,000 humans incapacitated and 400 deaths (1% mortality). It 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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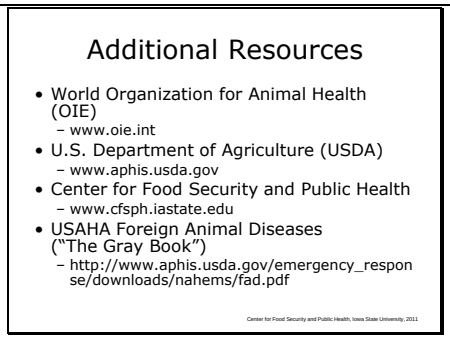

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