

Rabbit haemorrhagic disease

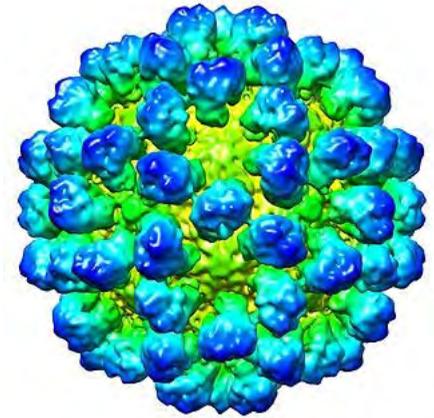
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Rabbit haemorrhagic disease (RHD), also known as **rabbit calicivirus disease (RCD)** or **viral haemorrhagic disease (VHD)**, is a highly infectious and often fatal disease that affects wild and domestic rabbits of the species *Oryctolagus cuniculus*. The infectious agent responsible for the disease is **rabbit haemorrhagic disease virus (RHDV)**, or **rabbit calicivirus (RCV)**, genus *Lagovirus* of the family Caliciviridae. The virus infects only rabbits, and has been used in some countries to control rabbit populations.

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CryoEM reconstruction of Rabbit Hemorrhagic Disease Virus (RHDV) capsid. EMDB entry EMD-1933 (<http://www.pdbe.org/EMD-1933>)^[1]

Virus classification

Group: Group IV ((+)ssRNA)

Order: Unassigned

Family: *Caliciviridae*

Genus: *Lagovirus*

Species: ***Rabbit hemorrhagic disease virus***

History

RHD first appeared in the Winter of 1983 in Jiangsu Province of the People's Republic of China. It was first isolated and characterized by S.J. Liu *et al.* in 1984.^[2] The Chinese outbreak was spread by the angora rabbit, which had originated in Europe. Fourteen million domesticated rabbits died within nine months in the outbreak.^[3]

In 1984 the virus that caused the disease was identified. The virus spread westward and reached Europe in 1988. The virus has since appeared in Mexico, Cuba, Australia, New Zealand and the United States.^[2] In 1992, the United Kingdom reported its first case of RHD in domestic show rabbits. By the late 1990s, RHD stretched to forty countries and had become endemic in wild and feral rabbit populations in Europe, Australia, New Zealand and Cuba.^[3] In Europe, there was a rapid increase in research into RHD, due to the importance of the

commercial breeding of rabbits for meat and fur production.

The first reported case in the United States was in Iowa on March 9, 2000. The affected breeds included Palominos and California Whites. By April 6, 25 of the 27 affected rabbits had died of the infection. In order to contain the disease, the remaining two rabbits were euthanized. No new introductions of rabbits were placed on the farm for two years after the discovery of RHD and August 1999 was the last time rabbits left and/or returned to the farm. The United States experienced other outbreaks of RHD in 2001 (Utah, Illinois, New York) and 2005 (Indiana).^[3]

In 2010, a new virus variant called rabbit hemorrhagic disease virus 2 (RHDV2) emerged in France.^[4]

World geographic distribution

Asia

Within a few months of RHD being reported in China in 1984, the disease was widely seen in many commercial rabbitries and had reached the Republic of Korea. RHD has also been reported in India and the Middle East.

Americas (North and South)

Since 1993, RHD has been endemic in Cuba; it is also believed to be thriving in Bolivia. From 1988 to 1992 Mexico dealt with an RHD endemic in domestic rabbits.^[3]

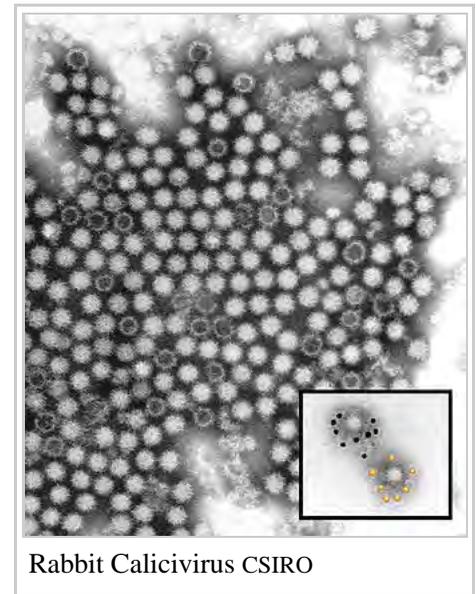
After outbreaks of RHD in 2000, 2001, and 2005 in domesticated rabbits, the United States has eradicated RHD from its rabbit populations. The native species, cottontails (*Sylvilagus floridanus*), black-tailed jackrabbits (*Lepus californicus*) and volcano rabbits (*Romerolagus diazzi*) seem not to be susceptible to the virus.^[3]

Australia

In 1991 a strain of the virus, Czech CAPM 351RHDV, was imported to Australia^[5] under strict quarantine conditions to research the safety and usefulness of the virus if it was used as a biological control agent against Australia and New Zealand's rabbit pest problem. Testing of the virus was undertaken on Wardang Island in Spencer Gulf off the coast of the Yorke Peninsula, South Australia. In 1995 the virus escaped quarantine and subsequently killed 10 million rabbits within 8 weeks of its release.^[6]

New Zealand

In July 1997, after considering over 800 public submissions, the New Zealand Ministry of Health decided not to allow RHDV to be imported into New Zealand to control rabbit populations. This was backed up in an early August review of the decision by the Director-General of Agriculture. However, in late August it was confirmed that RHDV had been deliberately and illegally introduced to the Cromwell area of the South Island.



An unsuccessful attempt was made by New Zealand officials to control the spread of the disease. It was, however, being intentionally spread, and several farmers (notably in the Mackenzie Basin area) admitted to processing rabbits that had died from the disease in kitchen blenders for further spreading.

Had the disease been introduced at a better time, there would have been a more effective control of the population. Unfortunately, it was released after breeding had commenced for the season, and rabbits under 2 weeks old at the time of the introduction were resistant to the disease. These young rabbits were therefore able to survive and breed rabbit numbers back up. Ten years on, rabbit populations (in the Mackenzie Basin in particular) are beginning to reach near pre-plague proportions once again though they have not yet returned to pre RCD levels.^{[7][8]}

Resistance to RHD in New Zealand rabbits has led to the widespread use of Compound 1080 (Sodium fluoroacetate). Farmers and land managers are having to increase their use of 1080 to protect pastoral land from rabbits and preserve the gains made in recent years through the use of RHD.^[9]

Europe

RHD is endemic throughout most of Europe. Italy's first case of RHD was recorded in 1986 and Spain's in 1988. France, Belgium (June) and Scandinavia followed in 1990. Within a few years of RHD's first appearance in Europe it had caused the largest mortality in domestic and wild rabbits in Germany, Austria, Spain and Italy. Spain was the worst affected by RHD, which in turn also affected the rabbit-specialized Iberian lynx.^{[10][11]}

When the United Kingdom's first case of RHD in 1992 was discovered, the disease was transmitted into the wild by domesticated pet rabbits. Sources vary in the number of confirmed cases of RHD; there were 9 known outbreaks in 1994, 32 cases but some sources believe there were as many as 512 cases of RHD in 1995, and around 30 RHD cases in 1996 throughout Scotland, England and Wales.

In April 2016, a highly lethal disease started affecting one of the northernmost feral rabbit populations in the world in Helsinki, Finland. The outbreak has since been identified to be caused by the new RHDV2 strain of the virus, being the first appearance of RHD in the country. Cases of viral transmission to domesticated pet rabbits have been confirmed and vaccinating rabbits has been recommended.^[12]

Transmission

Transmission of RHD occurs by direct contact with an infected animal and fomites. Rabbits acquire RHD through oral, nasal or conjunctival pathways. Urine, faeces and respiratory secretions may also shed the virus. The virus may also be carried by the wind. Carriers of the virus may remain infectious for up to a month depending on climate conditions; however, the virus has been known to persist for as little as 2 days and as long as 215 days. An infected carcass or hairs from an infected animal may also transmit RHD. Fomites such as clothing, contaminated food, cages, bedding, feeders and water will also harbour the virus. Even though the virus cannot reproduce in other mammals, predators and scavengers such as foxes, ferrets and some birds can excrete the virus through their faeces after ingesting an infected rabbit carcass. Flies, rabbit fleas, and mosquitoes can also spread the virus between rabbits.^[3]

Climate appears to play a crucial role in the transmission of RHD. In normal conditions, most outbreaks of RHD occur in winter or spring. High temperatures in late spring and summer will considerably reduce the spread of the virus. RHD will also be more prevalent in dry and semi-dry areas than in areas that are relatively cool and humid.^[6]

Signs

RHD primarily infects only adult rabbits. In fact, research has shown that rabbits younger than 8 weeks of age are resistant to the virus. The incubation period for the RHD virus is between 1 and 3 days, with death following 1 to 2 days after the infection. There is a wide range of RHD symptoms. Most rabbits will show no signs of external symptoms of RHD.

Symptomatic cases of RHD will display fever, squeals, and often coma leading to death within 12 to 36 hours. In less severe cases, rabbits may display uneasiness, excitement, anorexia, swollen eyelids, paralysis, ocular haemorrhages, and "paddling" or loss of skin. Convulsions may be seen as well. A fatal bloody discharge from the nose has been exhibited along with blood-stained cage floors, though these symptoms may have occurred after death. Rabbits who have recovered from the less severe symptoms usually develop severe jaundice with weight loss and lethargy. Diarrhoea, constipation and abdominal cramping are then exhibited right before death a few weeks later.

RHD causes rapid development of blood clot formation in major organs such as the heart, lungs and kidneys. The clots block blood vessels causing heart and respiratory failure. An infected rabbit that has died from RHD will often have its legs straight out and head over its neck.^[6]

Diagnosis

RHD may be indicated when several animals in the herd die after experiencing a fever and lethargy. Differential diagnosis includes pasteurellosis, myxomatosis, poisoning, heat exhaustion, and *E. coli* or *Clostridium perfringens* type E enterotoxemia.

Rabbits that die from RHD are usually in good outward state. However, the most frequent post-mortem lesions are necrosis of the liver, and splenomegaly. The liver of RHD rabbits may have a fine reticular pattern of necrosis outline each lobule and maybe yellow, gray or pale in colour. The liver is also usually friable and swollen. The spleen will be black in colour and also swollen with rounded edges, while the kidneys are dark brown in colour. Haemorrhages will also be seen many other organs and tissues. The trachea may present a foamy, bloody mucous. Enteritis of the small intestine and swollen meninges may also occur.

Laboratory tests such as reverse transcription polymerase chain reaction (RT-PCR), Western blotting, negative-staining immunoelectron microscopy, and ELISAs may be performed on samples from the liver, blood, spleen or other organs.

Morbidity, mortality, and immunity

RHD is extremely hard to locate in the wild since about 75% of rabbits with RHD will die in their burrows underground. Due to this difficulty, the morbidity and mortality estimates for RHD have a broad range. The morbidity rate ranges from 30% to 100% and the mortality rate from 40% to 100%; however, the typical mortality rate is usually around 90%.^[3]

In the wild, outbreaks in rabbits vary depending on the season, breeding cycles and geographical location. Some areas will see a high morbidity and mortality among its rabbit populations followed by calmer periods.

Maternal antibodies such as immunoglobulin G (IgG), which are readily transmitted to the young across the placenta, may explain why very young rabbits are resistant to RHD. Some scientists also believe that the

immature immune system of a young rabbit cannot produce the number of chemicals needed to initiate clotting in order to kill. Rabbits may develop immunity against other strains of the RHD virus, while others may endure persistent infections. The immunity does not survive through the next generation, leaving open the possibility of further outbreaks in the population.^[13]

Control

Countries that are uninfected by RHD may place restrictions on importation from endemic countries. According to the Merck/Merial Manual For Pet Health, Home Edition, 2007, RHD is a reportable disease in the United States. If a diagnosis is made by a veterinarian, a notification to the "appropriate government authorities" must be made.^[3]

Because of the highly infectious nature of the disease, strict quarantine is necessary when outbreaks occur. Depopulation, disinfection, surveillance and quarantines are the only way to properly and effectively eradicate the disease. Good disinfectants include 10% sodium hydroxide, 1-2% formalin, 2% One-Stroke Environ, and 10% household bleach. The RHD virus is resistant to ethers and chloroform. Deceased rabbits must be removed immediately and discarded in a safe manner. Surviving rabbits are quarantined or humanely euthanized. Test rabbits may be used to monitor the virus on vaccinated farms.^[3]

There are several vaccines available against VHD in the UK: Cylap, made by Fort Dodge Animal Health; Lapinject made by CEVA Animal Health; and Anivac, made by Animalcare Ltd. All last for 12 months and contain inactivated strains of VHD. A live combination vaccine, Nobivac Myxo-RHD, made by MSD Animal Health, has recently become available. Its active ingredient is a live myxoma-vectored RHD virus strain 009 and it offers a duration of immunity of 1 year against both RHD and myxomatosis.^[14]

Use as biological control agent

The European rabbit is the second most serious pest in New Zealand. Rabbits compete with livestock for grazing pasture, kill trees, shrubs, and have contributed to the extinction of some native plants. Consequently, rabbits contribute to soil erosion by eliminating the protective vegetation and disturb the soil by burrowing. The estimated combined cost of control and production losses in New Zealand as a result of rabbits is about \$23 million annually.^[15] This figure is only a small portion of the damage caused by rabbits. Parts of Australia have long experienced similar problems.

The use of RHD as a control agent is a recent tactic in a long string of efforts to reduce populations of European rabbits in areas where they are not native. With eventual, proper vaccination plans, the safety of domesticated (livestock and pet) rabbits might not be a concern regarding intentional use of RHD for this purpose.

See also

- Rabbits in Australia

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Further reading

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External links

- Disease card (http://www.oie.int/fileadmin/Home/eng/Animal_Health_in_the_World/docs/pdf/Disease_cards/RHD.pdf)

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