



# Caliciviridae

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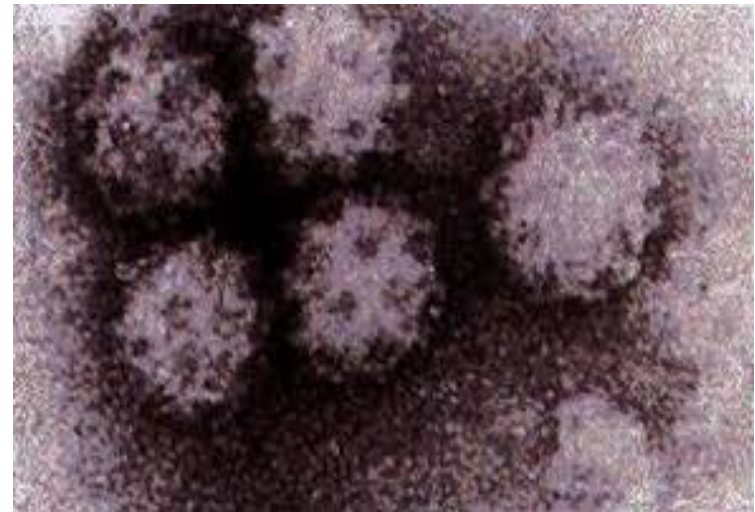
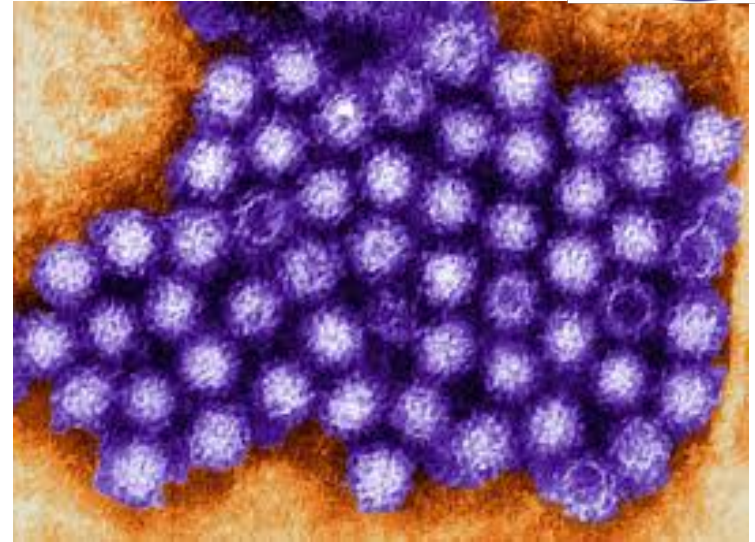
**Professor of Virology**



# Physical characters



- They are + sense ssRNA ,non-segmented , nacked viruses , cubic capsid with a diameter of 35–39 nm.
- seven species in this family, divided among 5 genera.
- The name calicivirus is derived from the Greek word *calyx* meaning cup or goblet, due to many strains having visible cup-shaped depressions.





# Physical characters

- **Caliciviridae family whose member genres are *Vesivirus*, *Lagovirus*, *Norovirus*, *Sapovirus*, and *Nebovirus*.**
- **The virions of this family are nonenveloped with icosahedral symmetry and are of 27–40 nm in diameter by negative-stain electron microscopy and 35–40 nm by cryo-electron microscopy.**
- **The capsid is composed of 90 dimers of the major structural protein VP1 arranged on a T = 3 icosahedral lattice. In noroviruses, the VP1 forms a subunit composed of a shell and two protruding domains.**



# Diseases by Caliciviridae



Diseases : **feline calicivirus** (respiratory disease); **rabbit hemorrhagic disease virus** (often-fatal hemorrhages) ; norwalk group of viruses: gastroenteritis.

Caliciviruses naturally infect vertebrates such as human, cattle, Pigs ,Cats, chicken, reptiles, dolphins, and amphibians.





# Physical characters

- A characteristic feature of calicivirus capsid architecture is the 32 cup-shaped depressions at each of the icosahedral five-fold and three-fold axes.
- In negative-stain virus preparations, some cup-shaped depressions appear distinct and well defined, while in others these depressions are less prominent.



# Viral proteins

- All the nonstructural proteins are encoded by a large polyprotein and expressed in the same order for each genus.
- The virions are predominantly composed of one major capsid protein, VP1 (58–60 kDa) and a second minor structural protein named VP2 (8.5–23 kDa) has been found in association with FCV and RHDV virions, and Norwalk virus-like particles.





# Taxonomy



- The *Caliciviridae* family includes:
- Genus *Lagovirus*; type species: *Rabbit hemorrhagic disease virus*
- Genus *Nebovirus*; type species: *Newbury-1 virus*
- Genus *Norovirus*; type species: *Norwalk virus*
- Genus *Sapovirus*; type species: *Sapporo virus*
- Genus *Vesivirus*; type species: *Vesicular exanthema of swine virus*



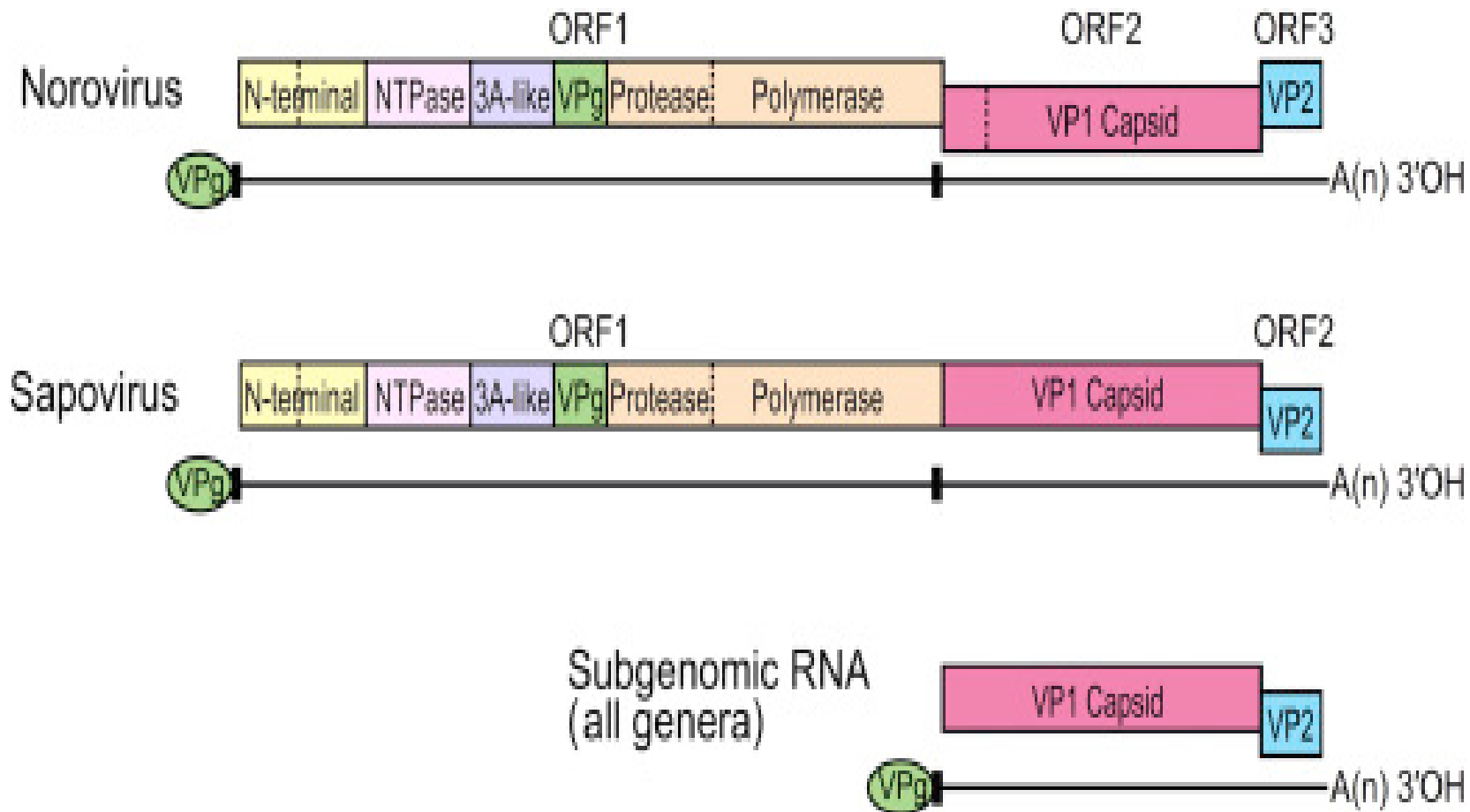
# Viral replication

- In the cytoplasm.
- Entry is achieved by attachment to host receptors, which mediates endocytosis.
- Positive stranded RNA virus → Translation.  
Vertebrates serve as the natural host.  
Transmission routes are fecal-oral

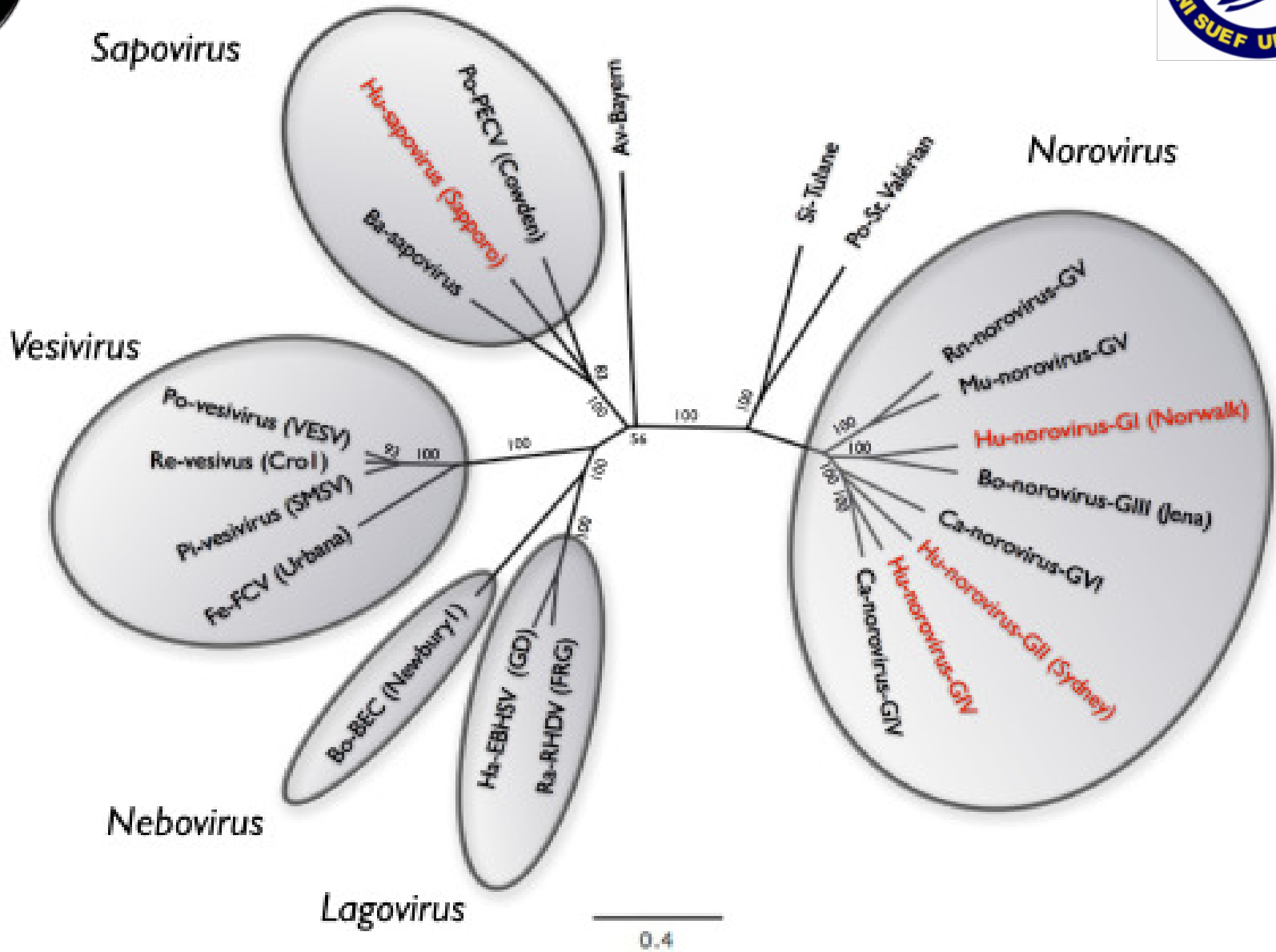




# Viral genome



**Caliciviruses have single stranded, positive sense genomic RNA (positive-strand RNA) organized into either two or three major ORFs.**





# Human disease

- Calicivirus infections commonly cause acute gastroenteritis, (e.g. the Norwalk Virus). Symptoms can include vomiting and diarrhea.
- These symptoms emerge after an incubation time of 2 days and the symptoms only generally last for 3 days.
- Most calicivirus infections do not call for medical attention, but those who are immunocompromised may need to be hospitalized for rehydration therapy.



# Animal viruses

- Feline calicivirus (FCV)—a member of the *Vesivirus*—represents an important pathogen of cats.
- Sapovirus, Norovirus and Vesivirus have been detected in pigs,.
- Rabbit hemorrhagic disease virus (RHDV) is a pathogen of rabbits that causes major problems throughout the world



# Rabbit haemorrhagic disease (RHD),



- **Rabbit Viral Hemorrhagic Disease (VHD) is a highly contagious disease caused by a calicivirus that affects only rabbits (wild and domesticated European rabbits)**
- **It has not been known to affect any North American native rabbits or hares, such as cottontails, snowshoe hares and jackrabbits.**
- **VHD is also known by several other acronyms: RHD (Rabbit Hemorrhagic Disease), RCV (Rabbit Calicivirus), and RCD (Rabbit Calicivirus Disease).**



# History



- RHD first in the [People's Republic of China](#). It was first isolated and characterized by S.J. Liu *et al.* in 1984
- 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.
- The virus spread westward and reached Europe in 1988.
- The virus has since appeared in Mexico, [Cuba](#), Australia, New Zealand and the United States.





In 1992, the United Kingdom reported its first case of RHD in domestic show rabbits.

The first reported case in the United States was in Iowa on March 9, 2000. [California Whites](#).

The United States experienced other outbreaks of RHD in 2001 ([Utah](#), [Illinois](#), [New York](#)) and 2005 ([Indiana](#)).

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



# Distribution





# Virus stability



- 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.



# Transmission

- Transmission 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;
- The virus persist for 2 days and as long as 215 days.
- An infected carcass or hairs from an infected animal may also transmit RHD.



# Transmission

- Fomites such as clothing, contaminated food, cages, bedding, feeders and water will also harbour the virus.
- foxes, ferrets and some birds can excrete the virus through their feces after ingesting an infected rabbit carcass.
- Flies, rabbit fleas, and mosquitoes can also spread the virus between rabbits.



# Clinical Signs



In fact, research has shown that rabbits younger than 8 weeks of age are resistant to the virus.

The incubation period 1 and 3 days, with death following 1 to 2 days

Most rabbits will show no signs of external symptoms of RHD.

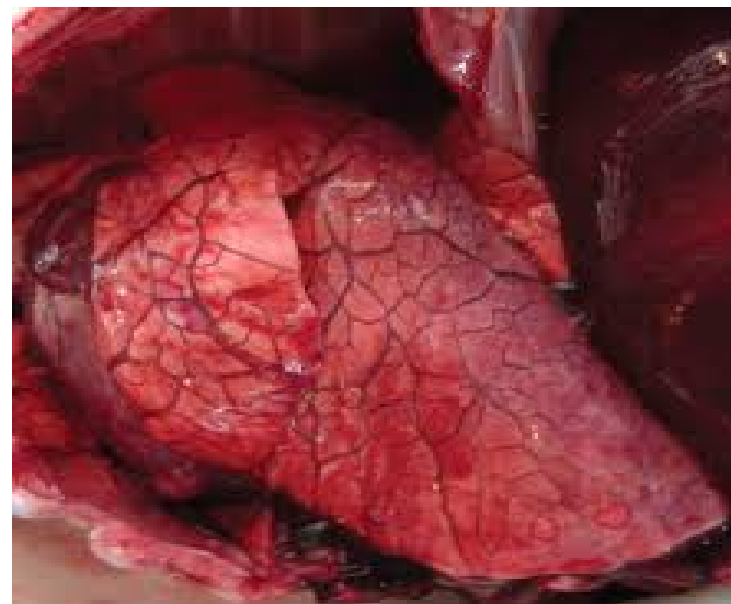
Symptomatic cases of RHD will display fever, and often coma leading to death within 12 to 36 hours.

In less severe cases, rabbits may display excitement, [anorexia](#), swollen eyelids, [paralysis](#), ocular [haemorrhages](#), and "padding" or loss of skin.

Convulsions may be seen as well.

A fatal bloody discharge from the nose 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](#).

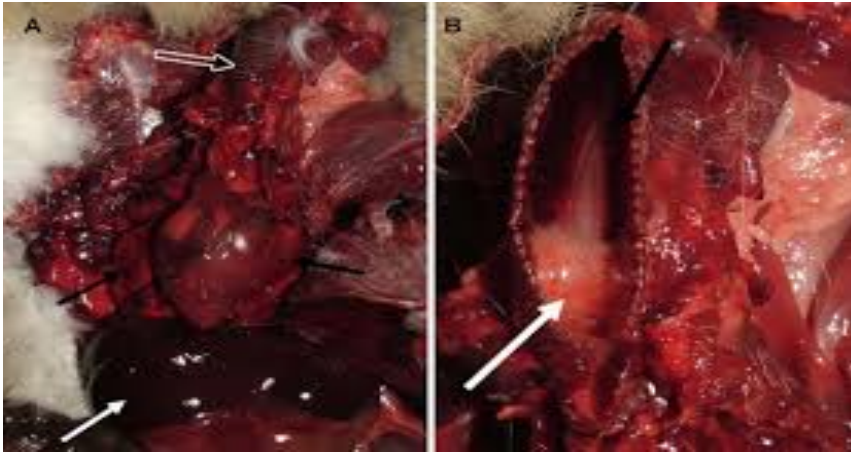
Diarrhoea, constipation and abdominal cramping are then exhibited right before death a few weeks later.

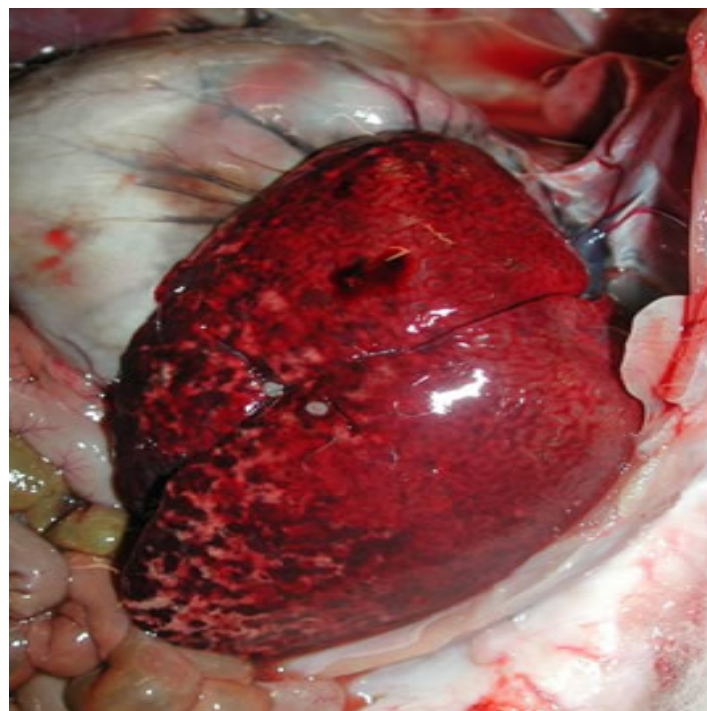
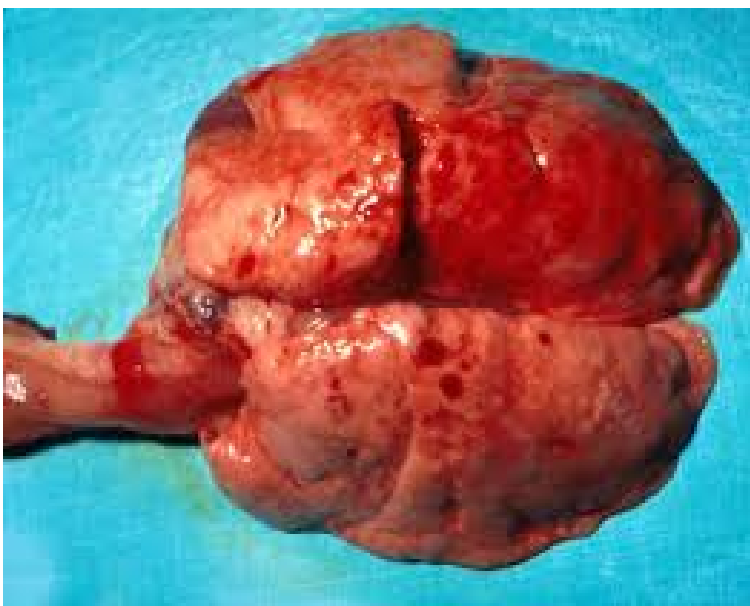
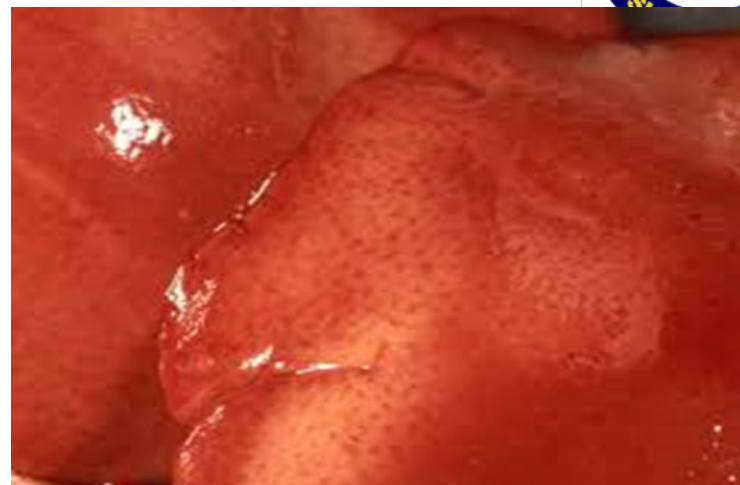
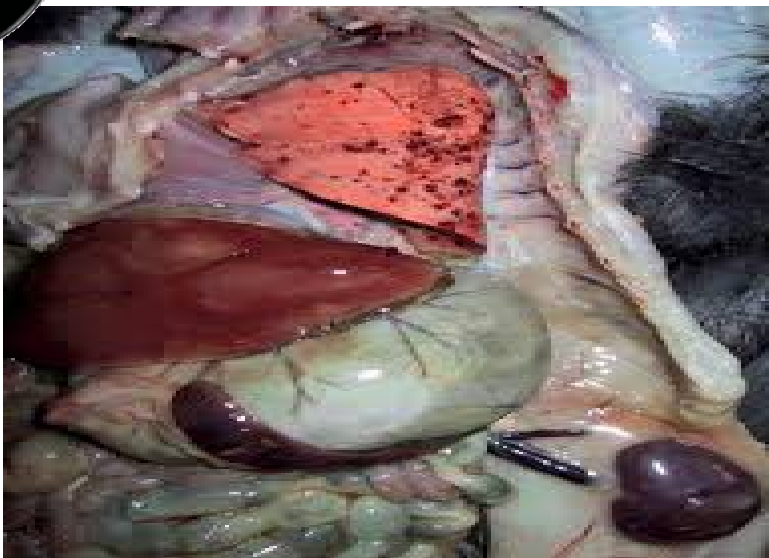




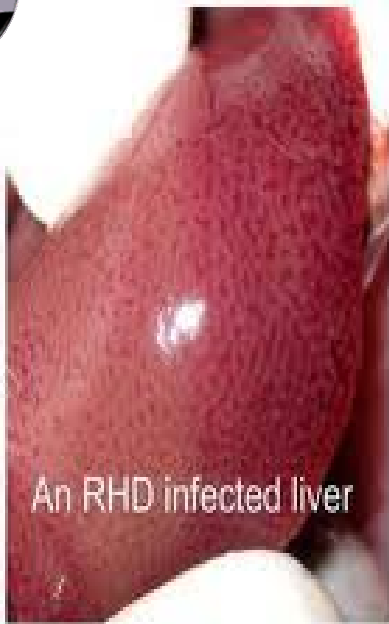


RHD causes rapid development of blood clot in the heart, lungs and kidneys. The clots block blood vessels causing heart and respiratory failure

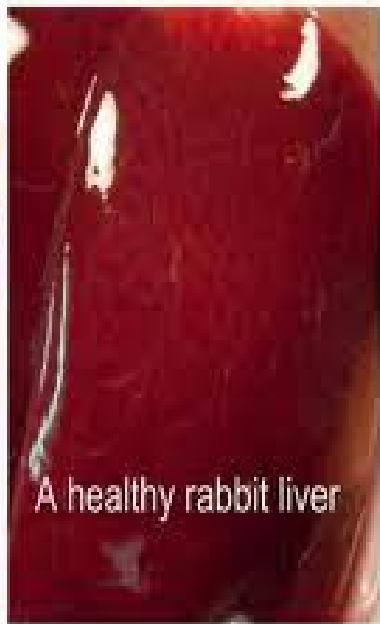




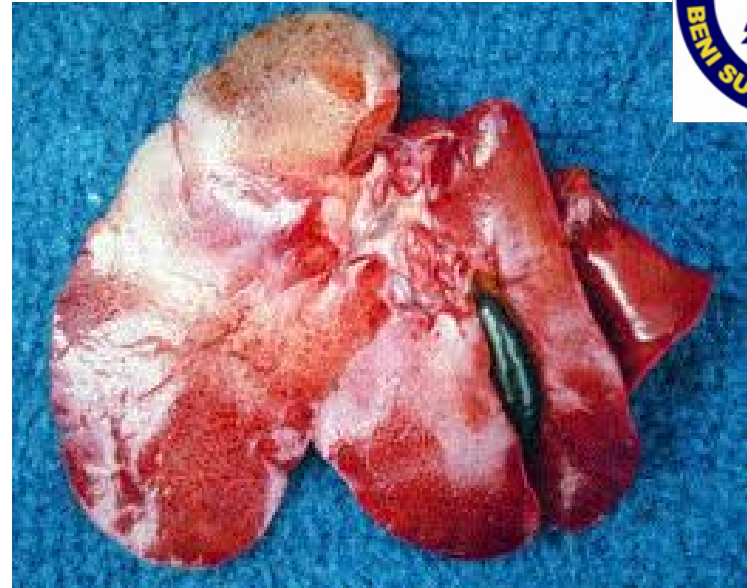




An RHD infected liver



A healthy rabbit liver







Vial of liquid RHDV suspension. Image: John Kovaliski





## 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.<sup>[3]</sup>

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.<sup>[3]</sup>

There are several vaccines available against VHD in the UK: Cylap, made by Fort Dodge Animal Health; Lapinject, made by CEVA Animal Health; Anivac, made by Animalcare Ltd and FILAVAC, made by Filavie. 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](#).<sup>[17]</sup> FILAVAC has been authorised by the VMD in April 2017 ; it is currently the only vaccine containing both classic and variant strain of VHD virus.<sup>[18]</sup>

## 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.<sup>[19]</sup> 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.<sup>[cit]</sup>



**VHD, however, is often a very swift and sudden killer, giving little warning. Rabbits may die without showing any symptoms at all. Some bleeding from the nose, mouth and rectum is sometimes seen. Any sudden rabbit death is suspicious and should be reported to your veterinarian or the State Veterinarian as a possible case of VHD. The incubation period of this disease is very short, and rabbits may die within 48 hours of exposure to the virus that causes VHD.**

**The death rate of rabbits exposed to this virus is very high, between 50 and 100%, with the latter number probably being closer to actual mortality rates. Rabbits who survive this disease are carriers and shed the virus for at least 42 days, perhaps longer.**

**Rabbit calicivirus is a very hardy virus, remaining viable in the environment for 105 days at 68F (i.e. remains stable for 105 days at room temperature) and for 225 days at 39F. It resists freezing.**

**There is no known cure for VHD. Vaccinations are available in countries where the disease is endemic, but there is no vaccine currently available in the US.**



