Rabbit Diseases

**Myxomatosis**
Myxomatosis is a severe, often fatal disease of the European rabbit (Oryctolagus) caused by myxoma virus. The virus is well-adapted to certain wild species of rabbits such as the South American cottontail (Sylvilagus) and these species are resistant to severe disease. However in the European rabbit it causes a systemic disease with a high mortality. All other mammals are refractory to the virus. Myxoma virus has been deliberately used in certain countries (e.g. Australia and France) for biological control of wild populations of the European rabbit.

**Etiology and Pathogenesis**
Myxoma virus is a member of the poxvirus family. It is a large, double-stranded DNA virus which replicates in the cytoplasm of infected cells. Biting insects are an important vector for transmission of myxoma virus. Such transmission is passive; the virus mechanically adheres to the mouthparts of the vector but no replication takes place. However the virus is also able to spread efficiently between rabbits in close contact in the absence of insect vectors. It is shed in ocular and nasal secretions and it is also potentially present in semen and genital secretions.

Following intradermal inoculation, initial replication of virus occurs at the inoculation site and within a few days the virus spreads from here to the draining lymph node. The virus spreads throughout the body via leucocytes to numerous secondary tissues and organs including lymphoid tissue, lungs, testes, conjunctivae, nasal mucosa and distal skin. Myxoma virus possesses a number of immunosuppressive mechanisms which assist viral survival and dissemination in the infected host. This may help explain why severe secondary bacterial infections are commonly seen in infected rabbits. Despite the immunosuppression, infected rabbits will develop an IgM and IgG antibody response which can be detected in the serum by ELISA and neutralization tests as early as days 6–10 after infection and both humoral and cell-mediated immunity is probably important in order to provide optimum resistance to disease. Myxoma virus can persist for prolonged periods in some rabbits and there are suggestions that latent infection may be a feature of the disease leading to later recrudescence of disease and virus shedding.

**Clinical and Pathological Findings**
Clinical signs depend on the strain of the virus and the route of infection. Two forms of the disease have been described; the classical (nodular) form and the amyxomatous (respiratory) form. Nodular myxomatosis is mainly transmitted by biting insects and predominately observed in wild and pet rabbits. It is characterised by multiple skin lesions and immunosuppression, usually accompanied by secondary bacterial infection of the respiratory tract. The evolution of clinical signs depends on the virulence of the infecting strain. Following infection with more virulent strains the initial sign is a swelling at the site of infection, which increases in size and often ulcerates. Following
this, acute inflammation of the conjunctivae and oedematous swelling of the eyelids and genital area occurs and secondary skin lesions usually appear on about the sixth or the seventh day post-infection. Death commonly occurs sometime between days 8 and 15 post-infection. The mortality rate ranges from 20 to 100%, according to the virulence of the infecting strain, and in surviving animals the lesions will progressively heal. Secondary bacterial infections of the upper and lower respiratory tract (e.g. with Pasteurellae) are typically seen in rabbits that live longer than around 10-14 days and this is probably the major cause of death in rabbits infected with less virulent strains.

The clinical signs of amyxomatous myxomatosis are mainly respiratory. This form is generally characterised by fewer skin lesions than the nodular type, although many of the other typical clinical signs such as conjunctivitis, swollen eyelids and genital area and rhinitis can be seen. This presentation of the disease form is more commonly seen in commercially farmed rabbits and it has been suggested that the amyxomatous form may represent an adaptation to contact spread via respiratory and conjunctival secretions. The virulence of amyxomatous strains seems to depend more on the presence of secondary bacterial pathogens such as *Pasteurella multocida*.

In peracute cases there may be no gross lesions. In rabbits that survive longer, findings at necropsy may include reduced body fat and haemorrhages in various organs (e.g. thymus, trachea and lungs); subcutaneous ecchymoses; multiple mucinous cutaneous nodules; oedema of the eyelids and anogenital region; swollen conjunctivae with mucopurulent ocular discharge; swollen nasal mucosae and mucopurulent nasal discharge; patchy consolidation in the lungs associated with secondary infections; swollen spleen and enlarged, oedematous and haemorrhagic lymph nodes.

**Diagnosis**

In many cases the typical clinical signs are sufficiently distinct to serve as the basis for diagnosis. If necessary, diagnosis can be confirmed in an individual case by isolation and identification of the virus or identification of viral antigen from skin lesions or sites of viral shedding (e.g. conjunctivae) and commercial PCR tests are now fairly widely available from a number of laboratories. Serologic tests (mainly ELISA) are also available to detect antibodies to the virus and these can be useful in confirming the overall prevalence of infection.

**Rabbit Haemorrhagic Disease**

Rabbit Haemorrhagic Disease - RHD (also known as Viral Haemorrhagic Disease – VHD and Rabbit Calicivirus Disease) is a highly contagious disease of the European rabbit (*Oryctolagus*) caused by a calicivirus (RHDV). The disease has a high morbidity and mortality rate in susceptible animals. After its emergence in China in the 1980s it has spread naturally, and rapidly throughout most of the rest of the world. As a consequence of its worldwide spread, RHDV differentiated into many genetically closely-related strains, all highly virulent. In addition, other non-virulent caliciviruses have been identified, both in commercial and wild rabbits, that are less closely genetically related and provide varying degrees of cross-protection against RHD. More recently, a new variant strain of virulent RHDV has emerged in Europe which seems capable of evading the high degree of protection provided by ‘classical’ RHDV vaccines. This new variant is designated as RHDV2.
**Etiology and Pathogenesis**

The etiological agent is a small RNA calicivirus which is very resistant to inactivation, particularly when protected by organic material, and may persist in decomposing carcasses in the environment, for some months. It is sensitive to phenol or formalin based disinfectants.

RHD affects both wild and domesticated members of the species *Oryctolagus cuniculus*, the European rabbit, although other rabbit species are not susceptible. Rabbits of all ages can be infected but animals younger than 40–50 days of age are refractory to disease. The morbidity rate varies from 30% to 100%, and the mortality rate is 40–100%.

Rabbits can become infected via oral, nasal or conjunctival routes following either direct contact with infected animals, exposure to an infected carcass, by means of fomites, including contaminated food, bedding and water and via mechanical transmission from flies and other insects. Rabbits which recover from disease may remain infectious for some weeks and continue to shed infection in their faeces.

Following infection the virus spreads and multiplies in splenic histiocytes and hepatocytes, in which it induces apoptosis and cell death. Substances released by the damaged cells are thought to initiate disseminated intravascular coagulation (DIC). It is this DIC and also the fulminant liver failure that causes rapid death in rabbits succumbing to acute disease.

**Clinical and Pathological Findings**

The course of the disease can be peracute, acute, subacute or chronic. Peracute RHD is characterised by sudden death, sometimes with signs of terminal haemorrhagic nasal discharge, and so clinical signs are normally only observed in the acute or subacute forms. The incubation period varies between 1 and 3 days and is followed by pyrexia (>40°C), anorexia, apathy, dullness, collapse, nervous signs (convulsion, ataxia, paralysis, opisthotonos, paddling) vocalisation, respiratory signs (dyspnoea, frothy and bloody nasal discharge), and cyanosis of mucous membranes. In these animals death often occurs within 12–36 hours of the onset of signs. During an outbreak 5–10% of rabbits may show signs of more chronic disease, characterised by generalised jaundice, lethargy and loss of weight. These animals usually die of liver failure within 1 or 2 weeks.

Due to the rapid course of this disease, most affected animals are normally found in good condition at necropsy. There is evidence of splenomegaly and primary liver necrosis, and a massive and widespread disseminated intravascular coagulopathy which results in the presence of clotted blood in vessels and petechial haemorrhages in all organs and tissues. The most severe lesions are in the liver, trachea and lungs. In subacute and chronic disease widespread icteric discoloration of the carcase is evident.

**Diagnosis**

A presumptive diagnosis can readily be made when there are multiple cases of sudden death in amongst unvaccinated animals, in some cases following a short period of lethargy and fever, and with characteristic hepatic necrosis and haemorrhages visible at necropsy.
The presumptive diagnosis can be confirmed by isolation and identification of virus or detection of viral antigen in samples of fresh liver, spleen or blood. A PCR test is available commercially which can detect viral RNA in a many organs, urine, faeces or serum.

Serum antibodies arising from natural infection or from immunisation appear within 4-6 days of infection in surviving animals. These can be measured using HI or ELISA tests.

*Source: Merck Vet Manual*