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Reoviridae

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Table of Contents

Viruses of the family Reoviridae (reo = respiratory, enteric, orphan) infect vertebrates, invertebrates, higher plants, fungi and bacteria. They are unique in that they possess a linear, double-stranded, segmented RNA genome. A number are important veterinary pathogens.

Viral Characteristics

- Reoviruses are naked double-stranded RNA viruses (60 - 80 nm in diameter) with an outer shelled (outer shell and core) icosahedral capsid containing 10, 11 or 12 segments of double-stranded RNA (see Fig. 16.1).
- They replicate conservatively in the cytoplasm, have a core-associated transcriptase and some (especially orthoreoviruses) produce large cytoplasmic perinuclear inclusions with a characteristic beehive pattern.
- Following entry into a host cell, the virion is partially uncoated. Unique to the Reoviridae, replication occurs within partially uncoated virions as all of the enzymes necessary for replication are present within the capsid. The dsRNA is transcribed to form +sense RNA, some of which is sent into the cytoplasm for translation by ribosomes. The remainder is packaged into partially assembled virions. Within the virions, the complementary -sense RNA is synthesized resulting in a dsRNA genome within the newly formed virions.
- Some serotypes share a common complement fixation antigen, but can be distinguished by hemagglutination inhibition and neutralization techniques.
- They vary in stability; the orthoreoviruses and rotaviruses retain infectivity over a wide pH range. Mammalian orthoreoviruses are resistant to a number of common disinfectants.

Figure 16-1. Reoviridae (60 - 80 nm). Virions are unique in that they possess three capsid layers. - To view this image in full size go to the IVIS website at www.ivis.org . -

Classification

The reoviruses of vertebrates are placed in five genera and those of insects and plants in four genera. The genera comprising the vertebrate viruses and their diseases are as follows:

Orbivirus (Have the capacity to replicate in some biting arthropods).
Bluetongue
African horse sickness

Equine encephalosis
Chuzan disease (Japan)
Epizootic hemorrhagic disease of deer
Ibaraki virus (A virus related to epizootic hemorrhagic disease virus of deer. Causes an often severe disease of cattle in Japan, Taiwan and Bali.)
Palyam virus [An orbivirus isolated from Culex species (India) and Culicoides species (Australia and Nigeria) that causes arthropod-borne disease characterized by fetal lesions and abortion].

Rotavirus

Rotavirus infections

Orthoreovirus These viruses, which only infect vertebrates, are generally minor causes of disease. They are spread by the fecal-oral and respiratory routes. Unlike orbiviruses and rotaviruses they can be propagated in cell cultures with relative ease. The mammalian orthoreovirus cause mild respiratory and enteric infections in many animal species and humans.

Avian orthoreoviruses cause significant infections in chickens and turkeys.

Coltivirus Members of this genus are mainly isolated from Ixodid ticks but also from humans, deer and some small animals.

Colorado tick fever virus: A human disease occurring in the northwest U.S.; acquired from the bite of infected tick; wild rodents probably serve as natural reservoirs.

Aquareovirus Species are recovered from sea and fresh water fish and some marine invertebrates including clams and oysters.

Orbivirus

Bluetongue

Cause

Bluetongue virus (BTV). Twenty-four serotypes are recognized. The virus contains 10 genome segments; three are large, three are medium and four are small.

Occurrence

This non-contagious disease of sheep, cattle, small domestic and wild ruminants occurs in many countries, including the southern United States. Major clinical signs are observed in infected sheep; cattle and goats are less seriously affected.

Transmission

Various species of biting Culicoides are the common vector for bluetongue viruses. Replication takes place in the insects without transovarial transmission. Virus inoculation occurs by biting insects.

Pathogenesis

The virus replicates initially in the regional lymph nodes with dissemination to other lymphoid tissues and further replication. The virus finally locates in the endothelium of small blood vessels where it replicates resulting in vascular damage, exudation, hemorrhage and hypoxia.

Clinical & Pathologic Features

The incubation period for sheep is usually 6 - 10 days. Although some sheep may experience only mild disease, typical infections are characterized by acute onset with high fever, depression, anorexia, nasal and ocular discharge, salivation, and ulcers on the lips, tongue, and dental pad. Swelling and tenderness of the coronary region of the hoof may result in lameness.

Principal changes observed at necropsy are the oral lesions, a generalized edema, and hemorrhages of skeletal and cardiac muscles. Pregnant ewes may abort or deliver lambs with hydranencephaly.

Bluetongue virus infection in cattle is usually subclinical but pregnant cows infected early in gestation may have mummified fetuses, abort or deliver calves with birth defects.

Bluetongue is a devastating disease of white-tailed deer and pronghorn antelope.

Diagnosis

- Clinical, specimens: whole blood, spleen, serum.
- A presumptive diagnosis is based on clinical signs and gross necropsy lesions with supportive serologic evidence of exposure.
- Confirmation requires isolation of the virus, which is best accomplished initially by the intravenous inoculation of chicken embryos and subsequently in cell cultures (e.g., Vero cell line). BT virus is among the most difficult animal viruses to isolate.
- The serologic tests most often used to determine exposure are the agar gel immunodiffusion (AGID) and a competitive ELISA. The latter is considered to be more sensitive and specific. Many cattle in the United States, particularly those in southeastern states, have antibodies to BT virus. In such endemic regions paired serum samples

and demonstration of rising titers may be required to demonstrate acute infection. Antigenically related orbiviruses may cross-react and give false negative results in AGID tests.
- Although not required for routine diagnosis, a nested PCR has been descried for identification of BTV nucleic acid.

Prevention
- Modified-live virus vaccines are effective but their use is not permitted in the United States. Protection is homologous and, in order to protect against multiple serotypes, polyvalent vaccines are required.
- Although BTV infections occur widely in ruminants in the United States, import restrictions are enforced in an attempt to prevent introduction of new serotypes. A number of other countries have similar restrictions.
- Reduction of insect vectors.

African Horse Sickness

Cause

African horse sickness virus. Nine serotypes have been identified by neutralization tests. There is a group specific complement fixation antigen.

Occurrence

Horses, mules, donkeys, zebras and dogs are naturally susceptible. Elephants, dogs and zebras are thought to be reservoir hosts. African horse sickness (AHS) is endemic in much of Africa and it has spread to the Middle East, India, Pakistan and to Spain and Portugal although the disease has not persisted outside of Africa.

Transmission

The virus is transmitted by biting of insect vectors (Culicoides species); dogs may also be infected by eating infected horse meat.

Pathogenesis

The primary sites of replication are thought to be lymph nodes, lungs and spleen. Following viremia, endothelial cells are infected with replication resulting in vascular damage resulting in increased vascular permeability, hemorrhage and edema.

Clinical & Pathologic Features

The disease occurs in severe, chronic and mild forms. In the severe pulmonary form there is acute onset of paroxysmal coughing, labored breathing, high temperature and edema of the respiratory tract. The more chronic form is characterized by hydropericardium, and hemorrhage and edema of the subcutis of the head and neck regions. Some horses may exhibit signs of both pulmonary and cardiac disease, whereas others may only experience a mild transient infection.
The mortality usually range from 20 to 95%.
The lesions observed at necropsy vary according to the form of the disease and may include edema of the lungs, hydrothorax, and gelatinous exudates in the subcutaneous, interlobular, and intramuscular tissues and lymph nodes.

Diagnosis
- Clinical specimens: freshly collected and refrigerated whole blood.
- A tentative diagnosis is made on the basis of clinical signs and pathologic changes.
- Laboratory confirmation is obtained by isolation of the virus in one-day-old mice inoculated intracerebrally, in embryonated eggs or in various cell cultures (e.g., Vero cells). The virus is identified by virus neutralization tests or immunofluorescence.
- ELISA, complement fixation and agar gel immunodiffusion procedures are used. for detection of antibodies and antigen.
- A RT(reverse transcriptase) -PCR procedure has been used to detect viral nucleic acid.
- There are nine different antigenic types of the virus that can be identified by serum neutralization tests. Their distribution varies with regions.

Prevention
- Strict import regulations are enforced to prevent introduction of AHS virus into countries free of the disease.
- Modified live polyvalent virus vaccines are used where the disease is endemic; however, these vaccines do not prevent viremia and reversion to virulence of vaccine strains has been reported.
- Control of insect vectors.

Equine Encephalosis

Equine encephalosis virus (seven serotypes) resembles closely the virus of AHS and causes a frequently fatal disease that resembles closely AHS. The disease has been reported from South Africa and is thought to be spread by biting arthropods and particularly Culicoides species.

Chuzan Disease
The cause of this infection is a tentative species in the genus Orbivirus. The disease occurs in southeast Asia and Japan and is characterized by congenital abnormalities in calves including hydronencephaly and cerebellar hypoplasia. Development of these abnormalities appears to be related to the age of the fetus at the time of infection, and is thought to occur most often when the fetus is infected at about four months of age. Affected calves may be blind and display seizures and opisthotonus. Beef cattle are more often affected than dairy cattle.
Transmission is by Culicoides oxystoma.
Diagnosis is usually based on clinical history, microscopic lesions, and supportive serologic results.

Epizootic Hemorrhagic Disease of Deer
Cause
Epizootic hemorrhagic disease (EHD) virus. There are eight serotypes of the EHD virus, but only two of these (New Jersey and Alberta) occur in the United States.

Occurrence
The disease occurs in white-tailed and mule deer; other deer species are not susceptible. Cattle, buffalo and non-white-tail deer are infected with various serotypes but do not develop clinical disease.

Transmission
The virus is transmitted by the biting gnat, Culicoides variipennis.

Clinical & Pathologic Features
The disease may be subclinical peracute, acute, or chronic. The peracute form is characterized by severe edema of the head and neck regions, including the tongue and conjunctiva, and rapid death. Edematous lungs are noted at necropsy but there are few if any signs of hemorrhage. Hemorrhages are more evident in animals that live longer (acute form), and are usually present in the heart, rumen, and intestine. There are also ulcerations on the tongue and dental pad and in the rumen and omasum.
The chronic form is characterized by lameness. Bluetongue virus may cause similar disease manifestations. The virus of EHD may infect cattle, but most infections are subclinical. One strain of EHD (Ibaraki) occurs in Southeast Asia and causes a disease in cattle clinically similar to bluetongue.

Diagnosis
- Clinical specimens: fresh heparinized blood, serum, and spleen.
- Diagnosis of EHD is often made on the basis of clinical signs and lesions. Confirmation requires isolation and identification of the virus. The virus can be propagated in embryonated chicken eggs inoculated intravenously and in various cell cultures, including the BHK-21 cell line.
- Fluorescent antibody may be used to identify virus in frozen sections of affected tissues.
- A high percentage of deer in the southeastern United States have antibodies to EHD virus as determined by the agar gel immunodiffusion test.

Prevention
There are no practicable preventive measures.

Rotavirus Infections
Rotaviruses cause gastroenteritis with diarrhea in many mammalian species and poultry worldwide. The disease is most common and severe in intensely-reared animals such as calves and piglets; however, it also an important disease in foals, puppies, kittens and poultry. The clinical signs are similar in all species affected and the outcome of the infection ranges from subclinical to severe gastroenteritis and even lethal infections. The disease usually affect young animals up to eight weeks of age; most often after the first week of life.

Cause
Seven serogroups, designated A through G, have been identified, based on differences in the major capsid antigen VP6.
- Most isolates causing disease belong to serogroup A.
- Fourteen serotypes have been identified in group A based on differences in the VP7 capsid antigen. Other groups also have different serotypes.
- The severity of the infection may be influenced by concurrent infections with other agents, including Salmonella species, Cryptosporidium species and E. coli or by stress such as chilling.
- Rotaviruses are species specific.

Occurrence
Rotaviruses occur widely in many animal species and humans. Rotavirus infection is endemic in many swine and dairy cattle herds.

Disease seems to occur most frequently when the immune status of the piglets or calves is lowered and there is an overwhelming buildup of the virus.
Rotaviruses can be recovered frequently from the intestine of many normal calves, pigs and other domestic species.

Transmission
By contact and animals are infected by the oral/fecal route. The virus is present in feces up to three weeks after infection and possibly longer.

Pathogenesis: General
- The mature epithelial cells of the distal half of the villi of the small intestine appear to be especially susceptible to rotavirus infection. Selective destruction of villous cells leads to villous atrophy, malabsorption, and diarrhea.
- Insufficient colostral antibody is thought to contribute to the development of these infections.
- Enteropathogenic E. coli may act in concert with rotavirus in causing diarrhea, particularly after the intestinal mucosa has been rendered vulnerable by necrosis and the loss of epithelial cells.

Clinical Signs: General
The incubation period may be less than 24 hours. Signs may include vomiting, anorexia, depression and a profuse, watery diarrhea of sudden onset, which quickly results in extreme dehydration.
Piglets - Rotaviral infection is widespread in swine herds throughout the world. The disease is seen most commonly in swine 1 - 4 weeks of age. The virus is present in feces up to three weeks after infection.
Calves - Rotavirus disease is seen most commonly in calves 1 - 7 days of age. Coronavirus infects calves from 1 day to 3 weeks of age. Both viruses are responsible for disease characterized by a profuse, watery diarrhea of sudden onset.
Poultry - Only group D viruses have been implicated in avian infections. Infections are considered to be common in domestic poultry and other avian species.
Other Animals - As mentioned above analogous rotavirus infection occurs in newborn foals, puppies and kittens.

Diagnosis
- Clinical specimens: portions of small intestine with fecal content.
- The ubiquity of rotaviruses must be taken into account in arriving at a diagnosis and also the possibility of coronavirus co- infection.
- It must be kept in mind that a number of other microbial (protozoa, virus, bacteria) agents cause gastroenteritis in young animals.
- Specific diagnosis is best accomplished by fluorescent antibody examination of frozen sections of intestine or by electron microscopic examination of feces and intestinal contents. Large numbers of rotaviruses are present in the feces of animals with clinical disease.
- Propagation of rotavirus using conventional cell culture systems is difficult.

Treatment
- Oral or intravenous electrolyte solutions to cope with dehydration.
- An antibiotic may be used in severe disease if there is complicating bacterial infection.

Prevention
- Given the widespread occurrence of rotaviruses (many carriers) eradication is not feasible.
- Modified live and killed vaccines are available. Vaccination of pregnant animals is helpful, although the value of oral vaccines in the newborn is questionable.
- Keep young animals warm and dry; provision for adequate colostrum and milk.
- Cleaning and disinfection of quarters reduces exposure to the virus large numbers of which are passed in he feces of infected individuals.

Orthoreovirus

Avian Orthoreoviruses

These non-mammalian orthoreoviruses share a common group antigen. The eleven serotypes produce syncytia in cell cultures and infections in chickens and turkeys. A variety of infections are produced depending upon the particular orthoreovirus involved. They include arthritis, tendinitis, gastroenteritis, hepatitis and myocarditis with weight loss. The infections are common in commercial flocks.
Virus isolation and identification, although strait forward, is not usually feasible. The viruses are readily identified by the fluorescent antibody staining of cryostat sections of tissues.
Good management practices with thorough cleaning and disinfection of quarters helps reduce losses. Active immunization is complicated by the involvement of different serotypes of virus.

Mammalian Orthoreoviruses

These viruses, three serotypes, have been associated with mild respiratory and enteric disease in many animal species.

Disease may be severe if complicated by secondary bacteria.

Glossary
Competitive ELISA: Antigen and the competitive substance (analog) will compete for specific antibodies. Concentration can be determined by comparison of the blocking effect (competition) by standardizing the concentrations of analog and antibody.
Hydranencephaly: In this condition fluid-filled cavities take the place of the cerebral hemispheres.
Nested PCR: PCR performed twice with two different primer sets, the second "nested" within the region amplified by the first set. In this manner, very low levels of PCR product can be made in greater quantity.
RT-PCR: Real-time PCR is a technique where PCR is monitored spectrophotometrically during the PCR process. This method is very sensitive to the detection of product prior to agarose gel electrophoresis.