Bunyaviridae and Bornaviridae

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Both families consist of negative-sense, single-stranded RNA viruses. Bunyaviridae is a large family of mainly arthropod-borne viruses (arborviruses) with several significant veterinary pathogens. Bornaviridae has only one species and horses and sheep appear to be the principal natural hosts.

Bunyaviridae

Bunyaviridae is the largest family of vertebrate viruses. Most bunyaviruses are transmitted by biting arthropods and, with the exceptions of Akabane disease, Cache valley, Rift valley fever, and Nairobi sheep disease, are of limited veterinary importance.

Viral Characteristics

- These viruses are 80 - 120 nm in diameter, have a helical nucleocapsid surrounded by an envelope, on the surface of which are glycoprotein projections. See Fig. 21.1.
- The genome consists of three segments of negative-sense single-stranded RNA.
- The segmented RNA genome may undergo genetic reassortment leading to new strains.
- With most of these viruses, genes are expressed in two disparate host systems, vertebrate and arthropod.
- The virus replicates in the cytoplasm and matures by budding into vesicles in the Golgi region and then released by exocytosis at the cell surface.
- These viruses are labile outside the host.

Figure 21-1. Bunyaviridae (80 to 120 nm). Helical nucleocapsid surrounded by an envelope with glycoprotein spikes. - To view this image in full size go to the IVIS website at www.ivis.org.
Classification

The term arbovirus (arthropod-borne virus) is often used to refer to any virus of vertebrates transmitted by an arthropod. It thus includes in addition to the viruses in Bunyaviridae, viruses in the families Arenaviridae, Togaviridae, Flaviviridae, Reoviridae and Rhabdoviridae. The name "arbovirus" is therefore not considered a legitimate taxonomic term.

There are presently five genera assigned to the Bunyaviridae and these genera contain serogroups. The genera are:

**Bunyavirus** - This genus consists of a large number of serologically grouped and ungrouped viruses. Most are mosquito-borne; some are tick-borne and some show transovarial transmission. Included of veterinary and human significance are:
- Akabane, Peaton and Aino viruses (members of the Simbu serogroup), which cause disease in sheep and cattle (described below under Akabane Disease).
- Cache Valley virus (see below).
- California encephalitis virus: Consists of more than a dozen serologically related mosquito-borne viruses that can occasionally cause encephalitis in humans in the USA.
- La Crosse virus is a strain of California encephalitis virus that was isolated from a fatal case of human meningoencephalitis in Wisconsin.

**Hantavirus**

At least 20 serologically related viruses that cause natural infection in small rodents (including mice). They are transmitted to humans by inhalation often causing fatal hemorrhagic fever.

**Nairovirus**
- Nairobi sheep disease virus.

**Phlebovirus**
- Rift Valley fever virus.

**Bunyavirus**

**Akabane Disease**

*(Congenital arthrogryposis-hydraencephaly)*

**Cause**

Akabane virus and probably the Peaton and Aino viruses.

**Occurrence**

Akabane disease occurs in cattle, sheep and goats mainly in Australia, some Asian countries, Argentina, South Africa, and the Middle East.

**Transmission**

The virus is transmitted to susceptible animals by biting-insects, particularly mosquitoes and midges (Culicoides).

**Clinical & Pathologic Features**

There are no overt clinical signs in adult animals exposed to these viruses other than an early febrile response. Fetal infections, which result in deformities of the fetus, may occur if pregnant cows are infected during the first trimester of gestation. There may be abortions, stillbirths, mummified fetuses, and premature live births. Arthrogryposis is the most common deformity noted, affecting a single joint in one limb to multiple joints in all limbs and the vertebral column. Severely affected animals may suffer difficult deliveries. Hydranencephaly is noted less frequently.

**Diagnosis**

- Clinical specimens: Placenta and fetus.
- A presumptive diagnosis is based on the clinical history and gross lesions in affected fetuses.
- The virus can be isolated by the intracerebral inoculation of young mice and in various cell cultures.
- Diagnosis is supported by detection of specific neutralizing antibodies in neonates and aborted calves, lambs and goats.

**Prevention**

- Killed vaccines are available.
- Akabane disease, although unlikely to occur in North America because of the reservoir and vectors, is reportable.

**Cache Valley Virus Infection**

Cache Valley virus has been associated with congenital malformations in sheep. These defects, which are principally arthrogryposis and hydranencephaly, are virtually indistinguishable from those observed with Akabane disease. Serologic evidence indicates that the virus is widely distributed in North America and that numerous mammalian species may be susceptible to infection.
**Nairovirus**

**Nairobi Sheep Disease**

**Cause**
Nairobi sheep disease virus.

**Occurrence**
Nairobi sheep disease occurs in sheep, goats and occasionally in humans (with fever and arthralgia) in East Africa.

**Transmission**
It is tick-borne (Rhipicephalus appendiculatus).

**Clinical Features**
The disease is characterized clinically by high fever, depression, anorexia, nasal discharge, and a severe non-contagious hemorrhagic gastroenteritis. Pregnant animals are likely to abort. The disease is more severe in sheep with the mortality rate ranging from 30 to 90%.

**Diagnosis**
- Clinical specimens: Whole blood, acute and convalescent sera, spleen, mesenteric lymph nodes.
- A presumptive diagnosis is made on the basis of clinical signs and history.
- Confirmation requires isolation and identification of the virus or the demonstration of a significant increase in antibody levels between acute and convalescent sera.
- The virus is most easily isolated by the intracerebral inoculation of infant mice. The virus also grows in a variety of cell cultures.

**Prevention**
- Dipping to control ticks is widely practiced in endemic regions.
- The disease is considered reportable in countries that are free of it.

**Phlebovirus**

**Rift Valley Fever**

**Cause**
Rift Valley fever virus.

**Occurrence**
Rift Valley fever occurs in Africa and the Middle East in sheep, goats, cattle, camels, antelopes and humans. Large outbreaks have occurred in Africa, Saudi Arabia and Yemen and considerable humans have succumbed.

**Transmission**
By mosquitoes but probably also by contact.

**Clinical & Pathologic Features**
Infection is most severe in young animals, and is characterized by a high fever, anorexia, weakness, and rapid death. Some affected animals may have nasal discharge and hemorrhagic diarrhea. Adult animals are less severely affected, but pregnant animals are likely to abort. Cattle are less severely affected than sheep.

The mortality rate may exceed 70% in young animals but is considerably less in adults. Humans may become infected by mosquitoes and through contact with diseased tissues. Infections are "flu-like", and can infrequently be severe and fatal.

A consistent and characteristic necropsy finding is severe liver necrosis.

**Diagnosis**
- Clinical specimens: Liver and spleen.
- A presumptive diagnosis is made on the basis of clinical signs and gross and microscopic lesions observed in the liver.
- Confirmation requires isolation and identification of the virus. The virus replicates on the chorioallantoic membrane of chicken embryos and in various cell cultures.

**Prevention**
- Modified live virus and killed virus vaccines are used in countries where the virus is endemic. The modified live vaccine should not be used in pregnant animals.
- Mosquito control reduces the chances of infection. In countries where the disease does not occur, outbreaks are dealt with by strict quarantine and slaughter.
**Bornaviridae**
This family is named after the town Borna in Germany where the disease in horses was first observed about 200 years ago. Borna disease virus is the only species in the only genus, Bornavirus. The virus has recently received considerable attention as a possible cause of mood disorders in humans. The host range of the virus is much greater than was earlier noted.

**Viral Characteristics**
- The virus is spherical, enveloped and about 90 nm in diameter. See Fig. 21.2.
- The genome consists of negative-sense, single-stranded RNA.
- Replication is in the cell nucleus with budding at the cell surface.
- The virus is genetically stable with different isolates showing high levels of sequence conservation.
- It is labile and its survival time outside the host is probably short.

As mentioned Bornaviridae contains only one genus, Bornavirus, and one species the cause of Borna disease.

Figure 21-2. Bornaviridae (80 - 100 nm in diameter). Helical nucleocapsid surrounded by an envelope with glycoprotein spikes. - To view this image in full size go to the IVIS website at www.ivis.org . -

**Bornavirus**

**Borna Disease**
What follows is mainly a description of the acute disease in the horse. Similar disease may also be seen in other species.

**Cause**
Borna disease virus. Although there is considerable genetic homogeneity, genotypes may adapt to particular hosts.

**Occurrence**
The disease in horses is endemic in some regions of Germany and Switzerland. In recent years infections have been reported in cattle, sheep, goats, monkeys, ostriches, cats and humans. Serological evidence from humans indicate that the virus is probably widespread in Europe and North America. Humans are infected by Borna disease virus and show an antibody response but not clinical disease. Whether or not these infections can be responsible for some psychiatric disorders is currently under investigation. Some serological evidence suggests they may be.

Questions that need to be answered are: What is the prevalence rate in humans? What is the source or sources of human infections? Is there a natural reservoir? Can humans transmit the disease in the way horses do?

**Transmission**
Spread is considered to occur by direct and indirect contact. The virus is present in nasal and oral secretions and urine.

**Clinical & Pathologic Features**
Following a protracted incubation period (weeks), the virus causes a meningoencephalomyelitis of horses with clinical signs that are similar to those produced by eastern, western and Venezuelan encephalomyelitis. They include depression, shaking and unsteady gait, and running into obstacles. The non-purulent encephalomyelitis mainly affects the gray matter of the brainstem and the cerebral hemispheres. Affected horses usually die.

Intranuclear inclusions may be present in neuronal cells of the hippocampus and olfactory lobes.

**Diagnosis**
- Clinical specimens: Brain.
- A presumptive diagnosis is often made on the basis of clinical signs and the finding of typical eosinophilic inclusions in brain tissue on histopathologic examination.
- Confirmation requires isolation and identification of the virus, which may be accomplished by the inoculation of embryonated chicken eggs via the chorioallantoic membrane or by the intracerebral inoculation of rabbits. The virus also grows in a variety of cell cultures but without observable cytopathic effects.
- Detection of specific antibodies by ELISA or immunofluorescence assay is supportive.
- A reverse-transcriptase PCR has been used to detect virus.

**Prevention**
- Affected and seropositive animal should be segregated.
**Glossary**

*Arthrogryposis:* Permanent flexure of a joint.

*Hydranencephaly:* An abnormal increase in the amount of cerebrospinal fluid in the cranial cavity. It is accompanied by enlargement of the cerebral ventricles and skull with atrophy of the brain.

*Reverse-transcriptase PCR:* A modification of the polymerase chain reaction that includes a first step utilizing the enzyme reverse transcriptase, which makes a DNA copy of viral RNA template. The DNA is then amplified utilizing polymerase chain reaction.

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