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Picornaviridae

G.R. Carter[1], **D.J. Wise**[2] and **E. F. Flores**[3]

[1]Professor Emeritus of the Department of Medical Sciences and Pathobiology, Virginia-Maryland Regional College of Veterinary Medicine, Virginia Tech, Blacksburg, Virginia, USA. [2]Department of Biology, Concord University, Athens, West Virginia, USA. [3]Department of Veterinary Preventive Medicine, Federal University of Santa Maria, Santa Maria, RS Brazil.

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This family consists of the smallest RNA viruses. They are naked, positive sense and single-stranded. There are six genera, four of which contain pathogens of veterinary importance.

Viral Characteristics

- The picornaviruses are small (22 - 30 nm), naked, icosahedral viruses (See Fig. 22.1).
- Replication takes place in the cytoplasm and the picornaviral RNA itself is infectious.
- The genome is approximately 8000 bases in length. It possesses a 3' polyA tail. However, the 5' end has a small virus-encoded protein called VPg or 3B.
- Near the 5' end is a region known as the internal ribosomal entry site (IRES), which is unique to the picornaviruses. This site functions to enhance ribosomal recognition of the virus RNA facilitating translation of viral proteins.
- Most picornaviruses can be propagated in cell culture producing a characteristic and rapid cytopathic effect. Exceptions are some rhinoviruses, which require a lower temperature and can be cultured in vitro in very few cell types such as human fetal tracheal cells.
- Most picornaviruses are host specific.
- Picornaviruses are able to survive in the environment for some time. They have been demonstrated to be infectious for several hours to one year, depending upon conditions.
- Picornaviruses are resistant to ether, chloroform and alcohol. They are susceptible to radiation, phenol, and bleach (chlorination). They are highly resistant to most disinfectants. However, 0.2% citric acid, 0.4% sodium carbonate, or acid-containing iodophore disinfectants are effective.

Figure 22-1. Picornaviridae (22 - 30 nm). Small, naked, icoshedral virions. - To view this image in full size go to the IVIS website at www.ivis.org . -

Classification

The Picornaviridae contains five genera, Enterovirus, Aphthovirus, Teschovius, Cardiovirus, and Hepatovirus. The significant veterinary diseases and viruses in each genus are as follows:

Enterovirus
- Teschen and Teschen-like diseases
- Swine vesicular disease
- Porcine enteroviruses
- Bovine enteroviruses
- Avian enteroviruses

Aphthovirus
- Foot-and-mouth disease virus

Cardiovirus
- Encephalomyocarditis virus

Hepatovirus
- Avian encephalomyelitis-like virus: a tentative species in this genus.
- Human hepatitis A virus

Parechovirus: Cause gastrointestinal and respiratory illness in humans.

Rhinovirus
- Three species of equine rhinoviruses.
- Bovine rhinoviruses 1, 2 and 3.
- More than 100 human rhinoviruses. They are widespread and cause usually mild respiratory infections.

Enterovirus

Teschen and Teschen-like Diseases

(Porcine encephalomyelitis)

Cause

The enteroviruses causing these diseases have been placed in one serological group, which is further divided into three subgroups. One of these subgroups includes porcine teschovirus 1; originally called porcine enterovirus serotype 1, the cause of Teschen disease. The cause of Talfan disease is in another subgroup.

Occurrence

Teschen disease, which is a severe porcine encephalomyelitis, is thought to occur rarely only in Europe and Africa. The less severe form, Talfan disease, probably occurs worldwide.

Transmission

The virus is shed in feces and saliva; infection is by ingestion. Spread is by direct and indirect contact.

Clinical & Pathologic Features

These viruses usually cause an infrequent disease in young pigs. The incubation period is approximately 10 days and pigs of all ages are affected during outbreaks. The most serious outbreaks (Teschen) have been reported from Europe.
Clinical signs are fever (104 to 106°F), ataxia, stiffness, tremors, dog-sitting position, nystagmus, convulsions, and prostration. Deaths usually occur within a few days after onset of signs. Mortality in Teschen disease is 50 - 75% or higher in young pigs.
The lesions include glial nodules, neuronal degeneration and lymphocytic perivascular cuffing mainly in the spinal cord. Talfan disease is clinically similar to Teschen disease but is less severe and the fatality rate is lower. The disease may be confused with pseudorabies, hog cholera, and hemagglutinating encephalomyelitis virus (HEV) infection.

Diagnosis
- Clinical specimens: Brain, spinal cord, and intestine.
- These viruses can be propagated in cell cultures of swine origin in which they produce cytopathic changes.

Identification is accomplished by virus neutralization tests using specific antisera. With regard to significance of viral isolation, it should be kept in mind that enteroviruses occur commonly in the intestine.

Prevention
- Animals that recover are immune.
- Live modified virus and an inactivated virus vaccine have been employed with success in Europe.

Swine Vesicular Disease

Cause
Swine vesicular disease virus (SVDV) of which there are several antigenically different strains. The SVD virus is closely related to the human enterovirus, Coxsackie B-5.

Occurrence
This disease was first reported in feeder pigs in Italy in 1966. It has since been reported in Great Britain (declared free in 1980), several European countries, and Asia. There have been reports of aseptic meningitis in humans caused by SVDV.

Transmission
Spread is by direct contact and fomites. Several outbreaks have been traced to uncooked or insufficiently cooked pork in garbage.

Clinical & Pathologic Features
The disease is clinically indistinguishable from foot-and-mouth disease (FMD), vesicular stomatitis (VS), and vesicular exanthema (VE).
Epithelial tissue is initially involved, followed by viremia with generalized infection of lymphoid tissues.
The first signs are reduced feed intake, lameness and tenderness of the feet, fever up to 106°F, and the formation of vesicles on the feet, snout, tongue, mouth, nostrils, and teats. The prognosis is favorable, but in most countries infected animals are slaughtered. Experimentally infected pigs may show central nervous system involvement.

Diagnosis
- Clinical specimens: Vesicular fluid, affected skin and mucous membranes, blood with anticoagulant, and serum.
- The virus can be propagated in cell cultures of porcine kidney. Cytopathic changes typical of picornavirus are produced in 2 - 4 days.
- In many countries regulatory officials should be contacted if SVD is suspected. They will collect appropriate clinical specimens to be tested, typically at a central government laboratory.
- Among the tests used is an ELISA to detect viral antigen in vesicular material. Because SVD resembles clinically FMD a correct diagnosis is imperative.

Prevention
- Vaccines are not available to prevent SVD.
- SVD is a reportable disease and, if it is suspected, strict measures of control including quarantine and slaughter are implemented.

Porcine Enteroviruses: Reproductive Infections
(SMEDI virus syndrome)

Cause
Porcine enteroviruses (Enterovirus). The viruses are designated by the name SMEDI, which is derived from Stillbirth, Mummification, Embryonic Death, Infertility).

Occurrence
The causal enteroviruses occur widely in swine herds.

Transmission
The viruses are present in feces and infection is presumably by direct and indirect contact.

Clinical & Pathologic Features
Susceptible pregnant gilts or sows are infected initially and then their embryos or fetuses. The SMEDI viruses have been isolated from stillborn pigs, "3-day" dead pigs, and fetuses found dead in the uterus in mid-pregnancy after hysterectomy. Herds from which these enteroviruses were recovered generally had small litter sizes and low survival rates.
Sows were immune after infection but the disease manifestations frequently appeared cyclically every 2 - 3 years; perhaps because of the susceptibility of new gilts. The typical disease manifestations of this group of viruses were produced experimentally. The five SMEDI virus groups reported fell into four groups of serologically related viruses. At least six

other enterovirus groups have been identified that are not associated with reproductive problems in sows.
Porcine parvovirus is considered to be the primary viral cause of reproductive problems in swine and little significance is given to the SMEDI viruses.

Diagnosis
- Clinical specimens: Tissue from fetuses and stillborn pigs.
- The viruses can be cultivated in primary pig kidney cell cultures; however, the frequency of isolations has been low, mainly because of the absence of viable virus at the time clinical disease becomes apparent.

Prevention
There are usually no attempts to prevent or control enterovirus infections in swine.

Bovine Enteroviruses
Two serotypes are recognized. Serotype 1 has been isolated from a wide range of animals species, while serotype 2 has only been recovered from cattle. Most infections are subclinical but abortion, stillbirths, and infertility in bulls has been reported.

Avian Enteroviruses
These include: duck hepatitis virus 1, duck hepatitis virus 3, avian nephritis virus and enteroviruses recovered from normal birds. Some strains have the capacity to cause serious hepatitis and nephritis in chickens and turkeys.

Aphthovirus
Foot-and-Mouth Disease

Cause
Foot-and-mouth disease virus (FMDV). A total of seven different serologic types are recognized. They are FMDV-A, FMDV-O, FMDV-C, FMDV-ASIA1, FMDV-SAT1, FMDV-SAT2 and FMDV-SAT3.
The first serotypes of FMD are often referred to as European types because they were first isolated in France and Germany, although they do occur in other countries. The SAT types were isolated in "Southern African Territories" and are restricted to Africa. Serotypes C, A and O have been isolated in South America; the recent (less than a decade) outbreaks in Argentina and Brazil were caused by serotypes A and O.
The Asia type has only been reported in various parts of Asia.
No serological/protection cross-reaction occurs between different types.

Occurrence
All cloven-footed animals including swine, sheep, goats, deer and water buffalo are susceptible. Guinea pigs, rabbits, mice and some other species can be infected experimentally. Contact with infected animals rarely results in infection of humans, which is characterized by development of vesicular lesions on the hands, feet, and in the mouth.
Foot-and-mouth disease (FMD) is widespread, occurring in South America, Africa, Europe, the Middle East and Asia. North America, New Zealand, Australia, and the United Kingdom are free at present. The Canadian outbreak of 1952 was traced to an European immigrant. A devastating outbreak occurred in Britain in 2001. A number of outbreaks occurred in Argentina, southern Brazil and Uruguay in 1999 - 2000.
Most South American countries are in the process of eradication with only a few small outbreaks in the last two to three years. Effective continental strategies of control and eradication have been implemented.

Transmission
The disease is spread by contact, fomites, and migratory birds. The mode of infection is by inhalation and ingestion. Airborne transmission has been reported and attributed to a combination of winds and humidity. The virus is considered particularly infectious and transmissible.

Clinical & Pathologic Features
The FMD virus produces a highly contagious disease of cloven-hoofed animals and is characterized by the production of vesicular lesions in the mouth, muzzle, interdigital space, and on the coronary band of the foot after a usual incubation period of 2 to 5 days. Vesicular lesions may also be found on the udder and teats of cows, and the snout of swine. The most common and characteristic sign is excessive salivation; the saliva is sticky, foamy, and stringy. The vesicles, which are pronounced on the buccal mucous membrane and tongue, break, erode, ulcerate, and eventually heal. Myocardial degeneration may be seen in the malignant form in calves but is rare. Pregnant animals may abort.
Morbidity is very high; mortality is low. Lameness and marked loss of condition are frequent sequellae. Affected animals may recover in one to two weeks. Some may become carriers but their role in transmission is controversial.

Diagnosis
- Clinical specimens: vesicular fluid, affected mucous membranes, pharyngeal and esophageal fluid (obtained with a

probang), blood, and serum.
- Diagnosis is based upon detection of FMDV in the aforementioned clinical materials. ELISA and complement fixation procedures are used.
- A mouse inoculation test is widely used to demonstrate virus. Suckling mice are inoculated intraperitoneally with liquid from vesicles and macerated tongue/foot lesions. If the material is positive, mice die in a few days. Several passages are made before the material is considered negative. This test is usually performed along with a serological test.
- The FMD virus can be isolated in a variety of cell cultures. Viral growth with accompanying cytopathology occurs best in primary cell cultures. Identification is accomplished by virus neutralization and complement fixation tests.
- A test for virus infection associated antigen detects antibody against the viral polymerase, which is considered present only during infection and not upon vaccination. It is used to distinguish active infection from vaccination with inactivated antigen.
- Real time PCR has been used to rapidly detect virus.

Prevention
- FMD is the most important economic disease of cattle and thus is reportable in many countries. Regulatory officials should be contacted if the disease is suspected. Confirmed outbreaks are dealt with in many countries by strict quarantine and slaughter. The difficulty of eradicating the disease once established was strikingly evident in the recent outbreak in Britain.
- In areas where the disease is endemic, vaccination is practiced using killed vaccines, of cell culture origin, containing the appropriate serotypes of virus for the region. The most effective vaccines in current use contain inactivated virus with an oil-adjuvant. Although requiring periodic revaccination, this type of vaccine has been quite effective and has contributed markedly to eradication in a number of countries.

Cardiovirus
Encephalomyocarditis Virus

Cause
Encephalomyocarditis (EM) virus. Although all strains have been shown to be antigenically identical, many differ in their biological behavior.

Occurrence
The virus and EM infection occur worldwide. Rats and mice are considered to be the natural hosts and principal reservoir for the virus. The virus has been recovered from squirrels, raccoons, llamas, sloths, certain antelope species, rhinoceros, pygmy hippopotamus, African elephants, and other vertebrates including humans. Affected nonhuman primates include orangutans, chimpanzees, baboons, cynomolgus monkeys, and lemurs. The disease is seen infrequently in pigs.

Transmission
Pigs are thought to be most often infected by eating feed contaminated with rodent urine and droppings.

Clinical & Pathologic Features
The virus causes a sporadic disease in young pigs characterized primarily by sudden deaths. Premonitory clinical signs may include anorexia, depression, and difficulty breathing.
Mortality may, be high in very young pigs but is usually subclinical in weanling pigs and adults. In utero infection may occur leading to fetal death.

Diagnosis
- Clinical specimens: Heart and brain.
- Gross necropsy lesions may reveal an enlarged heart with pale areas on the right ventricle.
- Confirmation of EM infection is best accomplished by fluorescent antibody examination of cryostat sections of affected tissue.
- The virus can be cultivated in a variety of cell cultures and in young mice inoculated intracerebrally.

Prevention
- Rodent control on swine premises is the principal means of prevention.
- Both an inactivated vaccine and a genetically-engineered, attenuated vaccine are available, but their effectiveness is variable. The inactivated vaccine is the more widely used.

Hepatovirus
Avian Encephalomyelitis
(Epidemic tremor)

Cause
Avian encephalomyelitis virus of which there are 15 serotypes.

Occurrence
Avian encephalomyelitis is an important, frequently occurring disease with worldwide distribution. It affects chickens, pheasants, turkeys, and quail.

Transmission
The virus is transmitted via the egg and by the oral/fecal route.

Clinical & Pathologic Features
Avian encephalomyelitis is principally a disease of young chicks during the first six weeks of age. The typical clinical disease usually occurs between 1 - 3 weeks of age. In laying birds, clinical signs are not apparent other than a decline in egg production, which may last 2 - 3 weeks.
Signs in young birds include tremor of the head, incoordination, and leg weakness with loss of condition followed frequently by prostration and death. Average mortality rate is about 20%.
Some infections are asymptomatic and are only diagnosed by the finding of brain lesions. The lesions in the brain and spinal cord consist of loss of neurons and perivascular cuffing that is mainly observed in the cerebellum, medulla, and pons. Diffuse lymphoid nodular hyperplasia is observed in the proventriculus, spleen, pancreas, and liver.

Diagnosis
- Clinical specimens: Brain and spinal cord.
- A presumptive diagnosis can be made clinically. Finding the typical microscopic lesions is supportive.
- Definitive diagnosis depends upon the demonstration of the virus by the intracerebral inoculation of day-old susceptible chicks. If virus is present, epidemic tremor develops in 10 - 12 days, and the brains can be harvested for histopathologic examination.
- Another diagnostic method is the inoculation of brain suspension into chicken embryos via the yolk sac; signs of encephalomyelitis infection in the chicks are observed after hatching. Tissues from these birds should be examined histologically after the signs appear.
- The virus can be cultivated in primary whole embryo cell cultures.
- Antibodies can be demonstrated by means of neutralization tests in chicken embryos employing an embryo-pathogenic strain of the virus.
- A commercial ELISA is available for the serologic monitoring of chicken flocks.

Prevention
A live virus vaccine is administered in the drinking water to 10 - 16 week-old birds. Killed vaccines are used to revaccinate breeders with poor antibody response. These vaccines are administered by the wing-web stick method.

Glossary
Probang: A slender flexible rod with a sponge on one end used to collect clinical material.
Real time PCR: This type of PCR utilizes a chemical amplicon, such as SYBR green, that emits a fluorescent signal during the DNA replication. The emitted signal is detected and indicates active DNA replication prior to running an agarose gel.