

# PORCINE TESCHOVIRUS



*Prepared for the Swine Health Information Center  
By the Center for Food Security and Public Health,  
College of Veterinary Medicine,  
Iowa State University  
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## SUMMARY

### Etiology

- Porcine teschovirus (PTV) is a non-enveloped RNA virus in the genus *Teschovirus*, family *Picornaviridae*.
- There are 13 known PTV serotypes. PTV-1 is associated with teschovirus encephalomyelitis; PTV-2, -3, and -5 are associated with Talfan disease (a milder presentation of polioencephalomyelitis). Additional presentations are seen with other serotypes.

### Cleaning and Disinfection

- PTV is stable over a wide range pH range (2–9) and can survive in liquid manure for long periods of time.
- Sodium chlorite, heat in the presence of halide ions, and 70% ethanol are effective methods for inactivating PTV.

### Epidemiology

- Swine, including wild boar, are the only known hosts for PTV.
- No swine-to-human transmission of PTV has been reported.
- PTV-1, which causes teschovirus encephalomyelitis, was first reported in Czechoslovakia in 1929; outbreaks have since occurred in Europe and Africa. Most recently PTV-1 was isolated in Haiti (2009) and Canada (2011). Less virulent PTV strains can be found worldwide including the United States.
- Teschovirus encephalomyelitis cause high morbidity and mortality in all age groups. Talfan disease mostly affects younger, post-weaning pigs, and low morbidity and mortality rates are observed.

### Transmission

- Transmission is fecal-oral. Fomites may also play a role. Transplacental transmission has been demonstrated experimentally, although fetal infection does not always occur.

### Infection in Swine/Pathogenesis

- PTV infection may be subclinical.
- Polioencephalomyelitis induced by PTV can result in severe disease (teschovirus encephalomyelitis) or mild disease (Talfan disease/benign enzootic paresis).

- Certain strains of PTV have also been linked to SMEDI syndrome (stillbirth [S], mummified fetus [M], embryonic death [ED], infertility [I]).
- PTV has been associated with diarrhea, but the virus can also be found in the feces of healthy pigs.
- Other signs linked to PTV include pneumonia, pericarditis, and myocarditis.

## **Diagnosis**

- PTV can be grown in swine-origin cell lines and identified via virus neutralization or immunofluorescent antibody assays.
- Reverse transcriptase polymerase chain reaction (RT-PCR) is also available, including a real-time assay that can differentiate PTV from other viruses including pseudorabies virus, PRRS virus, porcine parvovirus, porcine circovirus, and classical swine fever virus.
- An enzyme linked immunosorbent assay (ELISA) is available for detection of antibodies in teschovirus encephalomyelitis-affected individuals.

## **Immunity**

- Maternal antibodies are protective against PTV-induced reproductive disorders.
- Commercial vaccines for teschovirus encephalomyelitis were previously available (both attenuated and inactivated); however, because of the decrease in disease incidence, none remain in production.
- Cross-protection between numerous PTV strains is unlikely.

## **Prevention and Control**

- Quarantine, movement control, depopulation, and ring vaccination have previously been used in teschovirus encephalomyelitis outbreaks.

## **Gaps in Preparedness**

- Vaccines against teschovirus encephalomyelitis have been developed, but are not currently available.

## OVERVIEW

Porcine teschovirus (PTV) is a non-enveloped, positive-sense single-stranded RNA virus in the genus *Teschovirus* of the family *Picornaviridae*. Currently, there are 13 known serotypes of PTV. Pigs can be co-infected with more than one serotype and PTV is commonly isolated in healthy swine. Highly virulent strains of PTV-1 are known for causing teschovirus encephalomyelitis. Less virulent strains of PTV-1, in addition to PTV-2, PTV-3, and PTV-5, are associated with Talfan disease (also known as benign enzootic paresis), a milder presentation of polioencephalomyelitis than teschovirus encephalomyelitis. PTV is resistant to environmental conditions, surviving well in liquid feces and over a wide pH range.

PTV is endemic in most conventional swine herds throughout the world. Teschovirus encephalomyelitis was first seen in Czechoslovakia in 1929 and was a cause of major economic loss in Europe during a course of sporadic outbreaks from 1940–1960. During that time, the disease was also seen in Africa. The last report of teschovirus encephalomyelitis in Europe was in 1980; the disease has never been reported in the United States. More recently, outbreaks were reported in Haiti in 2009 and Canada in 2011.

Fecal-oral transmission of PTV is most common. However, PTV is hardy in the environment and fomites likely play a role in transmission as well. PTV infections are often asymptomatic, but in addition to polioencephalomyelitis, they can also induce a broad range of clinical syndromes including reproductive disorders, pneumonia, enteric disease, and pericarditis. In teschovirus encephalomyelitis, fever, inappetence, lethargy, and ataxia may be seen prior to paralysis or paresis. Paralysis begins in the hind limbs and travels cranially; once the respiratory muscles are involved the animal dies of suffocation. Reproductive disorders associated with PTV infection have been termed “SMEDI syndrome” (stillbirth [S], mummified fetus [M], embryonic death [ED], infertility [I]). There are no clinical signs seen in gilts or sows with SMEDI syndrome. When pericarditis or myocarditis is present, it is generally accompanied by polioencephalomyelitis.

PTV is easily propagated in cell cultures of porcine origin, most commonly using primary or secondary porcine kidney cells. The virus can then be identified using virus neutralization or immunofluorescent antibody assays. Alternatively, the reverse transcriptase polymerase chain reaction (RT-PCR) assay has proven to be a sensitive and specific method for rapid nucleic acid detection. Real-time PCR has also been described. An enzyme linked immunosorbent assay (ELISA) is available for detection of antibodies in teschovirus encephalomyelitis-affected individuals.

Humoral immunity is critical for protection against PTV-induced disease. Experimentally, cell-mediated immunity has been shown to be weak and local without significant anti-viral activity. Commercial vaccines have been available in the past to control teschovirus encephalomyelitis but are no longer available, due to a decrease in disease incidence and thus, a decrease in demand. Vaccination for SMEDI syndrome has not been used due to the challenges associated with vaccinating against the multiple PTV serotypes that cause it.

## LITERATURE REVIEW

### 1. Etiology

#### 1.1 Key Characteristics

Porcine teschovirus (PTV) is a non-enveloped, positive-sense single-stranded RNA virus belonging to the genus *Teschovirus* in the family *Picornaviridae*.<sup>1</sup>

#### 1.2 Strain Variability

PTV has 13 known serotypes that can be differentiated by *VP1* (1D) gene sequence or through cross-neutralization tests. PTV serotypes 1–10 were previously known as porcine enterovirus, belonging to cytopathic effect (CPE) group 1 (types 1–7 and 11–13).<sup>1</sup> PTV-12, discovered in 2011 in domestic swine in Spain, is believed to be the result of a mutation in the *VP1* gene of a previously known serotype.<sup>5</sup> PTV-13 was found in the feces of wild boar in Hungary.<sup>6</sup>

Highly virulent strains of PTV-1 are known for causing teschovirus encephalomyelitis. Less virulent strains of PTV-1, in addition to PTV-2, PTV-3, and PTV-5, are associated with Talfan disease (also known as benign enzootic paresis), a milder presentation of polioencephalomyelitis than teschovirus encephalomyelitis.<sup>2</sup>

### 2. Cleaning and Disinfection

#### 2.1 Survival

PTV isolates are resistant to many environmental conditions. The virus remains stable at a pH range of 2–9 and is also able to survive for long periods of time in liquid manure.<sup>2</sup>

#### 2.2 Disinfection

Heat, lipid solvents, and some disinfectants are ineffective in destabilizing PTV. Sodium chlorite, heat in the presence of halide ions, and 70% ethanol are effective methods for inactivating PTV.<sup>2,7,8</sup>

### 3. Epidemiology

#### 3.1 Species Affected

Swine are the only known host for PTV.<sup>1,2</sup> Wild boar are susceptible to PTV infection; however, little is known about the virus in wild suids.<sup>6,9</sup>

#### 3.2 Zoonotic Potential

PTV is not known to infect humans; there have been no reports of pig-to-human transmission.<sup>1,2</sup>

#### 3.3 Geographic Distribution

Teschovirus encephalomyelitis, caused by the highly virulent strain PTV-1, was first seen in Czechoslovakia in 1929, and sporadic outbreaks occurred in several European and African countries from 1940–1960, causing serious economic losses.<sup>2,10</sup> Europe has not reported an outbreak of the disease since 1980. Teschovirus encephalomyelitis never reached the United States but was reported in Haiti in 2009<sup>11</sup> and Canada in 2011.<sup>12</sup>

Remaining serotypes and less virulent strains of PTV-1 are ubiquitous throughout the world. Polioencephalomyelitis (Talfan disease or benign enzootic paresis) has occurred in Europe<sup>5,6</sup>, North America<sup>13</sup>, Australia<sup>2</sup>, and China.<sup>3</sup>

### 3.4 Morbidity and Mortality

Teschovirus encephalomyelitis causes high morbidity and mortality in all age groups.<sup>2</sup> In the 2009 outbreak in Haiti, 60% morbidity and 40% mortality was reported.<sup>11</sup> In 2011, Canada reported 100% mortality.<sup>12</sup> Talfan disease is associated with low morbidity and mortality and clinical disease is generally limited to younger, post-weaning animals.<sup>2,13</sup> With the exception of teschovirus encephalomyelitis, PTV infections usually occur when maternal antibodies wear off. Naïve animals are susceptible at any age.<sup>2</sup>

## 4. Transmission

Fecal-oral transmission of PTV is most common. However, PTV is hardy in the environment, and fomites likely play a role as well.<sup>2</sup>

When PTV-seronegative sows were orally inoculated with PTV, initial intestinal infection was followed by viremia that spread transplacentally to the fetus. Transplacental infection doesn't always result in fetal PTV infection as the blood-placenta barrier is protective in some cases. If transplacental infection does occur, the virus may spread to only one or a few fetuses.<sup>20</sup>

## 5. Infection in Swine/Pathogenesis

Once the virus is ingested, primary PTV replication occurs in the tonsils and intestinal tract.<sup>4,14</sup> Tonsils are believed to be important for virus entry, sustaining viral infection, and virus shedding.<sup>15</sup> The large intestine and ileum are more frequently infected, and at higher titers, than the duodenum and jejunum. More virulent strains are believed to cause viremia, which allows PTV access to the central nervous system (CNS) via the blood.<sup>16,17</sup>

Increased body temperature occurs four days post-infection, followed 24–48 hours later by diarrhea. Paralysis or paresis, both flaccid and spastic have been reported, is observed by 10–11 days post-infection.<sup>14</sup> Once respiratory paralysis/paresis occurs, the animal dies of asphyxiation.<sup>10</sup> Pigs infected experimentally intranasally developed CNS signs. Once introduced intranasally, the virus travels from the tonsils in a retrograde fashion, ascending to infect the brain.<sup>15</sup>

In reproductive disorders, the virus is thought to reach the placenta via the blood. Experimental nasal and oral inoculation have resulted in fetal infection in pregnant gilts.<sup>2,18</sup>

### 5.1 Clinical Signs

PTV infections are often subclinical; however, clinical syndromes are associated with certain serotypes.<sup>2</sup> It is possible for an animal to be co-infected with two or more serotypes simultaneously.<sup>3</sup>

Polioencephalomyelitis induced by PTV can result in severe disease (teschovirus encephalomyelitis) or mild disease (Talfan disease/benign enzootic paresis). In teschovirus encephalomyelitis, fever, anorexia, listlessness, and locomotor ataxia are seen prior to paralysis/paresis. Caudal ataxia leading to paresis or paralysis can be seen as early as two to three days post infection. Commonly, death occurs three to four days after the onset of clinical symptoms.<sup>11</sup> Milder cases of polioencephalomyelitis, caused by serotypes 1, 2, 3, and 5, affect naïve animals and younger animals, approximately four weeks of age, once maternal antibodies have waned and are no longer protective. Polioencephalomyelitis rarely progresses to complete paralysis.<sup>2</sup>

Reproductive disorders are associated with PTV-1, PTV-3, and PTV-6.<sup>1,2</sup> The term SMEDI syndrome (stillbirth [S], mummified fetus [M], embryonic death [ED], infertility[I]) was adapted to describe the variety of reproductive disorders caused by these serotypes.<sup>19</sup> SMEDI syndrome is also seen with parvovirus infections, which more frequently cause reproductive disorders in conventional herds than PTV. Infection in early to mid-gestation (40–70 days) leads to embryonic death and mummification while

infection during later stages of development may result in stillbirth or fetal development of antibodies coupled with survival.<sup>2,20</sup> PTV has also been linked to abortion in the field and in experimental studies.<sup>2,21</sup> SMEDI syndrome induced by PTV is rare because most sows have naturally been exposed to the virus prior to sexual maturity and are, therefore, immune at breeding. There are no clinical signs in the infected sow or gilt.<sup>20</sup> PTV has been isolated from the male reproductive tract, but experimental intrauterine inoculation of virus with sperm did not result in infection of embryos or prevent conception. Embryonic death or small litter size were not observed following intrauterine infection.<sup>2,20,22</sup>

Enteric disease has been linked to the following serotypes: PTV-1, PTV-2, PTV-3, or PTV-5. PTV has been isolated from the feces of pigs with diarrhea as well as healthy pigs; isolation from the intestinal tract may be a coincidental finding. However, gastrointestinal disease has been experimentally induced following PTV infection of pigs believed to be free of other pathogens. When seen, diarrhea is mild and transient.<sup>2</sup>

Pneumonia has been associated with PTV-1, PTV-2 and PTV-3, although not much is known about this clinical syndrome. It is unlikely that PTV alone is the cause of respiratory disease.<sup>2</sup>

Pericarditis and myocarditis have been linked to PTV-2 and PTV-3.<sup>2</sup> Fever develops approximately seven days post infection, followed by transient diarrhea. It is usually accompanied by polioencephalomyelitis.<sup>23</sup>

## 5.2 Postmortem Lesions

There are no gross lesions associated with severe or mild polioencephalomyelitis.<sup>17</sup> Histologic lesions include non-suppurative polioencephalomyelitis with lymphocytic vascular cuffing throughout the CNS. In the late stages of disease, neuronal degeneration (swelling, chromatolysis, axonal degeneration, and necrosis) is often present.<sup>10</sup>

Grossly, pericarditis is serofibrinous with a cloudy pericardial effusion that quickly forms a coagulum upon standing. Because pericarditis is seen in parallel with polioencephalomyelitis, histologic lesions include non-suppurative polioencephalomyelitis with lymphocytic vascular cuffing throughout the CNS and neuronal degeneration. Focal myocardial necrosis with cellular infiltrate is occasionally present.<sup>23</sup>

## 6. Diagnosis

### 6.1 Clinical History

Fever followed by ataxia and paralysis/paresis is suggestive of PTV infection. Gilts or sows that have litters with few or several stillborn or mummified fetuses is suggestive of PTV-induced reproductive disorder.<sup>2</sup>

### 6.2 Tests to Detect Nucleic Acids, Virus, or Antigens

PTV is easily cultured in cell lines of porcine origin; primary and secondary porcine kidney cells are most commonly used.<sup>2</sup> The virus also replicates well in some established cell lines, like IBRS-2 (porcine kidney cells).<sup>24</sup> Cultured PTV can be identified with virus neutralization (VN) or immunofluorescence antibody (IFA) assays.<sup>10</sup>

Immunohistochemistry on formalin-fixed paraffin embedded tissue can also be used for virus identification.<sup>25,26</sup>

RT-PCR is available for PTV, which can differentiate between porcine enterovirus and PTV-1.<sup>10,27</sup> RT-PCR is specific, sensitive and rapid, and does not cross react with pseudorabies virus, porcine reproductive and respiratory syndrome virus (PRRSV), porcine parvovirus, porcine coronavirus, porcine

reovirus, or picorna-like virus.<sup>28</sup> A real-time RT-PCR has been developed that reports high sensitivity and specificity, allowing for quantification of virus.<sup>15,29</sup> The assay does not amplify pseudorabies, PRRSV, porcine parvovirus, porcine circovirus or classical swine fever virus.

### **6.3 Tests to Detect Antibody**

PTV is a ubiquitous virus; therefore, one positive serological test is insignificant. However, a four-fold antibody titer increase with associated clinical signs can be considered positive for PTV-1.<sup>10</sup> An ELISA is available for detection of antibodies for teschovirus encephalomyelitis (PTV-1). However, because these viruses have high prevalence, serologic tests for the remaining serotypes may not be helpful.<sup>2</sup>

### **6.4 Samples**

#### *6.4.2.1 Preferred Samples*

Preferred samples for CNS disease include cerebrum, cerebellum, diencephalon, medulla oblongata, and cervical and lumbar spinal cord.<sup>10</sup>

For stillbirths or mummified fetuses, the fetal lung is the best tissue source for virus isolation.<sup>18</sup> Virus neutralization using fetal body fluids has also been successful. Isolation of PTV from gastrointestinal tissue is not necessarily indicative of causation as PTV is common in healthy animals.<sup>2</sup>

#### *6.4.2.2 Oral Fluids*

Specific data regarding the presence of PTV in oral fluids is unavailable.

## **7. Immunity**

### **7.1 Post-exposure**

The anti-PTV immune response is primarily a humoral response characterized by IgM and IgG antibodies. When the virus is introduced orally, anti-PTV IgA is produced within the intestinal tract and has been shown to be protective in enteric viral infections.<sup>30,31</sup> In an experimental study, cyclophosphamide, an immunosuppressant, was administered to pigs. The failure to produce antibody resulted in persistent virus infection within the gastrointestinal tract. The failure of animals to recover indicates the importance of IgA in protection against PTV at mucosal surfaces.<sup>32</sup> Cell-mediated immunity was shown to be weak and localized with no significant or specific antiviral activity.<sup>33</sup> However, more recent methods for measuring cell-mediated-immunity should be employed.

Maternal antibodies are protective against PTV-induced reproductive disorders. If maternal anti-PTV antibodies, specific to PTV strains associated with SMEDI syndrome, are present prior to pregnancy, it is protective against disease. It is believed that circulating anti-PTV antibodies prevent or reduce viremia, thereby preventing transplacental spread of PTV. Maternal antibody that develops after a sow is infected does not protect against spread of infection and transplacental spread of PTV is possible. PTV spreads to neighboring fetuses, presumably through fetal membranes. Intrauterine spread of PTV is slow, and fetuses die at various developmental stages.<sup>20</sup> Fetal development of anti-PTV antibodies, primarily IgM followed by IgG, begins approximately 68 days of gestation and reaches maturity around 84–96 days of gestation.<sup>34</sup> Anti-PTV antibody production in the fetus can be protective, resulting in no disease if infected during this stage. Maternal antibody acquired from colostrum is protective approximately until weaning.<sup>20</sup> In a prolonged outbreak of polioencephalomyelitis in Indiana, maternal colostrum antibody titers likely were not high enough to protect uncharacteristically large litter sizes, resulting in increased incidence of polioencephalomyelitis in piglets.<sup>13</sup>

## **7.2 Vaccines**

When PTV-induced disease was more prevalent, commercial vaccines were available. However, with disease decline, vaccines are no longer produced.<sup>10</sup> Attenuated and inactivated vaccines were used; both live and formalin-inactivated vaccines are equally protective.<sup>2</sup> Vaccination has not been used for milder cases of polioencephalomyelitis or for SMEDI syndrome. Vaccines for SMEDI syndrome may be justified. However, as SMEDI is caused by multiple serotypes, developing a multivalent PTV vaccine to protect against all strains poses a challenge.<sup>2</sup>

## **7.3 Cross-protection**

Humoral immunity plays an important role in protection against PTV-induced disease. Due to the large number of PTV serotypes, cross-protection is not likely.<sup>2,35</sup>

## **8. Prevention and Control**

There is no treatment for PTV infection. Pigs with milder presentations of polioencephalomyelitis may survive if their appetite returns after the transient paresis phase.<sup>2,11</sup>

Teschovirus encephalomyelitis should be reported to state or federal authorities.<sup>8</sup> In the past, successful control methods for teschovirus encephalomyelitis have included quarantine, movement controls, slaughter, and ring vaccination.<sup>2,8</sup> Restricting imports from countries that have teschovirus encephalomyelitis could help limit the spread of the virulent PTV-1 strain. Quarantine and slaughter would likely be effective control measures if teschovirus encephalomyelitis were to enter the United States.<sup>2</sup>

Vaccines are unavailable against the PTV serotypes that cause reproductive disorders. However, PTV infection is enzootic on most breeding farms and exposure can help prevent infection-induced disease. Gilts should not be raised in separate units and should be exposed to fecal material of weaned and feeder pigs to expose them to low levels of PTV. New breeding stock should be introduced into the unit more than one month prior to breeding in order to expose them to enzootic PTV strains and allow the development of immunity.<sup>20</sup>

Since PTV is easily isolated and grown in cell culture, protection is serotype-specific, and killed vaccines have been effective in the past, autogenous vaccines should be an option for induction of protective immunity.

## **9. World Organization for Animal Health (OIE) Terrestrial Animal Health Code**

PTV is not included in the 2015 OIE Terrestrial Animal Health Code. There are no restrictions on importation of animals from countries or zones infected with PTV. Teschovirus encephalomyelitis (previously Teschen or enterovirus encephalomyelitis) is included in the Manual of Diagnostic Tests and Vaccines for Terrestrial Animals 2015.

## **10. Gaps in Preparedness**

The introduction of teschovirus encephalomyelitis into the United States has the potential to cause serious economic loss. However, as this disease was seen in Europe throughout the 1950s and 60s, there are currently several diagnostic tests available and a vaccine has been developed and used, though it is not currently available.



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Authors, Center for Food Security and Public Health, College of Veterinary Medicine, Iowa State University:

- Sarah Horak, BS; 2<sup>nd</sup> year student,
- Kristin Killoran, PhD; 2<sup>nd</sup> year student
- Kerry Leedom Larson, DVM, MPH, PhD; Veterinary Specialist

Reviewers, Center for Food Security and Public Health, College of Veterinary Medicine, Iowa State University:

- Pamela Zaabel, DVM; Veterinary Specialist
- James A. Roth, DVM, PhD; Director

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