PORCINE RUBULAVIRUS  
(BLUE EYE)

The mission of the Swine Health Information Center is to protect and enhance the health of the United States swine herd through coordinated global disease monitoring, targeted research investments that minimize the impact of future disease threats, and analysis of swine health data.

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SUMMARY

IMPORTANCE
- Porcine rubulavirus (PoRV), also known as La Piedad Michoacán virus (LPMV), is a paramyxovirus of swine that causes CNS signs and high mortality in piglets, respiratory disease in pigs over 30 days-of-age, reproductive disease in sows and boars, and corneal opacity (“blue eye”) in pigs of all ages.
- As of 2021, PoRV has occurred only in Mexico. However, transboundary spread remains a concern for the U.S. pork industry.

PUBLIC HEALTH
- PoRV does not cause illness in humans. However, PoRV antibodies have been detected in serum from Mexican swine veterinarians.

INFECTION IN SWINE
- Suckling piglets develop progressive neurological signs often culminating in death. Ocular disease is also seen including blindness, nystagmus, swollen eyelids, and corneal opacity.
- Weaned pigs (>30 days-of-age) may develop respiratory disease and ocular disease. Neurological involvement is possible but much less common than in piglets.
- Reproductive failure occurs in pregnant gilts and sows. Early return to estrus, stillbirth, and mummification are seen most often. Abortion is not a typical feature of PoRV infection. Corneal opacity can also occur.
- Boars infected with PoRV develop anorexia, cough, and corneal opacity, as well as orchitis and epididymitis followed by testicular atrophy.

TREATMENT
- There is no treatment for PoRV infection.

CLEANING AND DISINFECTION
- Paramyxoviruses are typically labile and easily inactivated by heat, ultraviolet light, and low pH.
- Paramyxoviruses are susceptible to acids, alcohols, aldehydes, alkalis, halogens, and oxidizing agents, and have limited susceptibility to biguanides, phenolic compounds, and quaternary ammonium compounds.

PREVENTION AND CONTROL
- Standard biosecurity practices should be in place to prevent PoRV introduction.
• Replacement animals should be selected from PoRV-free sources and quarantined before they are introduced to the herd. Serological screening can be used to detect PoRV infection in replacements.
• There are licensed vaccines for PoRV in Mexico.

TRANSMISSION
• PoRV is found in nasal secretions, urine, and semen.
• The major route of transmission is direct contact (nose-to-nose). Subclinically infected pigs spread the disease to susceptible pigs. Transmission via semen and fomites may also be possible.

PATHOGENESIS
• PoRV binds sialic acid-expressing cells and replicates in the nasal mucosa and tonsil. It spreads to the brain via cranial nerves proximal to the oral cavity, and to other organs via the blood.

DIAGNOSIS
• Virus can be cultured in pig kidney cell lines. Antigens can be detected by direct immunofluorescence in tissue sections and monolayers. There are also quantitative reverse transcriptase polymerase chain reaction (qRT-PCR) assays that detect either the P (phosphoprotein) gene or the NP (nucleoprotein) gene across all strains of PoRV.
• Antibodies can be detected via hemagglutination inhibition, virus neutralization, and enzyme-linked immunosorbent assay (ELISA).

EPIDEMIOLOGY
• Only pigs develop clinical illness following natural exposure to PoRV. Experimentally, mice, rats, and chick embryos are susceptible to infection, and antibodies have been detected in rabbits, dogs, cats, and peccaries.
• PoRV has been reported only in Mexico. Most cases occur from April to July.
• In piglets, morbidity is 20–50%; mortality can reach 90%. Both are low in older pigs.

ETIOLOGY
• PoRV is an enveloped RNA virus in the genus Rubulavirus, family Paramyxoviridae.
• PoRV isolates have been divided into five subgroups based on HN gene sequencing. More recent phylogenetic analysis shows that PoRVs can be divided into two or three major groups depending on the genes that are sequenced (P, M, and HN vs. NP, F, and L).

HISTORY IN SWINE
• PoRV was first described on a sow farm in La Piedad, Michoacán, in 1980. Since then, it has become endemic in central Mexico.

IMMUNITY
• Lifelong immunity develops following natural infection with PoRV.
• There are two inactivated PoRV vaccines commercially available in Mexico. However, the efficacy of monovalent vaccines has been questioned since they may not prevent infection with all PoRV subgroups.

GAPS IN PREPAREDNESS
• PoRV has never been detected in the United States. However, PoRV is an economically important disease of swine in Mexico, and its emergence could harm the U.S. swine industry.
• There are no PoRV vaccines available for commercial use in the United States. Routine biosecurity practices can help prevent the introduction of PoRV.
LITERATURE REVIEW: PORCINE RUBULAVIRUS (BLUE EYE)

IMPORTANCE
Porcine rubulavirus (PoRV), also known as La Piedad Michoacán virus (LPMV), is a paramyxovirus of swine that causes CNS signs and high mortality in piglets, respiratory disease in pigs over 30 days-of-age, reproductive disease in sows and boars, and corneal opacity (“blue eye”) in pigs of all ages. As of 2021, PoRV has occurred only in Mexico. However, transboundary spread remains a concern for the U.S. pork industry.

PUBLIC HEALTH
PoRV does not cause illness in humans. A study of Mexican swine veterinarians showed that 2.3% and 5.8% were seropositive for PoRV, using the hemagglutination inhibition and virus neutralization assays, respectively.

INFECTION IN SWINE
Clinical signs are variable depending on the age of the pig.

- **Suckling piglets** (2 to 15 days-old) are most profoundly affected by PoRV. Initial signs include fever, rough hair coat, arching of the back, and constipation or diarrhea. Soon after, progressive neurological signs occur including ataxia, rigidity of the hind limbs, weakness, abnormal sitting positions, and hyperexcitability when handled. Possible ocular signs include blindness, nystagmus, dilated pupils, anterior uveitis, conjunctivitis, swollen eyelids with exudate, and corneal opacity (in up to 10% of affected piglets).

- In **weaned pigs** (>30 days-of-age), anorexia, fever, sneezing, and coughing occur. Nervous system involvement is less common. However, atypical outbreaks with 20% mortality and severe CNS signs have been observed in fattening and adult pigs. Corneal opacity occurs in up to 30% of weaned pigs. Experimentally, co-infection with swine influenza (H1N1) leads to increased respiratory signs in 6-week-old pigs.

- Reproductive failure can occur in **pregnant gilts/sows** resulting in early return to estrus, reduced farrowing rate, and increase in non-productive sow days. Stillbirths and mummification are often increased, but abortion is not a typical feature of PoRV. Corneal opacity is sometime seen in gilts and sows.

- **Boars** infected with PoRV may develop anorexia, cough, or corneal opacity. Orchitis and epididymitis occur, followed by testicular atrophy and decreased spermatozoon concentration and motility.

- Clinical signs other than mild anorexia and corneal opacity are not normally observed in **adult pigs**. Corneal opacity resolves spontaneously.

Gross lesions that may be seen include:

- **Piglets**: pneumonia (ventral tips of the cranial lung lobes); distended bladder and stomach; fibrinous peritoneal fluid accumulation; pericardial and renal hemorrhages; increased cerebral spinal fluid and cerebral congestion; conjunctivitis, chemosis, and corneal opacity; corneal vesicles and ulcers; and exudate in the anterior chamber.

- **Pregnant gilts/sows**: focal hemorrhages and congestion of the placenta and endometrium.

- **Fetuses**: mummification or small in size with areas of dermal ecchymoses.

- **Boars**: edema of the scrotum and tunica vaginalis; elevated yellow-white nodules on the head of the epididymis containing brown exudative fluid, and eventual testicular atrophy (often unilateral).
The main histological changes associated with PoRV include nonsuppurative encephalomyelitis affecting the gray matter of the thalamus, midbrain, and cerebral cortex, and interstitial pneumonia.\textsuperscript{1} Corneal opacity is due to corneal edema and anterior uveitis.\textsuperscript{1} Boars undergo epithelial degeneration in the head of the epididymis and testicles where inflammation has occurred.\textsuperscript{9} In the epididymal head vesicle formation can occur, along with loss of epithelial cilia and rupture of the epithelial wall. Severe infiltration of mononuclear cells is seen with phagocytosis of fragmented sperm.\textsuperscript{1, 9} Spermatic granulomas are possible in the head of the epididymis.\textsuperscript{6}

TREATMENT
There is no treatment for PoRV infection. Corneal opacity resolves spontaneously. Antimicrobial therapy is indicated for secondary infections.\textsuperscript{1}

Experimentally, the influenza neuraminidase inhibitor zanamivir and nucleoside triphosphates have been shown to partially or fully inhibit PoRV.\textsuperscript{10}

CLEANING AND DISINFECTION
SURVIVAL
Paramyxoviruses are typically labile and easily inactivated by heat and ultraviolet light, as well as low pH.

DISINFECTION
Paramyxoviruses are susceptible to acids, alcohols, aldehydes, alkalis, halogens, and oxidizing agents, and have limited susceptibility to biguanides, phenolic compounds, and quaternary ammonium compounds.\textsuperscript{11}

PREVENTION AND CONTROL
DISEASE REPORTING
PoRV is not an OIE-listed disease. There are no restrictions for importation of animals from countries or zones affected by PoRV. Any suspicious clinical or necropsy findings should always be reported to the USDA and your State Animal Health Official.

DISEASE PREVENTION
Standard biosecurity practices should be in place prevent PoRV introduction. Replacement animals should be selected from PoRV-free sources and quarantined before they are introduced to the herd.\textsuperscript{1} Serological screening can also be used to detect PoRV infection in replacements.\textsuperscript{1} There are licensed vaccines for PoRV in Mexico (see Immunity).

DISEASE CONTROL
PoRV has been eliminated from swine herds using management practices including herd closure, cleaning and disinfection, all-in/all-out production, elimination of clinically ill pigs (to prevent shedding and further transmission), and proper disposal of dead pigs.\textsuperscript{1} Seronegative sentinel pigs are tested along with the rest of the herd to confirm PoRV-free status.\textsuperscript{1}

TRANSMISSION
PoRV is found in nasal secretions, urine, and semen.\textsuperscript{1} Direct contact (nose-to-nose) is the major mode of transmission. Spread to new farms usually occurs through introduction of pigs with subclinical infection.\textsuperscript{1} Fomites may also contribute to transmission.\textsuperscript{1} Experimentally, intratracheal and intranasal exposure are also effective routes of transmission.\textsuperscript{1}

PATHOGENESIS
PoRV binds sialic acid-expressing cells. Initial replication occurs in the nasal mucosa and tonsil.\textsuperscript{1} PoRV spreads to the brain via cranial nerves proximal to the oral cavity.\textsuperscript{1} Thereafter, PoRV spreads to the lungs and to various organs throughout the body via the blood.\textsuperscript{1}
DIAGNOSIS
Suggestive signs include encephalitis in piglets, corneal opacity in pigs of all ages, reproductive failure in gilts/sows, and orchitis and epididymitis in boars.

TESTS TO DETECT NUCLEIC ACIDS, VIRUS, OR ANTIGENS
Virus can be cultured in PK-15 cells or primary pig kidney cells. Quantitative reverse transcriptase PCR (qRT-PCR) methods have been developed to detect the P12 gene or the NP13 gene across all known strains of PoRV. Compared to virus isolation, qRT-PCR assays have superior sensitivity. Additionally, antigen can be detected by direct immunofluorescence in tissue sections and monolayers.

TESTS TO DETECT ANTIBODY
Paired serum samples, collected 14 days apart, can be used to detect recent infection via the hemagglutination inhibition (HI) assay, virus neutralization, or enzyme linked immunosorbent assay (ELISA). HI is the most often used serological test. Bovine erythrocytes should be utilized to reduce false positives. A highly sensitive and specific blocking ELISA has been described for routine PoRV screening.

SAMPLES
Brain is the preferred tissue for virus isolation; however, lung and tonsil are also acceptable. PoRV may be isolated from ovary, placenta, uterus, and lymph nodes in infected pregnant females. Virus may also be isolated from fetal brain, lung, and liver.

Both nasal and oral swabs have been used for qRT-PCR. Oral fluids have not been specifically evaluated, but PoRV has been detected in saliva samples from suckling piglets.

EPIDEMIOLOGY
SPECIES AFFECTED
Only pigs become ill following natural exposure to PoRV. When inoculated experimentally, mice, rats, and chick embryos are affected. Rabbits, dogs, cats, and peccaries produce antibodies to PoRV.

GEOGRAPhic DISTRIBUTION
PoRV has been confined to Mexico since its discovery in La Piedad Michoacán in the 1980s (see History in Swine). Outbreaks have occurred in 16 of Mexico’s 31 states, most recently in central and west-central Mexico.

MORBIDITY AND MORTALITY
Approximately 20% of litters are affected during an outbreak. Within these litters, morbidity is 20–50% and mortality is approximately 90%. In the initial stages of an outbreak, suckling piglets often die within two days of symptom onset. Weeks later in the outbreak, piglets will die within 4–6 days of the onset of symptoms. In pigs older than 30 days, both morbidity and mortality are low. Depending on farm management, outbreaks can last between 2–9 weeks.

PoRV cases are observed throughout the year in Mexico, although most occur between April and July. Seroprevalence in four Mexican states ranged from 9–23.7% in non-vaccinated swine, making blue eye disease one of the four most important diseases affecting pigs in Mexico.

ETIOLOGY
CHARACTERISTICS OF PARAMYXOVIRUSES
PoRV is an RNA virus belonging to the family Paramyxoviridae. Paramyxoviruses are large (100–350nm), enveloped, single-stranded RNA viruses. Virions are pleomorphic, and can take on a spherical or elongated form. They have a layer of surface spikes and a herringbone-shaped nucleocapsid. Paramyxoviruses have six open reading frames (ORFs) encoding the structural genes N (nucleocapsid), L (polymerase), P (phosphoprotein), M (matrix) F, (fusion), and G/H/HN (attachment glycoproteins).
There are seven genera in the family, four of which affect mammals: *Rubulavirus*, *Henipavirus*, *Respirovirus*, and *Morbilivirus*. Paramyxoviruses of swine include:

- Menangle virus and PoRV (blue eye), genus *Rubulavirus*
- Nipah virus and Hendra virus, genus *Henipavirus*
- Porcine respirovirus 1 (porcine parainfluenza virus 1), genus *Respirovirus*

**CHARACTERISTICS OF PORCINE RUBULAVIRUS**

PoRV is believed to have originated from fruit bats in Central and South America. It does not share antigens with other paramyxoviruses, but is closely related to Mapuera virus, which was isolated from a fruit bat in Brazil.\(^\text{18}\)

Until 2016, only one complete genome sequence was available (LPMV, 1984).\(^\text{18}\) Garcia-Barrera and colleagues sequenced four additional PoRV isolates and found that recent neurovirulent strains (2008-2015) clustered in a separate clade from historical PoRVs based on the HN gene.\(^\text{15}\)

Additionally, PoRVs have been divided into subgroups based on the HN gene,\(^\text{19}\) which encodes for the highly immunogenic HN glycoprotein.\(^\text{20}\) There are five subgroups\(^\text{16}\) including:

- Subgroup II: PAC2 (1990), PAC3 (1992)
- Subgroup V: CIV (1999)

Subgroup prevalence varies by region in Mexico.\(^\text{16}\) Isolates from subgroup III (PAC6-PAC9)\(^\text{16}\) are considered to be highly neurovirulent vs. subgroup II isolates (PAC2 and PAC3).\(^\text{21}\)

More recently, phylogenetic analysis has shown that PoRVs can be divided into two or three major groups based on sequencing of the P, M, and HN genes or NP, F, and L genes, respectively.\(^\text{22}\) Although distinct PoRV variants have been identified, their virulence seems to be similar to isolates reported in the 1980s.\(^\text{23}\)

PoRV is a hemagglutinating, hemadsorbing virus.\(^\text{1}\)

**HISTORY IN SWINE**

The first descriptions of “blue eye” came from central Mexico in the 1980s. An outbreak was described on a 2500 sow farm in La Piedad, Michoacán, followed by other farms in neighboring states including Jalisco and Guanajuato.\(^\text{5}\) Corneal opacity was noted by farmers, and histology showed that changes in the brains of affected piglets were different than those caused by known neurotrophic viruses in Mexico. Specifically, non-suppurative meningoencephalitis was seen mainly in the thalamus, mid-brain, and cerebral cortex.\(^\text{5}\)

**IMMUNITY**

**POST-EXPOSURE**

Following natural infection, pigs develop lifelong immunity to PoRV.\(^\text{24}\) However, as PoRV lineages deviate, cross-reactivity between different isolates may decline and lead to decreased adaptive immunity.\(^\text{16}\)

**VACCINES**

Experimentally, inactivated oil-adjuvanted vaccines are safe and effective in preventing PoRV infection in suckling piglets, weaned piglets, adult pigs, and sows.\(^\text{25}\) Sows vaccinated at 81 and 96 days of gestation provide colostral antibodies to suckling piglets.\(^\text{25}\) More recently, a recombinant PoRV HN protein expressed in *Escherichia coli* has been tested in mice, where it successfully induced an antibody response.\(^\text{26}\) An ectodomain of PoRV HN (eHN) expressed in the yeast *Pichia pastoris* has also been shown to induce antibodies in mice.\(^\text{27}\)
There are two commercial, inactivated PoRV vaccines available in Mexico for use in pregnant gilts/sows, boars, and piglets. The efficacy of a monovalent vaccine has been questioned because it may not prevent infection with all PoRV subgroups. There is no PoRV vaccine licensed for use in the United States.

**CROSS-PROTECTION**
There is incomplete cross-reactivity among antibodies to different PoRV isolates.

**GAPS IN PREPAREDNESS**
PoRV is endemic to Mexico and has never been detected in the United States. However, it causes high morbidity and mortality, especially in piglets, and is an important economic disease. There are no PoRV vaccines licensed for use in the United States. Swine producers should be aware of the clinical signs associated with PoRV infection. Routine biosecurity practices can help prevent the introduction of PoRV.

**REFERENCES**


