PORCINE PARAINFLUENZA VIRUS 1

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SUMMARY

Etiology

- Porcine parainfluenza virus 1 (PPIV1) is an enveloped, non-segmented, single-stranded RNA virus that is a proposed member of the family *Paramyxoviridae*, subfamily *Paramyxovirinae*. The genus *Respirovirus*, to which the proposed PPIV1 belongs, contains four other recognized viruses: bovine parainfluenza virus 3 (BPIV3), human parainfluenza virus 1 (HPIV1), human parainfluenza virus 3 (HPIV3), Sendai virus (SeV, also known as mouse parainfluenza virus), and Simian virus 10. Other distantly related paramyxoviruses that cause serious disease in pigs include blue eye paramyxovirus, Menangle virus, and Nipah virus. Pigs are also potential hosts for Hendra virus, Newcastle disease virus, and BPIV3.
- Since 2013 three Chinese PPIV1 strains and two U.S. PPIV1 strains, which are closely related, have been identified and differentiated by genetic sequencing and phylogenetic analysis.

Cleaning and Disinfection

- Nothing is known about the survival and disinfection of PPIV1. Other viruses in the family *Paramyxoviridae* are known to have poor survivability outside the host. However, HPIVI1 can remain infective for years when frozen under certain circumstances.
- Paramyxoviruses in general are susceptible to acids, alcohols, aldehydes, alkalis, halogens and oxidizing agents, as well as heat.

Epidemiology

- To date, PPIV1 has been found only in domestic pigs.
- The virus has been identified in China and parts of the U.S. including Iowa, Illinois, Minnesota, North Carolina, Texas, Oklahoma, and Nebraska.
- There is no evidence that PPIV1 can infect humans; however, other paramyxoviruses are known to cause serious disease in a wide variety of animals including humans. Some paramyxoviruses such as Nipah virus are capable of cross-species transmission.
- Limited studies suggest that PPIV1 is widespread is some swine herds in the U.S. Serological testing of swine from eight states identified anti-PPIV1 antibodies in approximately 53% and 66% of samples.

Transmission

- PPIV1 is thought to be transmitted via the respiratory route. It is unclear whether other modes of transmission occur.

Infection in Swine/Pathogenesis

- Pigs infected with PPIV1 may suffer from mild to moderate respiratory disease or may be asymptomatic. Clinical disease is seen most often in pigs less than 21 days-of-age.
- PPIV1 causes no pathognomonic lesions, and the frequent presence of viral co-infections makes the interpretation of any observed changes difficult.

Diagnosis

- PPIV1 has not been cultured in cells. In situ hybridization can be used to visualize antigen in respiratory tissues.
- Reverse transcriptase polymerase chain reaction (RT-PCR) and quantitative RT-PCR (qRT-PCR) assays have been developed experimentally to identify PPIV1.
- Anti-PPIV1 antibody can be detected using an immunoprecipitation coupled to PCR detection assay (ICPD) and an indirect ELISA using a recombinant fusion (F) protein peptide (PPIV1 F ELISA).

Immunity

- There is currently no vaccines against PPIV1.
- Cross-reaction between PPIV1, HPIV1, and SeV may occur.

Prevention and Control

- There is no treatment for PPIV1.
- Common biosecurity practices should be followed on swine production sites. To reduce the risk of acquiring viral respiratory infections, stress should be avoided (e.g., overcrowding) and buildings should be adequately ventilated. Cleaning and disinfection protocols should be in place.

Gaps in Preparedness

- There is little known about PPIV1. More research is needed to describe the virus' host range, transmission modes, and pathogenesis. There is no vaccine. As some paramyxoviruses cause serious disease in humans, the potential for zoonotic transmission should also be examined.

OVERVIEW

Porcine parainfluenza virus 1 (PPIV1) is a newly characterized, proposed paramyxovirus (family *Paramyxoviridae*, subfamily *Paramyxovirinae)*. Like other paramyxoviruses, PPIV1 is an enveloped, non-segmented, single-stranded RNA virus. The genus *Respirovirus*, which contains the proposed PPIV1, also includes bovine parainfluenza virus 3 (BPIV3), human parainfluenza virus 1 (HPIV1), human parainfluenza virus 3 (HPIV3), Sendai virus (SeV, also known as murine parainfluenza virus), and Simian virus 10. Other more distantly related paramyxoviruses that cause significant disease in swine include blue eye paramyxovirus (BEP), Menangle virus, and Nipah virus. Pigs are also potential hosts for Hendra virus, Newcastle disease virus, and BPIV3.

PPIV1 was first identified in nasopharyngeal samples from slaughterhouse pigs in Hong Kong collected from 2008–2012. The virus was also found in clinical specimens from U.S. pigs with respiratory disease (from Iowa, Illinois, Minnesota, North Carolina, Texas, Oklahoma, and Nebraska) in early 2013. PPIV1 has since been detected in commercial swine from Oklahoma and Nebraska. U.S. strains appear to be very similar to PPIV1s identified in China.

Little is known about PPIV1 survival in the environment and disinfection. Other paramyxoviruses are known to have poor survivability outside the host. Paramyxoviruses are susceptible to acids, alcohols, aldehydes, alkalis, halogens and oxidizing agents, as well as heat. PPIV1 has been found only in naturally infected domestic pigs. There is no evidence that humans can be infected; however, paramyxoviruses are known to cause serious respiratory and neurological disease in a wide variety of species, including humans. Paramyxoviruses have the potential for cross-species transmission.

There is limited information on PPIV1-associated morbidity and mortality in pigs. In one study of slaughterhouse pigs from Hong Kong, reverse transcriptase polymerase chain reaction (RT-PCR) testing showed that 3.1% of nasopharyngeal samples and 0.7% of rectal swabs were positive for PPIV1. In the U.S., 6.1% of samples collected from Oklahoma pigs were positive for PPIV1 via quantitative RT-PCR (qRT-PCR). Serological studies involving eight U.S. states have shown prevalence rates of 52.5% and 66.1% when tested via an immunoprecipitation coupled to PCR detection assay (ICPD) and an indirect ELISA using a recombinant fusion (F) protein peptide (PPIV1 F ELISA).

PPIV1 is thought to be transmitted via the respiratory route. It is unclear whether other modes of transmission occur. The length of viral shedding is 2–10 days according to current data. PPIV1 should be considered when commercial pigs are showing symptoms of respiratory illness but test negative for known respiratory pathogens. Clinical signs associated with PPIV1 include lethargy, coughing, sneezing, and serous nasal discharge. However, the virus has also been detected in asymptomatic pigs. Young pigs (under 21 days) seem most likely to develop clinical disease. At this time it does not appear that experimental infections with PPIV1 have been conducted. There are no pathognomonic lesions caused by PPIV1, and the likelihood of viral co-infection makes the interpretation of observed signs and lesions difficult.

There is no vaccine and no treatment for PPIV1. Further studies are needed to understand the evolutionary history of the virus, as well as the host range, transmission modes, and pathogenesis of PPIV1. Paramyxoviruses are known for their ability to be transmitted across species, and some cause serious disease in humans (e.g., Nipah virus). Although PPIV1 has been found only in domestic pigs, further study is needed to determine whether zoonotic transmission occurs and if PPIV1 infection is a risk for humans in contact with pigs.

LITERATURE REVIEW

1. Etiology

1.1 Key Characteristics

Porcine parainfluenza virus 1 (PPIV1) is a newly characterized, proposed paramyxovirus (family *Paramyxoviridae*, subfamily *Paramyxovirinae).* Like other paramyxoviruses, PPIV1 is an enveloped, non-segmented, single-stranded RNA virus. The genus *Respirovirus*, which contains the proposed PPIV1, also includes bovine parainfluenza virus 3 (BPIV3), human parainfluenza virus 1 (HPIV1), human parainfluenza virus 3 (HPIV3), Sendai virus (SeV, also known as murine parainfluenza virus), and Simian virus 10.[1] Other more distantly related paramyxoviruses that cause significant disease in swine include blue eye paramyxovirus (BEP), Menangle virus[2], and Nipah virus.[3] Pigs are also potential hosts for Hendra virus[4], Newcastle disease virus[5], and BPIV3.[6-8]

1.2 Strain Variability

PPIV1 was first identified in samples from dead pigs collected in a Hong Kong slaughterhouse from 2008–2012.[9] A reverse transcriptase polymerase chain reaction (RT-PCR) assay was used to detect a region of the L gene common to respiroviruses; next, three complete genomes isolated from nasopharyngeal samples were amplified and sequenced.[9] Sharing <75% nucleotide identity with known paramyxoviruses, these isolates were deemed novel, but most closely related to SeV and HPIV1. A unique feature of PPIV1 was the presence of two G residues (instead of three to five) following the A_6 run at the editing site.[9] Among the three novel PPIV1 isolates detected (GenBank accession numbers JX857409–JX857411), nucleotide identity ranged from about 92% to 97%.[9]

A U.S. study of clinical specimens from pigs with respiratory disease (lung, nasal swabs, and/or oral fluids) was conducted in early 2013.[10] Using a nested pan-*Paramyxovirinae* PCR assay, targeting a conserved region of the L gene, sequences sharing 92.5% identity with PPIV1 were detected. Among the detected sequences, identity of 99–100% was observed.[10] There is also a report on the detection of PPIV1 in U.S. pigs using microarray technology.[11]

A study of pigs with clinical respiratory disease from Oklahoma recently identified PPIV1 in nasal swabs via RT-PCR and metagenomic sequencing.[12] PPIV1 was also identified in asymptomatic pigs from a breeding herd in Nebraska via quantitative RT-PCR (qRT-PCR) and metagenomic sequencing.[12] Full genome sequences of these two strains from Oklahoma (strain 1438-1, GenBank accession number KT749882) and Nebraska (strain 3103-1, GenBank accession number KT749883) revealed 97.7% pairwise identity to each other and 90.0–95.3% nucleotide identity to the three PPIV1 sequences previously identified from China.[9,12]

In the early 2000s, a novel paramyxovirus was isolated from pigs with respiratory and central nervous system disease in the northcentral U.S.[6] However, following further analysis including complete genome sequencing, it was determined that these viruses were in fact variants of BPIV3.[7,8]

2. Cleaning and Disinfection

2.1 Survival

Information on PPIV1 survival is lacking. Other viruses in the family *Paramyxoviridae* generally have poor survivability outside the host.[13] The human isolate HPIVI3 can survive for 4 hours on porous surfaces and 10 hours on nonporous surfaces.[14] HPIVI1 remains infective for years when frozen under certain circumstances.[14]

2.2 Disinfection
No information is available of the efficacy of specific disinfectants against PPIV1. Paramyxoviruses are generally susceptible to acids, alcohols, aldehydes, alkalis, halogens, and oxidizing agents. They are also very sensitive to heat.[1]

3. Epidemiology

3.1 Species Affected
To date, PPIV1 has been found only in domestic pigs.[9,10,12]

3.2 Zoonotic Potential
There is no evidence that PPIV1 can infect humans; however, other paramyxoviruses are known to cause systemic, exanthematous, respiratory and neurological disease in a wide variety of animals, including humans.[9] Paramyxoviruses such as Nipah virus are known for their potential to cross species barriers (from pigs to humans) and cause severe disease or epizootics in new hosts.[3]

3.3 Geographic Distribution
Little is known about the geographic distribution of PPIV1. The virus was first identified in slaughterhouse pigs in Hong Kong, where 12/386 (3.1%) of nasopharyngeal samples and 2/303 (0.7%) of rectal swabs tested positive for PPIV1 via RT-PCR.[9]

In the U.S., PPIV1 has been detected in commercial swine from Iowa, Illinois, Minnesota, North Carolina, Texas, Oklahoma, and Nebraska.[10,12] qRT-PCR testing showed that 17/279 (6.1%) samples collected from pigs in Oklahoma were PPIV1-positive.[12] Serological studies of commercial pigs, from naturally infected herds in eight states, found that 31/59 (52.5%) and 39/59 (66.1%) were positive for PPIV1 via the immunoprecipitation coupled to PCR detection assay (ICPD) and an indirect ELISA using a recombinant fusion (F) protein peptide (PPIV1 F ELISA).[12]

3.4 Morbidity and Mortality
PPIV1 has been identified in samples from young pigs. In one study, affected pigs ranged in age from neonates to 21 days.[10] A subsequent study found PPIV1-positive pigs to be between 10 and 21 days-of-age.[12] Eleven weaned pigs (18–19 days-of-age) from a PPIV1-positive farm in Oklahoma were transferred to the University of Nebraska-Lincoln animal research unit for a two-week observation period; however, no clinical signs developed in these pigs.[12] In these pigs, 6/11 (55%) were positive for PPIV1 on day one, and three additional pigs shed PPIV1 during the two-week study.[12] The lack of clinical signs suggests that age is important in the development of disease. No PPIV1-associated deaths have been described in pigs.

4. Transmission
PPIV1 is thought to be transmitted via the respiratory route. It is unclear whether other modes of transmission occur. The length of time for viral shedding appears to be 2–10 days.[12]

5. Infection in Swine/Pathogenesis
Little is known about PPIV1 pathogenesis. Virus has been detected in turbinate respiratory epithelial cells and to a lesser extent the trachea.[12]

5.1 Clinical Signs
Since PPIV1 was initially identified in swine nasopharyngeal samples, there is a suspected link between PPIV1 and respiratory disease.[9] Paramyxoviruses to which PPIV1 is related, SeV and HPIV1, are also known respiratory pathogens. In 2013, PPIV1 was identified in clinical samples from pigs with

respiratory disease.[10] Reported clinical signs included lethargy, coughing, and sneezing.[10] A similar study found that PPIV1-positive pigs exhibited coughing and sneezing with a serous nasal discharge.[12] Asymptomatic infection has been documented in pigs from a commercial breeding farm, as well as eleven-day-old pigs from a naturally infected farm during a two-week observation period.[12] At this time it does not appear that experimental infections with PPIV1 have been conducted.

5.2 Postmortem Lesions

In naturally infected PPIV1-positive pigs with respiratory disease, the lungs can have a lobular appearance.[10] Microscopically, bronchointerstitial pneumonia has been observed, with bronchiolitis and bronchiolar epithelial necrosis.[10] In another study of naturally infected pigs, histopathology revealed reduced numbers of cilia, goblet cells, or both in the trachea.[12] Mild lymphoplasmacytic rhinitis was also seen. However, because of the likelihood of viral co-infection, lesions cannot solely be attributed to PPIV1.[12]

6. Diagnosis

6.1 Clinical History

PPIV1 should be considered when pigs with respiratory disease test negative for the common viruses involved in the porcine respiratory disease complex (PRDC) such as porcine reproductive and respiratory syndrome virus (PRRSV), swine influenza virus (SIV), or porcine circovirus 2 (PCV2).[13]

6.2 Tests to Detect Nucleic Acids, Virus, or Antigens

Attempts to passage PPIV1 in various cell lines (including swine testicular cells, Vero cells, porcine alveolar macrophage cells, and primary porcine kidney cells) have been unsuccessful.[9,12] In situ hybridization (ISH) using a probe designed to detect PPIV1 in respiratory tissues has been described.[12] RT-PCR and qRT-PCR assays detecting the L gene have been developed[9,10], as well as a TaqMan qRT-PCR assay targeting the N region of the PPIV1 genome.[12] RT-PCR and gene sequencing (HN) are available at some veterinary diagnostic laboratories including Iowa State. There is one publication where microarray technology was used to identify PPIV1.[11]

6.3 Tests to Detect Antibody

An immunoprecipitation coupled to PCR detection assay (ICPD) and an indirect ELISA using a recombinant fusion (F) protein peptide (PPIV1 F ELISA) have been described.[12]

6.4 Samples

6.4.1 Preferred Samples

Preferred samples are nasopharyngeal swabs as the virus reproduces and is shed in the upper respiratory tract.[12]

6.4.2 Oral Fluids

PPIV1 has been detected in oral fluids.[12]

7. Immunity

7.1 Post-exposure

Studies have shown evidence of seroconversion 14 days post-exposure.[12]

7.2 Vaccines

There is currently no vaccine against PPIV1 and no vaccines are known to be in development.

7.3 Cross-protection

PPIV1 is most closely related to HPIV1 and SeV according to phylogenetic analysis. It has been shown that HPIV1 and SeV share high sequence homology and antigenic cross-reactivity.[15] PPIV1 may be cross-reactive with SeV and HPIV1[9], but experimental studies are needed to confirm this.

8. Prevention and Control

There is no specific treatment available for PPIV1. Common biosecurity practices should be implemented on swine production sites. To reduce the risk of acquiring viral respiratory infections, stress should be avoided (e.g., overcrowding) and buildings should be adequately ventilated. Cleaning and disinfection protocols should be in place.

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

PPIV1 is not covered in 2016 OIE Terrestrial Animal Health Code and there are no recommendations on importation of swine or pork.

10. Gaps in Preparedness

Very little is known about the evolutionary history of PPIV1.[12] Though the virus has recently been associated with respiratory disease in pigs, further studies are needed to describe the host range, transmission modes, and pathogenesis of PPIV1.[12] In general, paramyxoviruses are known for their ability to be transmitted across species, and some cause serious disease in humans (e.g., Nipah virus). Although PPIV1 has been found only in domestic pigs, further study is needed to determine whether zoonotic transmission occurs and if PPIV1 infection is a risk for humans in contact with pigs.

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