SWINE PAPILLOMAVIRUS

Prepared for the Swine Health Information Center
By the Center for Food Security and Public Health,
College of Veterinary Medicine,
Iowa State University
August 2015

SUMMARY

Etiology

- Swine papillomavirus (SPV) is a non-enveloped DNA virus that causes transmissible genital papilloma in swine.
- Two SPV variants have been described (*Sus scrofa* papillomaviruses type 1 variants a and b [SsPV-1a/b]).

Cleaning and Disinfection

- Papillomaviruses survive well in the environment and remain infective following exposure to lipid solvents and detergents, low pH, and high temperatures.
- No disinfection protocols specific to SPV are available; however, as a non-enveloped virus, SPV may be susceptible to hypochlorite and aldehydes such as formaldehyde and glutaraldehyde.
- A human papilloma virus, HPV16, was found to be susceptible to hypochlorite (0.525%) after 45 minutes. Glutaraldehyde had no ability to render HPV16 inactive. HPV16 was also susceptible to disinfection with a silver-based, 1.2% peracetic acid.

Epidemiology

- Papillomaviruses infect many species including humans, bovines, canines, equines, lagomorphs, and birds; the virus seems to be highly species-specific. SPV has only been documented in pigs.
- Humans are not at risk for infection with SPV.
- The geographic distribution of SPV is unclear. The few published reports that exist document SPV in England and Belgium.
- There is no information available on SPV-induced morbidity or mortality.

Transmission

- Transmission of SPV is sexual and occurs through natural servicing or artificial insemination of a gilt/sow by an infected boar.

Infection in Swine/Pathogenesis

- Infection with SPV results in small to moderately sized (1–3 cm), firm, papular to papillary lesions in the genital tract of pigs. The disease is typically mild and self-limiting.
- In gilts/sows the vulva is the site of infection while the preputial diverticulum is the site of infection in the boar. Lesions in boars tend to be larger and are more likely to be pedunculated.

Diagnosis

- The virus can be isolated in porcine kidney cell lines.
- Polymerase chain reaction (PCR) can be used to amplify the virus; SPV-specific primers have been described.
- No assays to detect anti-SPV-antibody have been described.

Immunity

- Disease caused by SPV is limited and resolves after a matter of weeks, once a sufficient anti-viral immune response has developed.
- No vaccine is available for SPV.

Prevention and Control

- To prevent transmission of SPV, semen can be screened before a boar is used for breeding.

Gaps in Preparedness

- There is little known about SPV. Although it seems to be a mild, self-limiting disease, more research is necessary to understand the potential impact of the infection on the reproductive health of swine herds. Studies are also needed to determine the best practices for SPV disinfection.

OVERVIEW

Swine papillomavirus (SPV) is a member of the *Papovavirus* group, in the family *Papillomavirus*. It is a small, non-enveloped, double-stranded DNA virus that causes a benign disease referred to as transmissible genital papilloma in swine. The virus may also reside in the skin of healthy pigs, but the significance of this finding is unclear. Like other papillomaviruses (PVs), SPV replicates in the epidermis and modulates the proliferation and differentiation of the stratified squamous epithelium in the genital tract. SPV has been isolated from the preputial diverticulum of boars at slaughter and results in the formation of small papular to papillary lesions following experimental infection of the vulvar or preputial diverticular mucosa. SPV is transmitted by the shedding of virion-laden sloughed cells from the stratum corneum of the stratified squamous epithelium. Semen can transmit SPV from boar to gilt/sow during artificial insemination and, presumably, during natural servicing.

Papillomaviruses are hardy viruses that can withstand exposure to lipid solvents and detergents, low pH, heat, and multiple disinfecting agents. In the case of an outbreak, disinfection of facilities could prove challenging.

Little has been published on SPV, leaving the details of its pathogenesis, the disease it causes, and its induced immune response largely unknown. There is no indication that SPV negatively impacts the reproductive health of swine herds. Specific assays to detect either SPV antigen or anti-SPV antibody have not been described, although the virus has been cultivated in porcine kidney cells after isolation from lesions, and may be easier to study now that the use of raft cultures for growing PVs is more common. Degenerate primers, which amplify PV non-specifically via polymerase chain reaction (PCR), have been used to further genomic analysis of two SPV variants. These variants were successfully detected using variant-specific primers by PCR.

As a sexually transmitted disease, SPV may pose a threat to swine herd health. There are no documented reports on SPV impacting reproductive health of swine, but more research is needed to understand whether SPV is a virus of no consequence or if it is a virus of which to take notice.

LITERATURE REVIEW

1. Etiology

1.1 Key Characteristics

Swine papillomavirus (SPV) is a member of the *Papovavirus* group, in the *Papillomavirus* family and, possibly, the *Alphapapillomavirus* genus[1]. SPV is a small, non-enveloped, double-stranded circular DNA virus with a genome that encodes eight to ten proteins. The virus is sexually transmitted and causes a benign disease known as transmissible genital papilloma in swine.[2,3] Although a recent report described two new variants that were found in healthy skin of domestic pigs[1], others have been unsuccessful in associating SPV with cutaneous fibropapillomatosis in piglets.[4]

1.2 Strain Variability

There is little information available on strain variability for SPV. The first report of SPV occurred before molecular techniques were available to sequence the genome. However, two SPV variants were recently described. *Sus scrofa* papillomaviruses type 1 variants a and b (SsPV-1a/b) were isolated from the skin of two healthy domestic pigs. These viruses were missing the E7 open reading frame that is normally present in PVs.[1]

2. Cleaning and Disinfection

2.1 Survival

Papillomaviruses survive well under diverse environmental conditions and remain infective following exposure to lipid solvents and detergents, low pH, and high temperatures.[5] SPV grows in cultured porcine kidney cells at 33, 36, and 39°C, demonstrating its ability to remain viable at various temperatures.[8]

2.2 Disinfection

As a non-enveloped virus, SPV may be susceptible to hypochlorite and aldehydes, such as formaldehyde and glutaraldehyde, for disinfection.[9] However, in one study, human papillomavirus 16 (HPV16) was only found to be susceptible to disinfection following 45 minutes of exposure to hypochlorite (0.525%). Glutaraldehyde had no ability to render HPV16 inactive. HPV16 was susceptible to disinfection with 1.2% peracetic acid silver-based disinfectant.[10] No published data is available on the disinfection of SPV.

3. Epidemiology

3.1 Species Affected

Papillomaviruses infect many species including, human, bovine, canine, equine, lagomorph, and avian.[5] Papillomaviruses are generally highly species-specific.[11] SPV has only been documented in pigs.[12-14]

3.2 Zoonotic Potential

SPV does not appear to be able to infect other species. Papillomaviruses found in butchers have been found to be human papillomaviruses, not papillomaviruses originating from other species.[14]

3.3 Geographic Distribution

There is no information on the current geographic distribution of SPV. Published reports demonstrate the presence of SPV in two boars in England in the 1960s[13] and two novel variants of SPV in the skin of healthy pigs in Belgium.[1]

3.4 Morbidity and Mortality

There is no information available on SPV-induced morbidity or mortality. The described self-limiting

nature of SPV-induced disease[13] suggests that SPV would not cause death.

4. Transmission

SPV can be transmitted during mating or artificial insemination.[7] Gilts/sows serviced or inseminated by infected boars would be expected to develop lesions four to ten weeks post-breeding.[13]

5. Infection in Swine/Pathogenesis

Replication of PVs requires the growth and differentiation of stratified squamous epithelial cells.[5] In the case of SPV, replication occurs in the mucous membranes of the vulva in the gilt/sow and the preputial diverticulum of the boar.[6] Initial infection occurs in the cells of the stratum basale, but the virus does not replicate within these cells. Instead, PVs remain in a proviral, latent state within basal cells. The genome remains episomal during this period[3] while simultaneously producing early viral gene products. These induce basal cell hyperplasia and delayed maturation of cells within the strata spinosum and granulosum.[5] When basal cells have matured sufficiently, progressing into the stratum spinosum, late viral gene products are produced and virions are assembled within the cells. Cells of the stratum granulosum are heavily laden with PV virions, which are shed when infected cells are exfoliated from the stratum corneum.[5]

5.1 Clinical Signs

Small to moderately sized (1–3 cm), firm, papular to papillary lesions are characteristic of SPV infection.[6,13] In one study, experimental lesions developed in an average of eight weeks post-intradermal inoculation or surface scarification of the vulva of the gilt or the prepuce of the boar. Inoculum was cell-free filtrate derived from preputial diverticular lesions discovered upon necropsy in two boars. Lesions were larger in experimentally infected boars than gilts, possibly due to the more protected position within the boar. The disease is limited in its course and resolves after a matter of weeks, once a sufficient anti-viral immune response has developed.[6] Experimentally infected pigs had resolution of lesions approximately three weeks after the first detection of lesion growth.[13]

5.2 Postmortem Lesions

Lesions induced by SPV were first described in 1961 in two boars upon necropsy. Grossly, a papular lesion was found in the preputial diverticulum of one and a papillary lesion found in the same location in the other boar. The lesions were firm and experimentally induced lesions in subsequently infected gilts and boars were of similar shape and firmness. Lesions in gilts were smaller than those in boars, whose lesions were often pedunculated.

Histologically, lesions caused by SPV are typical papillomas with extensive, uneven acanthosis and epithelial outgrowth. Large, spherical, intracytoplasmic inclusions stain with acid stains, often surrounded by a halo. Interface dermatitis characterized by mononuclear cell infiltrate is also seen.[2]

6. Diagnosis

6.1 Clinical History

As SPV infection induces a mild and self-limiting disease, there are no systemic clinical signs that have been associated with infection. Small, papular to papillary growths on the gilt/sow's vulva within the boar's preputial diverticulum are consistent with SPV infection.[6] Vulvar and preputial diverticular lesions in a herd should be examined and sampled, if possible.

6.2 Tests to Detect Nucleic Acids, Virus, or Antigens

Virus isolation and propagation may be performed by inoculating a PK-15 or PS cells, both porcine kidney cell lines.[8] Degenerate PV-specific primers may be used to amplify regions of the SPV genome

using polymerase chain reaction (PCR). Sequencing of the PCR products should be performed to further identify the amplicon. SsPV-1a/b specific primers have been described.[1]

6.3 Tests to Detect Antibody

No assays to detect anti-SPV-antibody have been described.

6.4 Samples

6.4.1 Preferred Samples

Scrapings or swabs from the preputial diverticulum of boars or the vulva of the female may be suitable for virus isolation and/or detection.[2,6]

6.4.2 Oral Fluids

The suitability of oral fluids for SPV isolation or detection is not known. SPV infects the genital tract and remains localized; therefore, it is unlikely that SPV will be found in oral fluids.

7. Immunity

7.1 Post-exposure

The antiviral immune response generated against PVs affords protection from reinfection and also against the existing growth, resulting in its regression and eventual sloughing. Data from rabbit papilloma-induced tumors studies demonstrated that exposure to inactivated virus was sufficient to protect rabbits against infection and subsequent tumor growth.[5] In spite of the ability to prevent reinfection, there was neutralizing activity of serum from experimentally SPV-infected pigs in only one of six pigs that had been repeatedly injected with SPV, while pigs only exposed to SPV a single time showed no serum-neutralization capacity.[12] Additionally, antigen-antibody precipitation assays were unable to demonstrate the presence of anti-PSV antibody.[12] The existence of a cell-mediated immune response to PSV is not known.

7.2 Vaccines

No information on vaccines for SPV is available. However, exposure to inactivated rabbit papillomavirus was sufficient to protect rabbits against infection[5], indicating that an inactivated SPV may be a potential vaccine candidate.

7.3 Cross-protection

There is no information available on cross-protection.

8. Prevention and Control

Viral screening of semen used for artificial insemination should be done prior to using it for breeding.[7] The self-limiting nature of the disease and lack of documented morbidity associated with it do not require extreme control measures. However, steps should be taken to ensure that uninfected animals are not bred to currently infected animals.

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

Swine papillomavirus is not included in the 2015 OIE Terrestrial Animal Health Code. There are no recommendations on restrictions for importations of pigs or pork from infected areas or zones.

10. Gaps in Preparedness

Swine papillomavirus has received little attention in the nearly 60 years since it was first described, and reports of SPV are few. More research is needed to understand the pathogenesis of SPV and the cost of any associated morbidities. Additionally, disinfection for PVs is challenging and more research into

effective disinfection methods for SPV is needed. Sexually transmitted infections may impact herd health; therefore, it is in the best interest of swine producers to understand the impact that SPV may have on their herds. Because SPV infection induces life-long protection from reinfection, better understanding of the immune response to SPV could lead to development of an effective vaccine.

ACKNOWLEDGEMENTS

Funding for this project was provided by the Swine Health Information Center, Perry, Iowa

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

- Kristin Killoran, PhD; 2nd 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

To cite:
Killoran K, Leedom Larson KR. Swine papillomavirus. Swine Health Information Center and Center for Food Security and Public Health, 2016. http://www.cfsph.iastate.edu/pdf/shic-factsheet-swine-papillomavirus.

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