

SENECAVIRUS A



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SUMMARY

Etiology

- Senecavirus A (SVA, formerly known as Seneca Valley virus) is a small, non-enveloped picornavirus discovered incidentally in 2002 as a cell culture contaminant. However, a retrospective serosurvey showed that the virus had been circulating silently in U.S. pigs since at least 1988.
- Only a single species is classified in the genus *Senecavirus*.
- The main significance of SVA is clinical resemblance to vesicular foreign animal diseases such as foot-and-mouth disease (FMD), swine vesicular disease (SVD), and vesicular exanthema of swine (VES).

Cleaning and Disinfection

- Studies on survival of SVA in the environment have not been reported.
- At 25°C (77°F), bleach (5.25%, 1:20 dilution) is highly effective against SVA on aluminum, rubber, plastic, stainless steel, and cured cement after a 10–15 minute contact time. At 4°C (39°F), bleach inactivates SVA within 5–15 minutes on all surfaces; disinfection is slightly less effective for rubber but still exceeds 99.9%.
- In the laboratory, an accelerated hydrogen peroxide-based disinfectant (Prevail® concentrate, Virox Technologies, Inc.) is also effective against SVA when applied at room temperature (1:20 dilution) for 10 minutes.
- The efficacy of many disinfectants against SVA remains unclear. Because vesicular diseases are clinically indistinguishable, disinfection protocols for FMD should be followed even if SVA is suspected. This includes use of sodium hydroxide, sodium carbonate, 0.2% citric acid, aldehydes, and oxidizing disinfectants including sodium hypochlorite.
- Below are specific EPA-approved disinfectants listed as effective for FMD by the USDA:

EPA Reg. No.	Product Name	Manufacturer	Active Ingredient(s)
1677-129	Oxonia Active (Alternate name: Oxysept 333)	Ecolab, Inc.	Hydrogen peroxide Peroxyacetic acid
6836-86	Lonza DC 101	Lonza, Inc.	Alkyl dimethyl benzyl ammonium chloride Didecyl dimethyl ammonium chloride Octyl decyl dimethyl ammonium chloride Diocetyl dimethyl ammonium chloride
10324-67	Maquat MQ615-AS	Mason Chemical Company	Alkyl dimethyl benzyl ammonium chloride

			Didecyl dimethyl ammonium chloride Octyl decyl dimethyl ammonium chloride Diocetyl dimethyl ammonium chloride
70060-19	Aseptrol S10-TAB	BASF Catalysts, LLC	Sodium chlorite Sodium dichloroisocyanurate dehydrate
70060-30	Aseptrol FC-TAB	BASF Catalysts, LLC	Sodium chlorite Sodium dichloroisocyanurate dehydrate
71654-6	Virkon S	E.I. du Pont de Nemours & Company	Sodium chloride Potassium peroxymonosulfate
74559-4	ACCEL (Concentrate) Disinfectant Cleaner (Alternate name: INTERVENTION Farm Animal Care Disinfectant Cleaner & Deodorizer)	Virox Technologies	Hydrogen peroxide

Epidemiology

- Neutralizing antibodies to SVA have been detected in small populations of swine, cattle, and wild mice in the United States. SVA nucleic acids have been detected in mice and houseflies in addition to pigs.
- SVA was identified in a single U.S. pig with vesicular lesions in 2010. Since July 2015, the virus has increasingly been identified in clinically affected pigs in the United States. SVA has also been reported in pigs with vesicular lesions in Canada, Brazil, China, Thailand, and Colombia.
- Morbidity and mortality in swine are variable. The highest morbidity has been reported in sows, but mortality is very low in adult swine. Morbidity in neonates can reach 70%, and reported case mortality ranges from 5–60%.
- There is no record of SVA causing symptomatic human disease. The virus has potent oncolytic abilities which are being explored in human cancer treatment research.

Transmission

- The transmission route(s) for SVA are not well understood. Both direct and indirect transmission likely play a role. SVA has been identified in mice and houseflies. There is some evidence that vertical transmission may occur. Another picornavirus, FMDV, is known to spread readily by direct contact with infected individuals, fomites, or exposure to aerosolized virus.

Infection in Swine/Pathogenesis

- Recently, inoculation with SVA has been clearly linked to vesicle development in swine.
- Vesicular lesions are found on the snout, lips, coronary bands, and/or interdigital spaces. Ruptured lesions form deep ulcerations that heal within about two weeks.
- In neonates, infection with SVA can lead to weakness, lethargy, neurologic signs, diarrhea, or death; however, clinical signs usually subside within 3–10 days and most piglets recover completely. Petechial hemorrhages of the kidney and ulcerative lesions of the tongue and coronary band have been reported, as well as subcutaneous and mesenteric edema in piglets with diarrhea.

Diagnosis

- SVA can be grown in several human and porcine-origin cell lines. Immunohistochemistry and in situ hybridization can be used to identify SVA antigen and nucleic acid in tissues. Monoclonal antibodies have been developed that do not cross-react with other vesicular diseases.

- Reverse transcription polymerase chain reaction (RT-PCR) is considered to be the gold standard for diagnosis and a number of conventional and quantitative methods have been published. Oral fluids can be tested via RT-PCR.
- Serological testing methods described include indirect and competitive enzyme linked immunosorbent assays (ELISAs) and virus neutralization.

Immunity

- In pigs, seroconversion occurs about 5 days post-infection. To date, it seems that new SVA infections have not been reported in previously affected swine herds.
- No vaccines are currently available for SVA.

Prevention and Control

- Proven methods for prevention and control of SVA are lacking. Vaccination and stamping out have been used to control FMD, which is caused by a similar virus.
- Common industry biosecurity practices should also be in place.
- There is no national surveillance for SVA.

Gaps in Preparedness

- Continued research on the epidemiology of SVA is needed.
- The development of more rapid, cost-effective diagnostic assays will be important in the future.
- More information is also needed on effective cleaning and disinfection practices for SVA.

OVERVIEW

Senecavirus A (formerly known as Seneca Valley virus) is a small, non-enveloped picornavirus, unknown until 2002 when it was discovered incidentally as a cell culture contaminant. However, a retrospective serosurvey showed that the virus had been circulating silently in U.S. pigs since at least 1988. Only a single species is currently classified in the genus *Senecavirus*, family Picornaviridae. Antibodies against the virus have been detected in swine, cattle, mice, and a single human sample, though the virus is not known to cause disease in humans. SVA nucleic acids have also been detected in mice and houseflies in addition to pigs. Outbreaks of idiopathic vesicular disease have been linked to SVA in the absence of other identified etiologic agents and also during concurrent infection with porcine circovirus and porcine enterovirus. While the pathogenicity of SVA was unclear previously, inoculation with the virus has now been clearly linked to the development of vesicular disease. SVA has also been identified in healthy pigs.

Swine SVA infection has occurred in Canada, the United States, Brazil, China, Thailand, and Colombia. Clinical signs of SVA, when present, are indistinguishable from those of foot-and-mouth disease (FMD), swine vesicular disease (SVD), vesicular exanthema of swine virus (VESV), all more serious and economically devastating foreign animal diseases (FADs). Erosions, ulcerations, and vesicular lesions of the snout, oral mucosa, and distal limbs, especially around the coronary band, may be observed. Hoof sloughing and lameness can also occur, as well as more general symptoms of illness such as fever, lethargy, and anorexia. In neonates, SVA causes weakness, lethargy, neurologic signs, diarrhea, or death; however, clinical signs usually subside within 3–10 days and most piglets recover completely.

SVA can be grown in several human and porcine-origin cell lines. Electron microscopy is not diagnostic; immunohistochemistry and in situ hybridization can be used to identify SVA antigen and nucleic acid in tissues. Monoclonal antibodies have been developed that do not cross-react with other vesicular diseases. Reverse transcription polymerase chain reaction (RT-PCR) is considered to be the gold standard for diagnosis and a number of conventional and quantitative methods have been published. Oral fluids can be tested via RT-PCR. Serological testing methods described include indirect and competitive enzyme linked immunosorbent assays (ELISAs) and virus neutralization.

Understanding the epidemiology of SVA and potential role of other species in virus transmission and origin, combined with continued development of rapid and specific diagnostics, will be crucial for pork producers to manage SVA in the future.

LITERATURE REVIEW

1. Etiology

1.1 Key Characteristics

Senecavirus A (formerly known as Seneca Valley virus) is a small, non-enveloped virus containing a single strand of positive-sense RNA within a protein capsid.^{1,2} It was originally discovered in 2002 as a cell culture contaminant, presumed to have been introduced through fetal bovine serum or porcine trypsin during the cultivation of human retinoblast (PER.C6[®]) cells at a laboratory in Gaithersburg, Massachusetts (near Seneca Creek State Park).^{3,4} However, retrospective serological studies of asymptomatic pigs from 1988–2008 suggest that SVA may have been silently circulating throughout the United States for some time.^{2,5} The main significance of SVA is that it cannot be differentiated from vesicular foreign animal diseases including foot-and-mouth disease (FMD), swine vesicular disease (SVD), and vesicular exanthema of swine (VES).⁶ SVA is also known for its ability to replicate in tumor cells and is being studied for treatment of neuroendocrine cancers in humans.^{1,7}

1.2 Strain Variability

The single species within the genus *Senecavirus* is known as Senecavirus A.⁸ There are approximately 7200 nucleotides (nt) in the SVA genome, plus 666 nt in the 5'UTR portion and 71 nt in the 3'UTR portion and a poly(A) tail.^{2,5} As described by Leme et al.,⁵ the prototype strain SVV-001 has the typical genome of other picornaviruses, with the standard L-4-3-4 layout (leader and 3 major protein regions named P1, P2, and P3, which are further divided into nonstructural polypeptides).² The polypeptides P1, 2C, 3C, and 3D of SVA are similar to those found in members of the genus *Cardiovirus*; however, differences have been noted in the 5'UTR, L, 2B, 3A, and 3'UTR regions⁹ as well as the internal ribosome entry site (IRES).¹⁰ Segales et al. have recently published an SVA review that summarizes further details regarding the genome.¹¹

The complete genome sequence was analyzed for SVV-001 and published in 2008.² Since then, more than 40 complete and partial SVA genomes have been entered in GenBank.¹² Known SVA strains are highly similar to each other; they are also similar to the prototype strain SVV-001, but to a lesser degree.⁵ Analyses of different SVA isolates suggests the existence of a common ancestor within the last three to four decades and a relatively recent introduction into United States swine herds.³

Senecavirus strains are currently grouped into three temporal clades. Clade I includes the prototype strain SVV-01, clade II contains the “historical” U.S. strains identified between 1988 and 1997, and clade III includes “contemporary” strains isolated from 2001–2016 in the United States, Brazil, Canada, China, Thailand, and Colombia.^{5,11} Within clade III, sequencing of the VP1 region shows that isolates are generally clustered by country of origin.⁵ However, the Colombian SVA strain identified in early 2016 is more similar to U.S. isolates than to those found in Brazil.¹³ Similarly, Chinese variants sequenced in 2016 and 2017 were found to be more closely related to U.S. isolates than other Chinese strains.^{14,15}

2. Cleaning and Disinfection

2.1 Survival

Studies on survival of SVA in the environment have not been reported, although the virus has been identified in environmental samples. In one study, SVA nucleic acids were detected in dust from an exhaust fan, in ground outside an affected farm, and in a tractor bucket used to haul dead pigs.¹⁶

2.2 Disinfection

Two recent studies evaluated disinfection of SVA under experimental conditions. At 25°C (77°F), bleach (5.25%, 1:20 dilution) was highly effective against SVA within 10–15 minutes on aluminum, rubber, plastic, stainless steel, and cured cement.¹⁷ At 4°C (39°F), bleach inactivated SVA within 5–15 minutes

on all surfaces; disinfection was slightly less effective for rubber but still exceeded 99.9%.¹⁷ Phenolic and quaternary ammonium disinfectants provided intermediate disinfection on all surfaces, inactivating only 82% and 78–99% of virus respectively, even after a 60 minute contact time and testing at both temperatures.¹⁷ An accelerated hydrogen peroxide-based disinfectant (Prevail® concentrate, Virox Technologies, Inc.) was effective against SVA when tested at room temperature (1:20 dilution) and a 10 minute contact time.¹⁸ The disinfectant retained its effectiveness under these conditions for 6 weeks following the initial preparation (when stored in a sealed bottle at room temperature).¹⁸

Until an FAD can be ruled out, an initial response to vesicular disease outbreaks in swine should follow protocols in place for such events.¹⁹ EPA-approved disinfectants for FMDV have been published by the USDA.²⁰ More research is needed on SVA-specific disinfection protocols to determine the effectiveness of existing methods. Generally, heat and alkaline or acidic disinfectants, such as sodium hydroxide (2%), sodium carbonate (4%),¹ and citric acid (0.2%), can deactivate FMDV, another picornavirus, although efficacy may decrease when the virus is dried.²¹ Aldehydes and oxidizing disinfectants, including sodium hypochlorite (3%), are also effective. Detergent and organic solvents are less effective in FMDV disinfection, though these are occasionally used in conjunction with a disinfectant to solubilize organic material.¹

3. Epidemiology

3.1 Species Affected

Neutralizing antibodies to SVA have been detected in small populations of swine, cattle, and wild mice in the United States, suggesting exposure to the virus without overt clinical signs. Similar serological testing of four primate species revealed no anti-SVA antibodies.⁴ SVA nucleic acids have been detected in mice and houseflies, as well as pigs.¹⁶ However, another study in mice showed no horizontal transmission, as measured by seroconversion, between infected and naïve mice during a 30 day period.³ Swine are thought to be a natural host of SVA.

3.2 Zoonotic Potential

There is no record of SVA causing symptomatic human disease,²² and normal primary human cells tested in vitro demonstrate resistance to infection. Presence of neutralizing anti-SVAV antibodies is rare in humans, suggesting that SVA exposure is not common or that the virus does not typically replicate enough in humans to stimulate a detectable humoral immune response. Further, SVV-001 does not bind human erythrocytes and is not inhibited by other components of human blood.²³ However, SVA can be readily propagated in human tumor cells showing neuroendocrine features. Due to its efficacy as an oncolytic agent, some attention should be given to the potential for viral adaptation and zoonotic infection in humans.³

SVA has also been identified as a virus of concern with porcine and human host range (able to infect humans or human cells in culture) in the preparation of biological products such as porcine trypsin that may be used in the production of vaccines or other human treatments. This suggests the need for revised and improved diagnostic testing of any and all reagents used for the production of products being given to humans.²⁴

3.3 Geographic Distribution

In 2007, the initial association of SVA with vesicular lesions was reported in pigs being transported from Canada to Minnesota for processing.¹⁹ The first known U.S. case occurred in Indiana in 2010, in a single 6-month-old pig with vesicular lesions in the oral cavity, around the nares, and on the coronary bands.⁶ Though clinical cases have been recognized only recently, a retrospective serological study of asymptomatic pigs from 1998–2008 suggests that SVA may have been silently circulating throughout the United States for years.²⁵

From 1988–2005, seven newly described picornavirus isolates, now known to be SVA, were identified from pigs with vesicular lesions in the United States (Minnesota, North Carolina, Iowa, New Jersey, Illinois, Louisiana and California).⁴ From mid-to-late 2015, the number of SVA cases detected in clinically ill pigs increased, and included pigs from Minnesota, Iowa, South Dakota, Nebraska, Illinois, Indiana, Missouri, Oklahoma, and North Carolina.²⁵ SVA was identified in pigs at two Iowa processing plants in 2016.²⁶ In the United States, Baker et al. report that SVA cases have occurred in breeding herds of all sizes with variable biosecurity in both swine dense and swine sparse areas.²⁷ The first report of SVA-associated neonatal mortality in the United States occurred in 2016.²⁸

Outside of the United States, SVA has been linked to vesicular disease outbreaks and outbreaks of sudden death in neonatal pigs (sometimes known as epidemic transient neonatal losses [ETNL]) in Brazil, first reported in 2015.^{29,30} The virus has also been detected in pigs with vesicular lesions and associated with neonatal death piglets in China since 2015.^{31,32} In 2016, the first detection of SVA was reported in pigs in Thailand and Colombia with vesicular lesions.^{13,33} SVA was once again confirmed in pigs with vesicular disease in Canada in 2016.³⁴

Idiopathic vesicular disease in swine has previously been reported in Australia,³⁵ New Zealand,³⁶ Florida,³⁷ and Indiana,³⁸ as well as Iowa and nearby states.³⁹ Cases of idiopathic vesicular disease could be caused by SVA or other pathogens such as swine enteroviruses, teschoviruses, porcine parvoviruses, or caliciviruses. Vesicular lesions in swine have also been reported in connection with mycotoxins, contact dermatitis, and feed containing marine products or the fungus *Sclerotinia sclerotiorum*.⁶ Historically, the potential involvement of SVA in most cases of idiopathic vesicular disease is unknown.

3.4 Morbidity and Mortality

From 1998–2008, isolates very similar to SVV-001 were identified in swine samples submitted to the National Veterinary Services Laboratories (NSVL) from multiple states.² Both the temporal and geographic distribution of these isolates suggested that SVV-001 was relatively common in the United States.² However, in a 2015 study of oral fluid samples (from pigs without clinical signs, submitted to the Iowa State University and University of Minnesota Diagnostic Laboratories), only 1.1% were positive for SVA by RT-PCR.⁴⁰

SVA morbidity varies widely depending on pig age, geographical region, and herd origin.⁵ Higher morbidity rates are seen in naïve herds. In weaners, 0.5–5% of pigs may be affected; in finishers and breeding animals, 5–30% morbidity can occur.⁵ The highest morbidity has been reported in sows, with up to 90% affected,²⁷ but mortality seems to be very low in adult pigs. In neonates, both high morbidity and mortality have been described. Morbidity rates can reach 70%.⁵ Leme et al. report that neonatal mortality varies from 15–30%.⁵ According to Segales et al., piglet mortality typically ranges from 5–60%.¹¹

4. Transmission

4.1 Pathogenesis

Two recent studies have definitively shown that SVA is a cause of vesicular disease in swine. Joshi et al. found that the strain SD15-26 caused vesicular disease in 15-week-old pigs following oronasal inoculation,⁴¹ and Montiel et al. found that intranasal inoculation with the strain SVA15-41901SD led to vesicle formation in nine-week-old pigs.⁴²

The tonsil is likely the primary SVA replication site; other lymphoid tissues (e.g., spleen and lymph nodes) are probably also involved in viral replication.⁴¹ As cited by Joshi et al.,⁴¹ this replication pattern is consistent with other picornaviruses including FMDV and encephalomyocarditis virus.

SVA is shed in oral secretions, nasal secretions, and feces for up to 28 days post-infection.⁴¹ Analysis of viral shedding following SVA infection in a breeding herd suggested that transmission risk is greatly reduced 30 days post-outbreak.⁴³ A similar study of viral shedding patterns in sows found that the viremic stage was relatively short. Only one SVA-positive sow remained at 9 weeks post-outbreak (laryngeal sample) and no SVA-positive sows were found at 6 or 9 weeks post-outbreak (rectal swab).⁴⁴ In experimentally infected animals, SVA was detected between days 3 and 7 post-infection in the lung, mediastinal and mesenteric lymph nodes, liver, spleen, small and large intestines, and tonsils.⁴¹ In convalescent pigs (i.e., 3.5 weeks post-infection), similar tissues contained SVA.⁴¹ Detectable levels of infectious virus have been found in nasal secretions, sputum, blood, urine, and stool in human cancer patients treated with intravenous SVV-001 in clinical trials.⁴⁵ The virus is also able to cross the blood-brain barrier in humans.⁴⁶

4.2 Routes of Transmission

Information on SVA transmission remains sparse. Vesicles caused by SVA infection have high virus loads,⁴⁷ making direct contact likely an important route of SVA transmission.⁵ As cited by Leme et al.,⁵ the virus is shed in the feces of clinically affected pigs, and SVA has been detected in the urinary epithelium.^{48,49} Environmental contamination could lead to possible SVA transmission in swine. In one study, SVA was not recovered from 30 environmental surfaces tested including waterers, feeders, pens, alleyways, and loadouts.⁵⁰ However, another showed that SVA nucleic acids could be detected in dust from an exhaust fan, in ground outside an affected farm, and in a tractor bucket used to haul dead pigs.¹⁶

SVA has been detected in mice and houseflies,¹⁶ though the role of non-swine animals in SVA transmission needs further investigation. Vertical transmission may also occur, as indicated by the detection of SVA in one-to-two day old piglets.⁴⁹ An investigation of affected U.S. breeding herds found that possible risk factors for SVA introduction included on-farm employee entry, carcass disposal and cull sow removal activities involving vehicle use, and breeding replacement entry, among others.²⁷ Another picornavirus, FMDV, is known to spread readily by direct contact with infected individuals, fomites, or exposure to aerosolized virus.¹

5. Infection in Swine/Pathogenesis

5.1 Clinical Signs

Inoculation with SVA leads to vesicle development on the snout, lips, coronary bands, and/or interdigital spaces.^{41,42} Ruptured vesicles form deep ulcerations that heal within about two weeks. Lesions observed in pigs infected with SVA cannot be distinguished clinically from those caused by FMDV or other vesicular diseases. However, Montiel et al. report that SVA lesions appeared on the feet several days before being recognized on the snout; lesions caused by FMDV typically appear on the snout and the feet at the same time.⁴² Additional clinical signs observed in experimentally infected pigs include lethargy, lameness, and anorexia.⁴¹ Fever of 40.3°C (104.5°F)–40.8°C (105.4°F) may be seen.¹¹ In the field, SVA has also been associated with weakness, lethargy, neurologic signs, diarrhea, or death in neonates; however, clinical signs usually subside within 3–10 days and most piglets recover completely.^{30,48}

5.2 Postmortem Lesions

Following experimental infection, ruptured vesicles became deep ulcers and skin erosions that evolve to crusted lesions.⁴¹ In a study of nine-week-old pigs, no other gross or microscopic lesions were seen.⁴² In 15-week-old pigs inoculated with SVA, mild to moderate lymphoid hyperplasia was documented in the tonsils, the spleen, and the lymph nodes; in the lungs, multifocal mild atelectasis occurred with diffuse congestion and multifocal mild perivascular accumulation of lymphocytes, plasma cells, and macrophages.⁴¹

In naturally infected neonates, gross lesions include petechial hemorrhages of the kidney and ulcerative lesions of the tongue and coronary band.⁴⁸ Histopathology revealed interstitial pneumonia as well as diphtheric glossitis, lymphocytic myocarditis, degeneration of the transitional epithelium of the urinary bladder and the ureters, and lymphoplasmacytic encephalitis.^{48,49} Subcutaneous and mesenteric edema have been seen in piglets with diarrhea.¹¹

6. Diagnosis

6.1 Clinical History

SVA cannot be diagnosed by clinical signs alone.

6.2 Tests to Detect Nucleic Acids, Virus, or Antigens

Human retinoblast (PER.C6[®]) cells² and human lung cancer cell monolayers (NCI-H1299^a)⁵¹ can be used for cultivation of SVA, as well as human non-small-cell lung carcinoma cells (H1299).⁴¹ Normal adult human cell lines not killed by SVAV produce almost no virus.^{22,23} Swine testis (ST) and swine kidney (SK-RST and PK-15) cells can also be used for virus isolation.¹¹ High virus titers are routinely produced and the virus is purified easily.

Electron microscopy studies of SVA samples reveal the presence of single or aggregate icosahedral particles that are small and indicative of picornavirus infection. Crystalline, lattice-like structures may be observed upon ultrastructural analysis of infected cells at 24 hours post-infection.² Histopathology alone is not diagnostic, but can aid in selection of tissues for further testing.⁵ Immunohistochemical (IHC) staining and *in situ* hybridization can be used to identify SVA antigen and nucleic acid in tissue samples.^{41,46,48,49,52,53} SVA-specific monoclonal antibodies (mAbs) have been produced that do not cross-react with other vesicular disease viruses (e.g., SVD, VES, and FMDV) as demonstrated by dot blot assay, and they are capable of specifically recognizing viral antigen in SVA-infected cell cultures as confirmed by IHC assay.⁵¹ Antibody reagents that can be used to detect SVA in skin with vesicular lesions have also been generated.⁵³ A fluorescent molecular probe that targets two regions of the SVA virus has been developed, then evaluated further for viral detection with light microscopy only.⁵³

As described by Leme et al.,⁵ RT-PCR is the most commonly used test to identify SVA, and a number of conventional RT-PCR^{16,29,54,55} and quantitative RT-PCR (qRT-PCR)^{13,16,28,47,54,56-60} protocols have been developed. qRT-PCR assays are considered the gold standard for vesicular disease because they are rapid, sensitive, and specific.⁵ One qRT-PCR assay, available at the South Dakota Animal Disease Research and Diagnostic Laboratory (ADRDL), was evaluated for its ability to detect SVA isolates from different geographic areas; targeting a conserved region of the SVA genome, the assay successfully identified isolates collected between 1988–2002 and those obtained from 2015–2016.⁶¹

6.3 Tests to Detect Antibody

Several enzyme linked immunosorbent assays (ELISAs) have been developed, including indirect^{51,56,62,63} and competitive^{51,64} methods as described by Leme et al.⁵ The cELISA is specific, easy to perform, and can detect antibodies from different species and different stages of the immune response. It does not require special reagents and can be modified to screen a large number of samples.⁵¹ Virus-neutralizing antibody detection has also been used in SVA identification^{51,64} Serological assays in development include a fluorescent microsphere immunoassay and a fluorescent focus neutralization assay.⁶³

6.4 Samples

6.4.1 Preferred Samples

Serum, tissue (vesicles), oral fluid, and vesicular fluid are suitable for virus isolation. These samples are also acceptable for RT-PCR, in addition to vesicular swabs. Blood, vesicular fluid, and epithelial tissue are typically collected for diagnostic workups in suspected vesicular FAD cases; esophageal/pharyngeal

samples (including tonsil) can also be tested.⁶⁵ Urine, feces, and nasal swabs from humans have been used to identify SVA by qRT-PCR.⁴⁵

6.4.2 Oral Fluids

Oral fluids have been used successfully in the identification of SVA.

7. Immunity

7.1 Post-exposure

Serological studies have revealed the occurrence of neutralizing anti-SVA antibodies in swine, cattle, and mice, but rarely in humans.⁴ In pigs, seroconversion occurs about 5 days post-infection.⁵ Higher SVA antibody titers have been observed in naturally infected pigs from Brazil compared to other countries. To date, it seems that new SVA infections have not been reported in previously affected swine herds.⁵

Human cancer patients in clinical trials have been shown to develop neutralizing antibodies within two weeks of intravenous treatment with SVV-001, with titer and swiftness of immune response dependent upon viral dose.⁴⁵ Mice will also develop neutralizing antibodies following intravenous injection of SVV-001.²³

7.2 Vaccines

No vaccines are currently available for SVA.

7.3 Cross-protection

No information was found on cross-protection between SVA isolates.

8. Prevention and Control

There are no treatments or vaccines available for SVA infection.⁵ Until more is known about SVA transmission and pathogenesis in swine, suggested methods of control are based on other picornaviruses which have been more extensively studied, such as FMDV. Strict biosecurity practices should be in place to prevent SVA entry onto a farm. Humans play a significant role acting as fomites for FMDV, as well as vehicles, equipment, and other objects.¹ Preventive measures should also be taken to avoid the possible spread of SVA by indirect transmission. Because SVA can be carried by houseflies and mice, vector control methods should be in place. Cleaning and disinfection of affected farms is critical. A few disinfectants have been specifically tested against SVA for efficacy.

Continued vigilance and awareness of the disease is essential. As of 2017, SVA is not found on the United States National List of Reportable Diseases.⁶⁶ The virus may be reportable in individual states; for example, California lists SVA as an emergency condition which must be reported to the State within 24 hours of discovery.⁶⁷ SVA is not federally reportable in Canada.⁶⁸

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

The 2017 OIE Terrestrial Animal Health Code does not include SVA. There are no recommendations regarding importation of cattle or swine from countries or zones infected with SVA. FMDV, which causes indistinguishable vesicular lesions, is listed by the OIE.⁶⁹

10. Gaps in Preparedness

According to Leme et al.,⁵ 2015 seems to have been a turning point for SVA epidemiology. In years prior, SVA was reported infrequently in pigs with clinical vesicular disease; however, the number of SVA reports have increased significantly in recent years. Increased morbidity and mortality rates have also been observed but the cause(s) of these changes remain unclear. Although SVA research has accelerated

recently,⁵ more biological and epidemiological studies on SVA are desperately needed to prevent further disruption to swine producers and mitigate consequences in United States markets.⁷⁰

Due to the clinical similarity of SVA to vesicular foreign animal diseases, rapid diagnosis of SVA in suspect cases is critical. The development of time-sensitive and cost-effective diagnostic assays could potentially prevent the need for costly FAD investigations and economic losses. More information is also needed on the environmental survival of SVA and effective cleaning and disinfection practices.

While pigs are a natural host of SVA, little is known about incidence of infection in other species. The close relationship of SVA to cardioviruses, known viruses of rodents, warrants further investigation into the potential for transmission of SVA from rodents to other species. The identification of similar isolates in additional species or locations could help to further our understanding of the origins of the virus.

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