Animal & Plant Health Agency

EMERGING PIG DISEASE ASSOCIATED WITH SENECA VALLEY VIRUS IN THE AMERICAS

This document summarises information about Porcine Idiopathic Vesicular Disease (PIVD) and Epidemic Transient Neonatal Losses (ETNL) associated with Seneca Valley virus detection reported in Brazil and the United States.

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1. Emerging disease associated with Seneca Valley virus

Two unusual disease presentations, Porcine (or Swine) Idiopathic Vesicular Disease (PIVD or SIVD) and Epidemic Transient Neonatal Losses (ETNL), have been described in multiple pig herds in Brazil since November 2014 (Vanucci and others, 2015) and in several herds in the US since July 2015. Detection of Seneca Valley virus, in the virus family *Picornaviridae*, has been a consistent, and in some the only, finding in these. Attempts to produce vesicular disease experimentally using contemporary SVV have recently been successful in the US. These recent findings are not the first detections of Seneca Valley virus (SVV) which has been identified previously but sporadically in North America. Current thinking is that SVV is a virus which emerged in pigs in the US in the early 1980s and then spread to other regions of the Americas. The virus may have evolved to one with greater virulence for pigs leading to the current outbreaks in the Americas. There is no known public health risk and no statutory legal/trade implications relating to SVV itself. The message to pig keepers remains that all disease incidents with vesicular lesions should be reported to APHA as suspect notifiable disease which will prompt investigation.

2. Virus nomenclature

Seneca Valley virus (SVV) was originally classified, in a species of the same name, as a member of a new picornavirus genus named *Senecavirus*. The species *Seneca Valley virus* was recently renamed *Senecavirus A* to fit into a more standardized picornavirus nomenclature and to distinguish the species name, *Senecavirus A*, from the virus name, Seneca Valley virus. It should not be referred to as 'Seneca A virus'. SVV may also be referred to as SVV-1 to indicate its (sero)type designation.

3. Main disease findings

PIVD:

- vesicles, coalescing erosions, crusting lesions on snouts, coronary bands, foot sole
- deep nail bed haemorrhages also a common findings
- transient and mild loss of appetite and lameness
- low fever (40^{o}C– 40.5^{o}C) in some pigs
- morbidity very variable from very low to very high and no mortality
- no effect on reproductive performance
- outbreaks are mostly self-limiting, lesions lasting approximately 1–2 weeks
- some herds have had persistent disease with about 5% of pigs each week showing lameness and vesicular disease
- significant presence of Seneca Valley virus RNA in the serum of pigs exhibiting vesicular and erosive lesions
- US study following finishers over time has found PCR positive oral fluid samples for four weeks so beyond resolution of vesicular lesions

ETNL:

- sudden onset mortality of neonatal piglets (5-70%)
- in affected litters, most neonatal piglets die

- most deaths occur 0-3 days old, up to 7-days-old may die or waste, older piglets unaffected
- deaths rapid (5-6 hours), not starvation – stomachs contain milk
- sometimes concurrent lethargy, neurological signs and/or diarrhoea in neonatal piglets
- surviving piglets in herds affected with piglet mortality rarely show vesicles, sows may
- outbreaks are self-limiting, lasting approximately 1–2 weeks
- PCR detection of SVV in lung, heart, liver, spleen, kidney and intestine of piglets from ETNL outbreaks but no pathology to explain deaths
- US study following unaffected and affected litters has found SVV in sows and piglets in both

The two age-related disease presentations described have occurred together on breeding units with PIVD in sows preceding piglet mortality due to ETNL in a recent US case, while in Brazil, ETNL cases preceded reports of PIVD in sows, possibly because the vesicles were mild and overlooked.

4. Experimental infection

In October 2015, the USDA and Iowa State University reproduced vesicular disease (classic lesions on snout, oral cavity and feet) by experimental infection of growing pigs in a study conducted by Dr Kelly Lager's group (USDA, Ames, IA - USA) using a contemporary 2015 US SVV field isolate from Dr KJ Yoon (Iowa State University, Ames, IA - USA). The findings were shared at the Swine Disease for Practitioners Conference at Iowa State University in November, 2015. The field isolate was from a case which had been investigated by animal health officials and notifiable vesicular diseases had been ruled out by testing.

5. Impact of disease

The main impact relates to the fact that the PIVD lesions closely resemble notifiable vesicular diseases (FMD, SVD, VS). Incidents have been reported to the Animal Health authorities and the investigations have required testing to rule out classical vesicular disease. This is costly and disruptive to the AH authorities and pig industry, especially when vesicles are detected at abattoirs. There is concern in Brazil that this PIVD could result in complacency with respect to reporting vesicular disease as suspect notifiable disease. The recommendation is that all disease incidents with any vesicular lesions present should be reported and trigger notifiable disease investigations.

There is minimal production loss in pigs affected with PIVD as it is clinically mild and of short duration, although lameness can cause concern if lesions become secondarily infected. The piglet mortality in ETNL is clearly a loss but is also very transient and only affects piglets up to one week old. There are no reports of repeat outbreaks in affected herds in Brazil so far.

In Brazil, up to 80% of the industry is estimated to have been affected between October 2014 and March 2015 with rapid spread across the country (SE to Midwest to South) into six states in three geographical regions (Leme and other, 2015 and Vannucci and other, 2015). The rapid emergence of SVV in Brazil suggests that infection was introduced into a naïve national herd.

In the US, from July to early November 2015, Seneca Valley virus has been detected in around 100 pig herds; around 38 breeding farms and 30 farms with growing pigs, rest unknown. Both commercial and exhibition/show pigs have been affected. These were investigated and negated by testing for notifiable vesicular diseases. There has been a sharp decline in SVV outbreaks since November 2015 in the US. Seroprevalence studies are still to be undertaken when an ELISA has been validated, it is suspected that SVV may be endemic in some areas of the US.

6. Spread of disease

The routes of transmission between herds and pigs are still unknown but there have not been obvious links with pig or semen sources and indirect virus transmission is considered to have been involved in spread of infection. Preliminary data from Brazil on risk factors show:

Positively associated factors: Neighbouring farm with ETNL, cattle nearby to unit, pelleted feed, bovine or swine plasma in feed (bovine had higher odds), some specific vaccines.

Not associated: feed company, source of corn, genetics, gilt source (internal external), equipment sharing, blood/bone meal in feed, water source, perimeter fencing, semen source.

There is limited published data and many uncertainties including routes and period of virus excretion, whether carrier status exists, the role of non-porcine hosts, virus survival etc. Samples from field studies have detected virus in oral fluids for at least four weeks from start of outbreak and beyond resolution of vesicular lesions. Virus has been detected in one boar's semen for a month in a field outbreak.

As the virus is a member of the *Picornaviradae* family of non-enveloped single-stranded RNA viruses (of which foot-and-mouth disease viruses, polioviruses and rhinoviruses are also members) it is likely to be relatively environmentally stable. Excretion of these viruses occurs in faeces, saliva and the presence of a viraemic stage means that blood, meat and meat products and other products of animal origin may be a source of virus with transmission pathways relating to ingestion or inhalation of these secretions, excretions or products, or to fomites contaminated with them. Therefore, although there are no proven transmission routes for Seneca Valley virus, a range of transmission pathways should be considered until further evidence is available. In addition, as the lesions in clinical disease involve the skin and feet, and there is a viraemic stage, mechanical transmission by vectors such as biting flies cannot be ruled out. A preliminary outbreak assessment identifying potential risk pathways for entry of SVV into the UK has recently been published by the International Disease Monitoring Team in APHA and is available on this link: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/510872/poa-seneca-america.pdf

7. Virology and testing

Knowles and others (AASV) characterised an unknown picornavirus isolate from US pigs from 1988 and were also provided with a sequence of a cell culture contaminant and found both to be a novel virus, named Seneca Valley virus (or *Senecavirus* A) . They also studied SVV isolates from pigs with and without vesicular lesions in different US states in subsequent years, all of which appeared to belong to the same genetic lineage suggesting recent emergence in US pigs in the early 1980s. Initial sequence analysis suggests that a strain of Seneca Valley virus has recently emerged in Brazil and similar contemporary strains have recently been detected in the US with 98.6 to 100% similarity. There is lower similarity (86.7 to 90.5%) between the Seneca Valley virus from current cases and previous Seneca Valley virus detected in pigs in the US and Canada in previous years, consistent with the evolution of a highly mutable RNA virus. Recent retrospective PCR screening of samples at the veterinary diagnostic laboratories at the Universities of Minnesota and Iowa has detected Seneca Valley virus in samples from a small number of herds (1.2% cases, 0.45% samples) in three US States, these herds did not have vesicular lesions evident. This points to low level circulation of virus. Retrospective investigation of material stored from sporadic, previously undiagnosed US cases of PIVD and ENTL dating back to the 1990s, has indicated presence of Seneca Valley virus in some. Further analysis is in progress to investigate the genetic diversity and evolution of Seneca Valley virus.

An ELISA is being validated now that experimental positive sera are available – seroprevalence studies can then be undertaken.

No virological or serological testing for Seneca Valley virus has been performed on pigs in the UK but it is considered that the national herd is likely to be naïve. The most likely alert to the presence of the vesicular disease manifestation in GB would be a report case to APHA of suspect notifiable vesicular disease in pigs as occurred in both Brazil and the US. It is highly likely that testing at Pirbright would then be required to negate notifiable vesicular disease. This provides the opportunity for submitted material to be tested for Seneca Valley virus at Pirbright once negated for notifiable disease. No notifiable disease investigations fitting the description of PIVD have been reported to APHA field services from 2014 to date.

An RT-PCR for Seneca Valley virus is being used in Brazil and the US. Serological tests being used in the US at present are reportedly not yet fully reliable.

8. Global and GB status

These disease manifestations associated with Seneca Valley virus detection have only been reported in Brazil and North America to date. Sporadic PIVD has been described in Australia, Italy and New Zealand but Seneca Valley virus was not investigated. There was reference in Leme and others (2015) to a 2007 vesicular disease investigation in pigs in Northern Ireland however the features of this incident provided by DARD do not raise any suspicion of possible PIVD.

No testing for Seneca Valley virus has been performed on pigs in the UK. No recent vesicular disease reports have been made to suggest that PIVD due to SVV is present or emerging. No testing of archived tissues or sera has been undertaken to determine if there is exposure to non-disease associated SVV in UK pigs.

If ETNL associated with Seneca Valley virus were to occur in GB, unless PIVD was seen concurrently, it may be not be investigated by farmers if mortality was low especially as it is transient and affects neonatal piglets. The higher the mortality, the more likely it would be for piglets to be submitted to APHA, SAC CVS, or external post-mortem providers for diagnostic investigation. The absence of gross and microscopic pathological findings means that these may result in being undiagnosed cases of systemic, enteric or nervous syndrome with clinical signs of found dead, diarrhoea or nervous disease being most likely. Diagnosis not reached (DNR) analysis of submissions with these presenting signs, and for systemic, enteric and nervous syndromes in neonatal piglets for the first nine months of 2015 showed that there were no statistically significant increases or incidents of concern.

9. Host range

a) Humans - the virus can infect humans but is considered harmless. In 2002, it was found as a contaminant in tissue culture, then found to be able to infect human cells in tissue culture, then found to be oncolytic so has been looked into as a tumour treatment (Burke and others, 2015). When inoculated into humans it is harmless, they seroconvert and become virus negative following viraemia and (in some) faecal excretion (Burke and others, 2015), the virus targets and replicates in tumour cells. Knowles and others (AASV) report limited serological analyses in the general human population and farmers which showed only one to have low level neutralizing antibody to Seneca Valley virus. Koppers-Lalic and others (2011) refer to this as evidence that exposure to Seneca Valley virus is not prevalent in the human population and is classified as a non-human virus not considered to be naturally infecting humans. The Human Animal Infections and Risk Surveillance (HAIRS) Group have been made aware of SVV in the Americas and have confirmed that SVV is not used in the UK for treatment of humans, If UK patients were enrolled in studies, the treatment would take place in US and in the studies done, one would not expect viral excretion in faeces on their return to UK.

b) Cattle - there is historical serological evidence reported of Seneca Valley virus infection in cattle in the US (Knowles and others, AASV). Also two risk factors identified for affected pig farms in Brazil were farms being close to cattle and bovine plasma in feed. The detection of Seneca Valley virus in 2002 as a cell culture contaminant was presumed to have been through introduction in bovine serum or porcine trypsin. There has been no increase in vesicular disease reports in cattle in Brazil or US indicating that if cattle are involved in virus transmission or acting as a virus reservoir, it is not causing disease in them. The APHA Cattle Expert Group has been made aware.

c) Rodents – seropositivity in rodents is reported. Koppers-Lalic and others (2011) refer to a study in mice which showed no evidence of horizontal transmission from mice injected with SVV and mixed with naïve mice. The closest evolutionary relatives to Seneca Valley virus are cardioviruses, which are principally rodent viruses.

d) Other - Further information about non-porcine hosts may come out of Brazilian and US studies on affected farms.

10. Knowledge gaps.

Investigations in the US continue into SVV infections in pigs and the epidemiology of the disease to address the many uncertainties including routes and period of virus excretion, whether carrier status exists, the role of non-porcine hosts, virus survival etc. Research is being commissioned in the US to address the key gaps in knowledge and includes:

- Confirmation of Seneca Valley virus as causal agent of ETNL and VS by challenge studies.
- Characterise Seneca Valley virus from diseased and non-diseased farms
- Development and validation of molecular and antibody-detection diagnostic tools.
- Describe population and individual infection dynamics (shedding duration and route)
- Perform epidemiological studies on regional prevalence and distribution.
- Evaluate the stability of Seneca Valley virus in disinfectants and the environment.
- Study the prevalence of Seneca Valley virus in other significant hosts and products.
- Conduct outbreak investigations including environmental and potential vector testing

11. References

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