

# PORCINE ASTROVIRUS



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## SUMMARY

### Etiology

- Porcine astrovirus (PAstV) is a non-enveloped RNA virus in the family *Astroviridae*.
- There are five known lineages with great genetic variability.

### Cleaning and Disinfection

- Astrovirus (AstV) is resistant to heat and requires very acidic pH for inactivation; it can survive for a long time in the environment.
- There is little information on specific disinfectants for AstVs. Non-enveloped viruses are typically susceptible to aldehydes and halogens (bleach).

### Epidemiology

- AstVs affect a wide variety of species and are mostly associated with gastrointestinal disease. PAstV was first isolated from the feces of pigs in 1980. AstVs have also been linked to neurological disease in humans, mink, cattle, and sheep. Recently, PAstV-associated polioencephalomyelitis has been reported in pigs in Hungary and the United States. PAstV has previously been found in pigs with congenital tremors but the significance of this is unknown.
- The zoonotic potential of AstVs is unclear; porcine-human AstV recombinants have been documented and human-to-pig transmission is suspected.
- PAstV has been isolated from pigs worldwide. Human AstV infections are most common in the winter, but there is little information about seasonal incidence of AstV infection in pigs. In Hungary, the incidence of PAstV-associated neurological disease spiked during the autumn.
- Prevalence of PAstV in swine feces can be very high; however, viral co-infection with other enteropathogens (e.g., rotavirus, transmissible gastroenteritis virus, porcine circovirus-2, and porcine hemagglutinating encephalitis virus) is often observed. The reported case fatality rates for PAstV-associated neurological disease on affected U.S. swine farms were 75 and 100%. In Hungary, about 1.5–2.0% of pigs were affected monthly by PAstV-associated neurological disease (over a two-year period).

### Transmission

- Transmission of PAstV is thought to be fecal-oral.

## **Infection in Swine/Pathogenesis**

- PAsV is thought to cause mild, self-limiting secretory diarrhea. Young pigs are most affected. Viral co-infections may contribute to observed clinical signs.
- Reported neurological signs associated with PAsV include hind limb weakness, posterior paraplegia, quadriplegia, convulsions, loss of consciousness, and flaccid paralysis of muscles. Congenital tremors may be related to PAsV infection in piglets but this is unclear.

## **Diagnosis**

- AstV is difficult to propagate. Reverse transcription polymerase chain reaction (RT-PCR) assays are used to detect viral RNA. Immunohistochemistry and indirect immunofluorescence have both successfully detected AstV antigens.
- Enzyme-linked immunosorbent assay (ELISA) and serum neutralization have been used to detect antibodies to AstV in pigs.

## **Immunity**

- There are currently no available vaccines against AstV in any species.

## **Prevention and Control**

- Cleaning and disinfection of affected facilities is critical to prevent enteric disease in swine.
- Standard biosecurity practices should also be in place.

## **Gaps in Preparedness**

- More information is needed about PAsV and its role as a swine pathogen. The virus has been associated with both gastrointestinal and neurological disease.
- Although no zoonotic cases have been reported, the potential for cross-species transmission exists. Vaccine development may be beneficial to both the human and animal medical communities.
- To prevent and control outbreaks, more information is needed on cleaning and disinfection protocols.

## OVERVIEW

Porcine astrovirus (PAstV) is a non-enveloped RNA virus belonging to the family *Astroviridae*. There are at least five distinct lineages (PAstV-1 to PAstV-5), all of which have been known to circulate in swine herds in the United States. Isolates from a single herd of pigs have shown high genetic diversity and variability. Virulence appears to vary by serotype.

Astrovirus (AstV) has a wide host range but infection is generally species-specific. PAstV is found worldwide with variable prevalence among herds. In swine, the virus causes a mild, self-limiting secretory diarrhea predominantly in piglets and weanlings; however, it has also been isolated from healthy adult pigs. In humans, astrovirus is the second leading cause of infantile gastroenteritis in children after rotavirus. AstVs have also been identified in humans, mink, cattle, and sheep with central nervous system (CNS) signs. More recently, PAstV-associated neurological disease has been identified on swine farms in the United States and Hungary. Though PAstV has also been found in pigs with congenital tremors in Sweden, the significance of these findings is unclear.

Though difficult to isolate, AstV has been successfully propagated in porcine kidney cells. Fecal samples are the primary source for virus isolation, although there are reports of extraintestinal AstV isolation from pigs, birds, humans, and mink. Reverse transcription polymerase chain reaction (RT-PCR) assays are used to detect viral RNA. Immunohistochemistry and indirect immunofluorescence have both successfully detected AstV antigens. Enzyme-linked immunosorbent assay (ELISA) and serum neutralization have been used to detect antibodies to AstV in pigs.

There are currently no available vaccines against AstV in any species. Promising polyclonal antibody titers have been shown in rabbits and chickens inoculated with a baculovirus-produced chicken AstV (CAstV) capsid protein vaccine. Whether or not the antibodies are protective remains to be seen. The development of this antigen has been utilized in diagnostic tests and vaccine trials, but further work is required.

AstV is a major concern in human infants, but no zoonotic cases have been reported to date. The ability of the virus to rapidly mutate, and the potential for an animal to become co-infected with two different strains, sets the stage for a recombination event from which a zoonotic strain could emerge. AstV is a public health concern in humans as it has been implicated in foodborne illnesses and can survive in ground water. Further research and investigation into the pathogenesis of AstV and vaccine development would benefit both veterinary and human medicine.

## LITERATURE REVIEW

### 1. Etiology

#### 1.1 Key Characteristics

Porcine astrovirus (PAstV) is a small, non-enveloped, single-stranded, positive-sense RNA virus named for its 5–6 pointed star-like morphology.<sup>1</sup> Astrovirus (AstV) belongs to the family *Astroviridae*, which is divided into two genera, *Mamastrovirus* and *Avastrovirus*. These genera affect mammals and avian species respectively.<sup>1</sup> PAstV was first recognized in the feces of diarrheic pigs from the United Kingdom in the 1980s.<sup>2</sup>

#### 1.2 Strain Variability

The genome of AstV is composed of three open reading frames that encode for nonstructural proteins (ORF1a), RNA-dependent RNA polymerase (ORF1b), and capsid proteins (ORF2) respectively.<sup>3</sup> An untranslated region (UTR) is present at the 5′ end. The 3′ end contains both a UTR and a poly-A tail.<sup>4</sup> There is a highly conserved nucleotide sequence among PAstV at the 5′ end of ORF2 which is useful for genomic analysis and PCR detection.<sup>5</sup>

A study from Canada found a highly conserved nucleotide sequence within the RNA-dependent RNA polymerase gene located between ORF1b and ORF2 in the genome of the *Astroviridae* family.<sup>5</sup> Analysis further grouped PAstV into 3 subgroups or clusters. Group I strains were closely related to PAstV 1, human AstV, and feline AstV strains; group II strains had little homology and lacked the nucleotide sequences between ORF 1b and ORF2 that is highly conserved among the other PAstV; and group III strains were related to mink, ovine, and some newly discovered human AstV strains.<sup>5</sup> This same study showed no evidence of recombination in AstV of swine.<sup>5</sup>

The diversity of PAstV is supported by data showing that strains collected from swine on a single farm and organized into subgroups seem to have relatively low homology.<sup>6</sup> Within PAstV, there are five distinct lineages (PAstV-1 to PAstV-5), each of which have been known to circulate in herds in the United States.<sup>7</sup> Based on phylogenetic analysis, each of the five lineages may have an independent origin, with vast genetic variability evidenced by greater homology between strains of different lineages than within strains of a single lineage.<sup>8</sup> Two PAstVs previously identified in pigs with and without congenital tremors belonged to lineages PAstV-2 and PAstV-5.<sup>9</sup> Isolates associated with recently reported neurological disease in the United States<sup>10</sup> and Hungary<sup>11</sup> have been classified as PAstV-3. PAstVs can also be classified into seven genotype species (MAstV 3, 22, 24, 26, 27, 31, and 32).<sup>12</sup> Co-infections of a single animal with multiple PAstV strains has been reported.<sup>7</sup>

It was previously accepted that AstVs were host restricted and species-specific, but phylogenetic analysis has suggested the possibility of interspecies recombination.<sup>13</sup> This evidence, coupled with the diverse array of species affected and the genetic diversity within *Astroviridae*, makes interspecies transmission with virus adaption a possibility.<sup>4</sup> A newly described PAstV detected in U.S. pigs with neurological disease was found to be more closely related to neurotropic AstVs from humans, minks, cows, and sheep than to other porcine isolates.<sup>10</sup> Evidence of cross-species AstV transmission exists between sheep and cattle.<sup>14</sup> A Chinese study published in 2011 showed that one particular PAstV strain, JWH-1, was closely associated with a novel AstV of deer.<sup>15</sup> Similarly, a bovine AstV isolated from the feces of cattle in Japan was found to cluster with PAstV; this isolate also contained an ORF2 region similar to ovine AstV.<sup>16</sup>

## 2. Cleaning and Disinfection

### 2.1 Survival

AstV remains stable and infectious within groundwater.<sup>17</sup> AstV persists in tap water at 4°C for 45 days with only a 1.2 log titer reduction (LTR).<sup>18</sup>

### 2.2 Disinfection

Mammalian AstVs are resistant to inactivation by acidic pH, heat, many detergents, and lipid solvents. Experimentally, PAstV resisted lipid solvents and remained stable when exposed to temperatures of 50°C for 30 minutes.<sup>1</sup> PAstV also retained its infectivity at pH 4.0 for 3 hours, but exposure to pH 3.0 for 3 hours decreased infectivity two-fold.<sup>1</sup> Infectivity of AstV when exposed to chlorine displayed 2.5 LTR after 1 hour contact time.<sup>18</sup>

## 3. Epidemiology

### 3.1 Species Affected

The family *Astroviridae* contains two genera: *Mamastrovirus* consisting of six mammalian species-specific viruses, and *Avastrovirus*, consisting of three avian species-specific viruses. AstV belonging to *Avastrovirus* cause more severe disease in their host species than do any of the *Mamastrovirus* viruses.

AstV was first detected in feces of human infants, and later, a cytopathic porcine strain was isolated from diarrheic feces of swine in 1980.<sup>1,2</sup> In humans, AstV is a recognized cause of diarrhea in the young, elderly, and immunocompromised.<sup>19</sup> Whether PAstV is a primary cause of porcine diarrhea remains unclear. The virus has been found in both symptomatic and asymptomatic pigs. Experimental infection with PAstV can cause diarrhea,<sup>1</sup> and co-infection with multiple strains of PAstV and/or other enteric viruses seems to be common.<sup>6,7</sup> AstV has been also detected in diarrheic cattle. Again, however, the association between AstV and diarrhea has been questioned, largely because experimental infections in cattle have not consistently produced disease.<sup>20-22</sup>

AstV has been found in other species (some with and some without enteric disease) including sheep,<sup>23,24</sup> farmed mink,<sup>25</sup> red deer,<sup>26</sup> European roe deer,<sup>27</sup> water buffalo,<sup>28</sup> yaks,<sup>29</sup> camels,<sup>30</sup> dogs,<sup>31,32</sup> cats,<sup>33,34</sup> rats,<sup>35</sup> rabbits,<sup>36</sup> marmots,<sup>37</sup> porcupines, shrews, and pikas,<sup>38</sup> cheetahs,<sup>39</sup> chickens,<sup>40</sup> ducks,<sup>41</sup> turkeys,<sup>13</sup> insectivorous bats,<sup>42,43</sup> and marine mammals.<sup>44</sup> Less commonly, AstV has been associated with respiratory disease in cattle<sup>45</sup> and in at least one case, a human infant.<sup>46</sup> AstV has also been isolated from nasopharyngeal swabs in camels positive for Middle East respiratory syndrome coronavirus (MERS-CoV).<sup>47</sup>

Recently, AstV has also been linked to neurological disease. As reported by Johnson et al., multiple human cases of AstV-associated encephalitis and meningitis have been identified, predominantly in the immunocompromised.<sup>19</sup> In farmed mink, AstV has been detected in animals with shaking, staggering, and ataxia (shaking mink syndrome).<sup>48</sup> Multiple reports have associated AstVs with nonsuppurative encephalitis in cattle<sup>49-57</sup> and sheep.<sup>14,58</sup> Neurological disease involving PAstV has been described in a piglet and two sows from the United States (identified at the Iowa State University Veterinary Diagnostic Laboratory)<sup>10</sup> and six 25-to-35 day old pigs from Hungary.<sup>11</sup> Archival brain and spinal samples from Hungary similarly tested positive for PAstV (from 2011 and 2014).<sup>11</sup> Non-CNS samples from pigs in Hungary (from the respiratory system, lymphoid system, circulatory system, and salivary glands of affected animals) were also positive for PAstV, but the virus was largely absent from feces.<sup>11</sup> In 2014, PAstV was associated with congenital tremors in piglets from an organic herd in Sweden; however, the virus was also demonstrated in the brain tissues of non-diseased controls, making the significance of these findings unclear.<sup>9</sup>

### 3.2 Zoonotic Potential

Emergence of porcine-human AstV recombinants has occurred in areas where pigs and humans live in close proximity with frequent interaction.<sup>4</sup> Viral transmission from humans to pigs is suspected while the reverse has not been described.<sup>4</sup>

Humans occupationally exposed to turkeys have been found to seroconvert to Turkey AstV-2 (TAstV).<sup>48</sup> A mammalian-like AstV was detected in the avian European Roller species for the first time in China in 2015.<sup>59</sup> Phylogenetic analysis of Canadian isolates showed that PAstV-1, PAstV-2, and PAstV-3 were more closely related to human AstVs and AstVs from other animals than to each other.<sup>7</sup>

A recombination event may have occurred between a human and sea lion isolate, suggesting either a human, a sea lion, or a third host was infected with both isolates simultaneously, resulting in emergence of a new strain.<sup>44</sup>

### 3.3 Geographic Distribution

PAstV has been isolated from pigs worldwide irrespective of age, season, or climate. PAstVs have been found in South Africa, the Czech Republic, Hungary, and Canada,<sup>5</sup> Columbia,<sup>4</sup> Croatia,<sup>8</sup> United States,<sup>7</sup> South Korea,<sup>60</sup> and China.<sup>15</sup> Distribution of each lineage is variable. PAstV-1 is predominant in Japan while PAstV-4 predominates in Hungary, South Korea, and the United States. PAstV-1, -2, and -3 are present in Canada.<sup>61</sup> In 2014, Croatia reported the presence of PAstV-3 viruses in a herd, the first time PAstV-3 has been detected in Europe.<sup>8</sup> PAstV associated with neurological disease has been reported recently in Hungary<sup>11</sup> and the United States.<sup>10</sup> PAstV was also found in pigs with congenital tremors in Sweden in 2014, although the clinical significance of this remains unclear.<sup>9</sup>

Human AstV seem to have the highest incidence of infection during winter months in temperate climates, but infections have also been reported in spring and summer months.<sup>4</sup> Little has been published regarding seasonal incidence of PAstV. However, in Hungary, reported cases of PAstV-associated neurological disease seemed to spike in the autumn.<sup>11</sup>

### 3.4 Morbidity and Mortality

Prevalence of PAstV on a single farm is variable and may be geographically dependent. Diagnostic testing of diarrheic samples from throughout North America found PAstV in 61.7% of samples, 20% of which were positive for PAstV alone while the remainder of positive samples contained PAstV and another known diarrhea-causing virus (such as rotavirus, transmissible gastroenteritis virus, porcine circovirus-2, and porcine hemagglutinating encephalitis virus).<sup>6</sup> A report from Canada detected PAstV-positive RT-PCR results from 80% of healthy pigs at time of slaughter for market.<sup>5</sup> Fecal samples from a high density farm in North Carolina had PAstV present in 75% of samples taken from healthy and diarrheic piglets.<sup>3</sup> Persistent infections have been reported in insectivorous bats<sup>42</sup> and in a human child,<sup>62</sup> and may be a reasonable explanation for AstV detection in fecal samples of a high percentage of apparently healthy adult pigs.<sup>63</sup> Seroconversion rates of swine herds have ranged as high as 83% in healthy adult pigs.<sup>1</sup>

In the U.S., pigs with PAstV-associated neurological disease were documented in a multistate swine production system in 2017. Samples from neurologic cases were submitted for testing on three occasions over a 9-month period. An affected sow farm reported a case-fatality rate of 100%, while two commercial grow-out facilities reported a case-fatality rate of 75%.<sup>10</sup> In Hungary, the index farm had experienced episodes of neurological disease over a two-year period (2015–2017).<sup>11</sup> About 30–40 weaned pigs (1.5–2% of the farm population) were affected each months. A spike in cases (about 80 cases/month, 4% of farm population) was seen during the autumn months.<sup>11</sup>

## 4. Transmission

All published reports support the fecal-oral route in PAsV transmission. Cesarean-delivered, colostrum-deprived (CDCD) gnotobiotic piglets developed mild diarrhea five days post-inoculation with filtered feces from a diarrheic piglet.<sup>64</sup> Following euthanasia, PAsV presence was confirmed in intestinal tissues by electron microscopy.<sup>64</sup> CDCD pigs orally inoculated with a PAsV isolate also developed mild diarrhea, seroconverted, and shed infectious PAsV in their feces.<sup>1</sup>

## 5. Infection in Swine/Pathogenesis

The pathogenesis of PAsV-induced diarrhea is poorly understood, especially in non-human mammals, and was previously thought to localize to the intestine. Bovine AstV has been shown to be M-cell trophic throughout the intestine resulting in mild pathology even in the absence of clinical disease.<sup>22</sup> A study of TAsV-2 in young poult revealed mild histopathological changes of the intestines, lacking inflammatory lesions and cell death, despite severe diarrhea.<sup>65</sup> A proposed mechanism for this is an increase in TGF- $\beta$ , a potent immunosuppressive cytokine.<sup>65</sup> A human AstV strain was found to experimentally induce diarrhea by disrupting tight junctions between intestinal epithelial cells, thus increasing permeability and access of the virus to underlying structures, including blood vessels.<sup>66</sup> Despite AstV being detected systemically, it is believed that viral replication is primarily limited to the absorptive epithelial cells of the intestinal tract.<sup>65</sup>

Extraintestinal AstV has been found in the brain tissue of mink with shaking mink syndrome,<sup>48</sup> from the brain of a human child suffering encephalitis,<sup>67</sup> and from CNS tissues of pigs with neurological disease in Sweden,<sup>9</sup> Hungary,<sup>11</sup> and the United States.<sup>10</sup> The virus has also been found in the liver of ducks with hepatitis<sup>41</sup> and the blood of pigs with PAsV-positive fecal samples.<sup>63</sup>

### 5.1 Clinical Signs

Pigs experimentally inoculated orally with PAsV develop a mild, self-limiting enteric disease characterized by secretory diarrhea.<sup>1</sup> Natural infections are more severe, likely due to viral co-infections contributing to clinical signs.<sup>1</sup> Healthy adult pigs are less likely to show gastrointestinal clinical signs when infected with PAsV.<sup>1</sup>

PAsV was found in pigs with and without congenital tremors in Sweden in 2014.<sup>9</sup> More recently, in 2017, PAsV-3 was identified in three U.S. pigs (a 5-week-old piglet and two sows) with nonsuppurative polioencephalomyelitis. All pigs reportedly exhibited hind limb weakness to quadriplegia and occasional convulsions.<sup>10</sup> Affected pigs from the 2015–2017 outbreak in Hungary (25-to-35 days old) presented with posterior paraplegia.<sup>11</sup> Loss of consciousness, paresis, and serious flaccid paralysis of muscles was later seen. Affected pigs were unable to eat or drink; they died from dehydration or were euthanized.<sup>11</sup> Hungarian archival brain and spinal cord homogenates that tested positive for PAsV from were collected from pigs that suffered from staggering and paralysis.<sup>11</sup> In cattle with AstV-associated encephalitis, one study found that the most frequently observed clinical signs were decreased awareness of surroundings, cranial nerve dysfunction, and recumbency.<sup>68</sup> AstV has also been linked to shaking mink syndrome, which results in ataxia, abnormal gait, tremors, and other neurological signs.<sup>48</sup>

Clinical signs vary among other species. Renal and hepatic involvement accompany intense enteric disease in avian species.<sup>4,41,59,65</sup>

### 5.2 Post Mortem Lesions

Studies investigating the anatomic pathology of PAsV are limited, likely due to the lack of PAsV-caused mortality. Minimal gross changes have been seen upon necropsy of PAsV-infected pigs while histopathological alterations have not been investigated.<sup>64</sup> In PAsV-associated cases of neurological disease, polioencephalomyelitis and neural necrosis have been seen.<sup>11</sup> In one instance, PAsV was

associated with congenital tremors; reported lesions included mild to moderate vacuolar changes of the white matter in the cerebrum, brain stem, and cerebellum.<sup>9</sup>

There have been investigations into the pathologic changes in turkey poults experimentally infected with TAsV-2. Upon post mortem examination, the intestines were dilated, 3–5 times normal size, and distended with gas and fluid.<sup>65</sup> Despite severe diarrhea, histopathology was unremarkable; observed changes included mild villous atrophy, very mild crypt hyperplasia, and minimal mononuclear infiltrate.<sup>65</sup>

## 6. Diagnosis

### 6.1 Clinical History

PAstV should be suspected in any piglet with diarrhea.<sup>4</sup> Viral co-infections are common.<sup>6</sup> PAstV should also be considered in cases of neurological disease.

### 6.2 Tests to Detect Nucleic Acids, Virus, or Antigens

Virus isolation for PAstV has proven difficult. PAstV isolation and propagation requires the use of pig kidney cells with the presence of trypsin.<sup>1</sup> Because of this, direct electron microscopy is often used to confirm PAstV infections clinically.<sup>64</sup>

Reverse transcription polymerase chain reaction (RT-PCR) is utilized to diagnose and analyze AstVs. Primers used for detection have been developed for bats which targets the 3' end of the ORF1b gene, a highly conserved region of the *Astroviridae* genome which encodes for the RNA dependent RNA polymerase.<sup>42</sup> This primer has been used in many studies to detect any member of the *Mamastrovirus* genus.<sup>42</sup> Primer sets specific for porcine strains have also been described.<sup>5</sup>

The PAstVs associated with congenital tremors in Sweden were identified in brain tissues by nested pan-AstV RT-PCR. In the United States, metagenomic sequencing was used to identify PAstV in samples from pigs with neurological disease (cerebrum, cerebellum, brain stem, and spinal cord).<sup>10</sup> Near-complete genomes obtained from one piglet and one sow were both identified as PoAstV3/USA/IA/7023/2017, which clustered with other known PAstV-3 strains.<sup>10</sup> Swine brain and spinal cord samples from Hungary (both from the current outbreak and previous outbreaks) were tested for PAstV using RT-PCR and in situ hybridization.<sup>11</sup> Isolates were also identified as PAstV-3.

Due to the limited knowledge of the pathogenesis of AstV and its poor growth in cell culture, development of virus-specific antigen tests is minimal. A baculovirus-produced CAstV capsid protein inoculated into rabbits resulted in polyclonal antiserum production, which was shown to be useful in indirect immunofluorescence, immunohistochemistry, and virus neutralization assays.<sup>40</sup> Indirect immunofluorescence and immunohistochemistry have been successfully performed for PAstV.<sup>1,40</sup>

### 6.3 Tests to Detect Antibody

Enzyme-linked immunosorbent assays (ELISAs) have been used for determining the rate of human seroconversion to TAsV.<sup>13,40</sup> Baculovirus-produced TAsV capsid protein was used as capture antigen while polyclonal anti-TAsV from capsid protein immunized rabbits was used for detection.<sup>13,40</sup> Similarly, baculovirus-expressed CAstV capsid protein was used as capture antigen in an ELISA to detect anti-CAstV antibody in chicken serum.<sup>15</sup> Serum neutralization has been used to accurately detect PAstV.<sup>1</sup>

## 6.4 Samples

### 6.4.1 Preferred Samples

PAstV has most successfully and consistently been isolated from the feces of affected animals.<sup>64</sup> More recently, PAstV has been isolated from the blood of pigs with PAstV-positive fecal samples.<sup>63</sup> The virus has also been found in CNS tissues of pigs with neurological disease.<sup>9,11</sup> Avian species appear to have



more systemic involvement with AstV infections; virus has been isolated from thymus, Bursa of Fabricius, spleen, liver, and jejunum.<sup>4</sup>

#### *6.4.2 Oral Fluids*

The suitability of oral fluids for PAsV diagnosis has not been evaluated.

## **7. Immunity**

### **7.1 Post-exposure**

Pigs experimentally infected with PAsV shed infectious virus in their feces seven days post-infection and developed neutralizing antibody titers 14 days post-infection.<sup>5</sup> Chickens, vaccinated with a baculovirus-expressed CAstV capsid protein fused to GST and administered with oil adjuvant, developed CAstV-specific antibody titers four weeks post-vaccination; however, chickens vaccinated with baculovirus-expressed CAstV capsid protein alone, in combination with oil adjuvant, did not develop virus-specific antibody until four weeks after a booster vaccination. In both experiments, the majority of chickens produced CAstV neutralizing antibody.<sup>40</sup> Whether the anti-CAstV antibodies produced by these animals will protect against challenge remains to be determined.

### **7.2 Vaccines**

There are no commercially available PAsV vaccines. Chickens immunized with a baculovirus-expressed CAstV capsid protein developed virus-specific antibody, and this technique of producing virus-like particles for vaccination shows great promise but is not currently available commercially.<sup>40</sup>

Antigenic diversity among PAsV strains in a given location<sup>6</sup> presents a challenge for vaccine development and disease prevention.

### **7.3 Cross-protection**

Cross protection has not been observed in humans with HAstV-1 antibodies when exposed to TAstV-2.<sup>13</sup> The antibodies appear to be specific to their respective capsid proteins.<sup>13</sup> Little is known of the antigenic relationship among the many strains of AstV. Antibodies to PAsV do not react with bovine AstV.<sup>69</sup>

## **8. Prevention and Control**

Due to the characteristics of AstV, its ubiquity, and its mutability, preventing AstV infections may prove to be difficult. As a hardy, non-enveloped virus that is resistant to heat and requires very acidic pH for inactivation, it can survive for a long time in the environment.<sup>1</sup> The best means to prevent infection would be immunization of sows allowing passive transfer of antibodies through colostrum to neonates, removal of diarrheic pigs from the herd, and implementation of greater sanitation standards within a facility.

## **9. World Organization for Animal Health Terrestrial Animal Health Code**

PAsV is not covered in 2017 OIE Terrestrial Animal Health Code and there are currently no recommendations on trade restrictions.

## **10. Gaps in Preparedness**

Porcine AstV causes a mild, self-limiting secretory diarrhea predominantly in piglets, but has been isolated from healthy adult pigs as well. The virus has also been recently isolated from pigs with neurological disease. Despite being extremely common in a wide range of hosts, the pathogenesis of AstV is poorly understood. Further investigation is needed to inform producers about prevention and treatment.

Because of its hardiness, mutability, and wide host range, there is potential for AstV zoonotic infection although there have been no reports to date. Despite evaluations of a potential CAstV capsid protein antigen as a vaccine candidate in chickens, little research has been performed evaluating the use of vaccines in swine. Additional investigation would better prepare both the veterinary and medical community in the event of a zoonotic infection and the possibility of an outbreak.

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