

Ju-Yi Peng, Cai-Zhen Jian, Chia-Yu Chang,  
and Hui-Wen Chang

---

## 11.1 Porcine Epidemic Diarrhea Virus Structure and Genome

Porcine epidemic diarrhea (PED) first appeared in England and Belgium in the 1970s. The etiological agent of the disease is porcine epidemic diarrhea virus (PEDV), which belongs to the order *Nidovirales*, genus *Alphacoronavirus*, and family *Coronaviridae* (EN 1977; Bridgen et al. 1993; Duarte et al. 1993). It consists of a single-stranded positive-sense RNA genome of approximately 28 kb in size with gene order 5'-replicase (1a/1b)-S-ORF3-E-M-N-3'. The viral genome encodes three nonstructural protein, Pol 1a/1b and ORF3, and four major structural proteins, the spike (S) glycoprotein, nucleocapsid (N) protein, membrane (M) glycoprotein, and envelope (E) protein. The S protein of PEDV is a type 1 transmembrane envelope protein and consists of the S1 and S2 domains. The S protein is responsible for the viral entry via specific binding of the S1 domain with the cellular receptor, fusion and interaction of the S2 domain with host cellular membrane, and for induction of neutralizing antibodies in the host (Bosch et al. 2003). The M and E proteins are associated with virus assembly via interacting with S and N proteins (Klumperman et al. 1994). The primary role of N protein is to pack the viral genomic RNA into viral particles (Spaan et al. 1983).

---

J.-Y. Peng • C.-Z. Jian • C.-Y. Chang • H.-W. Chang (✉)  
Graduate Institute of Molecular and Comparative Pathobiology,  
School of Veterinary Medicine, National Taiwan University, Taipei 10617, Taiwan  
e-mail: [huiwenchang@ntu.edu.tw](mailto:huiwenchang@ntu.edu.tw)

---

## 11.2 PEDV Transmission

PEDV is mainly transmitted via oral-fecal route, though aerosolized PEDV is also infectious (Alonso et al. 2014). The major transmission source of PEDV may be from the feces or vomitus. Other possible carriers for PEDV may be asymptomatic pigs or persons that carry contaminated fomites from farm to farm (Lowe et al. 2014). Besides horizontal transmission, potential route for vertical transmission of PEDV via sow milk is also suggested (Li et al. 2012; Sun et al. 2012).

---

## 11.3 PEDV Pathogenesis

PEDV establishes its infection majorly in porcine villous enterocytes, which express the cellular receptor, porcine aminopeptidase N (pAPN; CD13) (Li et al. 2007). PEDV replicates in the cytoplasm of villous epithelial cells in the small intestine and sometimes in the colon resulting in severe villous atrophy and leading to mal-absorptive diarrhea (Straw et al. 2006).

In the past, the prevalence of PED was low. It only caused endemic infection with very few mini-outbreaks. Suckling piglets are protected from the disease via maternal antibodies and immunity (Bandrick et al. 2014). The disease majorly appeared in postweaning pigs as the maternal antibody titer drops. Possibly due to the fast turnover time (2–3 days) of enterocytes from crypt stem cells in postweaning pigs as well as the low virulence of traditional PEDV strains, the affected piglets usually show transient diarrhea with low or without mortalities.

Since late 2010, however, new PEDV variants with evidence of increased virulence have been isolated in several countries. The novel PEDV variants attack neonatal piglets regardless of their vaccination status or maternal immunity, which derived from CV777-based vaccination or preexisting historic PEDV infection (Sun et al. 2012; Chiou 2015; Stevenson et al. 2013). Factors underlying the potential pathogenesis of the PEDV outbreaks and the high mortality in piglets include the mutation of the virus (Chiou et al. 2015; Pasick et al. 2014), the lacking of maternal antibodies for protection of the piglets, and the slower turnover rate of enterocytes (5–7 days) of the neonatal piglets as compared to postweaning pigs (2–3 days) (Jung and Saif 2015a; Straw et al. 2006).

---

## 11.4 Clinical Signs and Lesions in PEDV Infection

The major clinical signs of PED are watery diarrhea and/or vomiting. Piglets might die from dehydration and electrolyte imbalance due to severe diarrhea and vomiting. At necropsy, gross lesions majorly include distension of small intestine with

**Fig. 11.1** Gross lesions in a PED-affected 1-day-old piglet. Distension of small intestine with yellowish fluid content and thin and transparent intestinal walls were noted



yellowish fluid, thin and transparent intestinal walls (Fig. 11.1), and the stomach filled with curdle milk. Congestion of mesenteric vessels and edema of mesenteric lymph nodes are often seen. Under microscopic examination, an acute, diffuse, severe atrophic enteritis characterized by reduction in the villous height and crypt depth ratio, villous blunting and fusion, and cell exfoliation on the tips of villous enterocytes are often seen (Straw et al. 2006; Jung and Saif 2015a).

---

## 11.5 Differential Diagnosis Between Diarrheal Pathogens

Several viruses can cause diarrhea in pigs with similar clinical signs and pathologic features to PED. These viruses include porcine deltacoronavirus (PDCoV), transmissible gastroenteritis virus (TGEV), and porcine rotavirus. As listed in Table 11.1, these viral infections exhibit similar clinical signs, age tropisms, replication sites, gross lesions, and microscopic lesions. Therefore, a definitive diagnosis of PED majorly depends on molecular methods.

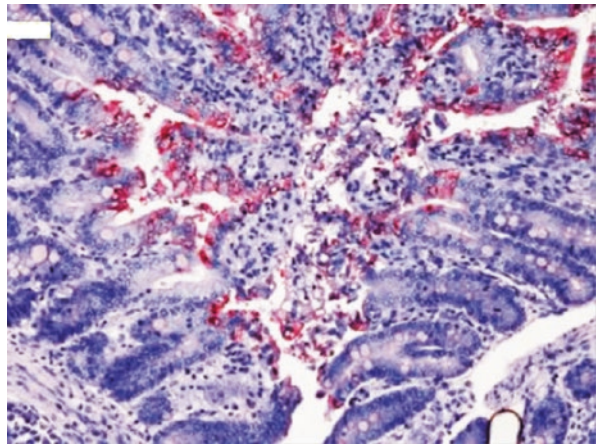
---

## 11.6 Diagnostic Methods of PEDV

Several laboratory diagnostic methods are available for the definitive diagnosis of PEDV infection, such as immunofluorescence assay (IFA) and immunohistochemistry (IHC) by using specific antibodies for the detection of PEDV antigen in paraffin-embedded tissues (Madson et al. 2014) (Fig. 11.2.), enzyme-linked immunosorbent assay (ELISA) for detecting virus or serum antibodies (Okda

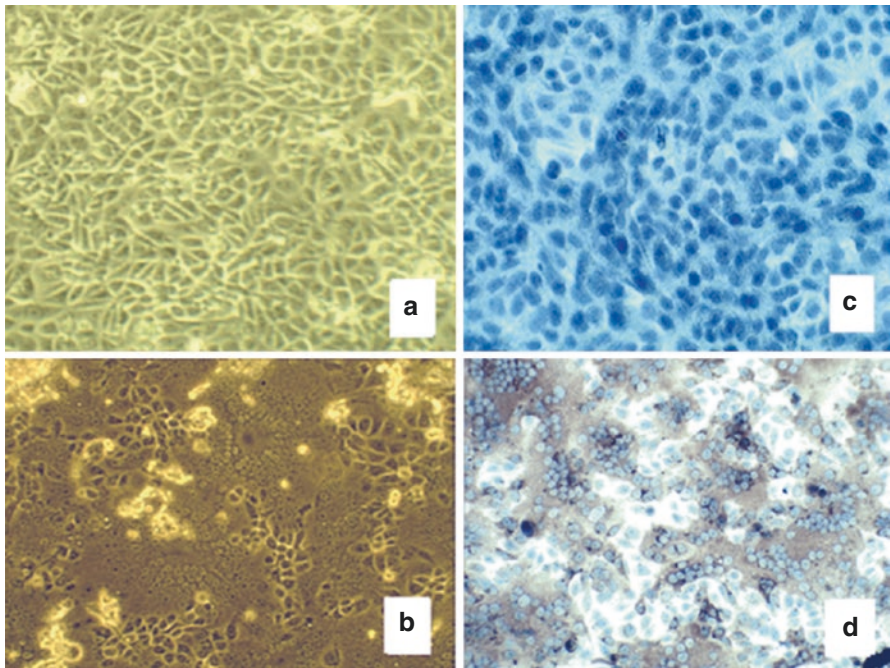
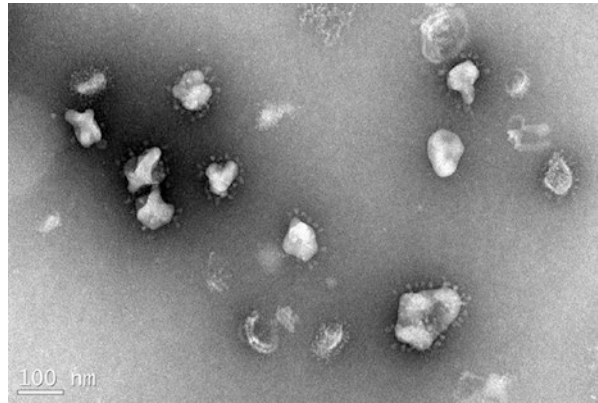
**Table. 11.1** Comparison of clinical and pathologic features among PEDV, PDCoV, PEDV, and TGEV infections

	PEDV	PDCoV	TGEV	Rotavirus
Etiology	Coronavirus	Coronavirus	Coronavirus	Rotavirus
Ages	All ages (Traditional PED: postweaning pigs; novel PED: neonatal piglets)	Young nursing piglets	All ages	Neonates
Replication site	Villous epithelium cells			
Clinical signs	Vomiting and profuse watery, yellowish diarrhea			
Gross lesions	1. The small intestine is distended with yellow, foamy fluid, and the wall is thin and transparent 2. The stomach is distended with curdled milk			
Microscopic lesions	Reduction in villous height to crypt depth ratio; cell exfoliation; vacuolation of superficial epithelial cells	Acute diffuse severe atrophic enteritis and vacuolation of superficial epithelial cells in cecum and colon	Reduction in villous height to crypt depth ratio; cytoplasmic vacuoles in villous enterocytes and Peyer's patches	Degeneration of villous epithelial cells

**Fig. 11.2** Detection of PEDV antigen in formalin-embedded tissues by the immunohistochemistry staining

et al. 2015; Gerber et al. 2014; Ren et al. 2011; Carvajal et al. 1995; Knuchel et al. 1992; van Nieuwstadt and Zetstra 1991), reverse transcription polymerase chain reaction (RT-PCR) for detecting the viral genome (Ben Salem et al. 2010; Ishikawa et al. 1997; Kweon et al. 1997), electron microscopy (EM) for demonstration of PEDV particles (Fig.11.3) in the diarrheal feces (Straw et al. 2006; Jung and Saif 2015a), and viral isolation together with immunocytochemistry (ICC) performed in Vero cells for propagation and in vitro characterization of the virus (Fig.11.4).

**Fig. 11.3** Transmission electron micrograph (TEM) of PEDV particles (*virions, round*) in a tissue culture sample



**Fig. 11.4** Isolation and detection of PEDV in Vero cells. As compared with mock-infected Vero cells (a, c), typical CPEs in PEDV-infected Vero cells are characterized by cell fusion and syncytial formation under the light microscopy (b) and distinct cytoplasmic signals under the immunocytochemistry staining (d)

## 11.7 Epidemiology of PEDV Worldwide

Molecular characteristics of the S gene of PEDV strains have been often investigated to better understand the genetic diversity of PEDVs. After the new PEDV

outbreaks, the global PEDVs have been divided into two major groups according to the phylogenetic analysis of S gene of PEDV. Group 1 (G1) comprises global new variants of PEDVs and US S non-INDEL strains in North America; group 2 (G2) is composed of CV777 and DR13 vaccine strains, historical PEDVs isolated in Asia and Europe before the recent outbreaks, and the emerging US S INDEL PEDVs. The G1 strains isolated from the USA, China, and Asia PED-affected piglets show high sequence identities to each other (Chiou et al. 2015; Chen et al. 2014; Pasick et al. 2014; Temeeyasen et al. 2014; Vui et al. 2014). These novel G1 PEDV strains are suggested to share a common ancestor. The G2 PEDV strains are suggested being less virulent and are reported circulating in Europe, the USA, and Asia (Vlasova et al. 2014; Dennis Hanke et al. 2015).

### 11.7.1 Epidemiology of PEDV in Asia

In Asia, historic PEDs are not uncommon in the field. Most of PEDV infections caused transient diarrhea in postweaning piglets and rarely any disease in suckling piglets. The new variants of PEDV, however, cause severe diseases and serious economic loss of the neonatal piglets in many Asian countries, including China (Tian et al. 2013; Li et al. 2012), Taiwan (Chiou et al. 2015; Lin et al. 2014), South Korea (Cho et al. 2014; Choi et al. 2014), Thailand (Temeeyasen et al. 2014), and Japan, raising the importance of PED in Asia. It has been demonstrated that new PEDV strains that emerged in Asia are distinct from previous historic PEDV strains. They cause higher morbidity and mortality in neonatal piglets than previous strains (Jung and Saif 2015b).

#### 11.7.1.1 China

In the past, the infection of PEDV was endemic, and the prevalence of PED was low with few mini-outbreaks reported in China. The CV777-based vaccine is frequently used in the field. Since late 2010, PEDV-infected piglets, regardless of vaccination or immune status, showed large-scale outbreaks of PED. These variants caused severe watery diarrhea in pigs of all ages and high death rate in neonatal and suckling piglets. Based on the phylogenetic analysis of full-length sequences of the S gene of PEDVs isolated in China, both G1 and G2 strains are concurrently isolated. While China G2 PEDV strains share 96–99 % homologies to the CV777-based vaccine strain, the China G1 PEDV strains only share 93–95 % similarity to the CV777-based vaccine strain as well as China historic PEDV strains. These China G1 PEDV strains present several nucleotides insertions and deletions in the S gene (Li et al. 2012). Comparing the G1 PEDV strains with the CV777-based vaccine strain, there are two to three amino acid mutations in the neutralizing epitope SS6 and one to eight amino acid differences in the CO-26 K equivalent epitope (COE) domain (499–638 aa) in the S protein. These mutations have been speculated to represent the viral evolution through escaping from the antibodies derived from the CV777-based vaccine or the historic PEDV strains in several studies (Chen et al. 2013; Hao et al. 2014).

### 11.7.1.2 Taiwan

Before outbreaks of new variants of PED, historically PED was endemic in Taiwan. PEDV infection only caused mild transient diarrhea in postweaning piglets. PEDV vaccines, such as the CV777-based or DR13-based vaccines, are not routinely used in Taiwan. Nearly at the same time as in North America, new variants of PEDV infection leading to dramatic outbreaks and losses of suckling piglets reemerged in late 2013 in Taiwan. Phylogenetic analysis of the S gene showed that new variants of Taiwan PEDV strains belong to G1 and are closely related to other G1 strains from the USA, Canada, and China. These new Taiwan PEDV strains share 99.2 to 99.3 % nucleotide sequence identity to China CH/ZMDZY/11 and 94.1 to 94.2 % homologies to historical Taiwan PEDV strains. Similar to other new global variants of PEDV G1 strains, three serine amino acid substitutions (A522S, A554S, and G599S) in the COE and two serine amino acid substitutions (L769S and D771S) in SS6 are also observed in the reemerging Taiwan PEDVs as compared with the CV777-based vaccine strain (Chiou et al. 2015).

### 11.7.1.3 Korea

In Korea, the endemic PED has been in the field for decades (Yeo et al. 2003; Kim and Chae 2000; Kubota et al. 1999), and live PEDV vaccine strains are also available (Song et al. 2007). In addition to the reemerging of new variants of G1 PEDV strains resulting in severe PED in suckling piglets (Lee and Lee 2014; Park et al. 2013, 2014; Cho et al. 2014), a novel G1 PEDV variant, MF3809, is identified containing numerous sequence variations in the S protein, including a large (204-aa) deletion at positions 713–916 and a 2-aa (D/NI) deletion at positions 163–164. The antigenicity/immunogenicity alteration of MF3809 is still unknown (Park et al. 2014).

## 11.7.2 Epidemiology of PEDV in North America

The first PED case in the USA was reported in April–May, 2013. There was no previous description of the disease in the country before that time. No PEDV vaccines were available in the USA as well. After the first outbreak, PEDV quickly spread throughout the USA, then to nearby countries, including Canada (Song et al. 2015; Pasick et al. 2014). The US PEDV strains distributed both in G1 and G2 groups. The strains causing severe outbreaks exhibit high similarity to G1 PEDVs and are designed as S non-INDEL strains. The S non-INDEL PEDV strains were most closely related to China PEDV strains of CH/ZMZDY/11 and AH2012 in G1 group. Later after the outbreak, variants of US PEDV strains are isolated and are clustered in G2 in the phylogenetic analysis. As compared with the original US G1 PEDV strains, the US G2 PEDV strains contain insertions and deletions in S protein and are designed as S INDEL strains. Based on the full-length S gene analysis of PEDVs, the US S non-INDEL strains in G1 shared 99.8–100 % homology to each other and shared 96.6–97.1 % homologies to other PEDV G2 strains from North America. The S INDEL and original S non-INDEL strains are suggestive co-circulating and could have been introduced simultaneously in North America (Anastasia et al. 2014).

### 11.7.3 Epidemiology of PEDV in Europe

The first PEDV was reported in Belgium in 1978. The virus then spread over Europe until the end of the 1990s. However, there were no well-documented reports for PEDV in Europe during the past decades; most of the countries have not implemented active monitoring for this particular disease (23). Recently, several European PEDVs variants, such as PEDV/GER/L00719/214 and PEDV/GER/L00721/2014 from Germany, FR/001/2014 from France, BEL/15 V010/2015 from Belgium, and some isolates from Portugal and Italy, have been isolated and studied. They shared high identity (99 %) with the USA/OH851 strain (S INDEL; G2) and the Chinese AH2012 strain, but less similar (97.1 %) to the historic isolate, CV777, which isolated from Europe (Grasland et al. 2015; Theuns et al. 2015; Dennis Hanke et al. 2015).

#### Conclusion

The recent global outbreaks of PED in pigs of all ages with the high mortality in neonatal piglets may be contributed by several factors, including the mutation of the virus, the lacking of maternal antibodies, and the slower turnover of enterocytes (5–7 days) of neonatal piglets (Jung and Saif 2015a; Straw et al. 2006). It had been demonstrated that current available vaccines, CV777 and the attenuated PEDV DR13 vaccines, might not be able to fully protect piglets against the infection or control disease progression due to the high genetic diversity of new variants of global PEDVs. A new generation of PEDV vaccine is therefore urgently in need.

### References

- Alonso C, Goede D, Morrison R, Davies P, Rovira A, Marthaler D, Torremorell M (2014) Evidence of infectivity of airborne porcine epidemic diarrhea virus and detection of airborne viral RNA at long distance from infected herd. *Vet Res* 45:73
- Anastasia N, Vlasova DM, Wang Q, Culhane MR, Rossow KD, Rovira A, Collins J, Saif LJ (2014) Distinct characteristics and complex evolution of PEDV strains, North America, May 2013–February 2014. *Emerg Infect Dis* 20(10):1620–1628
- Bandrick M, Theis K, Molitor T (2014) Maternal immunity enhances *Mycoplasma hyopneumoniae* vaccination induced cell-mediated immune responses in piglets. *BMC Vet Res* 10:124
- Ben Salem AN, Chupin Sergei A, Bjadovskaya Olga P, Andreeva Olga G, Mahjoub A, Prokhvatilova Larissa B (2010) Multiplex nested RT-PCR for the detection of porcine enteric viruses. *J Virol Methods* 165(2):283–293. doi:10.1016/j.jviromet.2010.02.010
- Bosch B, van der Zee R, de Haan C, Rottier P (2003) The coronavirus spike protein is a class I virus fusion protein: Structural and functional characterization of the fusion core complex. *J Virol* 77:8801–8811
- Bridgen A, Duarte M, Tobler K, Laude H, Ackermann M (1993) Sequence determination of the nucleocapsid protein gene of the porcine epidemic diarrhoea virus confirms that this virus is a coronavirus related to human coronavirus 229E and porcine transmissible gastroenteritis virus. *J Gen Virol* 74(Pt 9):1795–1804



- Carvajal A, Lanza I, Diego R, Rubio P, Carmenes P (1995) Evaluation of a blocking ELISA using monoclonal antibodies for the detection of porcine epidemic diarrhea virus and its antibodies. *J Vet Diagn Invest Off Publ Am Assoc Vet Lab Diagn Inc* 7(1):60–64
- Chen J, Liu X, Shi D, Shi H, Zhang X, Li C, Chi Y, Feng L (2013) Detection and molecular diversity of spike gene of porcine epidemic diarrhea virus in China. *Viruses* 5(10):2601–2613. doi:[10.3390/v5102601](https://doi.org/10.3390/v5102601)
- Chen Q, Li G, Stasko J, Thomas JT, Stensland WR, Pillatzki AE, Gauger PC, Schwartz KJ, Madson D, Yoon KJ, Stevenson GW, Burrough ER, Harmon KM, Main RG, Zhang J (2014) Isolation and characterization of porcine epidemic diarrhea viruses associated with the 2013 disease outbreak among swine in the United States. *J Clin Microbiol* 52(1):234–243. doi:[10.1128/JCM.02820-13](https://doi.org/10.1128/JCM.02820-13)
- Chiu HY, Huang YL, Deng MC, Chang CY, Jeng CR, Tsai PS, Yang C, Pang VF, Chang HW (2015) Phylogenetic analysis of the spike (S) gene of the new variants of porcine epidemic diarrhoea virus in Taiwan. *Transbound Emerg Dis*. doi:[10.1111/tbed.12357](https://doi.org/10.1111/tbed.12357)
- Cho YY, Lim SI, Kim YK, Song JY, Lee JB, An DJ (2014) Complete Genome Sequence of K14JB01, a novel variant strain of porcine epidemic diarrhea virus in South Korea. *Genome Announc* 2(3):e00505–e00514. doi:[10.1128/genomeA.00505-14](https://doi.org/10.1128/genomeA.00505-14)
- Choi JC, Lee KK, Pi JH, Park SY, Song CS, Choi IS, Lee JB, Lee DH, Lee SW (2014) Comparative genome analysis and molecular epidemiology of the reemerging porcine epidemic diarrhea virus strains isolated in Korea. *Infect Genet Evol J Mol Epidemiol Evol Genet Infect Dis* 26:348–351. doi:[10.1016/j.meegid.2014.06.005](https://doi.org/10.1016/j.meegid.2014.06.005)
- Dennis Hanke MJ, Petrov A, Ritzmann M, Stadler J, Valerij Akimkin SB, Pohlmann A, Schirrmeyer H, Beer M, Höper D (2015) Comparison of porcine epidemic diarrhea viruses from Germany and the United States, 2014. *Emerg Infect Dis* 21(3):493–496
- Duarte M, Gelfi J, Lambert P, Rasschaert D, Laude H (1993) Genome organization of porcine epidemic diarrhoea virus. *Adv Exp Med Biol* 342:55–60
- EN W (1977) An apparently new syndrome of porcine epidemic diarrhea. *Vet Rec* 100:243–244
- Gerber PF, Gong Q, Huang YW, Wang C, Holtkamp D, Opriessnig T (2014) Detection of antibodies against porcine epidemic diarrhea virus in serum and colostrum by indirect ELISA. *Vet J* 202(1):33–36. doi:[10.1016/j.tvjl.2014.07.018](https://doi.org/10.1016/j.tvjl.2014.07.018)
- Grasland B, Bigault L, Bernard C, Quenault H, Toulouse O, Fablet C, Rose N, Touzain F, Blanchard Y (2015) Complete genome sequence of a porcine epidemic diarrhea s gene indel strain isolated in france in december 2014. *Genome Announc* 3(3):e00535–e00515. doi:[10.1128/genomeA.00535-15](https://doi.org/10.1128/genomeA.00535-15)
- Hao J, Xue C, He L, Wang Y, Cao Y (2014) Bioinformatics insight into the spike glycoprotein gene of field porcine epidemic diarrhea strains during 2011–2013 in Guangdong, China. *Virus Genes* 49(1):58–67. doi:[10.1007/s11262-014-1055-y](https://doi.org/10.1007/s11262-014-1055-y)
- Ishikawa K, Sekiguchi H, Ogino T, Suzuki S (1997) Direct and rapid detection of porcine epidemic diarrhea virus by RT-PCR. *J Virol Methods* 69(1–2):191–195
- Jung K, Saif L (2015a) Porcine epidemic diarrhea virus infection: etiology, epidemiology, pathogenesis and immunoprophylaxis. *Vet J* 204:134–143
- Kim O, Chae C (2000) In situ hybridization for the detection and localization of porcine epidemic diarrhea virus in the intestinal tissues from naturally infected piglets. *Vet Pathol* 37(1):62–67
- Klumperman J, Locker J, Meijer A, Horzinek M, HJ G, Rottier P (1994) Coronavirus M proteins accumulate in the Golgi complex beyond the site of virion budding. *J Virol* 68:6523–6534
- Knuchel M, Ackermann M, Muller HK, Kihm U (1992) An ELISA for detection of antibodies against porcine epidemic diarrhoea virus (PEDV) based on the specific solubility of the viral surface glycoprotein. *Vet Microbiol* 32(2):117–134
- Kubota S, Sasaki O, Amimoto K, Okada N, Kitazima T, Yasuhara H (1999) Detection of porcine epidemic diarrhea virus using polymerase chain reaction and comparison of the nucleocapsid protein genes among strains of the virus. *J Vet Med Sci/Japanese Soc Vet Sci* 61(7):827–830
- Kweon CH, Lee JG, Han MG, Kang YB (1997) Rapid diagnosis of porcine epidemic diarrhea virus infection by polymerase chain reaction. *J Vet Med Sci/Japanese Soc Vet Sci* 59(3):231–232

- Lee S, Lee C (2014) Outbreak-related porcine epidemic diarrhea virus strains similar to US strains, South Korea, 2013. *Emerg Infect Dis* 20(7):1223–1226. doi:[10.3201/eid2007.140294](https://doi.org/10.3201/eid2007.140294)
- Li B, Ge J, Li Y (2007) Porcine aminopeptidase N is a functional receptor for the PEDV coronavirus. *Virology* 365:166–172
- Li W, Li H, Liu Y, Pan Y, Deng F, Song Y, Tang X, He Q (2012) New variants of porcine epidemic diarrhea virus, China, 2011. *Emerg Infect Dis* 18:1350–1353
- Lin CN, Chung WB, Chang SW, Wen CC, Liu H, Chien CH, Chiou MT (2014) US-like strain of porcine epidemic diarrhea virus outbreaks in Taiwan, 2013–2014. *J Vet Med Science/Japanese Soc Vet Sci* 76(9):1297–1299
- Lowe J, Gauger P, Harmon K, Zhang J, Connor J, Yeske P, Louia T, Levis L, Dufresne L, Main R (2014) Role of translocation in spread of porcine epidemic diarrhea virus infection, United States. *Emerg Infect Dis* 20:872–874
- Madson DM, Magstadt DR, Arruda PH, Hoang H, Sun D, Bower LP, Bhandari M, Burrough ER, Gauger PC, Pillatzki AE, Stevenson GW, Wilberts BL, Brodie J, Harmon KM, Wang C, Main RG, Zhang J, Yoon KJ (2014) Pathogenesis of porcine epidemic diarrhea virus isolate (US/Iowa/18984/2013) in 3-week-old weaned pigs. *Vet Microbiol* 74(1–2):60–68. doi:[10.1016/j.vetmic.2014.09.002](https://doi.org/10.1016/j.vetmic.2014.09.002)
- Okda F, Liu X, Singrey A, Clement T, Nelson J, Christopher-Hennings J, Nelson EA, Lawson S (2015) Development of an indirect ELISA, blocking ELISA, fluorescent microsphere immunoassay and fluorescent focus neutralization assay for serologic evaluation of exposure to North American strains of Porcine Epidemic Diarrhea Virus. *BMC Vet Res* 11:180. doi:[10.1186/s12917-015-0500-z](https://doi.org/10.1186/s12917-015-0500-z)
- Park S, Kim S, Song D, Park B (2014) Novel porcine epidemic diarrhea virus variant with large genomic deletion, South Korea. *Emerg Infect Dis* 20(12):2089–2092. doi:[10.3201/eid2012.131642](https://doi.org/10.3201/eid2012.131642)
- Park SJ, Song DS, Park BK (2013) Molecular epidemiology and phylogenetic analysis of porcine epidemic diarrhea virus (PEDV) field isolates in Korea. *Arch Virol* 158(7):1533–1541. doi:[10.1007/s00705-013-1651-5](https://doi.org/10.1007/s00705-013-1651-5)
- Pasick J, Berhane Y, Ojkic D, Maxie G, Embury-Hyatt C, Swekla K, Handel K, Fairles J, Alexandersen S (2014) Investigation into the role of potentially contaminated feed as a source of the first-detected outbreaks of porcine epidemic diarrhea in Canada. *Transbound Emerg Dis* 61(5):397–410. doi:[10.1111/tbed.12269](https://doi.org/10.1111/tbed.12269)
- Ren X, Suo S, Jang YS (2011) Development of a porcine epidemic diarrhea virus M protein-based ELISA for virus detection. *Biotechnol Lett* 33(2):215–220. doi:[10.1007/s10529-010-0420-8](https://doi.org/10.1007/s10529-010-0420-8)
- Song D, Moon H, Kang B (2015) Porcine epidemic diarrhea: a review of current epidemiology and available vaccines. *Clin Exp Vaccine Res* 4(2):166–176. doi:[10.7774/cevr.2015.4.2.166](https://doi.org/10.7774/cevr.2015.4.2.166)
- Song DS, Oh JS, Kang BK, Yang JS, Moon HJ, Yoo HS, Jang YS, Park BK (2007) Oral efficacy of Vero cell attenuated porcine epidemic diarrhea virus DR13 strain. *Res Vet Sci* 82(1):134–140. doi:[10.1016/j.rvsc.2006.03.007](https://doi.org/10.1016/j.rvsc.2006.03.007)
- Spaan WDH, Skinner M, Armstrong J, Rottier P, Smeekens S, van der Zeijst BA, Siddell SG (1983) Coronavirus mRNA synthesis involves fusion of non-contiguous sequences. *EMBO J* 2(10):1839–1844
- Stevenson GW, Hoang H, Schwartz KJ, Burrough ER, Sun D, Madson D, Cooper VL, Pillatzki A, Gauger P, Schmitt BJ, Koster LG, Killian ML, Yoon KJ (2013) Emergence of Porcine epidemic diarrhea virus in the United States: clinical signs, lesions, and viral genomic sequences. *J Vet Diagn Invest Off Publ Am Assoc Vet Lab Diagn Inc* 25(5):649–654. doi:[10.1177/1040638713501675](https://doi.org/10.1177/1040638713501675)
- Straw B, Zimmerman J, D’Allaire S, Taylor D (2006) *Diseases of swine*. 9th edn. Blackwell Publishing, Ames, Iowa.
- Sun R, Cai R, Chen Y, Liang P, Chen D, Song C (2012) Outbreak of porcine epidemic diarrhea in suckling piglets, China. *Emerg Infect Dis* 18:161–163
- Temeeyasen G, Srijangwad A, Tripipat T, Tipsombatboon P, Piriyaopngsa J, Phoolcharoen W, Chuanasa T, Tantituvanont A, Nilubol D (2014) Genetic diversity of ORF3 and spike genes of

- porcine epidemic diarrhea virus in Thailand. *Infect, Genet Evol J Mol Epidemiol Evol Genet Infect Dis* 21:205–213. doi:[10.1016/j.meegid.2013.11.001](https://doi.org/10.1016/j.meegid.2013.11.001)
- Theuns S, Conceicao-Neto N, Christiaens I, Zeller M, Desmarests LM, Roukaerts ID, Acar DD, Heylen E, Matthijnsens J, Nauwynck HJ (2015) Complete genome sequence of a porcine epidemic diarrhea virus from a novel outbreak in Belgium, January 2015. *Genome Announc* 3(3):e00506–e00515. doi:[10.1128/genomeA.00506-15](https://doi.org/10.1128/genomeA.00506-15)
- Tian Y, Su D, Zhang H, Chen RA, He D (2013) Complete genome sequence of a very virulent porcine epidemic diarrhea virus strain, CH/GDGZ/2012, isolated in Southern China. *Genome Announc* 1(4):00645–00613. doi:[10.1128/genomeA.00645-13](https://doi.org/10.1128/genomeA.00645-13)
- van Nieuwstadt AP, Zetstra T (1991) Use of two enzyme-linked immunosorbent assays to monitor antibody responses in swine with experimentally induced infection with porcine epidemic diarrhea virus. *Am J Vet Res* 52(7):1044–1050
- Vlasova AN, Marthaler D, Wang Q, Culhane MR, Rossow KD, Rovira A, Collins J, Saif LJ (2014) Distinct characteristics and complex evolution of PEDV strains, North America, May 2013–February 2014. *Emerg Infect Dis* 20(10):1620–1628. doi:[10.3201/eid2010.140491](https://doi.org/10.3201/eid2010.140491)
- Vui DT, Tung N, Inui K, Slater S, Nilubol D (2014) Complete genome sequence of porcine epidemic diarrhea virus in Vietnam. *Genome Announc* 2(4):e00753–e00714. doi:[10.1128/genomeA.00753-14](https://doi.org/10.1128/genomeA.00753-14)
- Yeo SG, Hernandez M, Krell PJ, Nagy EE (2003) Cloning and sequence analysis of the spike gene of porcine epidemic diarrhea virus Chinju99. *Virus Genes* 26(3):239–246