Porcine Deltacoronavirus (PDCoV)

Cross Species Transmission Potential

Intelligence Brief
May 2022

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SIGNAL SUMMARY

In a retrospective report, Lednicki et al (2021) describe the detection of Porcine deltacoronavirus (PDCoV) in three Haitian children. As part of ongoing monitoring of the health of school children, plasma samples from 369 children with acute undifferentiated febrile illness were collected between May 2014 and December 2015. The samples were tested for common pathogens that cause fever, including dengue, chikungunya and Zika viruses and the parasite that causes malaria.

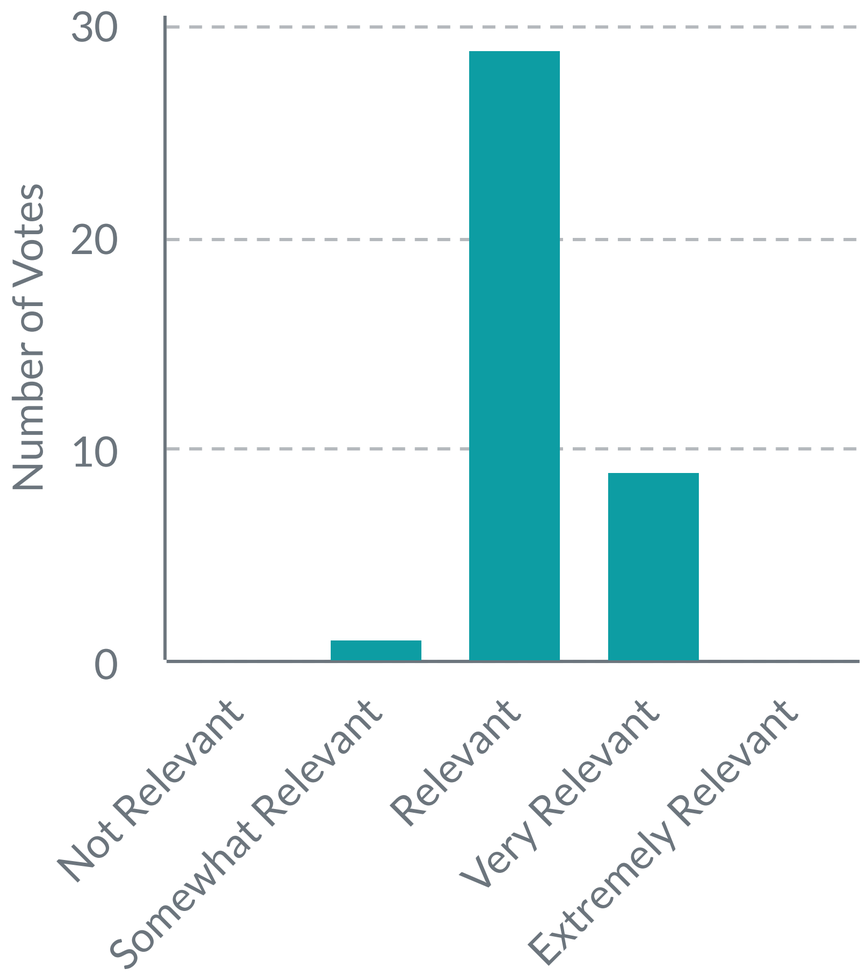
Samples that did not test positive for the common pathogens were placed onto VeroE6 cells to determine if any viruses were present. Very subtle cytopathic effect was observed in three of the samples. Through additional molecular testing methods, and transmission electron microscopy, it was determined that a coronavirus was present.

Gene sequencing demonstrated that there were at least two separate zoonotic events with non-recombinant strains of porcine deltacoronavirus. Two children at one school were found to have a coronavirus with 99.8% sequence similarity with a Chinese strain of PDCoV, whereas one child at a second school was found to be infected with a US strain of PDCoV.

All three children recovered uneventfully.

TRIAGE

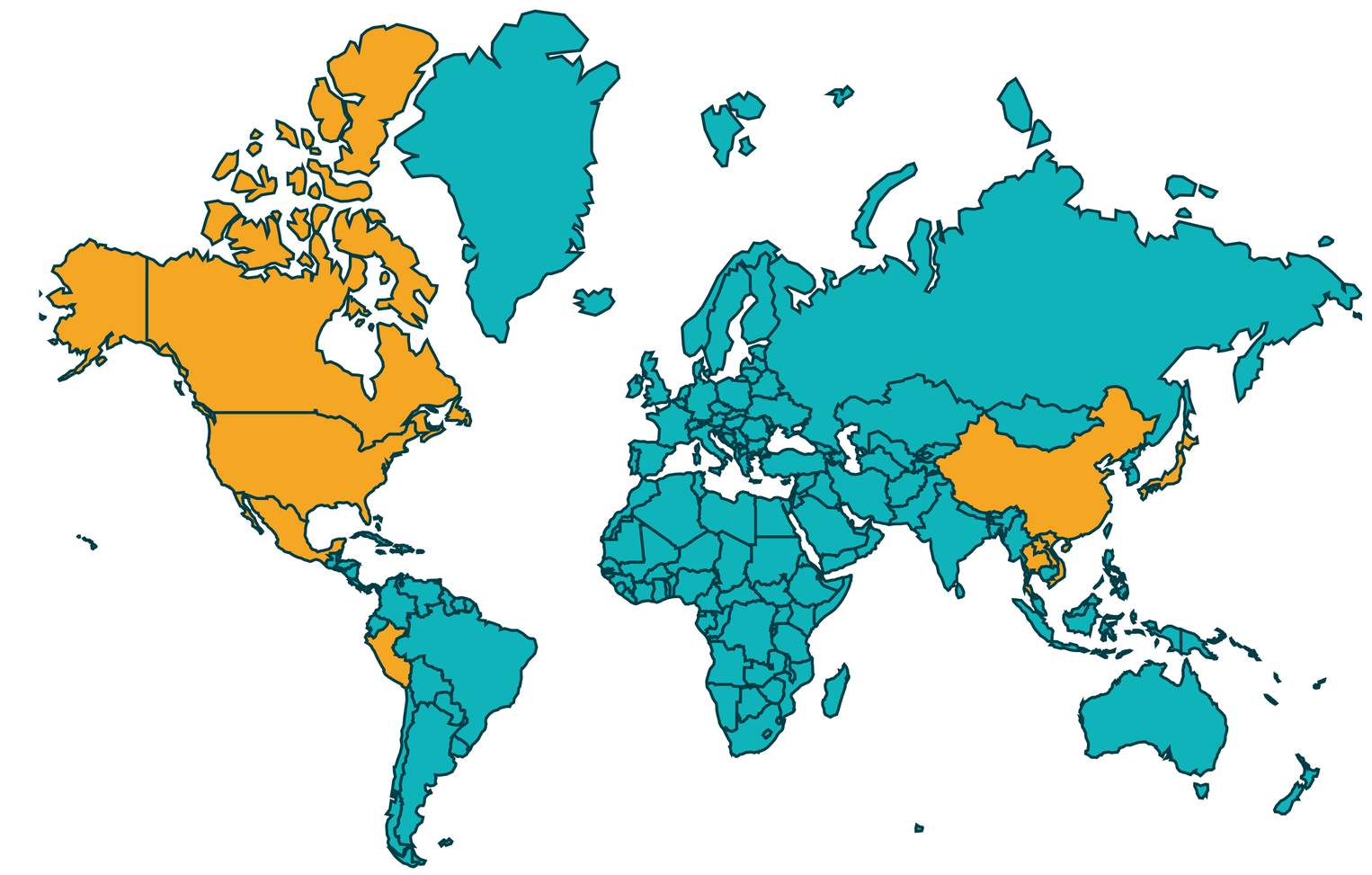
This event was considered in scope for the Community for Emerging and Zoonotic Diseases (CEZD), and was originally sent as a ping poll to the community for feedback on December 1, 2021. The report was considered somewhat relevant to very relevant by community members.



The COVID-19 pandemic raised global awareness of the zoonotic potential of coronaviruses. Subject matter experts in virology and swine health were consulted to share their perspectives on the disease presentation in swine, and the occurrence of the virus in children in Haiti to gain a greater understanding of the cross species transmission potential of PDCoV. This intelligence brief provides a summary of available information about the cross-species transmission potential of PDCoV.

GLOBAL DISTRIBUTION

PDCoV has a broad global distribution, having been identified in Hong Kong, the United States (Wang et al, 2014), Mainland China (Dong et al, 2015), South Korea (Lee et al, 2016), Thailand, Vietnam and Lao (Saeng-Chuto et al, 2017), Canada (Ajayi et al, 2018), Tibet (Wang et al 2018), Japan (Suzuki et al, 2018), Mexico (Perez-Rivera et al 2019), Peru (Vicente-Huaman 2021) and Haiti (Lednicki, 2021).



VIRAL TAXONOMY

Coronaviruses are enveloped, positive-sense, non-segmented, single-stranded RNA viruses, and members of family Coronaviridae in order Nidovirales.

They are classified into four genera containing viruses pathogenic to mammals.

ALPHA

- Porcine Epidemic Diarrhea virus (PEDv)
- Transmissible gastroenteritis virus (TGEV)
- Swine acute diarrhea syndrome coronavirus (SADS-CoV)
- Canine enteric coronavirus (CCoV)
- Feline infectious peritonitis virus (FIPV)
- Common cold (HCoV-229E, HCoV-NL63)
- Multiple Bat Coronaviruses

BETA

- Severe acute respiratory syndrome coronavirus (SARS-CoV)
- COVID19 (SARS-CoV-2)
- Middle East respiratory syndrome coronavirus (MERS-CoV)
- Murine hepatitis virus (MHV)
- Bovine coronaviruses
- Rat sialodacryoadenitis virus,
- Porcine hemagglutinating encephalomyelitis virus
- Canine respiratory coronavirus
- Equine coronavirus
- Common Cold (HCoV-OC43)

GAMMA

- Infectious bronchitis (IBV)
- Turkey coronavirus (TCoV)
- Beluga Whale CoV (BWCoV-SW1)

DELTA

- Sparrow coronavirus (SpCoV HKU17)
- Thrush coronavirus (ThCoV HKU12)
- Porcine Deltacoronavirus (PDCoV) has emerged fairly recently and is a member of this group

Scan QR code to view
Coronavirus Taxonomic Tree

VIRAL ORIGIN

Based on the genome sequences of 18 avian delta-coronaviruses and 100 PDCoVs, Ye et al (2020) constructed phylogenetic trees that indicate PDCoV shares a common ancestor with a sparrow-CoV, and that PDCoV likely emerged in Asia in the 1990's. Kong et al 2022, identify that the most likely ancestor is of avian origin, and less likely from another mammalian host, though there have been very closely related viruses found in Asian Leopard Cats and Chinese Ferret Badgers.

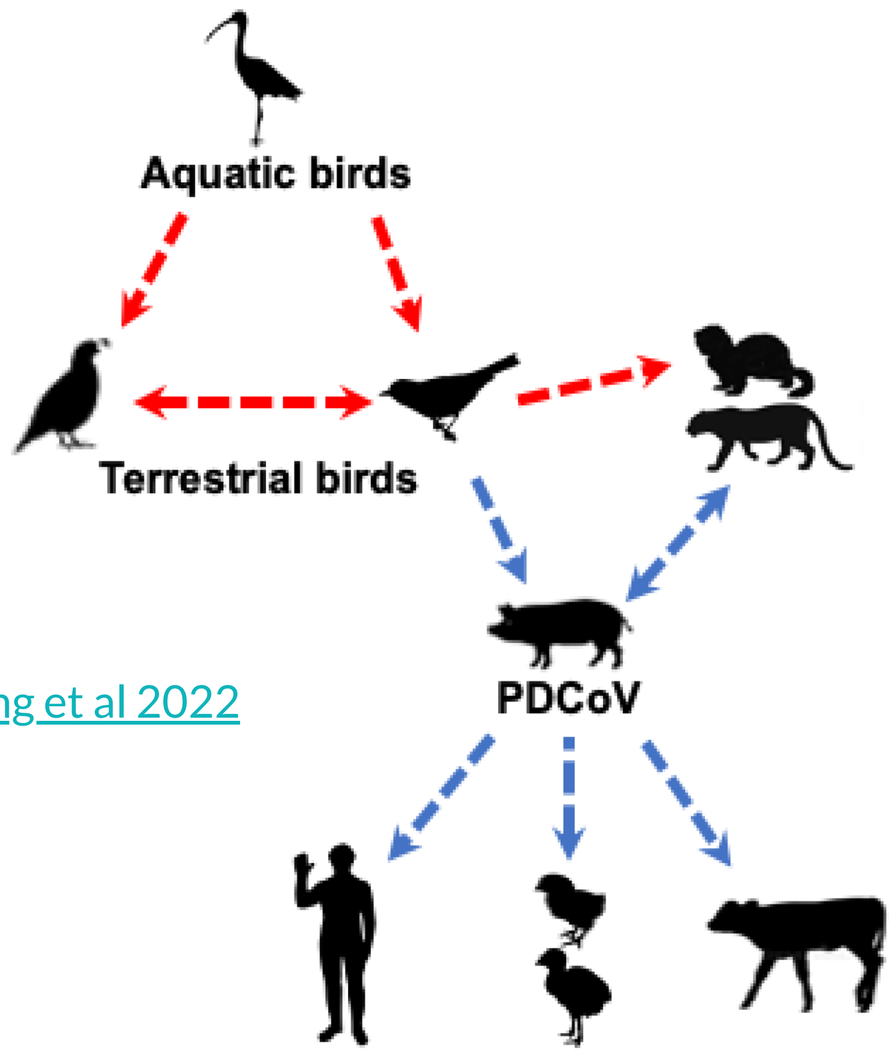


Figure credit: Kong et al 2022

Likely origin and routes of cross-species transmission of PDCoV. The red dashed line indicates potential, but unknown, transmission of δ-CoVs from avian to mammalian species; the blue dashed line indicates potential transmission of PDCoV based on epidemiology or experimental studies.

RECEPTOR USAGE

Porcine aminopeptidase N (pAPN) has been identified as an entry receptor to which the PDCoV spike protein attaches (Li et al 2018, Everest et al 2022). It is not necessarily the only mechanism for cell attachment and entry, as experimental studies with pAPN knock out porcine intestinal epithelial cells can still be infected with PCoV (Zhu, 2018) albeit at a reduced rate (Li et al, 2018). Other porcine viruses which use pAPN as a receptor include TGEV and PEDV. One human coronavirus (HCoV-229E) has been identified that uses APN as its receptor (Bonavia et al, 2003)

Aminopeptidase (APN) is a metalloprotease enzyme that serves a variety of physiological purposes; it is involved in pain sensation, regulation of blood pressure, motility of sperm cells, cell adhesion, and cancer related physiological functions of angiogenesis and metastasis (Chen et al, 2012). APN contains an interspecies conserved domain (Li et al, 2018).

SUSCEPTIBLE SPECIES AND CLINICAL SIGNS

PDCoV has been shown varying degrees of ability to infect pigs, chickens, turkeys, cattle and humans.

The findings in humans are limited to the detection of PDCoV in three Haitian children with acute undifferentiated febrile illness (Lednicki, 2021).

Pigs of all ages can be affected by PDCoV, but neonates are most susceptible. Clinical signs in neonatal piglets include diarrhea, dehydration, vomiting, lethargy, anorexia and variable levels of mortality (Duan, 2022). The entire intestine is affected; however, the primary sites of infection are the jejunum and ileum. Signs of PDCoV are far less severe than those of porcine epidemic diarrhea (PED) and transmissible gastroenteritis (TGE). (Jung et al, 2015). The minimum infectious dose is much lower in neonatal piglets than weaned piglets (Thomas et al, 2015).

Poultry can be experimentally infected with PDCoV (Boley et al, 2020). 14-day old chickens experimentally infected with PDCov showed transient diarrhea, with the majority of infected birds showing diarrhea within two days of inoculation. The infection was also passed to cohabited uninfected birds within 2 days. Pathology of the birds' intestine was only visible during the first week post infection and was normal 14 days post infection. Turkey poults were somewhat more susceptible to PDCoV, and still exhibited moderate diarrhea 14 days after infection. Gross pathology of all poult's intestines demonstrated distended gastrointestinal tracts containing yellow liquid and gas throughout the study period.

To determine susceptibility of calves, Jung et al (2017) experimentally infected four, 3–7-day old gnotobiotic animals. None of the infected animals showed clinical signs of disease, however all 4 shed PDCoV RNA in the feces. At the same time, 4 additional calves were experimentally challenged with PED virus, and no virus could be detected in the animals' feces during the experiment. No histological lesions were found in any of the animals' intestines.

DIAGNOSTICS

Diagnostic testing for PDCoV is readily available at veterinary diagnostic laboratories in Canada. Typical samples include feces, fecal swabs or oral fluids that can be tested using molecular diagnostic techiques; blood is a less reliable sample as viremia may not be prolonged (Neiderwerder et al, 2016).

TRANSMISSION

The primary mode of transmission of PDCov is via the fecal-oral route (Goyal, 2015, Neiderwerder et al, 2016). Laboratory studies indicate the possibility of aerosol transmission of PDCoV (Vitosh-Silman et al, 2016), however, it is thought that the mechanism of infection is actually oral ingestion of the aerosolized virus, rather than true aerosol spread. (Neiderwerder et al, 2016). McCluskey et al, 2015 sought to use a retrospective analysis to determine the source of introduction of PDCoV to the US in 2014, however, were unable to define the likely routes of introduction.

Greater information is available on the transmission mechanisms and epidemiology of PED Virus due to it's more severe effects, and PEDV controls should serve as a template for control of PDCoV.

SURVIVAL IN THE ENVIRONMENT

PDCoV can survive for >21 days outside the host can be difficult inactivate completely. Higher temperatures and lower humidity are more effective at inactivating the virus. PDCoV survives for extended periods of time in feces, feed, and feed ingredients; ranges include >3 to >7 weeks depending on the media tested and environmental conditions. This prolonged survival can be reduced by heat (Goyal, 2015). Given the long period of viability, exposure via the fecal-oral route is possible over long time periods.

KNOWLEDGE GAPS

The range of species that can be infected with PDCoV is not clearly known, given the conservation of the APN receptor across species, it is possible that other species, beyond poultry, pigs, gnotobiotic calves and humans, may be susceptible to infection with the virus.

Coronaviruses are known to recombine at a relatively high rate, in part due to their very large RNA genomes (Lai et al, 1996). Multiple example of CoV recombination are available in other species, including feline CoV's (Herrewegh et al, 1998), human CoV OC43 (Zhang, 2015), and avian delta coronaviruses (Wang et al, 2022). The ability for beta coronaviruses (e.g. SARS and MERS) to recombine has been modelled (Bannerjee et al, 2020). PDCoV infection in pigs frequently occurs concurrently with other enteric coronaviruses. The frequency of recombination of Porcine coronaviruses is not clearly described, and so the likelihood of changes to the virus are unknown.

Human infection with PDCoV cannot be quantified given the data available. Other than the three cases in Haitian children, there have been no reported detections of PDCoV in humans anywhere in the world, despite a large number of people in close contact with pigs globally. The Haitian cases at School A had 2 children with almost identical virus, but it was not possible to tell if the infection occurred from human to human or from a common source. It is important to note that given the large amount of whole genome sequencing of Coronaviruses that has occurred globally, due to the COVID-19 pandemic, it is unlikely that human infection with PDCoV is a widespread occurrence.

REFERENCES

Ajayi T, Dara R, Misener M, Pasma T, Moser L, Poljak Z. Herd-level prevalence and incidence of porcine epidemic diarrhoea virus (PEDV) and porcine deltacoronavirus (PDCoV) in swine herds in Ontario, Canada. Transbound Emerg Dis. 2018;65(5):1197–1207. https://onlinelibrary.wiley.com/doi/10.1111/tbed.12858

Bannerjee A, Doxey A, Tremblay B, Mansfield M, Subudhi S, Hirota J, Miller M, McArthur A, Mubareka S, Mossman K Predicting the recombination potential of severe acute respiratory syndrome coronavirus 2 and Middle East respiratory syndrome coronavirus 2020 Journal of General Virology 2020;101:1251–1260 http://dx.doi.org/10.1099/jgv.0.001491

Boley PA, Alhamo MA, Lossie G, Yadav K, Vasquez-Lee M, Saif LJ, et al. Porcine Deltacoronavirus Infection and Transmission in Poultry, United States. Emerg Infect Dis. 2020;26(2):255-265. https://doi.org/10.3201/eid2602.190346

Bonavia, A.; Zelus, B.D.; Wentworth, D.E.; Talbot, P.J.; Holmes, K.V. Identification of a receptor-binding domain of the spike glycoprotein of human coronavirus HCoV-229E. J. Virol. 2003, 77, 2530–2538. https://journals.asm.org/doi/10.1128/JVI.77.4.2530-2538.2003

Duan C (2022) An Updated Review of Porcine Deltacoronavirus in Terms of Prevalence, Pathogenicity, Pathogenesis and Antiviral Strategy. Front. Vet. Sci. 8:811187. https://www.frontiersin.org/articles/10.3389/fvets.2021.811187/full

Dong N, Fang L, Zeng S, Sun Q, Chen H, Xiao S. Porcine deltacoronavirus in mainland China. Emerg Infect Dis. 2015;21(12):2254–2255. https://doi.org/10.3201/eid2112.150283

Duan C (2022) An Updated Review of Porcine Deltacoronavirus in Terms of Prevalence, Pathogenicity, Pathogenesis and Antiviral Strategy. Front. Vet. Sci. 8:811187. https://doi.org/10.3389/fvets.2021.811187

Everest, H.; Stevenson, Leggett, P.; Bailey, D.; Bickerton, E.; Keep, S. Known Cellular and Receptor Interactions of Animal and Human Coronaviruses: A Review. Viruses 2022, 14, 351. https://www.mdpi.com/1999-4915/14/2/351

Herrewegh, A. A., I. Smeenk, M. C. Horzinek, P. J. Rottier, and R. J. de Groot. 1998. Feline coronavirus type II strains 79–1683 and 79–1146 originate from a double recombination between feline coronavirus type I and canine coronavirus. J. Virol. 72:4508–4514. https://doi.org/10.1128/JVI.72.5.4508-4514.1998

Jung K, Hu H, Eyerly B, Lu Z, Chepngeno J, Saif LJ. Pathogenicity of 2 Porcine Deltacoronavirus Strains in Gnotobiotic Pigs. Emerg Infect Dis. 2015;21(4):650-654. https://doi.org/10.3201/eid2104.141859

REFERENCES

Lednicky, J.A., Tagliamonte, M.S., White, S.K. et al. Independent infections of porcine deltacoronavirus among Haitian children. Nature 600, 133–137 (2021). https://doi.org/10.1038/s41586-021-04111-z

Lee JH, Chung HC, Nguyen VG, Moon HJ, Kim HK, Park SJ, Lee CH, Lee GE, Park BK. Detection and phylogenetic analysis of porcine deltacoronavirus in Korean swine farms, 2015. Transbound Emerg Dis. 2016;63(3):248–252. https://onlinelibrary.wiley.com/doi/10.1111/tbed.12490

Li, W.; Hulswit, R.J.G.; Kenney, S.P.; Widjaja, I.; Jung, K.; Alhamo, M.A.; van Dieren, B.; van Kuppeveld, F.J.M.; Saif, L.J.; Bosch, B.J. Broad receptor engagement of an emerging global coronavirus may potentiate its diverse cross-species transmissibility. Proc. Natl. Acad. Sci. USA 2018, 115, E5135–E5143. https://www.pnas.org/doi/full/10.1073/pnas.1802879115

Niederwerder M.C., Hesse R.A. Swine enteric coronavirus disease: a review of 4 years with porcine epidemic diarrhoea virus and porcine deltacoronavirus in the United States and Canada. Transboundary and Emerg Dis. 2018;65:660–675. https://onlinelibrary.wiley.com/doi/pdfdirect/10.1111/tbed.12823

Perez-Rivera C, Ramirez-Mendoza H, Mendoza-Elvira S, Segura-Velazquez R, Sanchez-Betancourt JI. First report and phylogenetic analysis of porcine deltacoronavirus in Mexico. Transbound Emerg Dis. 2019;66(4):1436–1441. https://onlinelibrary.wiley.com/doi/10.1111/tbed.13193

Saeng-Chuto K, Lorsirigool A, Temeeyasen G, Vui DT, Stott CJ, Madapong A, Tripipat T, Wegner M, Intrakamhaeng M, Chongcharoen W, Tantituvanont A, Kaewprommal P, Piriyapongsa J, Nilubol D. Different lineage of porcine deltacoronavirus in Thailand, Vietnam and Lao PDR in 2015. Transbound Emerg Dis. 2017;64(1):3–10. https://onlinelibrary.wiley.com/doi/10.1111/tbed.12585

Suzuki, T.; Shibahara, T.; Imai, N.; Yamamoto, T.; Ohashi, S. Genetic characterization and pathogenicity of Japanese porcine deltacoronavirus. Infect. Genet. Evol. 2018, 61, 176–182 https://pubmed.ncbi.nlm.nih.gov/29621617/

Thomas JT, Chen Q, Gauger PC, Giménez-Lirola LG, Sinha A, Harmon KM, et al. (2015) Effect of Porcine Epidemic Diarrhea Virus Infectious Doses on Infection Outcomes in Naïve Conventional Neonatal and Weaned Pigs. PLoS ONE 10(10): e0139266. https://doi.org/10.1371/journal.pone.0139266

Vicente-Huaman, J., & Gómez-Quispe, O. E. (2021). Evaluation of a Porcine deltacoronavirus eradication program in a full-cycle pig farm in Peru. Journal of advanced veterinary and animal research, 8(2), 300–306. https://doi.org/10.5455/javar.2021.h515

Thomas JT, Chen Q, Gauger PC, Giménez-Lirola LG, Sinha A, Harmon KM, et al. (2015) Effect of Porcine Epidemic Diarrhea Virus Infectious Doses on Infection Outcomes in Naïve Conventional Neonatal and Weaned Pigs. PLoS ONE 10(10): e0139266. https://doi.org/10.1371/journal.pone.0139266

REFERENCES

Vicente-Huaman, J., & Gómez-Quispe, O. E. (2021). Evaluation of a Porcine deltacoronavirus eradication program in a full-cycle pig farm in Peru. Journal of advanced veterinary and animal research, 8(2), 300–306. https://doi.org/10.5455/javar.2021.h515

Vitosh-Sillman S, Loy JD, Brodersen B, et al. Experimental infection of conventional nursing pigs and their dams with Porcine deltacoronavirus. Journal of Veterinary Diagnostic Investigation. 2016;28(5):486-497. doi:10.1177/1040638716654200

Wang L, Byrum B. Zhang Y (2014) Detection and genetic characterization of deltacoronavirus in pigs, Ohio, USA. Emerg Infect Dis. 2014;20(7):1227–1230. https://pubmed.ncbi.nlm.nih.gov/24964136/Wang

Wang M, Wang Y, Baloch AR, Pan Y, Tian L, Xu F, Shivaramu S, Chen S, Zeng Q. Detection and genetic characterization of porcine deltacoronavirus in Tibetan pigs surrounding the Qinghai-Tibet Plateau of China. Transbound Emerg Dis. 2018;65(2):363–369. https://onlinelibrary.wiley.com/doi/10.1111/tbed.12819

Wang Q, Zhou Z-J, You Z, et al. Epidemiology and evolution of novel deltacoronaviruses in birds in central China. Transbound Emerg Dis. 2022;69:632–644. https://doi.org/10.1111/tbed.14029

Woo PC, Lau SK, Lam CS, Lau CC, Tsang AK, Lau JH, et al. Discovery of seven novel mammalian and avian coronaviruses in the genus Deltacoronavirus supports bat coronaviruses as the gene source of alphacoronavirus and betacoronavirus and avian coronaviruses as the gene source of gammacoronavirus and deltacoronavirus. J Virol. 2012;86:3995–4008. https://doi.org/10.1128/JVI.06540-11.

Ye, X.; Chen, Y.; Zhu, X.; Guo, J.; Da, X.; Hou, Z.; Xu, S.; Zhou, J.; Fang, L.; Wang, D.; et al. Cross-Species Transmission of Deltacoronavirus and the Origin of Porcine Deltacoronavirus. Evol. Appl. 2020, 13, 2246–2253 https://onlinelibrary.wiley.com/doi/10.1111/eva.12997

Zhang J. Porcine deltacoronavirus: overview of infection dynamics, diagnostic methods, prevalence and genetic evolution. Virus Res. 2016;226:71–84. https://doi.org/10.1016/j.virusres.2016.05.028

Zhang Y., Li J., Xiao Y, Zhang J., Wang Y., Chen L., Paranhos-Baccalà G,Ren L., Wang J., Genotype shift in human coronavirus OC43 and emergence of a novel genotype by natural recombination. Journal of Infection, Volume 70, Issue 6, 2015, Pages 641-650 https://doi.org/10.1016/j.jinf.2014.12.005

Zhu, X.; Liu, S.; Wang, X.; Luo, Z.; Shi, Y.; Wang, D.; Peng, G.; Chen, H.; Fang, L.; Xiao, S. Contribution of porcine aminopeptidase N to porcine deltacoronavirus infection. Emerg. Microbes Infect. 2018, 7, 65. https://www.tandfonline.com/doi/full/10.1038/s41426-018-0068-3