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Recent updates on classical swine fever and its status in India

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Abstract
Pigs form an important component of the Indian economy, especially for the northeastern states and economically weaker sections of society. The decreasing trend in the pig population in recent animal censuses highlights the mortality and losses that occur to pig husbandry due to infectious diseases. Classical Swine Fever is an economically important, systemic, highly contagious, and fatal viral disease affecting domestic and wild pigs. The disease has a wide geographical presence worldwide and also shows endemic occurrence in nearly 23 states of India. Effective diagnosis along with strict control measures are needed due to the high economic value of the disease. A variety of conventional, serological, and molecular diagnostics are in currently use. Vaccination is the most important strategy to control CSF in domestic and wild populations. Live attenuated vaccines are widely used worldwide but the eradication of CSF needs effective marker vaccines for the differentiation of infected animals from vaccinated ones. Different marker vaccines have been launched in different countries including India and research is still underway to develop effective vaccination platforms for CSF control. The current review provides a comprehensive account of various aspects of CSF with special reference to its status in India.

Keywords: Pigs, classical swine fever, virus, diagnosis, vaccination

1. Introduction
According to the 20th livestock census, India has 9.06 million pigs and around 38.42% of this is contributed alone by the northeastern states of India [1]. In northeast India, pig farming is the main source of livelihood for most households where about 80% of households are engaged in pig farming and pork forms a key ingredient of their local diet. Classical swine fever (CSF) or hog cholera is a systemic, highly contagious, potentially fatal disease of domestic and wild pigs, important economically in India [2, 3]. This disease has never got proper attention since a major proportion of pig husbandry is restricted to socially backward classes of Indian society and to the fact that a major proportion of the pig population is present in North Eastern states. The decreasing trend in pig population to 9.06 million as per the 20th livestock census as compared to 11.1 million in the previous census may be attributed to losses incurred due to infectious diseases and lack of proper/rapid diagnostics and a short supply of quality vaccines to the aspiring pig farmers [1, 4, 5]. The presence of the CSF virus (CSFV) in pig herds has an economic impact on the meat production industry by causing widespread deaths due to the disease and trade restrictions on infected meat exports. A study conducted by the International Livestock Research Institute (ILRI) in three northeastern states of India *viz*. Assam, Mizoram, and Nagaland in 2011 revealed that Pig farmers in India incur an economic loss of over 2.224 billion Indian rupees each year due to mortality, treatment, and replacement costs [6]. CSF can spread in an epizootic form as well as establish enzootic infections in domestic and wild pig populations [7]. CSF remains widespread in many parts of the globe since the end of the 20th century. Successful eradication has been achieved in many countries, including North America, Australia, and parts of Northern Europe but the disease continues to be a problem in most of the pig-producing states of India.

2. Classical swine fever virus (CSFV)
CSFV is a member of the family *Flaviviridae* and the genus *Pestivirus* [7, 8]. The other members of this genus are the bovine viral diarrhea virus (BVDV) and the Border disease virus of sheep [9]. There is only one serotype of CSFV, although variability within the serotype has been reported [10]. The virus is enveloped with a 40-60 nm diameter having an electron-dense inner core structure of about 30 nm diameter [11].

The virus bears a single-stranded positive-sense RNA relatively stable genome spanning approximately 12.3 kbp and is made up of a single open reading frame (ORF) of 11.7 kbp flanked by a 5' and 3' untranslated region (UTR) [12]. The Schematic description of the genome organization and virion structure of CSFV is given in fig. 1.

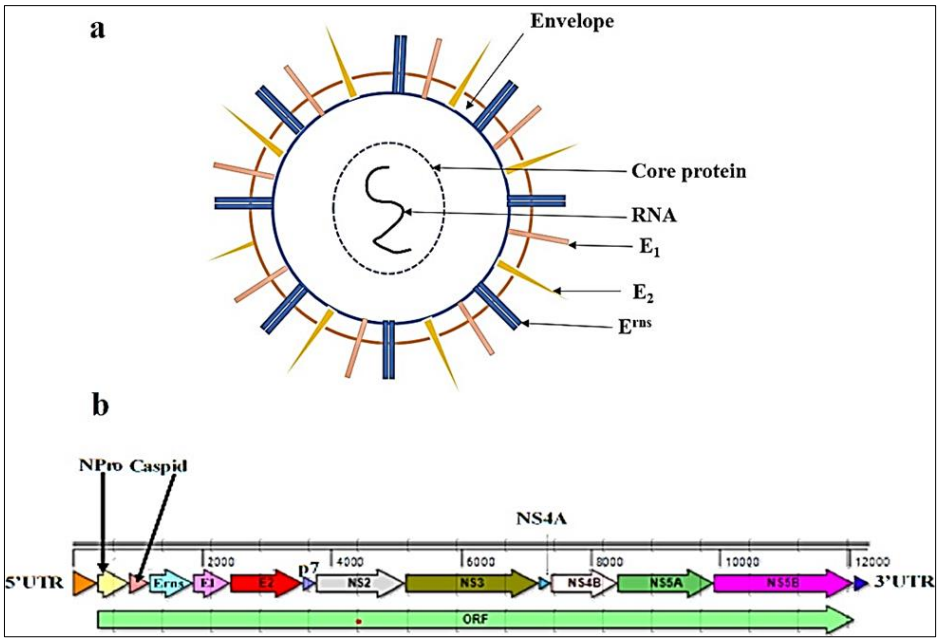

Fig 1: a. Structure of CSFV; b. Genome organization of CSFV

The UTRs contain conserved regions implicated in translational events [13]. Nevertheless, a recent study has indicated the possibility of recombination between strains [14]. The ORF is translated into a single polypeptide of about 3900 amino acids which is co-and post-translationally processed into mature peptides by several viruses and host-encoded proteases [15]. The virion consists of four structural proteins encoded at the 5' end of the genome, namely, C, E^{rns}, E1, and E2. The nucleocapsid coat of the virus is spherical and made up of numerous proteins whereas the surface is made of Erns, E1, and E2 present in homodimeric (E^{rns}, E2) or heterodimeric (E1E2) form [16]. The E1 and E2 structural proteins of the virion consist of transmembrane domains whereas Erns has no such domain and its attachment to the virion is rather weak. Apart from the structural proteins, the CSFV genome also encodes eight non-structural proteins, which comprise an N-terminal protease (Npro), p7, the non-structural proteins (NS) 2, 3, 4A, 4B, 5A, and finally 5B [17, 18]. CSFV is normally a non-cytopathogenic (ncp) virus. A rare cytopathogenic (cp) form can occur spontaneously in cell culture [19] and has also been found in wild boar [20]. Its significance in CSFV pathogenesis is unknown. The RNA of CSFV is infectious and acts as both the genomic and mRNA. The virus life starts with the attachment of envelope protein to host receptors which mediates the internalization of virus into the host cell through clathrin-mediated endocytosis. The viral envelope then fuses with the host endosomal membrane due to low pH and the RNA genome gets released into the cytoplasm. The positive-sense genomic ssRNA is then translated into a poly protein, which is cleaved to form all structural and non-structural proteins. Replication of the viral genome occurs at the surface of the endoplasmic reticulum in the cytoplasm. Virion assembly takes place at the endoplasmic reticulum and finally, it buds from the endoplasmic reticulum, is transported to the Golgi apparatus, and then exits the host cell via a secretory pathway [21].

3. Genetic diversity of CSFV

5'UTR, E2 glycoprotein gene, and 3'end of theNS5B polymerase gene (RdRp) are the three genomic regions that are recognized for the phylogenetic and genetic classification of CSFV isolates [22]. CSFV isolates from different parts of the world have been grouped into three genetic groups namely 1, 2, and 3, and each genetic group is further divided into subgroups. Genotype 1 is further divided into seven sub genotypes (1.1-1.7) whereas genotypes 2 and 3 are subdivided into three (2.1-2.3) and four (3.1-3.4) sub genotypes [23, 24]. Recently, due to high genetic variability, more subgroups have been identified within sub genotypes 2.1 and 2.2 which result in the segregation of genotype 2 into seven sub genotypes i. e. 2.1-2.7. Also, two new genotypes have been established namely 4 and 5 containing distantly related "congenital tremor" CSFV strain (Great Britain/1964) and two strains from Korea (KR/1998, KR/1999) [25]. Most isolates reported all over the world during 1980 and 1990 were of group 2. Most historical strains retrieved globally belong to genotype 1 which also contains in-use live attenuated vaccine strains. All field isolates reported from the American continent fall in genotype 1 but at the global level, genotype 2 emerged as the most dominant genotype over the last few decades. In India, the historical dominance of the 1.1 sub genotype was reported but in recent years the coexistence of three sub genotypes 1.1, 2.1 and 2.2 have been revealed by several reports with the dominance of 2.2 sub genotype [3, 22, 26-28]. The genetically similar isolates belonging to sub genotype 2.2 were also reported from the neighboring countries Nepal and Bangladesh [29, 30].

4. Geographical distribution

First reported in Ohio, USA, in the year 1833, CSF became widespread in Europe and America by 1866 [31]. Birch (1917) reported that the spread of virus infection may have been facilitated by the development of railways during the mid-

19th Century [32]. At the end of the 20th century, CSF remained widespread in many parts of the globe, but successful eradication was achieved in many countries of the world like Canada, America, and Australia. The first outbreak of CSF in Japan was recognized in 1888. With the development of the live attenuated GP vaccine in Japan in 1969, the outbreaks of CSF have decreased markedly but after a gap of 26 years, the disease has re-emerged in both domestic and wild pigs in Japan [33]. In South East Asia particularly in Indonesia, Korea, Malaysia, Myanmar, Mongolia, Philippines, Taiwan, and Vietnam, the disease is prevalent.

5. Status of CSF in India

In India, the first suspected case of CSF was reported from Aligarh, Uttar Pradesh, in 1944 [34]. Subsequently, the disease was reported in West Bengal, Andhra Pradesh, Maharashtra, Rajasthan, Bihar, Tamil Nadu, Punjab, Haryana, Himachal Pradesh, Meghalaya, Mizoram, Nagaland, Assam, Tripura, and Kerala [35]. According to the recent reports of All India coordinated research project on animal disease monitoring and surveillance (AICRP on ADMAS) from the National Institute of Veterinary Epidemiology and Disease Informatics, Bengaluru, CSF has emerged as the most reported viral disease of pigs in India during the year 2015-16 [3]. Since its first report in 1944 to the year 2017 outbreaks of CSF have been reported in 23 states of India [3, 22]. According to the data from OIE, a total of 2,618 outbreaks of CSF have been reported in India from 1996 to 2015 with a mortality of 29.04% [3]. The sporadic occurrence of disease throughout the year suggests the non-seasonal nature of disease occurrence in India. Based on Meta-Analysis data on CSF Prevalence in India, it was found that the prevalence of CSF ranges from 25-42% with 30% in the north; 37% in the west; 42% in the central; 41% in the east; 40% in northeast and 25% in south India [22, 36].

6. Transmission and pathogenesis and clinical signs

All species of domestic (Sus scrofa domesticus), feral and wild pigs, including European wild boar (Sus scrofa scrofa) and collared peccaries, are thought to be susceptible. Humans and other livestock species do not appear to be affected by CSF. Pigs usually become infected through the oronasal route by inhaling or ingesting the virus. Vertical transmission of CSFV from infected sows to their offspring can also occur and its secretion from all mucosal surfaces and in semen suggests its transmission through insemination [11, 37]. Frozen pork and its derived products can be a reservoir of the virus as CSFV has been reported to survive over long periods in these products [32]. Regardless of its route of entry virus primarily infects the epithelial cells of tonsillar crypts and then invades the lymphoid tissues. From lymphoid tissues, it is carried to regional lymph nodes and efferent blood capillaries leading to viremia. After that virus reaches the bone marrow and secondary lymphoid organs where it replicates. The parenchymatous organs are invaded late in the viremic phase. The immune system is a critical target for CSFV as it has a particular affinity for endothelial cells and the mononuclear phagocyte system, i.e. macrophages and dendritic cells (DCs) which play a crucial role in innate and adaptive immune response [22, 38, 39]. It is, therefore, evident that in CSFV infection breakdown of the immune system occurs which is accompanied by an aberrant pro-inflammatory response known as cytokine storm leading to an inability to control disease progression. Severe lymphopenia, lymphocyte apoptosis, thrombocytopenia, bone marrow, thymus atrophy, and thymocyte atrophy are also seen in CSF [23, 40]. Manifesting the highly variable clinical signs depending upon the virulence of virus strain and host immune system the CSFV infection may follow acute, sub-acute chronic, and unapparent subclinical courses. The acute infection caused by highly virulent strains of CSFV is characterized by symptoms of high fever, huddling, weakness, drowsiness, anorexia, conjunctivitis, and constipation followed by diarrhea [11]. Infected pigs may show purple discoloration of the skin in the abdomen, inner thighs, or ears and hemorrhages may be evident. The staggering gait followed by posterior paresis may also be seen in some cases. Vomiting bile may also occur and/or respiratory signs may develop. Although the incubation period of CSF is variable from 2-15 days, it is 3-7 days in acute cases and pigs in the acute stage of infection often die within 10-20 days after infection [41]. Sub-acute infections are caused by moderately virulent strains of CSFV and the clinical signs are less severe. However, the fever in sub-acute cases may persist for two to three weeks. When the immune system cannot eliminate the CSFV and the infection exceeds 30 days, infected pigs develop a chronic form of the infection where clinical signs are stunting, anorexia, intermittent pyrexia, and diarrhea [42-44]. Persistent infection may also be noticed, called Prenatal Course or 'late onset CSF.' Pregnant sows may be infected at any stage of gestation and the virus can pass placenta and infect the fetus. Infection caused by moderate to low virulent viral strains causes abortion, stillbirth, and mummification. Infection of sows around 50-70 days of gestation causes persistent infection in pigs born alive but they may develop a congenital tremor while others are asymptomatic at birth [23, 45]. These persistently infected pigs may not show signs for more than six months but shed the virus and spread the disease [42-45].

The postmortem lesions in CSF include hemorrhages in the skin, infarction in the spleen, and hemorrhagic enteritis, hemorrhagic mesenteric lymph nodes in the case of acute CSF form whereas necrotic tonsillitis and Button ulcers in the colon are the characteristic lesions in chronic CSF form [22,23].

7. Diagnosis of CSF

Rapid clinical and laboratory diagnosis is of utmost importance to for the effective control and treatment of CSF. Variability in clinical signs and post-mortem lesions along with persistent unnoticed infection often poses difficulty in the diagnosis of CSF [46]. Various diagnostic methods for the detection of CSFV antigens and antibodies are described in the OIE Manual of Diagnostic Tests and Vaccines for Terrestrial Animals, 2022 [47]. These methods include fluorescent antibody test (FAT), Immunoperoxidase staining using monoclonal antibodies for differentiation of pestiviruses, ELISA, Virus isolation in cell culture and Reverse transcription-polymerase chain reaction (RT-PCR). The serological diagnostic methods include the Fluorescent antibody virus neutralization test (FAVNT), Neutralizing peroxidase-linked assay (NPLA), and Antibody ELISAs [48]. The viral antigens are one of the most effective targets for molecular diagnosis and are detected by direct immunofluorescence or enzyme-linked immunosorbent assays (ELISAs). The virus can be easily grown and isolated in several cell lines of porcine origin including the porcine kidney cell line (PK15 and SK6) and swine testis endothelial

(STE) cells. However, the contamination of these cell lines with bovine viral diarrhea virus (BVDV) and other ruminant pestiviruses is a matter of concern that can interfere with the diagnosis [49]. The primary serological tests are widely used in India for surveillance and epidemiological investigations of CSF. ELISA based on E^{rns} and E_2 proteins is available for the serodiagnosis of CSFV which includes different variants of ELISA indirect, sandwich, and dot ELISA [50, 51].

During the past few decades, molecular or nucleic acid-based diagnostics emerged as a potential method of disease diagnosis, especially for pathogens with high genetic variability. Among these methods conventional Polymerase Chain Reaction (PCR), multiplex PCR, Reverse transcriptase polymerase chain reaction (RT–PCR), real-time quantitative PCR (qPCR), and RT-loop-mediated isothermal amplification (RT-LAMP) are at the forefront for CSF diagnosis [22, 23, 52, 53]. The CSFV RNA can also be detected in infected tissue using fluorescence-based in-situ hybridization (FISH) [54]. The advancement in genome sequencing techniques and next-generation sequencing platforms revolutionize the field of molecular diagnosis, particularly for genomic analysis of viruses. The complete genome sequences of Indian isolates belonging to genotypes 1 and 2 are also available and can be retrieved from the genomic databases [26-28].

8. Control of CSF

For economic reasons, proper reporting of disease, its control, and eradication is of huge importance. Following the strict biosecurity measures, restricted trans boundary movement of pigs, and investigations of infected wild pig populations are also important for controlling CSF in large pig farms. Vaccination is considered as the most effective and main choice for controlling CSF in countries where the disease is endemic along with stamping out policy with no vaccination [22, 23, 43]. Worldwide, live attenuated vaccines are widely used to control CSF both in domesticated and wild swine populations and paved a way for CSF eradication in several countries. Among the live attenuated CSFV strains used worldwide, the Lapinized Chinese (C) strain is the most common. The other regionally used stains are the Japanese guinea-pig exaltation-negative GPE strain, the Thiverval strain, the Riems strain, and the Mexican PAV strain [3, 22, 23, 55]. However, live attenuated vaccines are widely used for CSF control but these vaccines have a major disadvantage in that they cannot differentiate between infected the vaccinated animals (DIVA). Therefore, the need for marker DIVA vaccines was felt and subsequently two marker subunit DIVA vaccines Porcilis pesti and BayoVac developed by MSD animal health and BAYER AG respectively [22, 23, 56]. Both vaccines are based on the immunogenic E2 protein expressed in the baculovirus system and rely on the detection of antibodies against CSFV Erns protein employing the DIVA strategy. Although these vaccines provide a good platform for vaccination but also suffer from certain limitations like lower efficiency, slow immune response, incomplete protection against vertical transmission of CSFV, and incompatibility in oral delivery in wild boars. This led to the development of a second-generation marker vaccine in 2014, known as CP7_E2Alf (Suvaxyn) which contains a chimeric Pestivirus constructed in a BVDV backbone with E2 gene replaced by the E2 gene of CSF [57]. Although this vaccine addresses the disadvantages associated with the previously developed marker vaccines it lacks specificity as it shows cross-reactivity with BVDV or sera obtained from BVD-infected animals.

9. CSF vaccination in India

Due to its large economic impact CSF control in India has been prioritized by the government and hence Ministry of Fisheries, Animal Husbandry, and Dairying started the Classical swine fever control program (CSF-CP) in 2014-15. The program aims to control CSF by mass vaccination using live attenuated vaccines [22]. Lapinized vaccine using the Weybridge strain of CSFV has been used since 1964 but India suffered an acute shortage of vaccine as the need for vaccine is about 20 million doses per annum and the production is only 1.2 million doses per year [22, 56, 58]. It is clear from this data that it is difficult to meet the vaccine requirement through lapinized vaccines so attempts have been made to develop cell culture-based vaccines using either lapinized strain or local CSFV isolates. A few years back in 2020 an effective cell culture-based CSF vaccine has been developed by Indian Veterinary Research Institute which is marketed with the name ‘Raksha Class’ by Indian Immunologicals [22]. Apart from this, the reverse genetics strategy is also applied for the construction of cDNA clones using local CSF vaccine isolate which may present better and improved vaccine platforms in near future [59, 60].

10. Conclusion

The economic importance of CSF is attributed to its harmful effects on the pig industry worldwide. In India, the wide presence of CSF made it a disease of concern that needs to be addressed. Despite the extensive efforts taken to control CSF, it tends to re-emerge causing a continuous threat to the pig industry. In India also, significant efforts in CSF research, diagnosis, and vaccination has been made and are still in progress.

11. References

1. Department of Animal Husbandry, Dairying & Fisheries, Government of India, 20th Livestock Censuses; c2019.
2. Van Oirschot J. Hog cholera. In Coetzer JAW, Thomson GR, Tustin RC. (Eds) Infectious diseases of livestock. 2nd edn. Oxford University Press, Cape Town. 2004;2:975-986.
3. Singh VK, Rajak KK, Kumar A, Yadav SK. Classical swine fever in India: Current status and future perspective. Tropical Animal Health and Production. 2018;50:1181-1191.
4. India. Department of Animal Husbandry, Dairying & Fisheries, Government of India, 19th Livestock Censuses; c2012.
5. Sulabh S, Shivhare P, Kumari A, Kumar M, Nimmanapalli R. International Journal of Veterinary Sciences and Animal Husbandry. 2017;2(3):30-32.
6. Bett B, Deka RP, Padmakumar V, Sones KR. Prevention of Classical Swine Fever-An impact narrative from Northeast India. ILRI Research Brief 8. Nairobi, Kenya: ILRI; c2014.
7. Edward S, Fukusho A, Lefevre PC, Lipowski A, Pejsak Z, Roehe P, *et al*. Classical swine fever: The global situation. Veterinary Microbiology. 2000;73:103-119.
8. Simmonds P, Becher P, Bukh J, Gould EA, Meyers G, Monath T, *et al*. ICTV virus taxonomy profile: flaviviridae. Journal of General Virology. 2017;98:2-3.

9. Smith DB, Meyers G, Bukh J, Gould EA, Monath T, Muerho AS, *et al*. Proposed revision to the taxonomy of the genus Pestivirus, family Flaviviridae. Journal of General Virology. 2017;98:2106-2112.
10. Patrick J. Classical swine fever. In Foreign Animal Diseases, 7th Edition. St. Joseph, MO, USA: United States Animal Health Association; c2008. p. 197-205.
11. Moennig V, Floegel-Niesmann G, Greiser-Wilke I. Clinical signs and epidemiology of classical swine fever: a review of new knowledge. The Veterinary Journal. 2003;165:11-20.
12. Zhang H, Cao HW, Wu ZJ, Cui YD. A review of molecular characterization of classical swine fever virus (CSFV) Israel Journal of Veterinary Medicine. 2011;66:89-95.
13. Fletcher SP, Jackson RJ. Pestivirus internal ribosome entry site (IRES) structure and function: elements in the 52 untranslated region important for IRES function. Journal of Virology. 2002;76(10):5024-5033.
14. He DM, Qian KX, Shen GF, Zhang ZF, Li YN, Su ZL, Shao HB. Recombination and expression of classical swine fever virus (CSFV) structural protein E2 gene in *Chlamydomonas reinhardtii* chroloplasts. Colloids and Surfaces B: Bio interfaces. 2007;55(1): 26-30.
15. Rümenapf T, Unger G, Strauss JH, Thiel HJ. Processing of the envelope glycoproteins of pestiviruses. Journal of Virology. 1993;67(6):3288-3294.
16. Meyers G, Thiel HJ. Molecular characterization of pestiviruses. Advances in virus research 1996;47:53-118.
17. Falgout B, Pethel M, Zhang YM. Flaviviridae: The viruses and their replication. Journal of Virology. 1995;69(11):7232-7243.
18. Stark R, Rümenapf T, Meyers G, Thiel HJ. Genomic localization of hog cholera virus glycoproteins. Virology. 1990;174(1):286-289.
19. Mittelholzer C, Moser C, Tratschin JD, Hofmann MA. Analysis of classical swine fever virus replication kinetics allows differentiation of highly virulent from avirulent strains. Veterinary Microbiology. 2000;74(4):293-308.
20. Aoki H, Ishikawa K, Sakoda Y, Sekiguchi H, Kodama M, Suzuki S, *et al*. Characterization of classical swine fever virus associated with defective interfering particles containing a cytopathogenic sub genomic RNA isolated from wild boar. The Journal of Veterinary Medical Science. 2001;63(7):751-758.
21. Li S, Wang J, Yang Q, Naveed Anwar M, Yu S, Qiu HJ. Complex Virus-Host Interactions Involved in the Regulation of Classical Swine Fever Virus Replication: A Minireview. Viruses 2017;9:171. https://doi.org/10.3390/v9070171
22. Malik YS, Bhat S, Kumar ORV, Yadav AK, Sircar S, Ansari MI, *et al*. Classical Swine Fever Virus Biology, Clinicopathology, Diagnosis, Vaccines and a Meta-Analysis of Prevalence: A Review from the Indian Perspective. Pathogens. 2020;9(6):500. https://doi.org/10.3390/pathogens9060500
23. Ganges L, Crooke HR, Bohórquez JA, Postel A, Sakoda Y, Becher P, *et al*. Classical swine fever virus: the past, present and future. Virus research. 2020;289:198151. https://doi.org/10.1016/j.virusres.2020.198151
24. Garrido Haro AD, Barrera Valle M, Acosta A, Flores J. Phylodynamics of classical swine fever virus with emphasis on Ecuadorian strains. Trans boundary and Emerging Diseases. 2018;65:782-790. https://doi.org/10.1111/tbed.12803
25. Rios L, Nú˜nez JI, Díaz de Arce H, Ganges L, P´erez LJ. Revisiting the genetic diversity of classical swine fever virus: a proposal for new genotyping and sub genotyping schemes of classification. Trans boundary and Emerging Diseases. 2018;65:963-971. https://doi.org/10.1111/tbed.12909.
26. Rajkhowa TK, Hauhnar L, Lalrohlua I, Jagan MG. Emergence of 2.1 subgenotype of classical swine fever virus in pig population of India in 2011. Veterinary Quarterly. 2014;34:224-228.
27. Kumar R, Rajak KK, Chandra T, Thapliyal A, Muthuchelvan D, Sudhakar SB, *et al*. Whole-genome sequence of a classical Swine Fever virus isolated from the Uttarakhand state of India. Genome Announcement. 2014; 2:e00371-14. doi: https://doi.org/10.1128%2FgenomeA.00371-14
28. Kamboj A, Patel CL, Chaturvedi VK, Saini M, Gupta PK. Complete genome sequence of an Indian field isolate of classical Swine Fever virus belonging to sub genotype 1.1. Genome Announcement. 2014;2:e00886-14. doi: https://doi.org/10.1128/genomea.00886-14
29. Postel A, Jha VC, Schmeiser S, Becher P. First molecular identification and characterization of classical swine fever virus isolates from Nepal. Archives of Virology. 2013;158:207-210.
30. Sarkar S, Hossain ME, Gurley ES, Hasan R, Rahman MZ. An outbreak of classical swine fever in pigs in Bangladesh, 2015, Veterinary Medicine and Science. 2018;4:45-52.
31. Cole CG, Henley RR, Dale CN, Mott LO, Torrey JP, Zinober MR. History of hog cholera research in the US Department of Agriculture 1884-1960. Agriculture Information Bulletin No. 241, USDA, Washington DC; c1962.
32. Birch RR. Hog cholera transmission through infected pork. Journal of the American Veterinary Medical Association. 1917;51:303.
33. Postel A, Nishi T, Kameyama K, Meyer D, Suckstorff O, Fukai K, *et al*. Reemergence of classical swine fever, Japan, Emerging Infectious Diseases. 2019;25:1228-1231. https://doi.org/10.3201/eid2506.181578.
34. Krishnamurthy D, Adlakha SC. A preliminary report on the swine fever epidemic in Uttar Pradesh. Indian Veterinary Journal. 1962;39:406-419.
35. Sharma DK, Lal Krishna, Mishri J. Classical swine fever pigs and its status in India: A review. Indian Journal of Animal Science. 2008;78(12):1311-1317.
36. Patil SS, Suresh KP, Saha S, Prajapati A, Hemadri D, Roy P. Meta-analysis of classical swine fever prevalence in pigs in India: A 5-year study. Veterinary World. 2018;11: 297-303.
37. Floegel G, Wehrend A, Depner KR, Fritzemeier J, Waberski D, Moennig V. Detection of classical swine fever virus in semen of infected boars. Veterinary Microbiology. 2000;77:109-116.
38. Dahle J, Liess B. A review on classical swine fever infections in pigs: epizootiology, clinical disease and pathology. Comparative Immunology Microbiology and Infectious Diseases. 1992;15(3):203-11.
39. Ribbens S, Dewulf J, Koenen F, Laevens H, de Kruif A.

Transmission of classical swine fever. A review. Veterinary Quarterly. 2004;26:146-55.
40. Liu J, Fan XZ, Wang Q, Xu L, Zhao QZ, Huang W, *et al*. Dynamic distribution and tissue tropism of classical swine fever virus in experimentally infected pigs. Virology Journal 2011;8:201. https://doi.org/10.1186/1743-422X-8-201
41. Terpstra C. Hog cholera: an update of present knowledge. British Veterinary Journal. 1991;147(5):397-406.
42. Muñoz-González S, Ruggli N, Rosell R, Pérez LJ, Frías-Leuporeau MT, Fraile L, *et al*. Postnatal persistent infection with classical swine fever virus and its immunological implications. PLoS ONE 2015;10:e0125692.
43. Blome S, Staubach C, Henke J, Carlson J, Beer M. Classical Swine Fever-An Updated Review. Viruses 2017;9:86.
44. Rout M, Saikumar G. Virus load in pigs affected with different clinical forms of classical swine fever. Trans boundary and Emerging Diseases. 2012;59:128-133.
45. Boh´orquez JA, Mu˜noz-Gonz´alez S, P´erez-Sim´o M, Mu˜noz I, Rosell R, Coronado, *et al*. Foetal immune response activation and high replication rate during generation of classical swine fever congenital infection. Pathogens. 2020;9:285. https://doi.org/10.3390/pathogens9040285.
46. Moennig V, Becher P. Pestivirus control programs: how far have we come and where are we going? Animal Health Research Reviews. 2015;16:83-87. https://doi.org/10.1017/S1466252315000092.
47. World Organization for Animal Health (WOAH). Manual of diagnostic tests and vaccines for terrestrial animals [online]. Paris: WOAH; c2022. Classical swine fever. Available at: https://www.woah.org/fileadmin/Home/eng/Health_standards/tahm/3.08.03_CSF.pdf Accessed on 30 Nov 2022.
48. Postel A, Austermann-Busch S, Petrov A, Moennig V, Becher P. Epidemiology, diagnosis and control of classical swine fever: recent developments and future challenges. Trans boundary and Emerging Diseases. 2018;65:248–261. https://doi.org/10.1111/tbed.12676.
49. Postel A, Schmeiser S, Oguzoglu TC, Indenbirken D, Alawi M, Fischer N, *et al*. Close relationship of ruminant pestiviruses and classical Swine Fever virus. Emerging Infectious Diseases. 2015;21:668-672.
50. Sarma DK, Sarma PC. ELISA for detection of hog cholera virus antigen. Indian Journal of Animal Science. 1995;65:650-651.
51. Sarma DK, Meshram DJ. Comparison of sandwich and dot ELISA for detection of CSF virus antigen in pigs. Indian Veterinary Journal. 2008;85:915-918.
52. Depner K, Hoffmann B, Beer M. Evaluation of real-time RT-PCR assay for the routine intra vitam diagnosis of classical swine fever. Veterinary Microbiology. 2007;121:338-343.
53. Le Dimna M, Vrancken R, Koenen F, Bougeard S, Mesplede A, Hutet E, *et al*. Validation of two commercial real-time RT-PCR kits for rapid and specific diagnosis of classical swine fever virus. Journal of Virological Methods. 2008;147:136-142.
54. Nagarajan K, Saikumar G. Fluorescent in-situ hybridization technique for the detection and localization of classical swine fever virus in infected tissues. Veterinarski Arhiv. 2012;82:495-504.
55. Blome S, Moß C, Reimann I, K¨onig P, Beer M. Classical swine fever vaccines-state-of-the-art. Veterinary Microbiology. 2017;206:10-20.
56. Dong XN, Chen YH. Marker vaccine strategies and candidate CSFV marker vaccines, Vaccine. 2007;25:205-230.
57. Blome S, Wernike K, Reimann I, K¨onig P, Moß C, Beer M. A decade of research into classical swine fever marker vaccine CP7-E2alf (Suvaxyn® CSF Marker): a review of vaccine properties. Veterinary Research. 2017;48:51. https://doi.org/10.1186/s13567-017-0457-y.
58. Gupta PK, Saini M, Dahiya SS, *et al*. Molecular characterization of lapinized classical Swine Fever vaccine strain by full-length genome sequencing and analysis. Animal Biotechnology. 2011;22:111-117.
59. Kamboj A, Saini M, Rajan LS, Patel CL, Chaturvedi VK, Gupta PK. Construction of infectious cDNA clone derived from a classical swine fever virus field isolate in BAC vector using *in vitro* overlap extension PCR and recombination. Journal of virological methods. 2015;226:60-66. https://doi.org/10.1016/j.jviromet.2015.10.006
60. Coronado L, Perera CL, Rios L, Frías MT, Pérez LJ. A Critical Review about Different Vaccines against Classical Swine Fever Virus and Their Repercussions in Endemic Regions. Vaccines. 2021;9(2):154.