Review Article

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Swine Vesicular Disease: A clinical threat resembling Foot and Mouth Disease

Tridiganita I. Solikhah[1*], Aswin R. Khairullah[2], Syalzaesha A.F. Pengestu[1], Aloisius P. Alvaro[1], Ervina A. Lestari[1], Isma E. Cahyani[1], Muhammad Gufron[1], Yola F. Putri[1], Bantari W.K. Wardhani[3], Ikechukwu B. Moses[4], Daniah A. Afnani[5], Andi T. Khalisa[6], Dea A.A. Kurniasih[7], Syahputra Wibowo[8]

[1]*Division of Veterinary Clinic, Department of Health and Life Sciences, Faculty of Health, Medicine, and Life Sciences, Universitas Airlangga, Jl. Wijaya Kusuma No.113 Giri, Banyuwangi, East Java, 68422, Indonesia.*
[2]*Research Center for Veterinary Science, National Research and Innovation Agency (BRIN), Jl. Raya Bogor Km. 46 Cibinong, Bogor, West Java, 16911, Indonesia.*
[3]*Research Center for Pharmaceutical Ingredients and Traditional Medicine, National Research and Innovation Agency (BRIN), Jl. Raya Bogor Km. 46 Cibinong, Bogor, West Java, 16911, Indonesia.*
[4]*Department of Applied Microbiology, Faculty of Science, Ebonyi State University. Abakaliki 480211, Nigeria.*
[5]*Department of Microbiology and Parasitology, Faculty of Veterinary Medicine, Universitas Pendidikan Mandalika, Jl. Pemuda No. 59A, Dasan Agung Baru, Mataram, West Nusa Tenggara, 83125, Indonesia.*
[6]*Faculty of Military Pharmacy, Universitas Pertahanan, Kawasan IPSC Sentul, Sukahati, Citeureup, Bogor, West Java, 16810, Indonesia.*
[7]*Research Center for Public Health and Nutrition, National Research and Innovation Agency (BRIN), Jl. Raya Bogor Km. 46 Cibinong, Bogor, West Java, 16911, Indonesia.*
[8]*Eijkman Research Center for Molecular Biology, National Research and Innovation Agency (BRIN), Jl. Raya Bogor Km. 46 Cibinong, Bogor, West Java, 16911, Indonesia.*

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*Correspondence:

Corresponding author: Tridiganita Intan Solikhah
E-mail address: tridiganita-intan-s@fkh.unair.ac.id

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ABSTRACT

The contagious vesicular illness known as swine vesicular disease (SVD) affects pigs and has substantial veterinary and economic effects, primarily because its clinical signs are comparable to those of foot and mouth disease (FMD). Even while SVD is not zoonotic and seldom causes death, it can create emergency reactions that affect the trade in animals and livestock products, which makes it a serious problem. This illness is brought on by the Swine Vesicular Disease Virus (SVDV), a positive-stranded single-stranded RNA virus that is a member of the family Picornaviridae and genus Enterovirus. Since SVDV and human Coxsackievirus B5 share a high degree of genetic similarity, it is possible that the virus originated in humans and then crossed species to adapt to pigs. After being discovered in Italy for the first time in 1966, SVD has since been intermittently reported in many parts of Europe and Asia. Transmission happens by direct animal-to-animal contact, the fecal-oral route, and indirect channels including infected clothing, equipment, and vehicles. This virus poses a significant obstacle to eradication attempts due to its great resistance to environmental factors and disinfectants. Although subclinical infections are common, clinical symptoms include fever, weakness, and vesicles on the legs, muzzle, and around the nails. Control efforts depend on early discovery, animal culling, cleaning, and rigorous biosecurity implementation because there are no commercial vaccinations or targeted treatments available.

Introduction

Pigs that contract Swine Vesicular Disease (SVD) are infected by the Swine Vesicular Disease Virus (SVDV), a member of the Enterovirus genus that is a member of the Picornaviridae family (Tamba *et al*., 2020). Vesicular lesions from this disease are identical to those from Foot And Mouth Disease (FMD) (Fernández *et al*., 2008). SVD poses a risk to animal disease surveillance systems due to its similar clinical presentations, which can lead to misunderstanding in field diagnosis and policy overreaction if mistaken as FMD (Dekker, 2000). Since SVD affects trade and requires quick control, it is on the list of infectious animal diseases that need to be notified to the World Organization for Animal Health (WOAH/OIE) (Beltran-Alcrudo *et al*., 2019).

In 1966, SVD was originally recognized as a distinct disease entity in Italy following the identification of symptoms similar to FMD but with negative results on laboratory tests for FMD (Lin and Kitching, 2000). Later, in 1971, Hong Kong also experienced an SVD outbreak, which was later documented in other Asian and European nations (Dekker, 2000). SVDV is spread either directly by coming into touch with infected pigs or indirectly by contaminated feed, transportation, surroundings, and personnel who serve as mechanical vectors (Beltran-Alcrudo *et al*., 2019). The utilization of leftover food waste (swill feeding) tainted with the virus is a significant mode of transmission (Kedkovid *et al*., 2020). The virus has a significant risk of spreading indirectly due to its relative stability in the environment, particularly in situations with inadequate biosecurity and sanitation (Makovska *et al*., 2023).

Clinically, SVD takes two to seven days to incubate. Symptoms include vesicular lesions around the nails, on the legs, muzzle, and mouth (Chen *et al*., 2022). Sometimes the infection is subclinical, which makes it harder to identify and raises the possibility that the illness will spread unnoticed. Because SVD is so similar to other vesicular illnesses as FMD, Vesicular Stomatitis (VS), and Vesicular Exanthema of Swine (VES), clinical diagnosis of SVD is extremely challenging (Lin and Kitching, 2000). As a result, laboratory confirmation becomes crucial. The most common methods of diagnosis include RT-PCR, ELISA, and viral isolation (Reid *et al*., 2004). Since there is currently no commercially available treatment or vaccine, early discovery, isolation, culling of affected animals, and disinfection of contaminated sites are crucial to the control of SVD (Clemmons *et al*., 2021).

SVD's economic impact is often derived from policy ramifications rather than direct illness losses. International trade restrictions on pork products and their derivatives are immediately put in place once a nation is found to be positive for SVD (Dibaba, 2019). Usually, trading partners halt imports until the status of disease-free status is confirmed. This results in large financial losses, particularly for nations that export a lot of pork products (VanderWaal and Deen, 2018). Thus, even though SVD is categorized as a disease with minimal clinical impact, its existence raises serious concerns for livestock-based food security plans and animal health diplomacy.

Since it may influence global commerce in pork products, SVD has grown to be a serious animal health concern (Lin and Kitching, 2000). Despite having a low death rate and not being zoonotic, this disease is classified as an internationally notifiable animal disease, which means that prompt treatment and early discovery are necessary. Surveillance and control of this disease are crucial components of national veterinary policies in many nations, notably those in Southeast Asia, in order to stop its spread and major economic impact (Mai *et al*., 2024). The aim of this review article was to provide a comprehensive understanding of the various important aspects of this disease, including etiology, epidemiology, clinical manifestations, diagnostic methods, and control strategies for SVD.

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Etiology

In terms of virology, SVDV belongs to the Enterovirus genus, Enterovirus B species, and Picornaviridae family (Hyypiä *et al*., 1997). This virus is a non-enveloped, single-stranded RNA virus with positive polarity (+ssRNA) with a symmetrical, icosahedral capsid that is about 27–30 nanometers in size (Salmikangas *et al*., 2020). The single polyprotein chain encoded by the roughly 7,400 nucleotides that make up the viral genome is then broken down by viral proteases into structural and non-structural proteins (Inoue *et al*., 1989).

SVDV shares several genetic similarities with the human enterovirus Coxsackievirus B5 (CV-B5) (Huang *et al*., 2018). According to phylogenetic study, SVDV most likely started with CV-B5, which switched hosts from humans to pigs (Lomakina *et al*., 2016). It is believed that pigs are exposed to human excrement tainted with the virus through the fecal-oral route. Viral strains that may replicate effectively in pig tissues and induce distinctive clinical symptoms are created when the virus adapts to the new host. The resemblance between the 5'UTR genomic sequence typical of the human enterovirus group and the amino acid sequence of the VP1 protein reinforces this association (Gulholm *et al*., 2022).

The SVDV genome structurally encodes the four main capsid proteins, VP1, VP2, VP3, and VP4 (Kanno *et al*., 1999). The VP1 protein is essential for the virus's attachment to particular host cell surface receptors, which is the first stage of infection (Villanueva *et al*., 2005). Replication organelles (ROs) are modified internal membrane structures that serve as the site of viral RNA synthesis, allowing viruses to replicate only in the host cell's cytoplasm (Li *et al*., 2020). Similar to other enteroviruses, SVDV enters cells without a polymerase enzyme in its virion and uses its genome as mRNA to start making replication proteins (Escribano-Romero *et al*., 2000).

As is typical of enteroviruses, SVDV has a high capacity for environmental survival. This virus can withstand high temperatures, low pH (down to pH 3), organic solvents including ether and chloroform, and a variety of conventional disinfectants (Kristensen *et al*., 2021). This resistance facilitates indirect transmission through fomites by enabling the virus to persist for extended periods of time in feces, feed, drinking water, and cage surfaces (Dekker, 2000). This presents a significant obstacle to farm preventative and control initiatives.

History

In 1966, the Italian government recognized SVD as a disease for the first time (Lin and Kitching, 2000). At first, cases that were documented displayed the usual signs of vesicular disease, including fever, lameness, and blisters on the pig's foot and mouth. Animal health officials at the time believed that the case was FMD, a highly contagious vesicular illness that significantly affects the global animal commerce, because the clinical symptoms were identical (Chen *et al*., 2022). Further research was necessary, though, because laboratory results revealed that the causal culprit was distinct from the FMD virus (FMDV) (Kristensen *et al*., 2021).

A novel virus, later identified as Swine Vesicular Disease Virus (SVDV), which is a member of the family Picornaviridae and genus Enterovirus, was found to be the disease's causal agent through virological investigations (Lin and Kitching, 2000). It has been demonstrated that SVDV has a lot of genetic traits with the human virus Coxsackievirus B5 (Verdaguer *et al*., 2003). This suggests that the human virus that gave rise to SVDV most likely experienced adaptation and modification to become able to infect pigs. It is thought that this cross-species transmission is an instance of viral spillover, which leads to the development of novel cattle illnesses.

During the late 1960s and early 1980s, SVD spread to a number of other European nations after first appearing in Italy. Reports of cases have been made in Portugal, the UK, the Netherlands, and Belgium; patterns of dissemination indicate that the transit of pork products and the pig trade are important pathways of transmission (Lin and Kitching, 2000). Outbreaks of SVD happen occasionally in some regions, while the disease becomes endemic and endures for a long time in other regions, like Portugal and Italy (Tamba *et al*., 2020). As a result, nations have been compelled to strengthen their systems for monitoring and controlling diseases, which include outlawing the use of food waste as feed and boosting agricultural biosecurity.

An important turning point in animal health occurred in the 1960s when SVD was recognized as a distinct disease entity. This was because it showed how non-zoonotic viruses of the genus Enterovirus could cause a highly contagious disease in livestock that had a significant financial impact (Lin and Kitching, 2000). Since then, a number of nations have implemented specific vesicular disease surveillance programs for pigs and laboratory differentiation of all suspected FMD cases in order to predict the likelihood of SVD infection.

Epidemiology

Although the global spread of swine vesicular disease (SVD) is relatively recent, it has been a major problem in many parts of the world, particularly in Europe and Asia. Since its discovery in 1966 in Italy, SVD has reportedly spread to several European nations, including Portugal (Knowles *et al*., 2007), Spain (Mebus *et al*., 1993), England (Watson, 1981), the Netherlands (Terpstra *et al*., 1995), and Belgium (Pezzoni *et al*., 2021). The movement of live pigs, contaminated fomites, and contaminated pork products is the main way that the disease is transmitted (Beltran-Alcrudo *et al*., 2019). In these nations, SVD was endemic from the 1970s until the early 2000s.

The initial SVD outbreak epicenter was Italy, which saw recurrent outbreaks for almost 20 years (Tamba *et al*., 2020). Portugal too had a protracted SVD outbreak (Knowles *et al*., 2007). Once SVD-free, the UK saw multiple outbreaks between 1972 and 1982. Strict surveillance, animal movement restrictions, and a nationwide eradication program were used to manage the outbreaks (Donaldson *et al*., 1983). Over time, European nations have been able to lower the frequency of this disease by the introduction of policies to prohibit swill feeding, enhanced biosecurity, and international cooperation (Beltran-Alcrudo *et al*., 2019). The majority of European nations are currently SVD-free.

SVD case reports were documented in Taiwan during the late 1990s and early 2000s (Chen *et al*., 2013). Significant outbreaks have occurred in Taiwan, which has responded to the disease's growth by enacting a number of control measures, such as animal movement restrictions and stamping out. Few Asian nations outside of Taiwan have formally reported instances of SVD, but there is still a chance that the illness could spread, particularly in regions with a large pig trade, inadequate surveillance, and poorly controlled food waste management methods (Lin and Kitching, 2000).

The distribution of SVD is extremely restricted outside of Europe and Asia. No laboratory-confirmed SVD cases have been reported in Africa, Australia, or the Americas. This is mostly because of the robust veterinary surveillance systems and stringent biosecurity regulations in these regions. However, early discovery, required reporting, and import limitations from previously affected areas are necessary to retain these countries' SVD-free status.

Pathogenesis

The onset of SVD pathogenesis occurs when the virus enters a pig's body, typically by the oral-fecal route, direct contact with sick animals, or contaminated clothing and equipment (Dekker *et al*., 1995). This virus can persist in the external environment, such as in water, feed, and excrement, for an extended period of time (Gordon *et al*., 2019). SVDV enters the body through the oral mucosa or tiny skin wounds, infects local epithelial cells, and starts replicating right away (Bomsel and Alfsen, 2003). After then, the virus spreads to local lymphoid tissues like the tonsils and

the small intestine's Peyer's patches. From there, primary viremia is how the virus spreads throughout the body (Fenner *et al*., 1987). The epithelial cells of the skin and mucosa are the primary site of extensive viral replication, especially in regions with significant mechanical stress such the muzzle, legs, and nail area (Bomsel and Alfsen, 2003). The vesicular lesions that constitute the disease's clinical signature manifest here.

Vesicles are created when viral replication directly affects epithelial cells in a cytopathic manner (Netherton *et al*., 2007). The collection of fluid between cells (intercellular edema) is caused by this replication, which also results in cell death, the release of proteolytic enzymes, and a local inflammatory response. Vesicles may form and break, leaving erosions and ulcerations behind (Montiel *et al*., 2016). Laboratory diagnosis is necessary to make a conclusive differentiation because these vesicular lesions share morphological similarities with those produced by other vesicular disease viruses, including Vesicular Stomatitis Virus (VSV), Vesicular Exanthema of Swine Virus (VESV), and Foot and Mouth Disease Virus (FMDV) (Chen *et al*., 2022).

The host immune system starts to react to the infection by activating type I interferon and adaptive immune cells, and viremia is typically temporary (Seo and Hahm, 2010). The infection may only affect the intestinal mucosa in moderate or subclinical cases, with no overt clinical symptoms (Tamba *et al*., 2020). However, asymptomatic animals continue to be a significant source of transmission in the population because the virus can still be expelled in oral secretions and feces (Dekker *et al*., 1995). In contrast to the FMDV, SVDV does not result in latent infection or persistent viral infection. Animals often fully recover from acute infections and do not develop into virus carriers (Lin *et al*., 1998). Nonetheless, the primary obstacles to SVD pathogenesis are the extensive identification of subclinical infections and the virus's capacity to propagate via indirect pathways (fomites), which lengthens the cycle of transmission in pig populations, particularly in regions with inadequate biosecurity.

Immune response

SVDV infection triggers a complex immune response involving both the innate and adaptive immune systems. This virus usually enters the pig's body through the oral route or through wounds in the skin, then binds to specific receptors on the surface of host cells to initiate the replication process (Helke *et al*., 2015). Immediately after infection, the innate immune system responds through activation of immune sensors such as Toll-like receptors (TLRs), particularly TLR3 and TLR7, which recognize viral RNA as pathogen-associated molecular patterns (PAMPs) (Mogensen, 2009).

As a result of TLR activation, there is induction of production of pro-inflammatory cytokines and type I interferons (IFN-α and IFN-β) (Ivashkiv and Donlin, 2014). This interferon has an important role in limiting viral replication by activating the expression of interferon-stimulated genes (ISGs) which trigger antiviral mechanisms in cells (Lang *et al*., 2022). Dendritic cells will also process viral antigens and present them to T cells via the major histocompatibility complex (MHC), which is the initial step in adaptive immune activation (Broeke *et al*., 2013). Natural Killer (NK) cells may also play a role in recognizing and destroying infected cells before full T cell activation occurs (Cook *et al*., 2014).

In the adaptive immune phase, there is activation of two main pathways: T helper cells ($CD4^+$) and cytotoxic cells ($CD8^+$) (Taniuchi, 2018). Helper T cells will support the activation and differentiation of B cells into plasma cells that produce antibodies (McHeyzer-Williams *et al*., 2006). Neutralizing antibodies, particularly IgM and IgG, will play an important role in neutralizing circulating virus particles, preventing infection of new cells, and marking viruses for phagocytosis by macrophages (Neurath, 2008). However, in order to prevent the spread of the virus, cytotoxic T lymphocytes (CTL) that identify viral antigen fragments on MHC class I will eliminate infected host cells (Hewitt, 2003).

Following an SVDV infection, immunity is usually protective and creates memory cells that enable a quicker and more potent secondary immune response in the event of reexposure (Bugya *et al*., 2021). However, although this virus is more antigenically stable compared to other RNA viruses such as FMDV, the potential for slight antigenic alteration remains a worry, particularly in the context of vaccine development and serological diagnostic testing (Mateo *et al*., 2008).

An essential foundation for epidemiological surveillance is the identification of certain SVDV antibodies (by ELISA or virus neutralization test) (Yang *et al*., 2020). However, one of the primary reasons SVD vaccinations are not frequently utilized in control programs is because these antibodies are unable to discriminate between a natural infection and the reaction to vaccination. Despite the pig immune system's effectiveness in combating SVDV, control methods still depend on detection-based biosecurity and prevention and eradication rather than mass vaccination.

Clinical manifestations

SVD typically takes two to seven days to incubate after viral exposure. The first signs are usually a low-grade temperature (40–41°C), which might be followed by anorexia, lethargy, and a decrease in activity (Martín-Acebes *et al*., 2009). Then, vesicles (blisters) form on parts of the body that are vulnerable to pressure or friction, like the distal legs, nail beds, lips, tongue, and muzzle (Zhang *et al*., 2022). The size of these vesicles, which contain clear fluid, varies according to the infection's location and intensity. The vesicles that form typically rupture after 1-2 days, leaving behind painful erosions and ulcerations (Fry *et al*., 2003). Among the most noticeable symptoms is claudication, or limping, which can be caused by sores around the nails. Lesions in the nail bed may occasionally result in sloughing, or the nail falling off (Pasma *et al*., 2008). It is crucial to get a differential diagnosis because this could be mistaken for physical injuries or other illnesses.

Animals may exhibit no symptoms other than a transient fever or appetite loss in moderate or subclinical cases, particularly in populations that have already been infected. However, they are still able to spread the virus through their feces and secretions (Burrows *et al*., 1974). Therefore, even in the absence of clinical instances, serological surveillance becomes a crucial tool in determining the disease's prevalence. Young pigs may have less severe symptoms or no symptoms at all, but histopathologically, the epithelial tissue still has lesions (Kumar *et al*., 2017). The majority of pigs will recover in 7–10 days, and the death rate from SVD is often very low (Lin *et al*., 1998). Nonetheless, each suspected case should be handled as a veterinary emergency until laboratory testing proves otherwise due to its resemblance to FMD and its effect on the global animal trade.

Diagnosis

Feces, nasal and oral swabs, lesions (such as vesicular fluid, epithelial lining, scrapings, and swabs of deep erosions), and certain other secretions and excretions can all include SVDV, its antigens, and/or nucleic acids (Singh *et al*., 2012). Some tests, meanwhile, lack the sensitivity necessary to be applied to every kind of clinical sample. It is important to manage samples as though they contained the more delicate SVDV or FMDV, even though SVDV is a stable virus (Alexandersen *et al*., 2003).

ELISA is capable of detecting viral antigen in vesicular lesions. Typically, the antigen content in stool is too low for this test to detect (Yang *et al*., 2020). Although complement fixation and immunohistochemistry have been used in the past, other forms of antigen detection tests are rarely employed (Chen *et al*., 2022).

A range of clinical sample types, such as stool, oral and nasal swabs, and lesion material, can have their nucleic acids detected by RT-PCR testing (Reid *et al*., 2004). Pigs that are subclinically sick can be identified with the help of fecal samples. Oral fluids are promising as well. SVDV and viruses that cause other vesicular diseases, like vesicular stomatitis, vesicular exanthema, and foot and mouth disease in pigs, can be detected simultaneously by a number of published multiplex RT-PCR techniques (Lung *et al*., 2011). Assays for SVDV using lateral flow and loop-mediated

isothermal amplification have also been published (Fowler *et al*., 2016).

SVD can also be identified by virus isolation, albeit this is rarely done these days (Lin *et al*., 1998). If the presence of the virus is suggested by RT-PCR or ELISA antigen detection but not by clinical signs, serology, or an epidemiological connection to a herd outbreak, the World Organization for Animal Health (OIE) advises attempting SVDV isolation (Callens and De Clercq, 1999). SVDV is detected by antigen detection ELISA or RT-PCR and is present in pig cell lines, particularly IB-RS-2 cells (Paprocka, 2010). If there are other enteroviruses in the sample, false negative results could happen. Despite their ability to be differentiated during virus identification, these viruses have the potential to outgrow SVDV or interfere with its growth (Fry *et al*., 2003).

Serology is frequently used to identify swine vesicular disease, especially during export certification or surveillance. ELISA and viral neutralization (microneutralization test) are the most widely used serological tests (Yang *et al*., 2020). About 0.2–0.4% of unexposed pigs have positive or equivocal ELISA results, and roughly half of these samples are likewise positive when retested with virus neutralization (Yang *et al*., 2022). Occasionally, transient false-positive reactions are observed, albeit the source is unknown. Retesting these "single reactors" and their clusters will reveal them. The animal is not infected if there are no seropositive groups present and the second titer is steady, declining, or negative. Only antigen-specific IgM is seen in serum from single reactors, but serum from infected pigs typically contains specific IgG or both IgG and IgM (Butler *et al*., 2005). Sera from single reactors had a broad range of patterns in immunoblots, while sera from animals that tested positive responded nearly exclusively with the VP1 protein (Brocchi *et al*., 2006). Rare occurrences involving several reactors have been reported, although usually only one reactor is found in a swarm.

Differential diagnosis

Since the clinical signs and symptoms of SVD are quite similar to those of several other vesicular illnesses in pigs, differential diagnosis is essential to establishing a precise diagnosis. It is challenging to visually differentiate this condition from other vesicular disorders due to the characteristic lesions, which are vesicles (blisters) surrounding the mouth, tongue, nipples, and particularly the nail beds (Chen *et al*., 2022). Therefore, it is crucial to identify other illnesses that present with comparable symptoms in order to avoid improper handling and the application of quarantine regulations.

In order to make a differential diagnosis of SVD, Foot and Mouth Disease (FMD) is the first and most crucial condition to weigh in (Wong *et al*., 2020). The genus Aphthovirus, which causes FMD, is one of the most dreaded animal illnesses in the world because of its high rate of transmission and effects on trade (Brown *et al*., 2022). Pigs with FMD have symptoms that are extremely similar to those of SVD, such as a high temperature, mouth and hoof blisters, lameness, and decreased appetite (Kitching and Alexandersen, 2002). On the other hand, FMD frequently results in more widespread lesions, substantial population morbidity, and occasionally death, particularly in young animals (Longjam *et al*., 2011). Laboratory validation using RT-PCR, ELISA, or virus isolation is crucial to distinguishing between the two because of their clinical similarities (Khairullah *et al*., 2024).

Vesicular Stomatitis (VS), a vesicular disease brought on by a Vesiculovirus belonging to the Rhabdoviridae family, is another differential diagnosis (Liu *et al*., 2021). Pigs, horses, and cattle are among the many species that can be impacted by VS (Rozo-Lopez *et al*., 2018). Clinical manifestations include ulcers and vesicles in the foot, mouth, and muzzle (Urie *et al*., 2018). Seldom observed in Europe or Asia, VS is mostly widespread in the Americas, particularly in tropical and subtropical regions (Kumar *et al*., 2018). Despite their clinical similarities, VS and SVD can be distinguished from one another by distinctions in geographic distribution and test results (Blanco and Vizcaino, 2000).

Vesicular Exanthema of Swine (VES) is another vesicular disease to take into account. It is brought on by a virus belonging to the Caliciviridae family (Neill *et al*., 1998). Although the virus that causes VES is still present in marine animals, the disease was considered eradicated worldwide, particularly in the United States, in the 1950s (Smith and Akers, 1976). Therefore, even with a low probability, VES remains a meaningful differential diagnosis in scientific investigations or in extremely strict biosecurity circumstances (Zee *et al*., 1967).

A number of non-infectious diseases, including mechanical injuries to the foot or mouth, chemical burns from feed or poisonous materials, and secondary bacterial infections that result in ulcers or local inflammation, can also clinically resemble SVD in addition to primary vesicular disease. These illnesses do not spread as quickly as viral infections, though, and can typically be distinguished by obtaining a history and looking at the surrounding environment.

Transmission

SVDV can be contracted by ingesting, mucous membranes or broken skin, direct contact, or a contaminated environment (Glud *et al*., 2021). The virus is unlikely to transmit between pens unless there is an environmental or fomite transmission source, like a shared open drainage system, or pigs are moved or mixed. Airborne transmission is negligible (Hu *et al*., 2023). Pigs can expel SVDV through their urine, semen, feces, and nasal and oral fluids (Dekker, 2000). Transmission may start up to 48 hours before clinical symptoms appear. Vesicles are also home to the virus (Inoue *et al*., 2005). If pork is offered to other pigs in an uncooked or undercooked state, it can spread SVDV (Pezzoni *et al*., 2021). Rarely, animals can stay sick for up to three months, although most recover from the virus in two weeks (Escribano-Romero *et al*., 2000). The virus has been found in these pigs' tonsil and nasal secretions, as well as in their feces for extended periods of time (Lin *et al*., 1998).

Fomites are crucial to the transmission of SVDV, which can persist in the environment for extended periods of time (Pezzoni *et al*., 2021). The virus was discovered in farmers' nasal passages and in earthworms that had been buried with infected pigs (Escribano-Romero *et al*., 2000). This virus can endure a broad pH range, arid environments, and freezing temperatures since it is comparatively heat resistant (Lin and Kitching, 2000). Viable virus has been detected after 4-11 months at pH 2.5 to 12, when temperatures are between 12°C (54°F) and –20°C (-4°F) (Glud *et al*., 2021). In certain cases, SVDV can persist in dried, salted, or smoked meat for up to two years; in other cases, the virus can be rendered inactive in less than a year (McKercher *et al*., 1985). The various transmission pathways of SVDV are illustrated in Figure 1, which clearly distinguishes between direct transmission routes such as ingestion, exposure through mucous membranes or broken skin, and feeding undercooked pork, and indirect routes, including contact with contaminated surfaces, fomites (e.g., boots, equipment, drainage systems), and minimal airborne exposure from infected pigs or environmental sources.

Risk factors

The primary risk factors for SVD are tightly linked to biosecurity, animal mobility, and farm management techniques. Moving live pigs has a significant impact on the transmission of this illness, particularly if the animals are coming from affected areas or are not subjected to proper quarantine and health check procedures (Dekker *et al*., 1995). Additionally, because SVDV may live in contaminated animal products, using food waste (swill feeding) as feed poses a serious concern, particularly if it is not boiled first (Tamba *et al*., 2020). The transfer of viruses across cages or between farms is also facilitated by poor biosecurity, which includes things like a lack of disinfection protocols, unrestricted access to cages by outsiders, and inadequate environmental sanitation (Pezzoni *et al*., 2021). Pigs from various sources are mixed together without stringent

safeguards in slaughterhouses and livestock markets, increasing the risk (Dibaba, 2019). The situation is further exacerbated by farmers' ignorance of disease symptoms and inadequate disease reporting or monitoring systems, which permit the virus to spread covertly before preventative action is taken (Lin and Kitching, 2000).

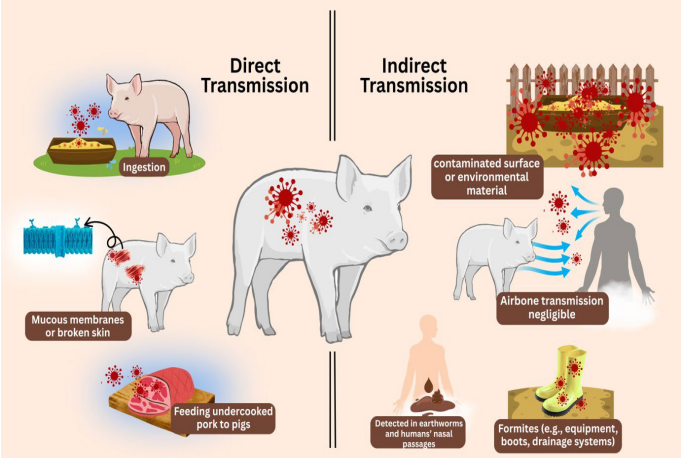

Figure 1. Transmission Pathways of Swine Vesicular Disease Virus (SVDV): Direct and Indirect Route

Public health importance

Even while SVD is not a zoonotic disease and cannot be spread to people, it is nevertheless very important in terms of public health (Beltran-Alcrudo *et al*., 2019). Particularly in areas where pigs are a significant source of animal protein and revenue, SVD epidemics have the potential to upset animal food supply chains, result in shortages of pork, and affect food security (Lin and Kitching, 2000). Socioeconomic stress can also result from epidemic management practices like mass extermination and trade restrictions, particularly in rural areas (Clemmons *et al*., 2021). Ineffective risk communication can also lead to a rise in public mistrust of food safety and worries about eating pig products (Chen *et al*., 2022). Since the SVD virus can persist in animal pens and waste for a considerable amount of time, inadequate biosecurity management also raises the possibility of other diseases developing, which could have a more extensive effect (Dekker, 2000). As a result, SVD prevention and control are crucial components of a One Health-based public health strategy that highlights the connections between human, animal, and environmental health.

Economic impact

International commerce disruption, especially with regard to the export of live pigs and their products, is one of the most important economic effects of SVD (Lin and Kitching, 2000). The World Organization for Animal Health (WOAH/OIE) has designated SVD as a notifiable illness, so when a case is found in a nation, trading partner nations may immediately block export access (Clemmons *et al*., 2021). This results in significant losses for the pig farming sector, particularly in the major exporting and producing nations. The revenue of farmers and exporters is directly impacted by these trade restrictions, but they also cause supply chain disruptions, lower selling prices, and market uncertainty (Kappes *et al*., 2023).

Systematic and expensive measures are needed to control SVD, ranging from surveillance, laboratory testing, and quarantine to the killing of diseased animals and cleaning up contaminated regions (Bellini *et al*., 2007). Farmers naturally suffer direct losses when exposed animals must be killed in large numbers to stop the disease from spreading (Tamba *et al*., 2020). Additionally, livestock owners who lose their animals as a result of the eradication campaign must receive financial compensation from the government (Kappes *et al*., 2023). The nation's economy is further burdened by the expenses of infrastructure, human resources, and logistics necessary to enable a prompt response to the outbreak (Hanson *et al*., 2022).

The indirect effects on productivity are nonetheless noticed even if SVD infections typically do not result in high mortality or appreciable production declines (Dekker, 2000). Reduced revenue will result from production, distribution, and marketing management problems for the impacted farms (Beltran-Alcrudo *et al*., 2019). Despite the fact that SVD cannot be spread to humans, consumers may also g*et al*armed or lose faith in the safety of domestic pig products (Lin and Kitching, 2000). The livestock industry may face additional financial strain if local markets see a decline in selling prices as a result of this decline in demand.

Governments and industry participants have been compelled by the rise in SVD cases to invest more on biosecurity measures, such as monitoring animal movements, expanding the capacity of diagnostic labs, and educating veterinary medical professionals (Pezzoni *et al*., 2021). Although this is a crucial step in stopping the spread, the expense of such investments frequently becomes an extra burden, particularly for poor nations with weak health systems. Outbreaks of SVD may eventually compel nations to redirect resources from other areas to animal health (Lin and Kitching, 2000).

Treatment

There is currently no specific antiviral medication or treatment that can directly cure SVD (Martín-Acebes *et al*., 2009). Infected animals are typically treated with supportive care, which aims to reduce symptoms and avoid secondary infections, particularly those that develop in the mouth and foot as sores or vesicles (Dekker, 2000). The course of treatment entails keeping the wound clean, giving additional antibiotics if needed to stop bacterial infection, and making sure the pig has enough food and water while it heals (Helke *et al*., 2015).

Vaccination

The majority of countries, especially those that have attained disease-free status, do not prescribe or employ vaccines for SVD, despite the fact that vaccination is a widespread method in the control of many infectious animal illnesses (Mowat *et al*., 1974). The reasons are less about mass vaccination and more about control and eradication measures that prioritize early discovery, prompt reporting, and culling of diseased animals.

The challenge of serologically differentiating between vaccinated and naturally infected pigs is one of the primary arguments against the use of the SVD vaccination (Yang *et al*., 2020). The use of vaccines can result in antibodies that resemble those produced by a natural illness, making serology-based surveillance schemes more challenging (Vashishtha and Kumar, 2024). This could conceal the virus's population-wide existence and postpone eradication attempts. As a result, a non-vaccine strategy is thought to be more successful in preserving disease-free status and safeguarding global trade in pigs and pork products.

Control

Controlling SVD is crucial to preserving the health of the swine population and shielding the livestock industry from large financial losses. Because of the highly contagious and long-lived nature of the virus that causes SVD, controlling the disease necessitates a rigorous, methodical strategy that is founded on the concepts of biosecurity and early identification (Dekker, 2000). The primary objective of SVD control is to preserve a disease-free status in order to facilitate international trade in pigs and pork products, in addition to limiting local transmission.

Rapid detection and reporting are the first steps in SVD control (Xu

et al., 2017). Although these symptoms can be confused with those of other vesicular diseases like FMD, farmers and animal health professionals should be able to identify clinical markers such vesicles on the muzzle, legs, and around the mouth (Montiel *et al*., 2016). Therefore, in every suspected case, laboratory confirmation is crucial. As soon as a case is identified, quarantine restrictions are put in place to limit the flow of people and animals to and from the outbreak site (Schwartz, 1982).

The selective culling (stamping out) of high-risk and diseased animals is one of the primary control methods (Clemmons *et al*., 2021). This is typically followed by a complete cleaning and disinfection of the surrounding area, vehicles, equipment, and cages (Kristensen *et al*., 2021). Since SVDV may live in feces and on damp surfaces, preventing the cycle of transmission requires rigorous sanitation (Lin and Kitching, 2000). Additionally, until additional testing determines that pork from the impacted areas is safe, all trade and distribution activities will be temporarily halted.

The two main pillars of SVD control are active and passive surveillance (Xu *et al*., 2017). Farmers report suspicious symptoms as part of passive monitoring, while veterinary authorities use sample and serological testing to conduct active surveillance, particularly in high-risk or outbreak-prone areas (Tamba *et al*., 2020). It was also made easier to track the origin and distribution of animals by strengthening the animal tracking and identification system.

Increased farm-level biosecurity measures, such as wearing protective gear, limiting access to pens, disinfecting tools and vehicles, and educating farmers and staff on the value of early disease detection and cleanliness, support this control strategy (Martín-Acebes *et al*., 2009). The government can also impose stringent rules, such prohibiting the feeding of swill, which is one of the primary ways that viruses infect pigs (Tamba *et al*., 2020).

Conclusion

Since SVD is an infectious animal disease that shares clinical characteristics with other vesicular diseases, especially FMD, it needs to be given careful consideration in the international animal health system. Even while SVD is not zoonotic and typically does not result in substantial mortality, it can lead to trade restrictions and lower market trust in pig products from impacted areas, which has a significant economic impact. The etiological agent, SVDV, belongs to the Enterovirus genus, which is highly resistant to environmental factors and is mainly transmitted by indirect contact and the fecal-oral route. Making the right diagnosis is crucial to distinguishing SVD from other, more severe vesicular illnesses. Control methods now rely more on early diagnosis, killing diseased animals, and the application of stringent biosecurity measures because there is no vaccine or particular treatment.

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Conflict of interest

The authors have declared no conflict of interest.

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