

Aujeszky's Disease (Pseudorabies) in pigs: An updated review of current knowledge and control measures

Jola Rahmahani^{1*}, Aswin R. Khairullah², Suwarno Suwarno¹, Muharam Saepullo², Imam Mustofa³, Abdul H. Furqoni⁴, Rury M. Wahyuni¹, Syahputra Wibowo⁵, Bima P. Pratama⁶, Sri S. Prihandani², Ricadonna Raissa⁷, Saifur Rehman⁸, Sheila M. Yanestria⁹, Ikechukwu B. Moses¹⁰

¹Division of Veterinary Microbiology, Faculty of Veterinary Medicine, Universitas Airlangga, Kampus C Mulyorejo, Jl. Dr. Ir. H. Soekarno, Surabaya, 60115, East Java, Indonesia.

²Research Center for Veterinary Science, National Research and Innovation Agency (BRIN), Jl. Raya Bogor Km. 46 Cibinong, Bogor, 16911, West Java, Indonesia.

³Division of Veterinary Reproduction, Faculty of Veterinary Medicine, Universitas Airlangga, Kampus C Mulyorejo, Jl. Dr. Ir. H. Soekarno, Surabaya, 60115, East Java, Indonesia.

⁴Center for Biomedical Research, National Research and Innovation Agency (BRIN), Jl. Raya Bogor Km. 46 Cibinong, Bogor, 16911, West Java, Indonesia.

⁵Eijkman Research Center for Molecular Biology, National Research and Innovation Agency (BRIN), Jl. Raya Bogor Km. 46 Cibinong, Bogor, 16911, West Java, Indonesia.

⁶Research Center for Process Technology, National Research and Innovation Agency (BRIN), KST BJ Habibie, Serpong, South Tangerang, 15314, Banten, Indonesia.

⁷Department of Pharmacology, Faculty of Veterinary Medicine, Universitas Brawijaya, Jl. Puncak Dieng, Kuncu, Kalisongo, Dau, Malang, 65151, East Java, Indonesia.

⁸Department of Pathobiology, Faculty of Veterinary and Animal Sciences, Gomal University, RV9W+GVJ, Indus HWY, Dera Ismail Khan, 27000, Pakistan.

⁹Department of Veterinary Public Health, Faculty of Veterinary Medicine, Universitas Wijaya Kusuma Surabaya, Jl. Dukuh Kupang XXV No.54, Dukuh Kupang, Dukuh Pakis, Surabaya, 60225, East Java, Indonesia.

¹⁰Department of Applied Microbiology, Faculty of Science, Ebonyi State University, Abakaliki, 480211, Nigeria.

ARTICLE INFO

Received: 01 July 2026

Accepted: 17 September 2026

*Correspondence:

Corresponding author: Jola Rahmahani
E-mail address: jola-r@fkh.unair.ac.id

Keywords:

Aujeszky's disease, Herpesvirus, Pig, Suid herpesvirus 1, Virus.

ABSTRACT

Pigs are the major reservoir and natural host of Aujeszky's disease, an infectious disease caused by Suid herpesvirus 1 (SHV-1). The illness is widespread throughout the world and has a major effect on pig farm output and animal health. Clinical symptoms can include neurological problems in piglets, respiratory diseases during the growth period, and reproductive disorders in pregnant sows, depending on the age and immune condition of the host. Establishing a latent infection in sensory nerve ganglia, which permits virus reactivation and sustains circulation within the population, is a crucial feature of SHV-1. Direct contact, aerosols, fomites, and vertical transmission from sow to fetus are all methods of transmission. The existence of feral pigs as an extra reservoir and farm management elements like population density and inadequate biosecurity increase epidemiological complexity. Clinical symptoms and pathology are combined with laboratory confirmation using molecular, serological, and immunohistochemical techniques to make the diagnosis. Aujeszky's disease control depends on the combination of active and passive surveillance, stringent biosecurity implementation, and vaccination, especially marker vaccines based on the DIVA method. Even though some nations have attained disease-free status, problems still exist because of animal migration and reintroductions from wild reservoirs. Thus, a risk-based control strategy is essential to permanently lessening the effects of this illness.

Introduction

Suid herpesvirus 1 (SHV-1), a member of the *Herpesviridae* family, subfamily Alphaherpesvirinae, is the infectious agent that causes Aujeszky's disease, often known as pseudorabies (Duan *et al.*, 2025). The main natural hosts and reservoirs are domestic pigs (*Sus scrofa domesticus*) and feral pigs (Ferrara *et al.*, 2021). Other mammalian species, including small ruminants, dogs, and cats, might unintentionally contract the infection, which usually results in death (Salwa, 2004; Thiry *et al.*, 2013; Papageorgiou *et al.*, 2025). This illness has a major influence on animal health and pig production systems worldwide, despite not being a major zoonosis (Zheng *et al.*, 2022).

According to epidemiology, Aujeszky's illness is found all over the world and has different levels of control in different places (Cano-Terriza *et al.*, 2019). Through organized eradication campaigns, some nations have successfully attained disease-free status, while the disease is still endemic in other areas (Yamane *et al.*, 2015). These variations are typically associated with vaccination rates, the efficacy of surveillance systems, and the degree of biosecurity implementation (Wang *et al.*, 2026). Another crucial element in sustaining viral circulation and perhaps resulting in re-introduction into domestic populations is the existence of reservoirs in feral pig populations (Wong *et al.*, 2019).

Clinically, the host's age and immunological condition have a significant impact on how the disease manifests (Sehl and Teifke, 2020). While respiratory discomfort, poor growth performance, and decreased production efficiency are the main signs in older pigs, infection frequently results in acute encephalitis with a high fatality rate in piglets (Papageorgiou *et al.*, 2017). Infection in pregnant sows can result in reproductive

problems that directly affect population productivity, such as abortion, fetal mummification, or the birth of weak piglets (Wang *et al.*, 2025).

A major contributing element to the persistence of infection in the population is the biological traits of SHV-1, which can create a latent infection in sensory nerve ganglia (Klupp, 2021). The virus can lie dormant for extended periods of time without producing any clinical signs, but it can reawaken in response to stress, immunosuppression, or environmental changes (Chen and Yu, 2024). This keeps the cycle of transmission within the livestock system going by enabling infected individuals to act as sources of recurrent infection (Hahn *et al.*, 1997).

Aerosols, contaminated fomites, and direct touch are the three ways that SHV-1 is spread (Cunningham *et al.*, 2021). The virus spreads more quickly in intensive, high-density livestock systems, and cross-regional distribution is facilitated by animal movement between farms (Liu *et al.*, 2022a). Additionally, the existence of feral pigs as an ecological reservoir makes disease control more difficult, especially in regions where domestic and wild populations coexist (Koshemetov *et al.*, 2021).

Due to death, decreased reproductive productivity, stunted growth, and expensive management and surveillance expenses, Aujeszky's illness results in substantial financial losses (Miller *et al.*, 1996). The economic burden is made worse by the extra effects of trade restrictions on live animals and their derivatives, especially in nations with commercial livestock systems that rely heavily on exports (Martínez-López *et al.*, 2009).

The efficacy of disease control has increased thanks to developments in molecular diagnostics, the creation of marker vaccines based on the Differentiating Infected from Vaccinated Animals (DIVA) method, and the application of risk-based biosecurity (Ma *et al.*, 2008). The existence of natural reservoirs, the dynamics of the animal trade, and the possibility

of dormant viruses reactivating in infected populations are still significant obstacles (Masot *et al.*, 2017).

Aujeszky's disease continues to be a crucial model for the research of viral diseases in animals because of the intricate relationships between the causal agent, host, and environment. In order to enable efficient and long-lasting population-level control efforts, a thorough understanding of this disease's features is crucial. The purpose of this review was to present a synthesis of the latest scientific knowledge on Aujeszky's disease, covering the characteristics of the causative agent, the mechanisms of pathogenesis, epidemiological patterns, clinical manifestations, and strategies for diagnosis, prevention, and control, to support more effective and sustainable disease management efforts.

Etiology

SHV-1, a member of the genus *Varicellovirus*, subfamily *Alphaherpesvirinae*, and family *Herpesviridae*, is the cause of Aujeszky's disease (Ferrara *et al.*, 2021). The double-stranded DNA genome of this enclosed DNA virus encodes a variety of structural and non-structural proteins involved in virulence, immunological evasion, and replication (Mettenleiter, 2000).

SHV-1's structure consists of an icosahedral capsid encased in a lipid envelope that contains significant surface glycoproteins including gB, gC, gD, and gE, as well as a tegument (Serena *et al.*, 2013). These glycoproteins are involved in cell-to-cell transmission, cell membrane penetration, and viral attachment to host cells (Nauwynck, 1997). The creation of marker vaccines utilized in the differentiation approach between infected and vaccinated animals (DIVA) has also been based on variations in the expression or function of specific glycoproteins, especially gE (Zheng *et al.*, 2022).

SHV-1 has a significant preference for lymphoid tissue, the neurological system, and epithelial tissue (Sehl and Teifke, 2020). One important biological feature underpinning illness development is the virus's capacity to reproduce effectively in the upper respiratory tract's epithelial cells before moving on to the central nervous system (Wong *et al.*, 2019). Additionally, the virus can create a latent infection in sensory nerve ganglia, which allows it to stay in the host for an extended period of time without causing any symptoms (Laval and Enquist, 2020).

Under farm conditions, SHV-1's biological stability is sufficient to allow transmission through direct touch and fomites, but it is comparatively limited in the external environment (Ukhovskiy *et al.*, 2022). The virus requires favorable environmental conditions to survive outside the host because it is sensitive to heat, common disinfectants, and severe pH levels (Gong *et al.*, 2020).

Despite the fact that SHV-1 often shows a high degree of genetic conservation, genetic diversity across isolates has been documented across geographical regions (Deblanc *et al.*, 2019). Variations in strains can affect host immunological responses, pathogenicity, and transmission patterns, which can have an impact on disease control and epidemiology (Liu *et al.*, 2022b). Importantly, the emergence of genetically divergent pseudorabies virus (PRV) variants has raised concerns regarding the adequacy of protection provided by classical vaccines such as Bartha-K61 (Zhang *et al.*, 2019). Since the emergence of novel PRV variants in vaccinated swine populations, particularly in China, several isolates have exhibited genetic and antigenic differences from classical PRV strains and have been associated with outbreaks despite extensive vaccination (Guo *et al.*, 2026). Molecular analyses have identified mutations and insertions in genes encoding major viral glycoproteins, including gB, gC, gD, and gE, which may alter antigenicity, virulence, and interactions with host immunity (Zheng *et al.*, 2022). Therefore, the observed genetic diversity of PRV should not be considered merely a phylogenetic characteristic, but also as a potential determinant of vaccine compatibility and disease control (Lin *et al.*, 2021).

However, the occurrence of vaccine-breakthrough infections should

not be interpreted as evidence that Bartha-K61 universally fails against contemporary PRV strains (An *et al.*, 2013). Experimental studies indicate that Bartha-K61 can provide strong protection against classical PRV but may provide incomplete protection against certain antigenically divergent variants, with differences in clinical protection, viral replication, and shedding (Tong *et al.*, 2015). Thus, the relationship between PRV genetic variation and vaccine protection is likely strain-dependent and requires continued comparative antigenic, genomic, and immunological investigation (Zhou *et al.*, 2022).

Epidemiology

The endemicity patterns of Aujeszky's disease are highly impacted by livestock production systems, control strategies, and the degree to which eradication programs are carried out in each nation (Aznar *et al.*, 2022). From an epidemiological perspective, the principal reservoirs that sustain viral transmission within the population are farmed pigs and wild boars (Liu *et al.*, 2022a). Figure 1 illustrates the transmission and epidemiological patterns of Aujeszky's disease caused by SHV-1, with domestic pigs and wild boars serving as the primary reservoirs that maintain the virus's continued circulation in the environment.

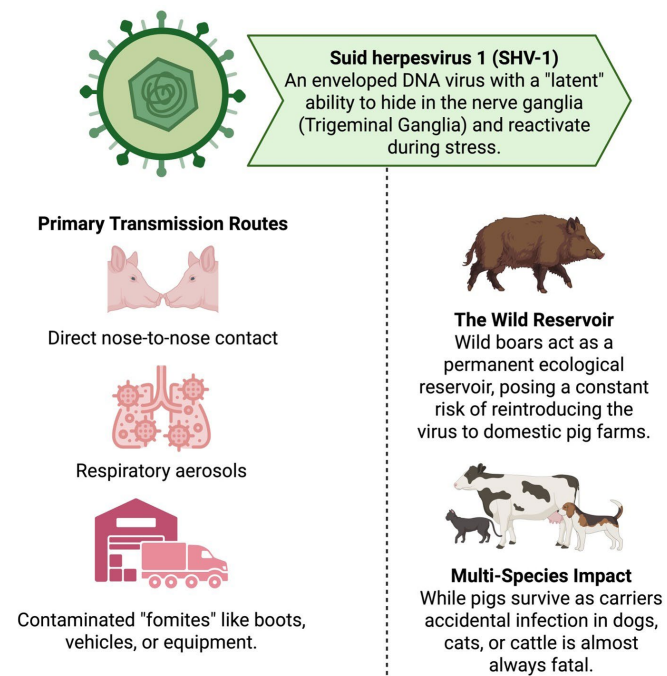


Figure 1. SHV-1 causes Aujeszky's disease through direct contact, aerosols, fomites, and wildlife reservoirs.

Due to effective eradication programs based on vaccination, surveillance, and culling of diseased animals, disease prevalence has dramatically decreased in areas with intensive pig farming sectors, such as parts of Europe and North America (Colomer *et al.*, 2020). Aujeszky's disease-free status in domestic pig populations has been attained by nations like the United States, Germany, the Netherlands, and the United Kingdom through a persistent, organized management strategy (Elbers *et al.*, 2000; Müller *et al.*, 2003; Hahn *et al.*, 2010; Peiso *et al.*, 2011). However, preventing viral reintroduction is still difficult due to the existence of reservoirs in wild pig populations (Boadella *et al.*, 2012).

On the other hand, Aujeszky's illness is still endemic in various parts of Asia, Latin America, and several developing nations, with regional variations in occurrence (Sehl and Teifke, 2020; Tan *et al.*, 2021; Serena *et al.*, 2023; Li *et al.*, 2024). This syndrome is typically associated with inadequate agricultural biosecurity, inconsistent vaccination coverage, and insufficient surveillance systems (Milicevic *et al.*, 2016). The virus spreads more quickly within local communities due to traditional, high-density livestock systems and lax animal transportation regulations (Bowden *et*

al., 2023).

A further epidemiological concern is the emergence and geographic dissemination of novel PRV variants in vaccinated swine populations (Liu *et al.*, 2022b). Since the emergence of variant PRV strains in China in 2011, outbreaks have been reported in farms with established Bartha-K61 vaccination programs, indicating that vaccination alone may not completely prevent infection or transmission by all circulating lineages (Wang *et al.*, 2016). These variant viruses have subsequently been detected in multiple regions, and their epidemiological importance is associated with their genetic divergence, variable pathogenicity, and reduced or incomplete protection afforded by some conventional vaccination programs (Favoreel, 2026). Such vaccine-breakthrough events are particularly important because apparently vaccinated populations may still contribute to viral circulation when vaccination reduces clinical disease but does not completely prevent infection or shedding (Mengeling *et al.*, 1992).

In the epidemiology of this illness, feral pigs' function as ecological reservoirs is receiving more and more attention (Papageorgiou *et al.*, 2025). In regions where wild habitats connect geographically with intensive production systems, wild boar populations have the capacity to sustain independent infection cycles and may operate as a source of reinfection for domestic livestock (Laidoudi *et al.*, 2022). Even if control in domestic populations is successful, this dynamic makes attaining total eradication at the regional level more difficult (Zhuang *et al.*, 2025).

The coexistence of genetically diverse PRV lineages in domestic and wild suid populations may further complicate control because wild reservoirs can maintain viral diversity and facilitate reintroduction into vaccinated production systems (Deblanc *et al.*, 2019). Consequently, epidemiological surveillance should move beyond serological monitoring and include molecular characterization of circulating isolates, particularly from outbreaks occurring in vaccinated herds (Chen *et al.*, 2022). Integrated genomic surveillance can help identify emerging variants, monitor their geographic spread, and determine whether particular lineages are associated with vaccine-breakthrough infections (Wu *et al.*, 2024).

Additionally, cross-regional dissemination is facilitated by the commerce in live animals and their derivatives, particularly where strict animal health inspections are lacking (Mettenleiter, 2020). One of the main ways that the virus spreads into areas free of disease is through the movement of infected animals, including those with latent infections (Prodanov-Radulović *et al.*, 2011). The movement of infected or latently infected animals may therefore contribute not only to the dissemination of classical PRV strains but also to the introduction of genetically divergent variants into previously controlled populations (Klupp, 2021).

Pathogenesis

The intricate process of Aujeszky's disease pathogenesis involves the dynamic interaction of viral replication, systemic spread, and the virus's capacity to remain latent in the host's nervous system (Zheng *et al.*, 2022). Usually, infection happens by the oronasal route, when the virus first attaches itself to oropharyngeal or upper respiratory tract epithelial cells (Thiry *et al.*, 2013). SHV-1 effectively multiplies locally during this first stage, creating new virions that infect local lymphoid tissues such as the tonsils and lymph nodes (Freuling *et al.*, 2023).

The virus either hematogenously or neurogenically enters the dissemination phase following primary replication (Pomeranz *et al.*, 2005). The virus enters by peripheral nerve terminals and travels retrogradely to the central nervous system (CNS) via the neurogenic route, which is thought to be the main mechanism of natural infection (Chen and Yu, 2024). Depending on the site of pathogen entry, axonal transport systems facilitate this movement, which enables the virus to reach the trigeminal or spinal ganglia (Papageorgiou *et al.*, 2022).

SHV-1 replicates rapidly in the central nervous system, resulting in a non-suppurative encephalitis marked by tissue edema, inflammatory cell infiltration, and neuronal death (Gerdtz *et al.*, 2000). Particularly in

piglets, these lesions cause distinctive neurological symptoms as tremors, ataxia, seizures, and high mortality (Müller *et al.*, 2011). Due to a better developed immune response, the infection is frequently more localized or asymptomatic in older animals (Mettenleiter, 2020).

The virus can move systemically to other organs like the lungs in addition to the nervous system, where it can replicate in the respiratory epithelium and cause interstitial pneumonia (Chen *et al.*, 2025a). Depending on the stage of gestation at the moment of infection, SHV-1 can pass through the placental barrier and infect the fetus in pregnant sows, causing miscarriage, mummification, or stillbirth (Iglesias and Harkness, 1988).

The ability of SHV-1 to remain dormant in sensory nerve ganglia is a crucial aspect of the pathophysiology of Aujeszky's disease (Wójcik *et al.*, 2026). The viral DNA stays in the cells during the dormant phase without generating active virions, which prevents the host immune system from identifying it (Deng *et al.*, 2022). However, the virus can reactivate and re-enter the active replication cycle in response to stress, immunosuppression, or other triggers, creating a new source of infection in the livestock population (Chen *et al.*, 2022).

Importantly, SHV-1 pathogenesis is also shaped by multiple viral immune-evasion mechanisms that operate during the early stages of infection (Zhu and Viejo-Borbolla, 2021). Several envelope glycoproteins and non-structural proteins interfere with host antiviral signaling and antigen presentation, thereby facilitating viral replication and persistence (Bude *et al.*, 2024). For example, gB has been implicated in modulation of host innate immune signaling, whereas gC and gE/gI contribute to interactions with host immune components and can influence complement activity, cell-to-cell spread, and immune recognition (Pomeranz *et al.*, 2005). The US3 protein kinase and other viral regulatory proteins further contribute to suppression of antiviral cellular responses, allowing productive replication to proceed despite activation of host defense pathways (Xie *et al.*, 2021). These mechanisms are particularly relevant because efficient suppression of early innate responses can increase the opportunity for viral dissemination before robust adaptive immunity is established (van Gent *et al.*, 2022).

At the molecular level, SHV-1 can interfere with type I IFN production and downstream IFN-stimulated antiviral responses (Gong *et al.*, 2022). Viral proteins can target components of pathways involving pattern-recognition receptors, interferon regulatory factors, and JAK-STAT signaling, thereby reducing the transcription or activity of interferon-stimulated genes (Ezeonwumelu *et al.*, 2021). This inhibition limits the establishment of an antiviral state in neighboring cells and may facilitate viral replication at mucosal and systemic sites (Dodantenna, 2026). The ability of SHV-1 to modulate several points within the IFN pathway rather than relying on a single viral protein highlights the multifactorial nature of its innate immune evasion (Su *et al.*, 2016).

SHV-1 also interferes with antigen presentation, which can reduce recognition of infected cells by cytotoxic T lymphocytes (Tomescu *et al.*, 2003). Viral immune-evasion proteins have been associated with disruption of major histocompatibility complex class I (MHC-I) expression or intracellular trafficking, thereby decreasing the presentation of viral peptides on the surface of infected cells (Wu *et al.*, 2025). Reduced MHC-I availability can impair CD8⁺ T-cell recognition and provide an additional mechanism for prolonging viral replication and persistence (Gainey *et al.*, 2012). These effects complement the virus's ability to establish latency, during which viral gene expression is markedly restricted and immune visibility is further reduced (Geljc *et al.*, 2021).

The combined effects of IFN signaling inhibition, modulation of antigen presentation, and reduced immune recognition therefore represent an important molecular link between acute SHV-1 replication and subsequent persistence (Lukhele *et al.*, 2019). Nevertheless, the contribution of individual viral proteins may vary according to viral strain, cell type, and experimental conditions (Danastas *et al.*, 2020). Further comparative studies using contemporary field isolates are therefore required to determine whether differences in immune-evasion activity contribute to

variation in virulence, tissue tropism, and vaccine protection among circulating SHV-1 strains (de Freitas *et al.*, 2019).

Immune response

Coordination between innate and adaptive immunity is necessary for the immune response to Aujeszky's disease (Nie *et al.*, 2023). Together, these immune responses define the infection's severity, the virus's ability to be controlled, and the success of establishing latency (Mettenleiter, 1996). The innate immune system acts as the first line of defense during the early stages of infection by producing type I interferons (IFN- α/β) and activating infected macrophages, dendritic cells, and epithelial cells (Laval *et al.*, 2018). By creating an antiviral state in nearby cells and boosting the production of antigen-presenting molecules, interferons are essential for preventing viral replication (Song *et al.*, 2026).

However, the antiviral activity of IFN- α/β can be substantially attenuated by SHV-1 immune-evasion mechanisms (Melchjorsen *et al.*, 2009). Viral modulation of pattern-recognition receptor signaling, interferon regulatory factors, and downstream JAK-STAT signaling can reduce both IFN production and the expression of interferon-stimulated genes (Fleming, 2016). In parallel, interference with MHC-I antigen processing and surface expression can diminish the ability of CD8⁺ T cells to recognize infected cells (Cruz *et al.*, 2025). Thus, SHV-1 immune evasion operates at both the innate signaling and antigen-presentation levels, providing complementary mechanisms that favor viral replication and persistence (Nie *et al.*, 2023).

By disrupting the interferon signaling cascade and altering dendritic cell activity, SHV-1 can dodge or suppress the innate response, enabling initial replication to take place before the full activation of adaptive immunity (Lamote *et al.*, 2017). Pro-inflammatory cytokines like IL-1 β , IL-6, and TNF- α are produced more often at this point, which promotes local inflammation and immune cell recruitment to the infection site (Delva *et al.*, 2022).

A crucial element in the management of systemic infections is the adaptive immune response (Ye *et al.*, 2022). The generation of specialized antibodies against viral surface proteins, especially the gB, gC, and gD glycoproteins, which are involved in neutralizing virions and inhibiting infection of new cells, is what defines humoral immunity (Bude *et al.*, 2024). Additionally, these antibodies aid in opsonization and complement system activation, which improves the removal of viruses from the circulation and peripheral tissues (Wang *et al.*, 2021).

However, cellular immune response is essential for getting rid of infected cells, especially when it comes to activating cytotoxic T lympho-

cytes (CD8⁺), which are able to identify viral antigens shown by MHC class I (Gaïney *et al.*, 2012). By generating cytokines like IFN- γ , which boost macrophage activity and effector cell development, helper T cells (CD4⁺) facilitate this response (Yin *et al.*, 2022). However, the host's age, immunological state, and the virulence of the virus strain can all affect how effective the cellular response is (Salinas-Zacarias *et al.*, 2020).

The interaction between viral immune evasion and cellular immunity is particularly important during persistent infection (Wang *et al.*, 2024a). By limiting IFN-mediated antiviral activity and reducing the efficiency of MHC-I-dependent antigen presentation, SHV-1 may decrease the probability of complete elimination of infected cells (Xia *et al.*, 2019). These mechanisms do not act independently of latency; rather, they may facilitate the transition from productive infection to a state in which viral replication is restricted and immune recognition is minimized (Orr *et al.*, 2005).

SHV-1 has the special capacity to avoid total eradication through latency in sensory ganglia, even while the adaptive immune response can manage the acute stage of infection (Deng *et al.*, 2022). Viral gene expression is so low during this stage that it doesn't cause a noticeable immunological reaction (Maes *et al.*, 1997). Because the immune system is unable to eradicate the infection entirely, the virus can continue to live inside the host for the rest of its life (Pannwitz *et al.*, 2012).

Pathology

The pathological abnormalities caused by Aujeszky's illness are mainly indicative of the virus's preference for lymphoid tissue, the respiratory tract, and the central nervous system (Narita *et al.*, 1991). The brain system and respiratory organs exhibit the most consistent lesion pattern, although pathological characteristics vary based on age, immunological condition, and infection route (Chen *et al.*, 2025b). Table 1 summarizes the pathological features of Aujeszky's disease caused by SHV-1 in various major organ systems.

Although meningeal congestion and mild to moderate cerebral edema may be present in acute cases, macroscopic alterations in the central nervous system are typically not noticeable (Zhang *et al.*, 2015). According to histopathological analysis, the main lesion is a non-suppurative encephalitis with neuronal degeneration, localized necrosis, perivascularitis, and mononuclear cell infiltration, including macrophages and lymphocytes (Laval and Enquist, 2020). In reaction to the damage to the nerve tissue, these alterations are frequently accompanied by reactive gliosis (Schulze *et al.*, 2010).

Necrotic rhinitis and interstitial pneumonia are prevalent in the re-

Table 1. Pathological features of Aujeszky's disease across different organ systems.

Organ system	Gross pathological changes	Histopathological changes	Characteristic lesions	Clinical implications	References
Central nervous system (CNS)	Usually no obvious gross lesions; meningeal congestion and mild-moderate cerebral edema may occur in acute cases	Non-suppurative encephalitis, neuronal degeneration, focal necrosis, perivascularitis, infiltration of lymphocytes and macrophages, reactive gliosis	Predominantly mononuclear inflammatory lesions with neuronal involvement	Neurological manifestations including tremors, ataxia, seizures, and high mortality in piglets	Zhang <i>et al.</i> (2015); Laval and Enquist (2020); Schulze <i>et al.</i> (2010)
Respiratory tract	Necrotic rhinitis; pulmonary congestion and edema	Interstitial pneumonia, degeneration and necrosis of nasal mucosal epithelium, alveolar septal thickening, inflammatory cell infiltration	Eosinophilic intranuclear inclusion bodies in respiratory epithelial cells	Coughing, dyspnea, respiratory impairment, and reduced performance	Shibata <i>et al.</i> (2003); Robinson <i>et al.</i> (2026); Yu <i>et al.</i> (2026)
Lymphoid tissues (tonsils and lymph nodes)	Mild enlargement or absence of specific gross lesions	Follicular necrosis, lymphocyte depletion, and early viral replication in lymphoid tissues	Disruption of lymphoid follicular architecture	Local immunosuppression and initiation of systemic viral dissemination	Ukhovskiy <i>et al.</i> (2020); Narita <i>et al.</i> (1998)
Reproductive system (pregnant animals)	Placentitis; gross lesions may be absent or inconspicuous	Placental infection, fetal infection, and multifocal fetal organ necrosis (particularly liver and CNS)	Systemic fetal lesions with extensive tissue degeneration	Abortion, fetal mummification, stillbirth, and neonatal mortality	Li <i>et al.</i> (2026a); Bowden <i>et al.</i> (2023)
General tissues (multiple organs)	No consistent gross lesions	Intranuclear inclusion bodies in epithelial cells and neurons (not consistently observed throughout infection)	Histological evidence suggestive of active herpesvirus replication	Supports etiological confirmation of Suid herpesvirus 1 (SHV-1) infection	Balasch <i>et al.</i> (1998a)

spiratory tract, especially in young pigs (Shibata *et al.*, 2003). Herpesvirus infection is characterized by degeneration, necrosis, and eosinophilic intranuclear inclusions in the nasal mucosal epithelium (Robinson *et al.*, 2026). Alveolar septa thickening in the lungs as a result of edema and inflammatory cell infiltration can lead to poor gas exchange and clinical dyspnea (Yu *et al.*, 2026).

Significant alterations, such as follicular necrosis and lymphocyte depletion, are also seen in lymphoid tissues such the tonsils and lymph nodes (Ukhovskiy *et al.*, 2020). Before the virus spreads throughout the body, it first replicates in local lymphoid tissues, which is reflected in these lesions (Narita *et al.*, 1998). Intranuclear inclusions can occasionally be observed in neurons and epithelial cells, albeit this is not always the case throughout the course of infection (Balasch *et al.*, 1998a).

Pathology, such as placentitis and fetal infection, can affect the reproductive system in pregnant animals (Li *et al.*, 2026a). Depending on the gestational age during infection, fetal abnormalities include numerous organ necrosis, especially of the liver and central nervous system, linked to miscarriage, mummification, or stillbirth (Bowden *et al.*, 2023).

Clinical manifestations

Age, immune status, and degree of virus infection all have a significant impact on the clinical signs of Aujeszky's illness, with piglets usually experiencing the most severe symptoms (Wang *et al.*, 2026). Neurological, respiratory, and reproductive issues are among the many clinical

symptoms of the disease that might occur concurrently or primarily affect one system (Zheng *et al.*, 2022). Table 2 presents the variation in clinical manifestations of Aujeszky's disease based on age group and physiological status of the animal.

Infection in newborn piglets is severe and frequently lethal (Casal *et al.*, 2004). Anorexia, sadness, tremors, and incoordination are among the initial signs; seizures, opisthotonos, and paralysis follow (Sehl and Teifke, 2020). Due to the neurovirulent virus's high tropism for the immunologically immature nervous system, mortality in this group can approach 100% within a short period of symptom onset (Klupp, 2021). Figure 2 shows the variation in clinical manifestations of Aujeszky's disease based on age group and physiological status of the pig after SHV-1 infection.

Clinical symptoms are more erratic and not necessarily lethal in young piglets and growers (Prodanov-Radulović *et al.*, 2015). Reduced appetite and limited growth are frequently accompanied by respiratory symptoms as coughing, sneezing, dyspnea, and nasal discharge (Verpoest *et al.*, 2017). Although neurological symptoms are still present, they are usually less severe than in newborns. Sometimes an illness is asymptomatic, resulting merely in a reduction in productivity (Favoreel, 2026).

Due to a highly developed immune system, infections in adult pigs are frequently subclinical or mild. Nonetheless, mature animals continue to be a significant viral reservoir (Zhao *et al.*, 2018). When symptoms do manifest, they typically include temporary fever, moderate respiratory discomfort, and decreased productivity without overt neurological symptoms (Chen and Yu, 2024).

Table 2. Clinical manifestations of Aujeszky's disease according to age group and physiological status.

Animal group	Predominantly affected system	Main clinical manifestations	Severity	Clinical notes	References
Neonatal piglets	Central nervous system (CNS)	Anorexia, depression, tremors, incoordination, seizures, opisthotonos, paralysis	Very severe (mortality may approach 100%)	Acute onset with rapid progression; marked SHV-1 neurotropism in the immature nervous system	Casal <i>et al.</i> (2004); Sehl and Teifke (2020); Klupp (2021)
Young pigs (growers)	Respiratory ± neurological	Coughing, sneezing, dyspnea, nasal discharge, reduced appetite, growth retardation	Moderate	May be accompanied by mild neurological signs or remain subclinical; clinical presentation is variable	Prodanov-Radulović <i>et al.</i> (2015); Verpoest <i>et al.</i> (2017); Favoreel (2026)
Adult pigs	Mild respiratory / minimal systemic involvement	Mild fever, mild respiratory disturbances, decreased production performance	Mild to subclinical	Serve as an important viral reservoir with continued virus shedding despite limited clinical signs	Zhao <i>et al.</i> (2018); Chen and Yu (2024)
Pregnant sows	Reproductive system	Abortion, fetal mummification, stillbirth, birth of weak piglets	Variable (depending on gestational stage)	Early gestational infection is associated with embryonic resorption or mummification, whereas late infection more commonly results in abortion or stillbirth	Yamane <i>et al.</i> (2015); Amoroso <i>et al.</i> (2020)

Table 3. Diagnostic approaches for Aujeszky's disease in pigs.

Diagnostic stage	Method / approach	Detection target	Role in diagnosis	Clinical / laboratory notes	References
Clinical suspicion (presumptive diagnosis)	Clinical and epidemiological observation	Neurological, respiratory, and reproductive manifestations	Establishes initial case suspicion	Clinical signs are not specific and require laboratory confirmation	Yu <i>et al.</i> (2014); Balasch <i>et al.</i> (1998b); Gu <i>et al.</i> (2025)
Differential diagnosis	Evaluation of alternative diseases	Classical swine fever (CSF), porcine reproductive and respiratory syndrome (PRRS), and other bacterial or viral infections	Excludes diseases with similar clinical presentations	Essential during acute outbreak investigations due to overlapping signs	Bo and Li (2022)
Molecular detection (gold standard)	PCR / Real-time PCR	SHV-1 DNA	Definitive etiological confirmation	High sensitivity and specificity; applicable for early and subclinical infection detection	Pérez and de Arce (2009); Černe <i>et al.</i> (2023)
Virus isolation	Cell culture	Viable virus and cytopathic effects (CPE)	Reference confirmation method	Requires specialized laboratory facilities and longer processing time	Moiseenko <i>et al.</i> (2025); Zhou <i>et al.</i> (2022)
Serological testing	ELISA, serum neutralization test (SNT)	Antibodies against SHV-1	Population surveillance and immune status assessment	Interpretation should consider vaccination history and DIVA strategy implementation	Serena <i>et al.</i> (2013); Leamcharaskul <i>et al.</i> (1991); Kondibaeva <i>et al.</i> (2021)
Tissue antigen detection	Immunohistochemistry (IHC)	SHV-1 antigen in infected tissues	Diagnostic confirmation in cases with inconclusive results	Particularly useful for CNS lesions and lymphoid tissues by correlating antigen localization with histopathological changes	Grieco <i>et al.</i> (1997); Yıldırım <i>et al.</i> (2017)

Significant reproductive problems, including abortion, fetal mummification, stillbirth, or the birth of poor piglets, can result from SHV-1 infection in pregnant sows (Yamane *et al.*, 2015). The stage of gestation at the time of infection greatly influences the severity of reproductive diseases; early infections typically result in mummification or embryo resorption, whereas late infections more frequently cause abortion or stillbirth (Amoroso *et al.*, 2020).

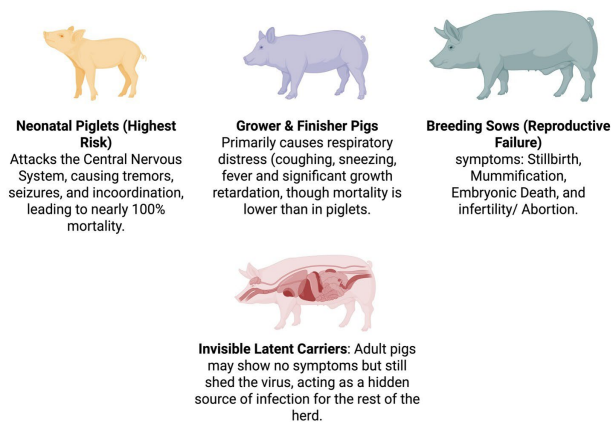


Figure 2. Aujeszky's disease affects pigs differently by age, causing neurological, respiratory, reproductive, or latent infection.

Diagnosis

Given the range of symptoms that can resemble those of other neurological and respiratory conditions in pigs, diagnosing Aujeszky's disease necessitates a thorough approach that incorporates clinical observation, pathological investigation, and laboratory confirmation (Yu *et al.*, 2014). Clinical indications alone typically do not allow for a reliable diagnosis, hence agent detection techniques are essential to case confirmation (Balasch *et al.*, 1998b). Table 3 illustrates the stepwise approach to the diagnosis of Aujeszky's disease, starting from clinical suspicion to laboratory confirmation.

A combination of common clinical signs, including as acute neurological abnormalities in piglets, respiratory problems during the growth period, and miscarriages in pregnant sows, can raise suspicions of infection in the early stages (Gu *et al.*, 2025). Differential diagnosis, however, necessitates taking into account other illnesses such classical swine fever, porcine reproductive and respiratory syndrome, and other neurotropic bacterial or viral infections because these symptoms are nonspecific (Bo and Li, 2022).

Molecular techniques, especially polymerase chain reaction (PCR), which has a high sensitivity and specificity in identifying SHV-1 genetic material from tissue samples such brain, tonsil, lung, or nasal swabs, are typically used to confirm the etiology (Pérez and de Arce, 2009). Additionally, viral load quantification and early subclinical infection identification are made possible by real-time PCR techniques (Černe *et al.*, 2023).

Although its usage is becoming less common due to the need for specialized laboratory facilities and the comparatively long time required, virus isolation is still regarded as the reference approach in some circumstances (Moiseenko *et al.*, 2025). Cell cultures from infected tissue can be used to isolate the virus, which can then be identified by its distinctive cytopathic effects and confirmed by serology or genetic analysis (Zhou *et al.*, 2022).

Antibodies to SHV-1 are found using serological assays such serum neutralization tests and enzyme-linked immunosorbent assay (ELISA) (Serena *et al.*, 2013). These techniques are particularly helpful in marker-based vaccination eradication efforts (DIVA tactics) and population monitoring and animal immune status assessment (Leamcharaskul *et al.*, 1991). However, because of the potential for cross-reactions or vaccine antibodies, vaccination history must be taken into account when interpreting serological results (Kondibaeva *et al.*, 2021).

Furthermore, viral antigens in infected tissues can be directly identified using immunohistochemistry (IHC) techniques, especially in lymphoid tissues and diseases of the central nervous system (Grieco *et al.*, 1997). In situations where PCR results are unclear, this technique helps to confirm the diagnosis by establishing a link between the presence of viral antigens and histopathological alterations (Yildirim *et al.*, 2017).

Differential diagnosis

Because Aujeszky's disease's clinical signs are ambiguous and can resemble a number of infectious disorders affecting the neurological, pulmonary, and reproductive systems in pigs, a thorough differential diagnosis is crucial (Yamane *et al.*, 2015). Particularly in situations of acute outbreaks with significant piglet mortality, accurate differential diagnosis is essential to prevent misinterpretation (Wang *et al.*, 2024b).

Aujeszky's disease must be distinguished from porcine teschovirus encephalomyelitis and classical swine fever (CSF) among illnesses exhibiting neurological symptoms (Greiser-Wilke *et al.*, 2007). In contrast to Aujeszky's disease, CSF usually exhibits a combination of high fever, systemic bleeding, and hemorrhagic lesions in the kidneys and lymphoid organs (Ratta *et al.*, 2010). Teschovirus infection, on the other hand, more frequently causes encephalomyelitis with a distinct lesion distribution and less respiratory involvement (Yamada *et al.*, 2014).

When it comes to respiratory involvement, this illness can resemble influenza A infection in pigs and porcine reproductive and respiratory syndrome (PRRS) (Saade *et al.*, 2020). While influenza A often manifests as an abrupt respiratory onset and is highly contagious without significant neurological involvement, PRRS is characterized by chronic interstitial pneumonia and persistent reproductive impairment (Chun *et al.*, 2023). In the early stages of infection, this differentiation is crucial for differentiating overlapping clinical presentations (Moghadami, 2017).

Aujeszky's illness must be differentiated from leptospirosis and porcine parvovirus infection in terms of reproduction (Pacini *et al.*, 2021). Leptospirosis is more frequently linked to miscarriages with evidence of septicemia and multi-organ dysfunction, whereas parvovirus mostly causes reproductive failure with fetal mummification without systemic symptoms in the sow (Khairullah *et al.*, 2024). Neurological or respiratory involvement, which is not always present in either condition, is another characteristic of Aujeszky's disease in both sows and piglets (Presti *et al.*, 2021).

Acute neurological symptoms like meningitis and encephalitis can also be brought on by certain bacterial infections, such *Streptococcus suis* (Choi *et al.*, 2012). However, unlike the viral cause of Aujeszky's disease, bacterial infections usually react to antibiotic therapy and offer distinct bacteriological evidence (van Samkar *et al.*, 2015).

Transmission

Pigs are the main host and epidemiological reservoir for Aujeszky's illness, which spreads by a complicated interplay of direct, indirect, and vertical transmission pathways (Didkowska *et al.*, 2025). The virus's capacity to excrete large amounts both during the active infection phase and following reactivation from a dormant state has a significant impact on successful transmission (Wong *et al.*, 2019).

SHV-1 spreads mostly via horizontal transmission via direct contact (Mocsári *et al.*, 1989). In high-density herds, inhaling infectious particles is a major pathway because the virus is expelled through respiratory aerosols, saliva, and nasal secretions (Gillespie *et al.*, 1996). The buildup of airborne virus particles is accelerated and the efficiency of transmission between individuals within a population is increased in intensive rearing circumstances with little ventilation (Christensen *et al.*, 1993).

Apart from direct touch, polluted farm equipment, worker apparel, feed, and transportation vehicles are examples of indirect transmission (Ukhovskiy *et al.*, 2022). Particularly in agricultural systems with inad-

quate biosecurity, mechanical transmission might contribute to the spread of the infectious agent between production units since the virus can live for a brief amount of time under specific environmental conditions (Gong *et al.*, 2020).

Additionally, vertical transmission is important, especially in pregnant infected sows (Pacini *et al.*, 2020). Abortion, mummification, and stillbirth are just a few of the reproductive outcomes that can occur when SHV-1 infiltrates the fetus across the placental barrier (Wang *et al.*, 2025). The stage of pregnancy at the time of infection determines how severe the reproductive effects are; early infections are more likely to result in embryonic failure, whereas late infections are more likely to cause fetal mortality (Su *et al.*, 2024).

Furthermore, after being exposed to the virus from pigs, a number of non-porcine species, including dogs, cats, and small ruminants, may unintentionally become infected (Ciarello *et al.*, 2020). Although the infection in these species is terminal and does not contribute to the cycle of transmission, it is nevertheless an important epidemiological indication of viral circulation in the agricultural setting (Chen and Yu, 2024).

Transmission dynamics are reinforced at regional and cross-regional scales by management factors such as animal mobility between farms, the absence of quarantine systems, and inadequate biosecurity practices (Zhuang *et al.*, 2025). Additionally, stress that causes latent viruses in infected people to reactivate serves as a source of recurring infections, sustaining the virus's persistence in the community (Li *et al.*, 2023).

Risk factors

Numerous interrelated risk variables, such as biological features, farm management, the environment, and animal movement dynamics, affect the incidence and spread of Aujeszky's illness (Didkowska *et al.*, 2025). The degree of population vulnerability and the rate of virus transmission within a production system are determined by the combination of these parameters (Masiuk *et al.*, 2021). Table 4 summarizes the various risk factors contributing to the occurrence and spread of Aujeszky's disease, caused by SHV-1.

Because it increases the frequency of direct contact with individuals and promotes aerosol transmission, high pig population density is a significant risk factor (Hu *et al.*, 2016). These conditions are made worse by intensive housing systems with inadequate ventilation, which speeds up the virus's propagation both within and between housing units on a farm (Kumar *et al.*, 2021).

The risk of SHV-1 entry and transmission is also significantly in-

creased by weak biosecurity (Zhang *et al.*, 2025). Indirect transmission channels can be created by practices including shared facilities between housing units, insufficient equipment cleaning, and a lack of human and vehicle access controls (Liu *et al.*, 2022a). Additionally, the possibility of introducing animals harboring viruses, including those with latent diseases, increases when additional animals are brought in without proper quarantine (Mettenleiter, 2020).

One significant biological mechanism that contributes to the reactivation of latent viruses is animal stress (Chen *et al.*, 2022). Transportation, environmental changes, overcrowding, and malnutrition can all lower the host's immunological response, which increases the likelihood of virus excretion back into the environment and spread to other animals in the community (Chen and Yu, 2024).

Susceptibility to infection is also influenced by immunological health and age (Claeys *et al.*, 2025). Due to their underdeveloped immune systems, newborn piglets are most vulnerable to serious clinical illness, but older pigs frequently serve as asymptomatic repositories that sustain the population's infection cycle (Papageorgiou *et al.*, 2017). Additionally, vulnerable populations that promote virus persistence may be created by inadequate or uneven vaccination status (Bo and Li, 2022).

Animal commerce and mobility across nations or regions are significant contributors to the spread of illness, particularly in places with patchy control initiatives (Gao *et al.*, 2025). New outbreaks may result from the transfer of diseased animals into groups that are disease-free, particularly in the absence of sufficient diagnostic screening (Evans *et al.*, 2024).

Economic impact

Due to lower productivity, higher mortality, and expensive control and eradication expenses, Aujeszky's disease has a major financial impact on the pig farming sector (Suprani *et al.*, 2026). Depending on the endemic status and the efficacy of the management system in a given area, economic losses may be direct or indirect and may occur over a short or lengthy period of time (Liu *et al.*, 2019).

The primary causes of direct losses include the high mortality rate of neonatal piglets, poor growth performance during the expansion period, and reproductive issues in the mother, including stillbirth, fetal mummification, and abortion (Yamane *et al.*, 2015). The number of piglets generated per reproductive cycle is reduced as a result of this combination of diseases, greatly lowering production efficiency (Evans *et al.*, 2024).

The necessity for laboratory diagnostics, vaccination regimens, and

Table 4. Risk factors associated with Aujeszky's disease in pig production systems.

Risk factor category	Specific factor	Mechanism contributing to SHV-1 transmission	Epidemiological impact	References
Farm management	High population density	Increases direct animal-to-animal contact and facilitates aerosol transmission	Accelerates virus spread within and between housing units	Hu <i>et al.</i> (2016); Kumar <i>et al.</i> (2021)
Housing environment	Poor ventilation in intensive production systems	Promotes accumulation of viral particles in the air and increases inhalation exposure	Enhances respiratory transmission and facilitates viral dissemination	Kumar <i>et al.</i> (2021)
Biosecurity	Inadequate disinfection, unrestricted access, shared facilities and equipment	Facilitates indirect transmission through contaminated fomites	Increases the risk of virus introduction and spread between production units	Zhang <i>et al.</i> (2025); Liu <i>et al.</i> (2022a)
Animal introduction management	Absence of quarantine for newly introduced animals	Allows entry of infected animals, including latent carriers	Creates a source of new outbreaks in previously disease-free populations	Mettenleiter (2020)
Host biological factors	Stress (transportation, environmental changes, overcrowding, poor nutrition)	Suppresses immune responses and promotes latent virus reactivation	Increases viral shedding and secondary transmission	Chen <i>et al.</i> (2022); Chen and Yu (2024)
Age and immune status	High susceptibility in neonates; adults frequently remain asymptomatic	Differences in immune competence and infection severity influence disease expression	Neonates experience high mortality, whereas adults may act as reservoirs maintaining transmission	Claeys <i>et al.</i> (2025); Papageorgiou <i>et al.</i> (2017)
Vaccination status	Inadequate or uneven vaccination coverage	Creates susceptible subpopulations within the herd	Supports viral persistence and continued circulation within the population	Bo and Li (2022)
Animal movement	Trade and transportation across farms, regions, or countries	Facilitates geographical dissemination of infected animals	Introduces SHV-1 into disease-free areas and triggers new outbreaks	Gao <i>et al.</i> (2025); Evans <i>et al.</i> (2024)

extra biosecurity measures raises medical and animal health management costs in addition to productivity losses (Parsons *et al.*, 1990). The use of marker vaccinations and eradication operations focused on the removal of positive animals can significantly raise operating costs in impacted livestock systems (Aznar *et al.*, 2022).

Restrictions on the trade of live animals and products derived from them due to the notifiable illness status in a number of nations are another example of indirect effects (Ukhovskiy *et al.*, 2022). These limitations may have an impact on access to foreign markets, lower export values, and upset the supply chain stability of the pork business (Mettenleiter, 2020). Aujeszky's disease can be a major barrier to animal health certification in the context of international trade (Carella *et al.*, 2023).

Disease outbreaks can also affect the overall production system, resulting in higher biosecurity expenses, lower labor productivity, and the need to reorganize livestock populations (Kouam and Moussala, 2018). The quick spread of the virus might worsen the economic impact on farms with intensive systems, leading to overall losses in a production unit (Liu *et al.*, 2022a).

Treatment

There is currently no targeted and efficient antiviral treatment to eradicate SHV-1 in Aujeszky's disease (Zheng *et al.*, 2022). As a result, population control and supporting measures are prioritized over curative medicine in the field of disease management (Guo *et al.*, 2024). This has to do with the virus's capacity to spread quickly during the acute phase and linger in latent form in nerve ganglia, making pharmaceutical treatment challenging (Cohen, 2020).

In order to lessen clinical severity and enhance animal welfare, infected animals are typically treated symptomatically (Laval *et al.*, 2018). Supportive management should be individualized according to the clinical condition and may include maintaining hydration, nutritional support, and minimizing environmental stress. However, these measures are supportive rather than antiviral and have not been established to eliminate SHV-1 infection or prevent viral latency (Spickler, 2024; Molitor, 2026). Nevertheless, these treatments are not very effective, particularly in piglets that already have serious illnesses of the central nervous system (Papageorgiou *et al.*, 2022).

Environmental management, such as better air quality, less housing density, and higher ventilation, is essential for promoting recovery in infections that primarily affect the respiratory system (Bourgueil *et al.*, 1992). Instead of treating the viral agent directly, antibiotics should only be used to manage subsequent bacterial infections, which frequently exacerbate the clinical situation (Wong *et al.*, 2019).

There are no treatment measures that can stop transplacental transmission in pregnant sows or enhance reproductive results after infection (Rollinson *et al.*, 1988). As a result, management is more concerned with preventing illness through vaccination and biosecurity than with treating infection after it has already happened (Tan *et al.*, 2021).

A "test and remove" strategy, also known as selective depopulation, is frequently used in contemporary livestock systems as part of control initiatives, especially in regions where diseases are being eradicated (Masiuk *et al.*, 2021). In order to break the cycle of transmission, this method entails identifying diseased animals using laboratory diagnostics and then eliminating them (Thiry *et al.*, 2013).

Vaccination

Aujeszky's disease control methods heavily rely on vaccination, particularly in endemic regions where complete eradication has not yet been attained (Pensaert and Morrison, 2000). Vaccination's main objective is to minimize the economic and epidemiological effects by lowering clinical incidence, virus shedding, and dissemination among animal populations (Zhang *et al.*, 2025).

A variety of vaccinations have been created, including as live attenuated vaccines, inactivated vaccines (killed vaccines), and recombinant vaccines based on marker technology (DIVA: Differentiating Infected from Vaccinated Animals) (Nie *et al.*, 2023). Because live attenuated vaccines can concurrently elicit humoral and cellular immune responses, they often have higher immunogenicity (Liu *et al.*, 2026). However, the possibility of residual pathogenicity and possible reactivation under specific circumstances must be taken into account when using them (Balasch *et al.*, 1998a).

Because they don't contain live viruses, inactivated vaccines have a higher safety profile (Kondibaeva *et al.*, 2021). However, they often evoke a more restricted immune response and need boosters to maintain sufficient protection (Xing *et al.*, 2024). In order to increase immunogenicity, these vaccines are therefore more frequently employed in conjunction with adjuvants (Zhang *et al.*, 2023).

One important advancement in Aujeszky's disease control and eradication initiatives is the marker vaccine method (DIVA) (Pensaert *et al.*, 2004). By eliminating or altering particular antigens, like the gE glycoprotein, this vaccine enables serological testing to distinguish between animals that are naturally infected and those who have received the vaccination (Bude *et al.*, 2024). Because it makes it possible to accurately identify animals that have viruses, this tactic is essential in surveillance-based eradication campaigns (Stegeman, 1997).

Nevertheless, the effectiveness of conventional Bartha-K61 vaccination should be critically considered in the context of emerging PRV variants (Zhou *et al.*, 2017). Although Bartha-K61 remains effective against classical PRV strains and can substantially reduce clinical disease and viral dissemination, outbreaks in vaccinated herds have been associated with antigenically and genetically divergent PRV variants (Delva *et al.*, 2020). Experimental studies suggest that vaccination may provide incomplete protection against some of these variants, particularly with respect to preventing infection, viral replication, and shedding (Liu *et al.*, 2025). This indicates that vaccine protection is not necessarily uniform across genetically distinct PRV lineages and that antigenic divergence may contribute to vaccine-breakthrough infections (Zheng *et al.*, 2022).

The emergence of these variants does not necessarily indicate complete immune escape from Bartha-K61 (Nie *et al.*, 2023). Rather, it highlights a potential mismatch between vaccine strains and circulating field strains and suggests that protection should be evaluated using contemporary PRV isolates rather than relying exclusively on historical vaccine-challenge models (Zhou *et al.*, 2022). Genetic and antigenic surveillance of circulating PRV strains is therefore important for identifying changes in major protective antigens and determining whether existing vaccines remain sufficiently matched to prevalent viruses (Bo and Li, 2022).

Population coverage, program compliance, and integration with biosecurity measures all have a significant impact on vaccination efficacy (Segalés and Sibila, 2025). The creation of vulnerable subpopulations that permit the virus to spread can result from unequal vaccination (Engel and Wierup, 1999). Moreover, mother immune status, ambient infection pressure, and the animal's age at the time of vaccination all have an impact on vaccination success (Pomorska-Mól *et al.*, 2010). Accordingly, vaccination should be integrated with strict biosecurity, movement control, DIVA-based surveillance, and molecular monitoring of vaccine-breakthrough cases (Chen and Yu, 2024). The development of updated or broadly protective vaccines targeting conserved and immunologically relevant PRV antigens may also be necessary to improve protection against genetically divergent variants and reduce the risk of continued viral circulation in vaccinated populations (Zhou *et al.*, 2023).

Control

In order to break the chain of transmission and reduce virus circulation in pig herds, controlling Aujeszky's illness necessitates an integrated

strategy that combines vaccination, biosecurity, surveillance, and population management (Kit, 1990). Complete eradication is difficult because the virus can remain dormant in nerve ganglia, necessitating a long-term, risk-based control approach (Wójcik *et al.*, 2026). Figure 3 illustrates an integrated control approach for Aujeszky's disease, emphasizing early detection using molecular methods such as PCR, the application of marker vaccines (DIVA) to differentiate between infected and vaccinated animals, strengthening farm biosecurity, and the elimination of positive animals to break the chain of transmission.

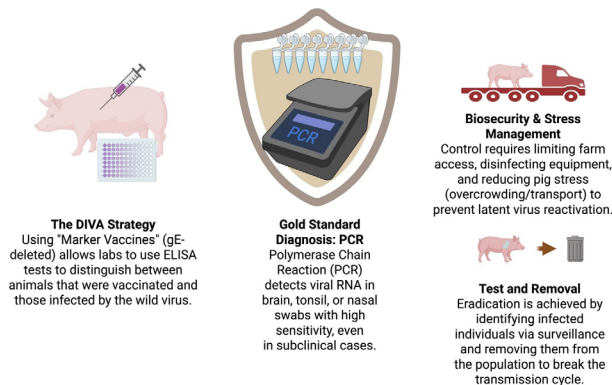


Figure 3. Aujeszky's disease control relies on PCR diagnosis, DIVA vaccination, biosecurity, and removal of infected animals.

Implementing biosecurity is essential to stopping the introduction and spread of SHV-1 (Ciarello *et al.*, 2020). Controlling animal movement, putting in place a quarantine system for new animals, routinely disinfecting buildings and equipment, and limiting vehicle and human access to agricultural areas are some of these precautions (Mettenleiter, 2020). Infection pressure and the frequency of interpersonal contact are both lowered by decreasing population density (Chen *et al.*, 2025c).

In order to lower clinical incidence and viral shedding, vaccination programs are essential (Mengeling *et al.*, 1992). Differentiating between naturally infected and vaccinated animals is made possible by the use of a vaccination marker (DIVA), which supports eradication campaigns based on serological surveillance (Pasick, 2004). High population coverage and uniform dosage across all vulnerable age groups are critical for vaccination efficacy (Segalés and Sibila, 2025).

To track the dynamics of infection within the community, both active and passive surveillance are required (Ouagal *et al.*, 2010). While molecular techniques like PCR are utilized to identify infected animals, including those in the subclinical period, serological surveillance is employed to find SHV-1 antibodies (Yang *et al.*, 2022). Zone-based eradication or control decisions are based on this surveillance data (Wang *et al.*, 2024b).

In certain endemic nations, eradication tactics include a "test and removal" strategy, also known as selective depopulation, which entails locating and getting rid of animals that test positive in order to stop the cycle of transmission (Assavacheep and Thanawongnuwech, 2022). To stop the reintroduction of viruses, this strategy is frequently paired with population reorganization and higher biosecurity norms (Ketusing *et al.*, 2014).

Additionally, as stress can enhance SHV-1 excretion and cause latent viral reactivation, managing animal stress is also essential to disease control (Tanaka and Mannen, 2003). To lower the risk of reactivation, factors like transportation, environmental changes, and congestion should be reduced (Li *et al.*, 2026b).

Conclusion

SHV-1 is the source of Aujeszky's disease, a serious viral illness that affects both farm productivity and animal health in pigs. The virus is difficult to manage and may remain in the population due to its neurotropic nature, ability to replicate systemically, and formation of latent infection

in nerve ganglia.

Pigs are the main reservoir for SHV-1, which spread epidemiologically through direct, indirect, and vertical transmission. Neurological diseases in piglets, respiratory illnesses throughout the growth phase, and reproductive disorders in pregnant sows are among the clinical symptoms that vary according to age and immunological condition.

Vaccination, biosecurity, and monitoring are the three main components of disease control, with marker vaccines (DIVA) being crucial to eradication efforts in a number of nations. However, the possibility of latent viral reactivation and the existence of reservoirs in feral pig herds continue to be significant obstacles to complete eradication.

Acknowledgement

The authors thank Badan Riset dan Inovasi Nasional for the funding support for this study.

Conflict of interest

The authors declare that there is no conflict of interest.

References

- Amoroso, M.G., Di Concilio, D., D'Alessio, N., Veneziano, V., Galiero, G., Fusco, G., 2020. Canine parvovirus and pseudorabies virus coinfection as a cause of death in a wolf (*Canis lupus*) from southern Italy. *Vet. Med. Sci.* 6, 600–605. doi: 10.1002/vms3.270.
- An, T.Q., Peng, J.M., Tian, Z.J., Zhao, H.Y., Li, N., Liu, Y.M., Chen, J.Z., Leng, C.L., Sun, Y., Chang, D., Tong, G.Z., 2013. Pseudorabies virus variant in Bartha-K61-vaccinated pigs, China, 2012. *Emerg. Infect. Dis.* 19, 1749–1755. doi: 10.3201/eid1911.130177.
- Assavacheep, P., Thanawongnuwech, R., 2022. Porcine respiratory disease complex: Dynamics of polymicrobial infections and management strategies after the introduction of the African swine fever. *Front. Vet. Sci.* 9, 1048861. doi: 10.3389/fvets.2022.1048861.
- Aznar, M.N., Bessone, F.A., Segurado, R., Duffy, S.J., 2022. Assessment of an Aujeszky's Disease Control Strategy in a Highly Prevalent Pig Farm Based on Systematic Vaccination With an Inactivated gE-Negative Marker Vaccine. *Front. Vet. Sci.* 9, 852650. doi: 10.3389/fvets.2022.852650.
- Balasch, M., Pujols, J., Segalés, J., Plana-Durán, J., Pumarola, M., 1998a. Study of the persistence of Aujeszky's disease (pseudorabies) virus in peripheral blood mononuclear cells and tissues of experimentally infected pigs. *Vet. Microbiol.* 62, 171–183. doi: 10.1016/s0378-1135(98)00208-9.
- Balasch, M., Pujols, J., Segalés, J., Pumarola, M., 1998b. Aujeszky's disease (pseudorabies) virus detection in cerebrospinal fluid in experimentally infected pigs. *Vet. Microbiol.* 60, 99–106. doi: 10.1016/s0378-1135(97)00156-9.
- Bo, Z., Li, X., 2022. A Review of Pseudorabies Virus Variants: Genomics, Vaccination, Transmission, and Zoonotic Potential. *Viruses* 14, 1003. doi: 10.3390/v14051003.
- Boadella, M., Gortázar, C., Vicente, J., Ruiz-Fons, F., 2012. Wild boar: an increasing concern for Aujeszky's disease control in pigs? *BMC Vet. Res.* 8, 7. doi: 10.1186/1746-6148-8-7.
- Bourguet, E., Hutet, E., Cariolet, R., Vannier, P., 1992. Air sampling procedure for evaluation of viral excretion level by vaccinated pigs infected with Aujeszky's disease (pseudorabies) virus. *Res. Vet. Sci.* 52, 182–186. doi: 10.1016/0034-5288(92)90008-p.
- Bowden, C.F., Kiser, J.N., Miller, R.S., Buckley, A.C., Boggiano, P.M., Giglio, R.M., Brown, V.R., Garrick, D., Neiberghs, H.L., Piaggio, A.J., Speidel, S.E., Smyser, T.J., 2023. Genomic regions associated with pseudorabies virus infection status in naturally infected feral swine (*Sus scrofa*). *Front. Genet.* 14, 1292671. doi: 10.3389/fgene.2023.1292671.
- Bude, S.A., Lu, Z., Zhao, Z., Zhang, Q., 2024. Pseudorabies Virus Glycoproteins E and B Application in Vaccine and Diagnosis Kit Development. *Vaccines* 12, 1078. doi: 10.3390/vaccines12091078.
- Cano-Terriza, D., Martínez, R., Moreno, A., Pérez-Marín, J.E., Jiménez-Ruiz, S., Paniagua, J., Borge, C., García-Bocanegra, I., 2019. Survey of Aujeszky's Disease Virus in Hunting Dogs from Spain. *Ecohealth* 16, 351–355. doi: 10.1007/s10393-019-01426-2.
- Carella, E., Caruso, C., Moreno, A., Di Blasio, A., Oberto, F., Vitale, N., Masoero, L., 2023. Meat Juice and Oral Fluid as Alternatives to Serum for Aujeszky Disease Monitoring in Pigs. *Microorganisms* 11, 2418. doi: 10.3390/microorganisms11102418.
- Casal, J., Planasdemunt, L., Varo, J.A., Martín, M., 2004. The use of different vaccination schedules for sows to protect piglets against Aujeszky's disease. *J. Vet. Med. B Infect. Dis. Vet. Public Health* 51, 8–11. doi: 10.1046/j.1439-0450.2003.00721.x.
- Černe, D., Hostnik, P., Toplak, I., Juntos, P., Paller, T., Kuhar, U., 2023. Detection of Pseudorabies in Dogs in Slovenia between 2006 and 2020: From Clinical and Diagnostic Features to Molecular Epidemiology. *Transbound. Emerg. Dis.* 2023, 4497806. doi: 10.1155/2023/4497806.
- Chen, J., Li, G., Wan, C., Li, Y., Peng, L., Fang, R., Peng, Y., Ye, C., 2022. A Comparison of Pseudorabies Virus Latency to Other α -Herpesvirinae Subfamily Members. *Viruses* 14, 1386. doi: 10.3390/v14071386.
- Chen, J., Zhao, G., Yang, Y., Li, Y., Song, Y., Li, D., Du, Q., Tong, D., Huang, Y., 2025a. Pseudorabies virus induces natural killer cell depletion by GSDMD-mediated inflammation and pyroptosis to promote infection and lung injury. *J. Virol.* 99, e0041525. doi: 10.1128/jvi.00415-25.
- Chen, W., Fan, G., Huang, Y., Zhou, K., Chen, Z., Chen, K., Zhang, H., Li, Z., 2025b. Characteristics of the pseudorabies virus strain GDWS2 with severe neurological signs and high viral shedding capacity in pigs. *Front. Vet. Sci.* 12, 1530765. doi: 10.3389/fvets.2025.1530765.
- Chen, X., Yu, Z., 2024. Insight into the Interaction Mechanism of Pseudorabies Virus Infection. *Biology (Basel)* 13, 1013. doi: 10.3390/biology13121013.
- Chen, Y., Gao, J., Hua, R., Zhang, G., 2025c. Pseudorabies virus as a zoonosis: scientific and public health implications. *Virus Genes* 61, 9–25. doi: 10.1007/s11262-024-02122-2.
- Choi, S.M., Cho, B.H., Choi, K.H., Nam, T.S., Kim, J.T., Park, M.S., Kim, B.C., Kim, M.K., Cho, K.H., 2012. Meningitis caused by *Streptococcus suis*: case report and review of the literature. *J. Clin. Neurol.* 8, 79–82. doi: 10.3988/jcn.2012.8.1.79.
- Christensen, L.S., Mortensen, S., Bøtner, A., Strandbygaard, B.S., Rønsholt, L., Henriksen, C.A., Andersen, J.B., 1993. Further evidence of long distance airborne transmission of Aujeszky's disease (pseudorabies) virus. *Vet. Rec.* 132, 317–321. doi: 10.1136/vr.132.13.317.
- Chrun, T., Maze, E.A., Roper, K.J., Vatzia, E., Paudyal, B., McNee, A., Martini, V., Manjegowda, T., Freimanis, G., Silesian, A., Polo, N., Clark, B., Besell, E., Booth, G., Carr, B.V., Edmans, M., Nunez, A., Koopaeuw, S., Wanasen, N., Graham, S.P., Tchilian, E., 2023. Simultaneous co-infection with swine influenza A and porcine reproductive and respiratory syndrome virus potentiates adaptive immune responses. *Front. Immunol.* 14, 1192604. doi: 10.3389/fim-

- mu.2023.1192604.
- Ciarellio, F.P., Capucchio, M.T., Ippolito, D., Colombino, E., Gibelli, L.R.M., Fiasconaro, M., Martin, A.M.M., Di Marco Lo Presti, V., 2020. First Report of a Severe Outbreak of Aujeszky's Disease in Cattle in Sicily (Italy). *Pathogens* 9, 954. doi: 10.3390/pathogens9110954.
- Claeys, M.S.C., Brabant, S.G.A.L., Rosshaert, S., Van Waesberghe, C., Favoreel, H.W., 2025. Age-dependent differences in type I interferon, IL-12 and pro-inflammatory cytokine production by porcine peripheral blood mononuclear cells in response to pseudorabies virus-infected cells. *Front. Immunol.* 16, 1596490. doi: 10.3389/fimmu.2025.1596490.
- Cohen, J.I., 2020. Herpesvirus latency. *J. Clin. Invest.* 130, 3361–3369. doi: 10.1172/JCI136225.
- Colomer, M.A., Margalida, A., Fraile, L., 2020. Vaccination Is a Suitable Tool in the Control of Aujeszky's Disease Outbreaks in Pigs Using a Population Dynamics P Systems Model. *Animals* 10, 909. doi: 10.3390/ani10050909.
- Cruz, F.M., Orellano, L.A.A., Chan, A., Rock, K.L., 2025. Alternate MHC I Antigen Presentation Pathways Allow CD8+ T-cell Recognition and Killing of Cancer Cells in the Absence of β 2M or TAP. *Cancer Immunol. Res.* 13, 98–108. doi: 10.1158/2326-6066.CIR-24-0320.
- Cunningham, M.W., Onorato, D.P., Sayler, K.A., Leone, E.H., Conley, K.J., Mead, D.G., Bradley, J.A.C., Maes, R.K., Kiuppel, M., Shindle, D.B., Wisely, S.M., Subramaniam, K., Wise, A.G., Clemons, B.C., Cusack, L.M., Jansen, D., Schueller, P., Hernández, F.A., Waltzek, T.B., 2021. Pseudorabies (Aujeszky's disease) is an underdiagnosed cause of death in the Florida panther (*Puma concolor coryi*). *J. Wildl. Dis.* 57, 784–798. doi: 10.7589/JWD-D-20-00119.
- Danastas, K., Miranda-Saksena, M., Cunningham, A.L., 2020. Herpes Simplex Virus Type 1 Interactions with the Interferon System. *Int. J. Mol. Sci.* 21, 5150. doi: 10.3390/ijms21145150.
- de Freitas, L.F.D., Oliveira, R.P., Miranda, M.C.G., Rocha, R.P., Barbosa-Stancio, E.F., Faria, A.M.C., da Fonseca, F.G., 2019. The Virulence of Different Vaccinia Virus Strains Is Directly Proportional to Their Ability To Downmodulate Specific Cell-Mediated Immune Compartments In Vivo. *J. Virol.* 93, e02191-18. doi: 10.1128/JVI.02191-18.
- Deblanc, C., Oger, A., Simon, G., Le Potier, M.F., 2019. Genetic Diversity among Pseudorabies Viruses Isolated from Dogs in France from 2006 to 2018. *Pathogens* 8, 266. doi: 10.3390/pathogens8040266.
- Delva, J.L., Nauwynck, H.J., Mettenleiter, T.C., Favoreel, H.W., 2020. The Attenuated Pseudorabies Virus Vaccine Strain Bartha K61: A Brief Review on the Knowledge Gathered During 60 Years of Research. *Pathogens* 9, 897. doi: 10.3390/pathogens9110897.
- Delva, J.L., Van Waesberghe, C., Van Den Broeck, W., Lamote, J.A., Vereecke, N., Theuns, S., Couck, L., Favoreel, H.W., 2022. The Attenuated Pseudorabies Virus Vaccine Strain Bartha Hyperactivates Plasmacytoid Dendritic Cells by Generating Large Amounts of Cell-Free Virus in Infected Epithelial Cells. *J. Virol.* 96, e0219921. doi: 10.1128/jvi.02199-21.
- Deng, J., Wu, Z., Liu, J., Ji, Q., Ju, C., 2022. The Role of Latency-Associated Transcripts in the Latent Infection of Pseudorabies Virus. *Viruses* 14, 1379. doi: 10.3390/v14071379.
- Didkowska, A., Klich, D., Matusik, K., Kwiecień, E., Tchórz, W., Welz, M., Skibniewski, B., Kwiecieński, P., Mierkiewicz, M., Anusz, K., 2025. Serological survey and associated risk factors of Aujeszky's disease virus in wild boar from south and central Poland. *J. Vet. Res.* 69, 177–181. doi: 10.2478/jvetres-2025-0031.
- Dodattenna, N., 2026. Viral Mastery: The Dynamic Regulation of Interferon Signaling. *Viruses* 18, 674. doi: 10.3390/v18060674.
- Duan, S.H., Li, Z.M., Yu, X.J., Li, D., 2025. Alphaherpesvirus in Pets and Livestock. *Microorganisms* 13, 82. doi: 10.3390/microorganisms13010082.
- Elbers, A.R., Braamskamp, J., Dekkers, L.J., Voets, R., Duinhof, T., Hunneman, W.A., Stegeman, J.A., 2000. Aujeszky's disease virus eradication campaign successfully heading for last stage in The Netherlands. *Vet. Q.* 22, 103–107. doi: 10.1080/01652176.2000.9695034.
- Engel, M., Wierup, M., 1999. Vaccination and eradication programme against Aujeszky's disease in five Swedish pig herds with special reference to herd owner attitudes. *Acta Vet. Scand.* 40, 213–219. doi: 10.1186/BF03547019.
- Evans, D., Horgan, V., Taylor, R.A., Kelly, L., 2024. A qualitative risk assessment of imports of animal feed as a potential pathway for Aujeszky's disease virus incursion. *Microb. Risk Anal.* 27–28, 100314. doi: 10.1016/j.mran.2024.100314.
- Ezeonwumelu, I.J., Garcia-Vidal, E., Ballana, E., 2021. JAK-STAT Pathway: A Novel Target to Tackle Viral Infections. *Viruses* 13, 2379. doi: 10.3390/v13122379.
- Favoreel, H.W., 2026. Human infection with pseudorabies virus: review of evidence, risk assessment, and future directions. *J. Virol.* 100, e00080-26. doi: 10.1128/jvi.00080-26.
- Ferrara, G., Longobardi, C., D'Ambrosi, F., Amoroso, M.G., D'Alessio, N., Damiano, S., Ciarica, R., Iovane, V., Iovane, G., Pagnini, U., Montagnaro, S., 2021. Aujeszky's Disease in South-Italian Wild Boars (*Sus scrofa*): A Serological Survey. *Animals (Basel)* 11, 3298. doi: 10.3390/ani1113298.
- Fleming, S.B., 2016. Viral Inhibition of the IFN-Induced JAK/STAT Signalling Pathway: Development of Live Attenuated Vaccines by Mutation of Viral-Encoded IFN-Antagonists. *Vaccines (Basel)* 4, 23. doi: 10.3390/vaccines4030023.
- Freuling, C.M., Hlinak, A., Schulze, C., Sehl-Ewert, J., Wysocki, P., Szentiks, C.A., Schmitt, K., Wohlsein, P., Kluth, G., Reinhardt, I., Mettenleiter, T.C., Müller, T., 2023. Suid alphaherpesvirus 1 of wild boar origin as a recent source of Aujeszky's disease in carnivores in Germany. *Virol. J.* 20, 110. doi: 10.1186/s12985-023-02074-3.
- Gainey, M.D., Rivenbark, J.G., Cho, H., Yang, L., Yokoyama, W.M., 2012. Viral MHC class I inhibition evades CD8+ T-cell effector responses in vivo but not CD8+ T-cell priming. *Proc. Natl. Acad. Sci. U S A* 109, E3260–E3267. doi: 10.1073/pnas.1217111109.
- Gao, W., Zhang, M., Zhu, Z., 2025. The prevalence of pseudorabies virus in China from 2010 to 2024: a systematic review and meta-analysis. *BMC Vet. Res.* 21, 513. doi: 10.1186/s12917-025-04924-4.
- Geljić, I.S., Brilic, P.K., Musak, L., Karner, D., Ambriović-Ristov, A., Jonjic, S., Schu, P., Rovis, T.L., 2021. Viral Interactions with Adaptor-Protein Complexes: A Ubiquitous Trait among Viral Species. *Int. J. Mol. Sci.* 22, 5274. doi: 10.3390/ijms22105274.
- Gerdts, V., Beyer, J., Lomniczi, B., Mettenleiter, T.C., 2000. Pseudorabies virus expressing bovine herpesvirus 1 glycoprotein B exhibits altered neurotropism and increased neurovirulence. *J. Virol.* 74, 817–827. doi: 10.1128/jvi.74.2.817-827.2000.
- Gillespie, R.R., Hill, M.A., Kanitz, C.L., 1996. Infection of pigs by aerosols of Aujeszky's disease virus and their shedding of the virus. *Res. Vet. Sci.* 60, 228–233. doi: 10.1016/s0034-5288(96)90044-2.
- Gong, L., Deng, Q., Xu, R., Ji, C., Wang, H., Zhang, G., 2020. Effects of physical and chemical factors on pseudorabies virus activity in vitro. *BMC Vet. Res.* 16, 358. doi: 10.1186/s12917-020-02573-3.
- Gong, L., Ou, X., Hu, L., Zhong, J., Li, J., Deng, S., Li, B., Pan, L., Wang, L., Hong, X., Luo, W., Zeng, Q., Zan, J., Peng, T., Cai, M., Li, M., 2022. The Molecular Mechanism of Herpes Simplex Virus 1 UL31 in Antagonizing the Activity of IFN- β . *Microbiol. Spectr.* 10, e0188321. doi: 10.1128/spectrum.01883-21.
- Greiser-Wilke, I., Blome, S., Moennig, V., 2007. Diagnostic methods for detection of Classical swine fever virus--status quo and new developments. *Vaccine* 25, 5524–5530. doi: 10.1016/j.vaccine.2006.11.043.
- Grieco, V., Gelmetti, D., Finazzi, G., Brocchi, E., Finazzi, M., 1997. Immunohistologic diagnosis of pseudorabies (Aujeszky's disease) using monoclonal antibodies. *J. Vet. Diagn. Invest.* 9, 326–328. doi: 10.1177/104063879700900320.
- Gu, N.Y., Ryu, G.S., Park, G.N., Lee, J.Y., Cho, Y.S., Yang, D.K., Lee, H.J., 2025. Enhanced susceptibility of porcine muscle-derived mesenchymal stem cells to Aujeszky's virus compared Vero cells. *Anim. Biotechnol.* 36, 2479677. doi: 10.1080/10495398.2025.2479677.
- Guo, H., Liu, Q., Yang, D., Zhang, H., Kuang, Y., Li, Y., Chen, H., Wang, X., 2024. Brincidofovir Effectively Inhibits Proliferation of Pseudorabies Virus by Disrupting Viral Replication. *Viruses* 16, 464. doi: 10.3390/v16030464.
- Guo, Z., Kang, H., Feng, Z., Zhang, X., Shi, J., Li, J., Song, Z., Xiang, L., Gong, B., Xu, H., Leng, C., Zhou, G., Wang, Q., Tang, Y., An, T., Cai, X., Tian, Z., Peng, J., Zhang, H., 2026. Persistent Circulation of Pseudorabies Virus Variants in China: Genomic Features, Pathogenic Characteristics, and Cross-Protective Efficacy of Variant Strain Vaccines. *Transbound. Emerg. Dis.* 2026, 5341313. doi: 10.1155/tbed/5341313.
- Hahn, E.C., Fadl-Alla, B., Lichtensteiger, C.A., 2010. Variation of Aujeszky's disease viruses in wild swine in the USA. *Vet. Microbiol.* 143, 45–51. doi: 10.1016/j.vetmic.2010.02.013.
- Hahn, E.C., Page, G.R., Hahn, P.S., Gillis, K.D., Romero, C., Anelli, J.A., Gibbs, E.P., 1997. Mechanisms of transmission of Aujeszky's disease virus originating from feral swine in the USA. *Vet. Microbiol.* 55, 123–130. doi: 10.1016/s0378-1135(96)01309-0.
- Hu, D., Lv, L., Zhang, Z., Xiao, Y., Liu, S., 2016. Seroprevalence and associated risk factors of pseudorabies in Shandong province of China. *J. Vet. Sci.* 17, 361–368. doi: 10.4142/jvs.2016.17.361.
- Iglesias, J.G., Harkness, J.W., 1988. Studies of transplacental and perinatal infection with two clones of a single Aujeszky's disease (pseudorabies) virus isolate. *Vet. Microbiol.* 16, 243–254. doi: 10.1016/0378-1135(88)90028-4.
- Ketusing, N., Reeves, A., Portacci, K., Yano, T., Olea-Popelka, F., Keefe, T., Salman, M., 2014. Evaluation of strategies for the eradication of Pseudorabies virus (Aujeszky's disease) in commercial swine farms in Chiang-Mai and Lampoon Provinces, Thailand, using a simulation disease spread model. *Transbound. Emerg. Dis.* 61, 169–176. doi: 10.1111/tbed.12017.
- Khairullah, A.R., Kusala, M.K.J., Fauziah, I., Furqoni, A.H., Suhendro, I., Effendi, M.H., Raissa, R., Moses, I.B., Silaen, O.S.M., Yuliatun, L., Yanestria, S.M., Riwi, K.H.P., Hasib, A., Ayuti, S.R., 2024. Deciphering leptospirosis: Insights into an emerging global threat. *J. Adv. Vet. Res.* 14, 1065–1071.
- Kit, S., 1990. Genetically engineered vaccines for control of Aujeszky's disease (pseudorabies). *Vaccine* 8, 420–424. doi: 10.1016/0264-410x(90)90240-m.
- Klupp, B.G., 2021. Pseudorabies Virus Infections. *Pathogens* 10, 719. doi: 10.3390/pathogens10060719.
- Kondibaeva, Z.B., Yespembetov, B.A., Abeuov, K.B., Mussayeva, A.K., Siyabekov, S.T., Nussupova, S.T., Akmatova, E.K., Pazylov, Y.K., Maikhin, K.T., Syrym, N.S., 2021. Inactivated vaccine against Aujeszky's disease. *Vet. World* 14, 2957–2963. doi: 10.14202/vetworld.2021.2957-2963.
- Koshmetov, Z.K., Kondibaeva, Z.B., Mussoyev, A.M., Abishov, A.A., Omarbekova, U.Z., 2021. Epizootic situation of Aujeszky's disease within the territory of the Republic of Kazakhstan. *Open Vet. J.* 11, 135–143. doi: 10.4314/ovj.v11i1.20.
- Kouam, M.K., Moussala, J.O., 2018. Assessment of Factors Influencing the Implementation of Biosecurity Measures on Pig Farms in the Western Highlands of Cameroon (Central Africa). *Vet. Med. Int.* 2018, 9173646. doi: 10.1155/2018/9173646.
- Kumar, P., Kausar, M.A., Singh, A.B., Singh, R., 2021. Biological contaminants in the indoor air environment and their impacts on human health. *Air Qual. Atmos. Health* 14, 1723–1736. doi: 10.1007/s11869-021-00978-z.
- Laidoudi, Y., Davoust, B., Watier-Grillot, S., Oger, A., Le Potier, M.F., Deblanc, C., 2022. Serological Survey of Aujeszky's Disease in Wild Boar from Southeastern France. *Pathogens* 11, 1107. doi: 10.3390/pathogens11101107.
- Lamote, J.A.S., Kestens, M., Van Waesberghe, C., Delva, J., De Pelsmaeker, S., Devriendt, B., Favoreel, H.W., 2017. The Pseudorabies Virus Glycoprotein gE/gI Complex Suppresses Type I Interferon Production by Plasmacytoid Dendritic Cells. *J. Virol.* 91, e02276-16. doi: 10.1128/JVI.02276-16.
- Laval, K., Enquist, L.W., 2020. The Neuropathic Itch Caused by Pseudorabies Virus. *Pathogens* 9, 254. doi: 10.3390/pathogens9040254.
- Laval, K., Vernejoul, J.B., Van Cleemput, J., Koyuncu, O.O., Enquist, L.W., 2018. Virulent Pseudorabies Virus Infection Induces a Specific and Lethal Systemic Inflammatory Response in Mice. *J. Virol.* 92, e01614-18. doi: 10.1128/JVI.01614-18.
- Leamcharakul, P., Renner-Müller, I.C., Reimann, M., Munz, E., 1991. A serological survey of the prevalence of Aujeszky's disease antibodies in Thailand using enzyme-linked immunosorbent assays (ELISA), serum neutralization (SN) and latexagglutination tests (LT). *Rev. Elev. Med. Vet. Pays Trop.* 44, 135–140.
- Li, H.X., Fong, M.W.C., Rahaman, N.Y.A., Low, S.E., Lee, J.X., Cheah, E.H.C., Kam, K.Y., Yong, R.L.H., Ooi, P.T., 2024. Serological Investigation of Aujeszky's Disease Between 1919 and 2021 in Peninsular Malaysia. *Pertanika J. Trop. Agric. Sci.* 47, 1109–1120. doi: 10.47836/pjtas.47.4.04.
- Li, H.Y., Xu, T., Wu, X., Liu, B.L., Yan, Y.X., Shao, L.N., Huang, B.Z., Qing, Y., Ge, L.P., Liu, Z.H., Sun, J., Zeng, X., Xu, Z.W., Zhu, L., 2026a. Pathogenesis of pseudorabies virus in mouse placenta: insights into maternal-infant transmission mechanisms. *Microbiol. Spectr.* 14, e0364825. doi: 10.1128/spectrum.03648-25.
- Li, L.T., Liu, J., Luo, M., Liu, J.S., Zhang, M.M., Zhang, W.J., Chen, H.C., Liu, Z.F., 2023. Establishment of pseudorabies virus latency and reactivation model in mice dorsal root ganglia culture. *J. Gen. Virol.* 104. doi: 10.1099/jgv.0.001921.
- Li, Y., Yang, F., Zou, D., Liu, P., Qi, K., Wang, J., Sun, C., Tang, Y., Zhang, R., Ren, J., Cui, Z., Li, R., Ji, Y., Qi, S., Gan, L., 2026b. Curcumin maintains pseudorabies virus latent infection by inhibiting the phosphorylation level of EGFR protein. *Vet. Microbiol.* 320, 111114. doi: 10.1016/j.vetmic.2026.111114.
- Lin, Y., Tan, L., Wang, C., He, S., Fang, L., Wang, Z., Zhong, Y., Zhang, K., Liu, D., Yang, Q., Wang, A., 2021. Serological Investigation and Genetic Characteristics of Pseudorabies Virus in Hunan Province of China From 2016 to 2020. *Front. Vet. Sci.* 8, 762326. doi: 10.3389/fvets.2021.762326.
- Liu, A., Xue, T., Zhao, X., Zou, J., Pu, H., Hu, X., Tian, Z., 2022a. Pseudorabies Virus Associations in Wild Animals: Review of Potential Reservoirs for Cross-Host Transmission. *Viruses* 14, 2254. doi: 10.3390/v14102254.
- Liu, G., Zhao, X., Lin, Y., Wang, X., Liu, D., 2026. A Comparative Review of Veterinary and Human Vaccine Development Strategies: Insights into Herpesvirus Vaccinology from Latency to Elimination. *Vaccines* 14, 249. doi: 10.3390/vaccines14030249.
- Liu, Q., Kuang, Y., Li, Y., Guo, H., Zhou, C., Guo, S., Tan, C., Wu, B., Chen, H., Wang, X., 2022b. The Epidemiology and Variation in Pseudorabies Virus: A Continuing Challenge to Pigs and Humans. *Viruses* 14, 1463. doi: 10.3390/v14071463.
- Liu, Y., Chen, Q., Rao, X., Diao, X., Yang, L., Fang, X., Hogeveen, H., 2019. An economic assessment of pseudorabies (Aujeszky's disease) elimination on hog farms in China. *Prev. Vet. Med.* 163, 24–30. doi: 10.1016/j.prevetmed.2018.12.005.
- Liu, Y.Y., Zhang, T.T., Zhao, Y., Li, N.W., Malhi, K.K., Yao, X., Li, J.L., 2025. Maternal antibodies to Bartha-K61 vaccine did not protect newborn piglets from challenge with novel recombinant pseudorabies virus. *Vet. J.* 314, 106463. doi: 10.1016/j.tvjl.2025.106463.
- Lukhele, S., Boukhaled, G.M., Brooks, D.G., 2019. Type I interferon signaling, regulation and gene stimulation in chronic virus infection. *Semin. Immunol.* 43, 101277. doi: 10.1016/j.smim.2019.05.001.
- Ma, W., Lager, K.M., Richt, J.A., Stoffregen, W.C., Zhou, F., Yoon, K.J., 2008. Development of real-time polymerase chain reaction assays for rapid detection and differentiation of wild-type pseudorabies and gene-deleted vaccine viruses. *J. Vet. Diagn. Invest.* 20, 440–447. doi: 10.1177/104063870802000405.
- Maes, R.K., Sussman, M.D., Vilnis, A., Thacker, B.J., 1997. Recent developments in latency and recombination of Aujeszky's disease (pseudorabies) virus. *Vet. Microbiol.* 55, 13–27. doi: 10.1016/s0378-1135(96)01305-3.
- Martínez-López, B., Carpenter, T.E., Sánchez-Vizcaino, J.M., 2009. Risk assessment and cost-effectiveness analysis of Aujeszky's disease virus introduction through breeding and fattening pig movements into Spain. *Prev. Vet. Med.* 90, 10–16. doi: 10.1016/j.prevetmed.2009.03.004.
- Masiuk, D., Kokariyev, A., Holda, K., Vasilenko, T., Hlebeniuk, V., 2021. Evaluation of the effectiveness of various vaccination protocols for pigs against aujeszky disease. *Adv. Anim. Vet. Sci.* 9, 483–489. doi: 10.17582/journal.aavs/2021/9.4.483.489.
- Masot, A.J., Gil, M., Risco, D., Jiménez, O.M., Núñez, J.I., Redondo, E., 2017. Pseudorabies virus infection (Aujeszky's disease) in an Iberian lynx (*Lynx pardinus*) in Spain: a case report. *BMC Vet. Res.* 13, 6. doi: 10.1186/s12917-016-0938-7.
- Melchjorsen, J., Matikainen, S., Paludan, S.R., 2009. Activation and evasion of innate antiviral immunity by herpes simplex virus. *Viruses* 1, 737–759. doi: 10.3390/v1030737.
- Mengeling, W.L., Lager, K.M., Volz, D.M., Brockmeier, S.L., 1992. Effect of various vaccination pro-

- cedures on shedding, latency, and reactivation of attenuated and virulent pseudorabies virus in swine. *Am. J. Vet. Res.* 53, 2164–2173.
- Mettenleiter, T.C., 1996. Immunobiology of pseudorabies (Aujeszky's disease). *Vet. Immunol. Immunopathol.* 54, 221–229. doi: 10.1016/s0165-2427(96)05695-4.
- Mettenleiter, T.C., 2000. Aujeszky's disease (pseudorabies) virus: the virus and molecular pathogenesis—state of the art, June 1999. *Vet. Res.* 31, 99–115. doi: 10.1051/vetres:2000110.
- Mettenleiter, T.C., 2020. Aujeszky's Disease and the Development of the Marker/DIVA Vaccination Concept. *Pathogens* 9, 563. doi: 10.3390/pathogens9070563.
- Milicevic, V., Radojicic, S., Valcic, M., Ivovic, V., Radosavljevic, V., 2016. Evidence of Aujeszky's disease in wild boar in Serbia. *BMC Vet. Res.* 12, 134. doi: 10.1186/s12917-016-0758-9.
- Miller, G.Y., Tsai, J.S., Forster, D.L., 1996. Benefit-cost analysis of the national pseudorabies virus eradication program. *J. Am. Vet. Med. Assoc.* 208, 208–213.
- Mocsári, E., Szolnoki, J., Glávits, R., Zsák, L., 1989. Horizontal transmission of Aujeszky's disease virus from sheep to pigs. *Vet. Microbiol.* 19, 245–252. doi: 10.1016/0378-1135(89)90070-9.
- Moghadami, M., 2017. A Narrative Review of Influenza: A Seasonal and Pandemic Disease. *Iran. J. Med. Sci.* 42, 2–13.
- Moiseenko, D., Chernyshev, R., Kamalova, N., Gavrilova, V., Igolkina, A., 2025. Evolution of Porcine Virus Isolation: Guidelines for Practical Laboratory Application. *Microorganisms* 13, 2658. doi: 10.3390/microorganisms13122658.
- Molitor, T., 2026. Pseudorabies in pigs. Merck Veterinary Manual. Reviewed by Alejandro Ramirez. Last updated March 2026.
- Müller, T., Bätza, H.J., Schlüter, H., Conraths, F.J., Mettenleiter, T.C., 2003. Eradication of Aujeszky's Disease in Germany. *J. Vet. Med. B* 50, 207–213. doi: 10.1046/j.1439-0450.2003.00666.x.
- Müller, T., Hahn, E.C., Tottewitz, F., Kramer, M., Klupp, B.G., Mettenleiter, T.C., Freuling, C., 2011. Pseudorabies virus in wild swine: a global perspective. *Arch. Virol.* 156, 1691–705. doi: 10.1007/s00705-011-1080-2.
- Narita, M., Imada, T., Kobayashi, M., 1991. Pathogenesis of Aujeszky's disease virus infection in swine tracheal organ culture. *J. Comp. Pathol.* 105, 439–444. doi: 10.1016/s0021-9975(08)80113-2.
- Narita, M., Zhao, Y.M., Kawashima, K., Arai, S., Hirose, H., Yamada, S., Ezura, K., 1998. Enteric lesions induced by different pseudorabies (Aujeszky's disease) virus strains inoculated into closed intestinal loops of pigs. *J. Vet. Diagn. Invest.* 10, 36–42. doi: 10.1177/104063879801000107.
- Nauwynck, H.J., 1997. Functional aspects of Aujeszky's disease (pseudorabies) viral proteins with relation to invasion, virulence and immunogenicity. *Vet. Microbiol.* 55, 3–11. doi: 10.1016/s0378-1135(96)01299-0.
- Nie, Z., Zhu, S., Wu, L., Sun, R., Shu, J., He, Y., Feng, H., 2023. Progress on innate immune evasion and live attenuated vaccine of pseudorabies virus. *Front. Microbiol.* 14, 1138016. doi: 10.3389/fmicb.2023.1138016.
- Orr, M.T., Edelmann, K.H., Vieira, J., Corey, L., Raulet, D.H., Wilson, C.B., 2005. Inhibition of MHC class I is a virulence factor in herpes simplex virus infection of mice. *PLoS Pathog.* 1, e7. doi: 10.1371/journal.ppat.0010007.
- Ouagal, M., Hendrikx, P., Saegerman, C., Berkvens, D., 2010. Comparison between active and passive surveillance within the network of epidemiological surveillance of animal diseases in Chad. *Acta Trop.* 116, 147–151. doi: 10.1016/j.actatropica.2010.07.004.
- Pacini, M.I., Forzan, M., Cilia, G., Bernardini, L., Marzoli, F., Pedonese, F., Bandecchi, P., Fratini, F., Mazzei, M., 2020. Detection of Pseudorabies Virus in Wild Boar Foetus. *Animals* 10, 366. doi: 10.3390/ani10020366.
- Pacini, M.I., Forzan, M., Cilia, G., Bertelloni, F., Fratini, F., Mazzei, M., 2021. Detection and Characterization of Viral Pathogens Associated with Reproductive Failure in Wild Boars in Central Italy. *Animals* 11, 304. doi: 10.3390/ani11020304.
- Pannwitz, G., Freuling, C., Denzin, N., Schaarschmidt, U., Nieper, H., Hlinak, A., Burkhardt, S., Klopries, M., Dedeck, J., Hoffmann, L., Kramer, M., Selhorst, T., Conraths, F.J., Mettenleiter, T., Müller, T., 2012. A long-term serological survey on Aujeszky's disease virus infections in wild boar in East Germany. *Epidemiol. Infect.* 140, 348–358. doi: 10.1017/S0950268811000033.
- Papageorgiou, K., Bouzalas, I., Giamoustari, K., Wróbel, M., Doukas, D., Stoikou, A., Athanasakopoulou, Z., Chatzopoulos, D., Papadopoulos, D., Pakos, S., Karapetsiou, C., Billinis, C., Petridou, E., Kritas, S.K., 2025. Detection of Pseudorabies Virus in Hunting Dogs in Greece: The Role of Wild Boars in Virus Transmission. *Pathogens* 14, 905. doi: 10.3390/pathogens14090905.
- Papageorgiou, K.V., Burriel, A.R., Filioussis, G., Psychas, V., Nauwynck, H., Kritas, S., 2017. Aujeszky's Disease (Pseudorabies). An old threat in current pig industry? Part I. Pathogenetic information and implications. *J. Hellenic Vet. Med. Soc.* 62, 29–37. doi: 10.12681/jhvm.14833.
- Papageorgiou, K., Grivas, I., Chiotelli, M., Theodoridis, A., Panteris, E., Papadopoulos, D., Petridou, E., Papaioannou, N., Nauwynck, H., Kritas, S.K., 2022. Age-Dependent Invasion of Pseudorabies Virus into Porcine Central Nervous System via Maxillary Nerve. *Pathogens* 11, 157. doi: 10.3390/pathogens11020157.
- Parsons, T.D., Pitcher, P.M., Johnstone, C., 1990. Economic analysis of an epizootic of pseudorabies and subsequent production following the institution of a vaccination program in a Pennsylvania swine herd. *J. Am. Vet. Med. Assoc.* 197, 188–191.
- Pasick, J., 2004. Application of DIVA vaccines and their companion diagnostic tests to foreign animal disease eradication. *Anim. Health Res. Rev.* 5, 257–262. doi: 10.1079/ahr.200479.
- Peiso, O.O., Bronsvort, B.M., Handel, I.G., Volkova, V.V., 2011. A review of exotic animal disease in Great Britain and in Scotland specifically between 1938 and 2007. *PLoS One* 6, e22066. doi: 10.1371/journal.pone.0022066.
- Pensaert, M., Labarque, G., Favoreel, H., Nauwynck, H., 2004. Aujeszky's disease vaccination and differentiation of vaccinated from infected pigs. *Dev. Biol. (Basel)* 119, 243–254.
- Pensaert, M., Morrison, R.B., 2000. Challenges of the final stages of the ADV eradication program. *Vet. Res.* 31, 141–145. doi: 10.1051/vetres:2000112.
- Pérez, L.J., de Arce, H.D., 2009. Development of a polymerase chain reaction assay for the detection of pseudorabies virus in clinical samples. *Braz. J. Microbiol.* 40, 433–438. doi: 10.1590/S1517-83822009000300002.
- Pomeroy, L.E., Reynolds, A.E., Hengartner, C.J., 2005. Molecular biology of pseudorabies virus: impact on neurobiology and veterinary medicine. *Microbiol. Mol. Biol. Rev.* 69, 462–500. doi: 10.1128/MMBR.69.3.462-500.2005.
- Pomorska-Mól, M., Markowska-Daniel, I., Pejcz, Z., 2010. Evaluation of humoral and antigen-specific T-cell responses after vaccination of pigs against pseudorabies in the presence of maternal antibodies. *Vet. Microbiol.* 144, 450–454. doi: 10.1016/j.vetmic.2010.01.015.
- Presti, V.D.M.L., Moreno, A., Castelli, A., Ippolito, D., Aliberti, A., Amato, B., Vitale, M., Fiasconaro, M., Ciarrelli, F.P., 2021. Retrieving Historical Cases of Aujeszky's Disease in Sicily (Italy): Report of a Natural Outbreak Affecting Sheep, Goats, Dogs, Cats and Foxes and Considerations on Critical Issues and Perspectives in Light of the Recent EU Regulation 429/2016. *Pathogens* 10, 1301. doi: 10.3390/pathogens10101301.
- Prodanov-Radulović, J., Došen, R., Pušić, I., Petrović, T., Apić, J., Stojanov, I., Polaček, V., 2015. Emergence of pseudorabies virus (morbus aujeszky) infection at large swine farms in ap vojvodina (Serbia). *Serbian J. Agric. Sci.* 64, 105–111.
- Prodanov-Radulović, J., Došen, R., Pušić, I., Stojanov, I., Lupulović, D., Ratajac, R., 2011. The transmission and spreading routes of Aujeszky's disease in swine population. *Biotechnol. Anim. Husb.* 27, 867–874. doi: 10.2298/BAH1103867P.
- Ratta, B., Nautiyal, B., Ravindra, P.V., Chaturvedi, U., Kumar, S., Subudhi, P.K., Chindera, K., Tiwari, S., Barmann, N.N., Tiwari, A.K., 2010. Characterization and expression of e2 glycoprotein of classical Swine Fever virus in a eukaryotic expression system. *Indian J. Virol.* 21, 69–75. doi: 10.1007/s13337-010-0009-9.
- Robinson, A.L., Bianchessi, L., Rocchi, M.S., Dagleish, M.P., 2026. A review of the pathology of herpesvirus infections in pinnipeds. *J. Comp. Pathol.* 226, 42–56. doi: 10.1016/j.jcpa.2026.01.007.
- Rollinson, E.A., White, G., Thiry, E., Dubuisson, J., Pastoret, P.P., 1988. Therapy of Aujeszky's disease (pseudorabies) in naturally infected and artificially inoculated piglets using BW B759U [9-(1,3-dihydroxy-2-propoxymethyl) guanine]. *Res. Vet. Sci.* 45, 54–61.
- Saade, G., Ménard, D., Hervet, C., Renon, P., Hue, E., Zhu, J., Dubreil, L., Pallot, R., Pronost, S., Bourry, O., Simon, G., Dupont, J., Bertho, N., Meurens, F., 2020. Porcine Reproductive and Respiratory Syndrome Virus Interferes with Swine Influenza A Virus Infection of Epithelial Cells. *Vaccines (Basel)* 8, 508. doi: 10.3390/vaccines8030508.
- Salinas-Zacarias, I., Guzman-Bautista, E.R., del Carmen Ramirez-Estudillo, M., Chacón-Salinas, R., Vega-López, M.A., 2020. Mucosal and systemic immune responses to Aujeszky's disease virus (ADV) in early vaccinated piglets. *Comp. Immunol. Microbiol. Infect. Dis.* 68, 101400. doi: 10.1016/j.cimid.2019.101400.
- Salwa, A., 2004. A natural outbreak of Aujeszky's disease in farm animals. *Pol. J. Vet. Sci.* 7, 261–266.
- Schulze, C., Hlinak, A., Wohlsein, P., Kutzer, P., Müller, T., 2010. Spontaneous Aujeszky's disease (pseudorabies) in European wild boars (*Sus scrofa*) in the federal state of Brandenburg, Germany. *Berl. Munch. Tierarztl. Wochenschr.* 123, 359–364.
- Segalés, J., Sibila, M., 2025. Speculative Review on the Feasibility of Porcine Circovirus 2 Elimination. *Animals (Basel)* 15, 2744. doi: 10.3390/ani15182744.
- Sehl, J., Teifke, J.P., 2020. Comparative Pathology of Pseudorabies in Different Naturally and Experimentally Infected Species—A Review. *Pathogens* 9, 633. doi: 10.3390/pathogens9080633.
- Serena, M.S., Cappuccino, J., Fossaroli, M., Williams, M.M., Dibarbora, M., Brizzio, R., Metz, G.E., Aspitia, C.G., Perez, A., Carpinetti, B.N., Echeverría, M.G., 2023. Characterization of new strains of Pseudorabies virus in Argentina: Detection of interspecies transmission. *Open Vet. J.* 13, 419–426. doi: 10.5455/OVJ.2023.v13.i4.3.
- Serena, M.S., Geisler, C., Metz, G.E., Corva, S.G., Mórtoia, E.C., Larsen, A., Jarvis, D.L., Echeverría, M.G., 2013. Expression and purification of Suid Herpesvirus-1 glycoprotein E in the baculovirus system and its use to diagnose Aujeszky's disease in infected pigs. *Protein Expr. Purif.* 90, 1–8. doi: 10.1016/j.pep.2013.04.008.
- Shibata, I., Yazawa, S., Ono, M., Okuda, Y., 2003. Experimental dual infection of specific pathogen-free pigs with porcine reproductive and respiratory syndrome virus and pseudorabies virus. *J. Vet. Med. B Infect. Dis. Vet. Public Health* 50, 14–19. doi: 10.1046/j.1439-0450.2003.00605.x.
- Song, J., Bai, R., Xing, D., Li, C., Chen, X., Zheng, F., Lei, M., Wang, Y., Liu, Y., Tang, J., Liu, P., Cheng, C., Yuan, J., Zhang, R., 2026. Pseudorabies virus TK protein antagonizes alpha interferon response by interfering with the JAK1-STAT1 interaction. *Virol. Sin.* 41, 132–143. doi: 10.1016/j.virs.2026.01.004.
- Spickler, A.R., 2024. Aujeszky's disease (Pseudorabies). Center for Food Security and Public Health, Iowa State University. Last updated January 2024.
- Stegeman, A., 1997. Aujeszky's disease (pseudorabies) virus eradication campaign in The Netherlands. *Vet. Microbiol.* 55, 175–180. doi: 10.1016/s0378-1135(96)01301-6.
- Su, B.Q., Yang, G.Y., Wang, J., Ming, S.L., Chu, B.B., 2024. Pseudorabies virus inhibits progesterone-induced inactivation of TRPM1 to facilitate viral entry. *PLoS Pathog.* 20, e1011956. doi: 10.1371/journal.ppat.1011956.
- Su, C., Zhan, G., Zheng, C., 2016. Evasion of host antiviral innate immunity by HSV-1, an update. *Virol. J.* 13, 38. doi: 10.1186/s12985-016-0495-5.
- Suprani, V., Agnusi, G.P., Romanelli, C., Aragrande, M., Canali, M., 2026. The economic sustainability of biosecurity in pig farming: a systematic review with bibliometric, network and content analysis. *Front. Anim. Sci.* 7, 1738787. doi: 10.3389/fanim.2026.1738787.
- Tan, L., Yao, J., Yang, Y., Luo, W., Yuan, X., Yang, L., Wang, A., 2021. Current Status and Challenge of Pseudorabies Virus Infection in China. *Virol. Sin.* 36, 588–607. doi: 10.1007/s12250-020-00340-0.
- Tanaka, S., Mannen, K., 2003. Effect of mild stress in mice latently infected pseudorabies virus. *Exp. Anim.* 52, 383–386. doi: 10.1538/expanim.52.383.
- Thiry, E., Addie, D., Belák, S., Boucraut-Baralon, C., Egberink, H., Frymson, T., Gruffydd-Jones, T., Hartmann, K., Hosie, M.J., Lloret, A., Lutz, H., Marsilio, F., Möstl, K., Pennisi, M.G., Radford, A.D., Truyen, U., Horzinek, M.C., 2013. Aujeszky's disease/pseudorabies in cats: ABCD guidelines on prevention and management. *J. Feline Med. Surg.* 15, 555–556. doi: 10.1177/1098612X13489211.
- Tomescu, C., Law, W.K., Kedes, D.H., 2003. Surface downregulation of major histocompatibility complex class I, PE-CAM, and ICAM-1 following de novo infection of endothelial cells with Kaposi's sarcoma-associated herpesvirus. *J. Virol.* 77, 9669–9684. doi: 10.1128/jvi.77.17.9669-9684.2003.
- Tong, W., Liu, F., Zheng, H., Liang, C., Zhou, Y.J., Jiang, Y.F., Shan, T.L., Gao, F., Li, G.X., Tong, G.Z., 2015. Emergence of a Pseudorabies virus variant with increased virulence to piglets. *Vet. Microbiol.* 181, 236–240. doi: 10.1016/j.vetmic.2015.09.021.
- Ukhovskiy, V.V., Kornienko, L.Y., Pyskun, A.V., Chechet, O.M., Drozhzhe, Z.M., Polupan, I.M., Alekseeva, G.B., Moroz, O.A., Romanov, O.M., 2020. Spread of Aujeszky's disease among wild boars and domestic pigs in Ukraine. *Regul. Mech. Biosyst.* 13, 46–52. doi: 10.15421/022206.
- Ukhovskiy, V.V., Romanov, O.M., Borisevich, B.V., Tarasov, O.A., Ukhovska, T.M., Pyskun, A.V., Solomon, V.V., Ayshpur, O.Y., 2020. Pathologic changes in pig organs, infected with the Aujeszky's disease. *Ukr. J. Ecol.* 10, 8–15.
- van Gent, M., Chiang, J.J., Muppala, S., Chiang, C., Azab, W., Kattenhorn, L., Knipe, D.M., Osterrieder, N., Gack, M.U., 2022. The US3 Kinase of Herpes Simplex Virus Phosphorylates the RNA Sensor RIG-I To Suppress Innate Immunity. *J. Virol.* 96, e0151021. doi: 10.1128/JVI.01510-21.
- van Samkar, A., Brouwer, M.C., Schultze, C., van der Ende, A., van de Beek, D., 2015. Streptococcus suis Meningitis: A Systematic Review and Meta-analysis. *PLoS Negl. Trop. Dis.* 9, e0004191. doi: 10.1371/journal.pntd.0004191.
- Verpoest, S., Cay, B., Favoreel, H., De Regge, N., 2017. Age-Dependent Differences in Pseudorabies Virus Neuropathogenesis and Associated Cytokine Expression. *J. Virol.* 91, e02058-16. doi: 10.1128/JVI.02058-16.
- Wang, C., Li, L., Zhai, X., Chang, H., Liu, H., 2024a. Evasion of the Antiviral Innate Immunity by PRV. *Int. J. Mol. Sci.* 25, 13140. doi: 10.3390/ijms252313140.
- Wang, H., Li, H., Tang, B., Ye, C., Han, M., Teng, L., Yue, M., Li, Y., 2024b. Fast and sensitive differential diagnosis of pseudorabies virus-infected versus pseudorabies virus-vaccinated swine using CRISPR-Cas12a. *Microbiol. Spectr.* 12, e0261723. doi: 10.1128/spectrum.02617-23.
- Wang, J., Guo, R., Qiao, Y., Xu, M., Wang, Z., Liu, Y., Gu, Y., Liu, C., Hou, J., 2016. An inactivated gE-deleted pseudorabies vaccine provides complete clinical protection and reduces virus shedding against challenge by a Chinese pseudorabies variant. *BMC Vet. Res.* 12, 277. doi: 10.1186/s12917-016-0897-z.
- Wang, J., Han, H., Liu, W., Li, S., Guo, D., 2021. Diagnosis and gl antibody dynamics of pseudorabies virus in an intensive pig farm in Hei Longjiang Province. *J. Vet. Sci.* 22, e23. doi: 10.4142/jvs.2021.22.e23.
- Wang, T.Y., Li, C., Cai, X.H., Shan, T., Tang, Y.D., 2026. Spillover of pseudorabies virus variants to humans: an urgent call for pseudorabies eradication in domestic pigs. *Lancet Microbe* 7, 101351. doi: 10.1016/j.lanmic.2026.101351.
- Wang, Y., Jin, Y., Wang, Y., Li, Y., Wang, X., Li, Z., Zhou, J., 2025. Sow reproductive disorders: a key issue affecting the pig industry. *Front. Vet. Sci.* 12, 1535719. doi: 10.3389/fvets.2025.1535719.
- Wójcik, W., Didkowska, A., Orłowska, B., Nowak, S., Sell, B., Anusz, K., Pfaff, F., Hoffmann, B., 2026. Aujeszky's Disease in a Grey Wolf (*Canis lupus*) in Poland. *Viruses* 18, 449. doi: 10.3390/v18040449.
- Wong, G., Lu, J., Zhang, W., Gao, G.F., 2019. Pseudorabies virus: a neglected zoonotic pathogen in humans? *Emerg. Microbes Infect.* 8, 150–154. doi: 10.1080/22221751.2018.1563459.
- Wu, J., Zhang, J., Zhou, J., Luo, Y., Wang, X., Yang, R., Zhu, J., Jia, M., Zhang, L., Fu, L., Yan, N., Wang, Y., 2024. Prevalence and Genetic Variation Investigation of the Pseudorabies Virus in Southwest China. *Animals* 14, 3103. doi: 10.3390/ani14213103.
- Wu, Y., Sun, Z., Xia, L., Tian, P., Jiao, L., Li, Y., Wei, Z., Wang, X., Li, X., Zhang, G., 2025. MHC-I pathway disruption by viruses: insights into immune evasion and vaccine design for animals. *Front. Immunol.* 16, 1540159. doi: 10.3389/fimmu.2025.1540159.
- Xia, S., Tao, Y., Cui, L., Yu, Y., Xu, S., 2019. MHC Class I Molecules Exacerbate Viral Infection by Disrupting Type I Interferon Signaling. *J. Immunol. Res.* 2019, 5370706. doi: 10.1155/2019/5370706.
- Xie, J., Zhang, X., Chen, L., Bi, Y., Idris, A., Xu, S., Li, X., Zhang, Y., Feng, R., 2021. Pseudorabies Virus US3 Protein Inhibits IFN- β Production by Interacting With IRF3 to Block Its Activation. *Front.*

- Microbiol. 12, 761282. doi: 10.3389/fmicb.2021.761282.
- Xing, G., Li, H., Lu, C., Li, H., Jin, Y., Yan, Y., Shang, S., Zhou, J., 2024. The attenuated Pseudorabies virus vaccine Bartha K61 induces a weak cellular immunity: implications for the development of PRV-vectored vaccines. *Front. Immunol.* 15, 1489268. doi: 10.3389/fimmu.2024.1489268.
- Yamada, M., Miyazaki, A., Yamamoto, Y., Nakamura, K., Ito, M., Tsunemitsu, H., Narita, M., 2014. Experimental teschovirus encephalomyelitis in gnotobiotic pigs. *J. Comp. Pathol.* 150, 276–286. doi: 10.1016/j.jcpa.2013.08.004.
- Yamane, I., Ishizeki, S., Yamazaki, H., 2015. Aujeszky's disease and the effects of infection on Japanese swine herd productivity: a cross-sectional study. *J. Vet. Med. Sci.* 77, 579–582. doi: 10.1292/jvms.14-0385.
- Yang, L., Long, Y., Li, Q., Song, W., Huang, Y., Liang, G., Yu, D., Zhou, M., Xu, G., Chen, Y., Huang, C., Tang, X., 2022. Detection of suid herpesvirus 1 infectivity in pigs by propidium monoazide-qPCR. *Front. Vet. Sci.* 9, 975726. doi: 10.3389/fvets.2022.975726.
- Ye, G., Liu, H., Zhou, Q., Liu, X., Huang, L., Weng, C., 2022. A Tug of War: Pseudorabies Virus and Host Antiviral Innate Immunity. *Viruses* 14, 547. doi: 10.3390/v14030547.
- Yıldırım, S., Özkan, C., Yener, Z., Çetin, M., Kozat, S., 2017. Immunohistochemical diagnosis of Pseudorabies (Aujeszky's Disease) in a cow in Van, Turkey. *Kafkas Univ. Vet. Fak. Derg.* 23, 173–176. doi: 10.9775/kvfd.2016.16071.
- Yin, Y., Ma, J., Van Waesberghe, C., Devriendt, B., Favoreel, H.W., 2022. Pseudorabies virus-induced expression and antiviral activity of type I or type III interferon depend on the type of infected epithelial cell. *Front. Immunol.* 13, 1016982. doi: 10.3389/fimmu.2022.1016982.
- Yu, L., Chen, Y., Zhu, Z., Li, X., 2026. Pseudorabies Virus Infection Triggers PANoptosis to Enhance Inflammatory Responses Both In Vitro and In Vivo. *Microorganisms* 14, 303. doi: 10.3390/microorganisms14020303.
- Yu, X., Zhou, Z., Hu, D., Zhang, Q., Han, T., Li, X., Gu, X., Yuan, L., Zhang, S., Wang, B., Qu, P., Liu, J., Zhai, X., Tian, K., 2014. Pathogenic pseudorabies virus, China, 2012. *Emerg. Infect. Dis.* 20, 102–104. doi: 10.3201/eid2001.130531.
- Zhang, C., Liu, Y., Chen, S., Qiao, Y., Guo, M., Zheng, Y., Xu, M., Wang, Z., Hou, J., Wang, J., 2019. A gD&gC-substituted pseudorabies virus vaccine strain provides complete clinical protection and is helpful to prevent virus shedding against challenge by a Chinese pseudorabies variant. *BMC Vet. Res.* 15, 2. doi: 10.1186/s12917-018-1766-8.
- Zhang, H.L., Zhang, R.H., Liu, G., Li, G.M., Wang, F.X., Wen, Y.J., Shan, H., 2023. Evaluation of immunogenicity of gene-deleted and subunit vaccines constructed against the emerging pseudorabies virus variants. *Virol. J.* 20, 98. doi: 10.1186/s12985-023-02051-w.
- Zhang, L., Zhong, C., Wang, J., Lu, Z., Liu, L., Yang, W., Lyu, Y., 2015. Pathogenesis of natural and experimental Pseudorabies virus infections in dogs. *Virol. J.* 12, 44. doi: 10.1186/s12985-015-0274-8.
- Zhang, Z., Wei, Q., Wu, C., Ye, Z., Qin, L., Chen, T., Sun, Z., Tian, K., Li, X., 2025. Isolation and pathogenicity of a novel recombinant pseudorabies virus from the attenuated vaccine and classical strains. *Front. Vet. Sci.* 12, 1579148. doi: 10.3389/fvets.2025.1579148.
- Zhao, H., Wang, S., Liu, C., Han, J., Tang, J., Zhou, L., Ge, X., Guo, X., Yang, H., 2018. The pUL56 of pseudorabies virus variant induces downregulation of swine leukocyte antigen class I molecules through the lysosome pathway. *Virus Res.* 251, 56–67. doi: 10.1016/j.virus-res.2018.04.007.
- Zheng, H.H., Fu, P.F., Chen, H.Y., Wang, Z.Y., 2022. Pseudorabies Virus: From Pathogenesis to Prevention Strategies. *Viruses* 14, 1638. doi: 10.3390/v14081638.
- Zhou, J., Li, S., Wang, X., Zou, M., Gao, S., 2017. Bartha-k61 vaccine protects growing pigs against challenge with an emerging variant pseudorabies virus. *Vaccine* 35, 1161–1166. doi: 10.1016/j.vaccine.2017.01.003.
- Zhou, M., Abid, M., Cao, S., Zhu, S., 2023. Recombinant Pseudorabies Virus Usage in Vaccine Development against Swine Infectious Disease. *Viruses* 15, 370. doi: 10.3390/v15020370.
- Zhou, Q., Zhang, L., Liu, H., Ye, G., Huang, L., Weng, C., 2022. Isolation and Characterization of Two Pseudorabies Virus and Evaluation of Their Effects on Host Natural Immune Responses and Pathogenicity. *Viruses* 14, 712. doi: 10.3390/v14040712.
- Zhu, S., Viejo-Borbolla, A., 2021. Pathogenesis and virulence of herpes simplex virus. *Virulence* 12, 2670–2702. doi: 10.1080/21505594.2021.1982373.
- Zhuang, L., Gong, J., Shen, J., Zhao, Y., Yang, J., Liu, Q., Zhang, Y., Shen, Q., 2025. Advances in molecular epidemiology and detection methods of pseudorabies virus. *Discover Nano* 20, 45. doi: 10.1186/s11671-025-04217-7.