Review Article

Journal of Advanced Veterinary Research
(2026) Volume 16, Issue 4, 546-556

A review of canine distemper in domestic dogs

Tridiganita I. Solikhah[1*], Aloisius P. Alvaro[1], Archena T.P. Putra[1], Rizky A. Ibrahim[1], Aswin R. Khairullah[2], Muhammad Akram[3]

[1]Division of Veterinary Clinic, Department of Health and Life Sciences, Faculty of Health, Medicine, and Life Sciences, Universitas Airlangga, Jl. Wijaya Kusuma No.113 Giri, Banyuwangi, East Java, 68422, Indonesia.
[2]Research Center for Veterinary Science, National Research and Innovation Agency (BRIN), Jl. Raya Bogor Km. 46 Cibinong, Bogor, West Java, 16911, Indonesia.
[3]Department of Eastern Medicine, Government College University Faisalabad, 38000, Pakistan.

ARTICLE INFO

Recieved: 01 April 2026

Accepted: 03 June 2026

*Correspondence:

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

Keywords:

Canine distemper virus (CDV), Disease, Epidemiology, Prevention, vaccination.

ABSTRACT

Canine distemper (CD) represents a highly infectious and frequently lethal viral disorder with multisystemic involvement that impacts domestic dogs as well as a wide range of carnivorous species globally. The causative pathogen, Canine Distemper Virus (CDV), belongs to the genus *Morbillivirus* under the family *Paramyxoviridae* and demonstrates remarkable genetic variability, encompassing at least seventeen genotypes identified across different regions of the world. Although effective vaccines are available, CDV continues to persist endemically in numerous areas, largely attributed to insufficient immunization coverage, ongoing viral mutation, and interspecies transmission facilitated by wildlife reservoirs. This review comprehensively summarized the etiology, epidemiology, transmission routes, risk factors, pathogenesis, clinical manifestations, diagnostic approaches, hematological and clinicopathological findings, as well as therapeutic, vaccination, and preventive strategies for CD. The virus primarily targets epithelial, lymphoid, and nervous tissues, producing severe respiratory, gastrointestinal, and neurological symptoms. Diagnostic confirmation relies on molecular and serological assays such as RT-PCR and ELISA, which offer high sensitivity for detecting viral RNA or antibodies. Although treatment is mainly supportive, prevention through timely and widespread vaccination remains the cornerstone of control. Furthermore, the persistence of novel viral lineages and spillover events from domestic dogs to wildlife underscore the need for continuous molecular surveillance and global cooperation. Understanding CDV's pathogenesis, epidemiological dynamics, and economic implications is crucial for developing integrated control strategies to mitigate the impact of canine distemper disease on animal health, biodiversity, and the veterinary public health sector.

Introduction

The CDV was initially documented in 1746 by Antonio de Ulloa y de la Torre-Giral, who provided the earliest description of a canine disease occurring in Quito, South America. The infection rapidly spread across the continent and was later reported in Europe, where severe outbreaks occurred. In 1760, an outbreak occurred in Spain, resulting in the deaths of approximately 900 dogs within a single day in Madrid. The disease subsequently spread to Great Britain in 1764 and later to Italy in 1770. During the early nineteenth century, Edward Jenner observed that young dogs exhibited greater vulnerability to the infection than adults, and that those which recovered developed resistance to subsequent infections, resembling the immunity seen in human measles. Historical and molecular evidence further suggests that CDV may have originated in South America after the adaptation of the measles virus to dogs during European colonization, before being transported to Europe, where it caused large-scale epidemics and eventually became endemic (Quintero-Gil *et al*., 2019).

Based on global surveillance, the distribution and prevalence of CDV vary by geography, climate, vaccination coverage, and host health. In domestic dogs, reported prevalence reached 56.6% in Italy, 16.1% in Austria, 7.4% in asymptomatic and 3% in symptomatic shelter dogs in the United States, 35.3% in community-acquired and 22.4% in hospital-acquired infections in Thailand, and 40% in free-roaming dogs in Cambodia. Despite the extensive implementation of vaccination programs, CDV still leads to lethal outbreaks among domestic dogs and various carnivorous species (Krstić *et al*., 2025).

Morbillivirus canis or CDV, a member of the genus *Morbillivirus* in the family *Paramyxoviridae*, causes an acute, highly contagious, and often fatal infection in domestic dogs (*Canis lupus familiaris*) and other carnivores such as canids and mustelids, with a high mortality rate (Liang *et al*., 2024; Wipf *et al*., 2025). Until 2014, nine genetic lineages of CDV were identified based on H gene sequence similarity. However, the number has gradually expanded, with seventeen major genotypes now recognized globally, including America-1 (vaccine strains), America-2–America-4, Europe/South America-1, South America-2 and -3, Europe-2/European Wildlife, Europe-3/Arctic, Asia-1–Asia-6, and Africa-1 and -2. Domestic dogs remain the primary host and reservoir, as all sequenced genotypes have been detected in this species. Some rare variants—such as South America-3, Asia-2, Asia-4, and Asia-5—have been reported exclusively in domestic dogs, underscoring their key role in CDV classification and global dissemination (Wipf *et al*., 2025).

Although an effective vaccine exists, CD remains a significant pathogen in dogs and has recently expanded into various wildlife species, including members of five orders and two families of nonhuman primates. CDV's capacity for cross-species infection reflects its remarkable evolutionary adaptability, establishing it as one of the most virulent viruses within the *Morbillivirus* genus (Uhl *et al*., 2019). CDV remains one of the most important and lethal viral agents infecting domestic dogs and various wildlife species. Despite the wide availability of vaccines, severe and often fatal outbreaks persist across the world. CDV attacks several organ systems, including the respiratory, gastrointestinal, and central nervous systems, and causes immunosuppression that increases vulnerability to secondary infections. Because of its high transmissibility, broad host range, and ability to cross species, a comprehensive understanding of CDV pathogenesis, diagnostic methods, and preventive measures is vital for effective disease control (Wilkes, 2022).

The significance of studying CD provides a comprehensive foundation that allows readers and researchers to explore various aspects of this viral disease in domestic dogs. This review serves as a key reference

ISSN: 2090-6277/2090-6269/

for understanding the multifaceted nature of CD, including its etiology and causative agent CDV, epidemiological patterns, transmission routes and risk factors, pathogenesis, clinical signs and pathological changes, diagnostic and hematological findings, as well as treatment, vaccination, control, and prevention strategies.

This review aimed to provide a comprehensive overview of the mechanisms of CDV infection, including its molecular and pathological features, epidemiology, clinical signs, hematology, clinicopathology, treatment strategies, vaccination efforts, and its broader effects on animal health and the economy. By integrating findings from various scientific studies, this paper sought to deepen the understanding of CD as a major infectious disease in domestic dogs and to serve as a foundation for future research and disease control initiatives.

Etiology and causative agent

CDV is a highly infectious systemic disease that primarily affects domestic dogs but can also infect a wide range of carnivores, including members of Canidae such as foxes, wolves, and coyotes; Procyonidae such as raccoons; Mustelidae such as ferrets and minks; Ursidae such as giant pandas; Ailuridae such as red pandas; and Felidae such as lions and tigers. Occasional infections have also been recorded in Artiodactyla, Primates, Rodentia, and Proboscidea. Despite ongoing vaccination programs, infections continue to occur in dogs due to antigenic variations between vaccine strains and circulating field viruses. The disease is caused by Canine *Morbillivirus*, a negative sense, single stranded RNA virus with a nonsegmented, enveloped genome of about 15,690 nucleotides (Rendon-Marin *et al*., 2019). Morphologically, CDV displays pleomorphic, predominantly spherical particles measuring approximately 150 to 250 nanometers in diameter (Rivera-Martínez *et al*., 2024). The CDV genome produces eight proteins organized into six transcription units in the order N, P, M, F, H, and L, which are separated by intergenic untranslated regions (UTRs) of relatively consistent length, except for the longer and more variable UTR located between the matrix (M) and fusion (F) genes (Rendon-Marin *et al*., 2019).

Figure 1 illustrates the morphology and genomic organization of CDV, highlighting the arrangement of its structural and non-structural proteins that play crucial roles in viral replication, assembly, and host interaction.

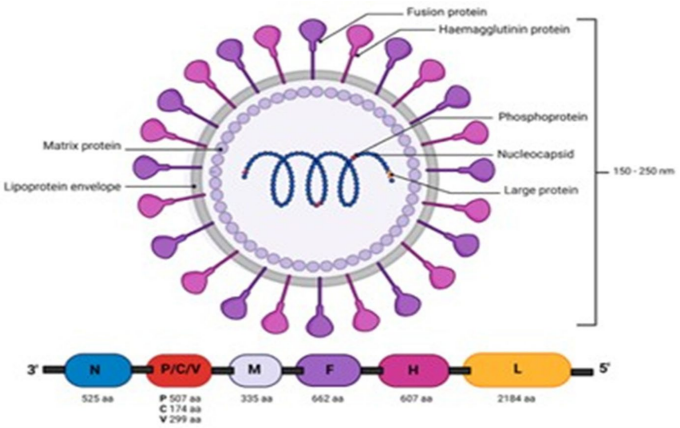

Figure 1. Morphology and genomic organization of CDV.

The CDV genome encodes six structural proteins, namely nucleocapsid (N), phosphoprotein (P), matrix (M), fusion (F), hemagglutinin (H), and polymerase (L), as well as two nonstructural proteins, V and C (Wilkes, 2022). The P gene produces proteins V and C through RNA editing, inserting non-templated G residues during mRNA synthesis and leaky scanning. The V protein regulates the innate immune response by suppressing the nuclear translocation of STAT1 and STAT2 and by blocking MDA5-mediated synthesis of interferon beta (Rendon-Marin *et al*., 2019). Protein C serves as a polymerase cofactor for RNA synthesis and prevents dsRNA formation to evade immunity, with its deficiency attenuating CDV virulence (Wilkes, 2022). Protein N encapsulates and protects the RNA genome, forming ribonucleoprotein (RNP) complexes with P and L as templates for transcription and replication. Protein L possesses polymerase activity, including RNA synthesis, capping, and methylation domains (Rendon-Marin *et al*., 2019).

Figure 2 presents the reverse genetics approach applied to generate a recombinant wild-type CDV, illustrating the key steps involved in the recovery of infectious virus from cloned cDNA.

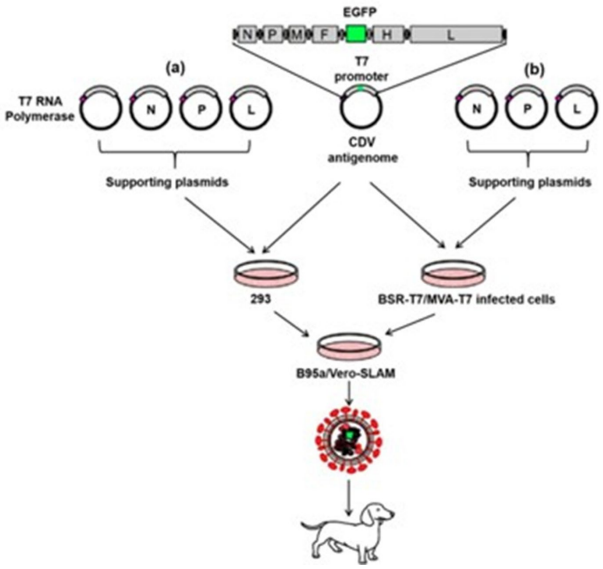

Figure 2. Reverse genetics approach for generating recombinant wild-type CDV.

This method utilizes five recombinant plasmids, including a T7 promoter driven full length cDNA plasmid that carries the enhanced green fluorescent protein (EGFP) gene inserted between the fusion (F) and hemagglutinin (H) genes, together with four cytomegalovirus (CMV) promoter regulated helper plasmids encoding the nucleocapsid (N), phosphoprotein (P), and large (L) proteins, along with the T7 polymerase plasmid. The T7 polymerase plasmid can alternatively be substituted with baby hamster kidney cells that constitutively express T7 RNA polymerase (BSR T7) or with the modified vaccinia Ankara (MVA T7) virus. Recombinant CDV is obtained by cotransfecting all plasmids into 293 cells or into BSR T7 or MVA T7 infected cells, followed by detection of EGFP expression in infected foci and cocultivation with B95a or Vero SLAM cells (Vero cells expressing the signaling lymphocytic activation molecule receptor) for subsequent viral propagation (Zhao *et al*., 2020).

The envelope glycoproteins H and F play essential roles in CDV pathogenesis. The H protein mediates viral attachment to host receptors, including SLAM on lymphoid cells and nectin 4 on epithelial cells. It lacks neuraminidase activity and represents the most variable CDV protein, exhibiting up to 11 percent nucleotide divergence, which supports phylogenetic analyses and contributes to the virus's wide host range. Protein F mediates membrane fusion, allowing RNP entry into the cytoplasm. Protein M bridges the RNP and envelope proteins, essential for assembly and budding, interacting with N, H, and F proteins. CDV budding occurs independently of the ESCRT machinery, mediated by M protein, and the virus depends on envelope cholesterol for infectivity, with depletion reducing syncytium formation; it is labile to detergents, surviving briefly at room temperature but longer in cold conditions. Morphologically, particles feature a helical nucleocapsid of N protein around the RNA, enveloped by H and F spikes, with M protein bridging the structure; the spike complex includes H tetramers and F trimers, and envelope proteins partition into detergent-resistant membranes to aid assembly (Rendon-Marin *et al*., 2019). The glycosylation sites of the H protein differ between vaccine and wild type strains, affecting the antigenic properties of the virus (Ke *et al*., 2015).

Figure 3 illustrates the mechanism of CDV entry into host cells, its intracellular replication cycle, and the subsequent release of newly formed virions in infected dogs.

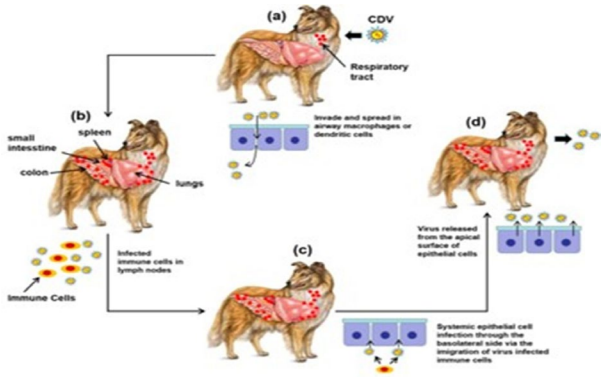

Figure 3. Mechanism of entry, replication, and release of CDV in infected dogs.

Initially, the virus attaches to the signaling lymphocytic activation molecule (SLAM) receptor on macrophages or dendritic cells within the respiratory tract (a). After infecting these immune cells, CDV travels to the lymph nodes, replicates, and subsequently disseminates to secondary lymphoid organs such as the spleen and thymus (b). It then targets epithelial tissues by binding to the nectin 4 receptor located on the basolateral surface of epithelial cells (c). Finally, the virus exits through the apical surface of these cells, allowing viral shedding and transmission to new hosts (d) (Zhao *et al*., 2020).

Transmission mainly occurs through direct contact with infected animals during activities such as mating, fighting, grooming, or predation, as well as through respiratory droplets, aerosolized secretions, and occasionally contaminated objects (Wilkes, 2022). Transplacental transmission has also been reported (Saaed and Al-Obaidi, 2021). Taxonomically, CDV is classified within the order *Mononegavirales*, family *Paramyxoviridae*, and genus *Morbillivirus*, under the species *Morbillivirus canis*. It is closely related to other members of this genus, including *Measles morbillivirus*, *Small ruminant Morbillivirus*, *Phocine Morbillivirus*, *Cetacean Morbillivirus*, and the now extinct *Rinderpest Morbillivirus* (Wilkes, 2022). CDV shares genetic links with human and animal *Morbillivirus*es, featuring conserved amino acids, nucleotides, and epitopes, with phylogenetic analysis suggesting a common ancestor with morbilli-related viruses (Rivera-Martínez *et al*., 2024). Its evolutionary rate ranges from 4.433×10^{-4} to 9.10×10^{-4} substitutions per site per year based on H gene data, with nucleotide and amino acid similarities of 87.2-100% and 82.5-100%, respectively (Wang *et al*., 2023). CDV genotypes are defined by less than 5 percent nucleotide divergence and more than 95 percent similarity in the H protein, forming approximately 17 to 22 geographically clustered lineages. These include America 1 (comprising most commercial vaccine strains), America 2 to America 5, Arctic, Rockborn like, Asia 1 to Asia 6, Africa 1 and Africa 2, European Wildlife, Europe or South America 1, South America 2 and 3, Canada 1, Caspian, North America 1 and 2, and Australia (Rendon-Marin *et al*., 2019).

CDV causes a multisystemic infection that affects a wide range of mammals, including domestic dogs, foxes, wolves, ferrets, raccoons, felids, and some primate species. The virus invades the gastrointestinal and respiratory tracts as well as the central nervous system, producing clinical signs such as fever, conjunctivitis, ocular and nasal discharge, coughing, vomiting, diarrhea, and neurological disorders including blindness, paralysis, convulsions, and fatal demyelination (Kocatürk *et al*., 2025). Commonly referred to as Hardpad Disease, CDV is a major viral infection that affects the digestive, respiratory, and central nervous systems of domestic dogs, wild carnivores such as foxes and ferrets, and marine mammals. The virus belongs to the genus *Morbillivirus* within the family *Paramyxoviridae* and the order *Mononegavirales* (Dik *et al*., 2023). As the causative agent of a widespread viral disease in domestic and wild carnivores, CDV is a negative sense RNA virus classified within the family *Paramyxoviridae* and the genus *Morbillivirus*, carrying important epidemiological significance for both human and animal health (Echeverry-Bonilla *et al*., 2022). CDV is a single stranded RNA virus belonging to the genus *Morbillivirus* within the family *Paramyxoviridae*. It is closely related to other *Morbillivirus*es, including *Measles morbillivirus*, *Cetacean Morbillivirus*, *Feline morbillivirus*, *Small ruminant Morbillivirus*, *Phocine Morbillivirus*, and *Rinderpest Morbillivirus* (Kim *et al*., 2021).

History and epidemiology

CDV is a highly contagious RNA virus belonging to the genus *Morbillivirus* within the family *Paramyxoviridae*, first discovered in 1905 by Henri Carré in France (Naveenkumar *et al*., 2025). It is an enveloped virus with a single-stranded, negative-sense RNA genome of approximately 15 kb, encoding eight proteins, including the nucleocapsid (N), phosphoprotein (P), matrix (M), fusion (F), hemagglutinin (H), and polymerase (L) proteins, with additional V and C proteins produced through RNA editing (Franzo *et al*., 2024). The most recent common ancestor of CDV dates back to 1868 in the USA, with subsequent spread to continental Europe in 1948 and rapid dissemination to other continents, identifying the Canidae family as the original host and source of spread (Wang *et al*., 2023). CDV has become an endemic disease in canine populations worldwide, posing significant threats due to its high morbidity, mortality, and neurological sequelae in domestic dogs (Franzo *et al*., 2024; Freire *et al*., 2025).

Epidemiologically, CDV exhibits remarkable host flexibility, primarily affecting species in the order Carnivora, including families such as Canidae (dogs, foxes, wolves), Mustelidae (ferrets, badgers), Felidae (lions, tigers), and others, with spillover to non-carnivore taxa like Primates and Rodentia (Franzo *et al*., 2024). Of 217 scientific articles on CDV in non-dog hosts, only 51.8% report clinical signs, varying from subclinical infection to nearly 100% mortality, as seen in domestic cats and ferrets (Weckworth *et al*., 2020). The virus is transmitted through aerosolized particles from infected secretions, leading to immunosuppression and secondary infections, with clinical manifestations including catarrhal symptoms (pyrexia, conjunctivitis, cough, gastrointestinal signs) and neurological forms (myoclonus, seizures, ataxia). Despite vaccination, CDV persists in vaccinated animals, with incomplete protection and variable coverage influenced by socio-economic factors, particularly in low-income areas where free-ranging dogs interact with wildlife (Franzo *et al*., 2024).

Geographical clustering reveals 18 lineages, with strong regional patterns; for instance, in Italy, lineages include Europe/South America-1, Europe Wildlife, and Arctic-like, the latter first reported in dogs in the early 21st century and linked to epidemics affecting foxes, badgers, and martens (Alfano *et al*., 2025). In India, outbreaks have impacted domestic dogs and endangered species like Asiatic lions and leopards, emphasizing conservation needs (Naveenkumar *et al*., 2025). In Vietnam, limited studies exist, with genotypes such as America-1, Asia-1, and novel clades identified, but no prior reports on partial F gene sequences from the Mekong Delta (Van *et al*., 2025). Globally, 11 lineages co-circulate, with effective population size showing exponential growth phases between 2000–2005 and 2010–2012 (Wang *et al*., 2023). Risk factors include unvaccinated or incompletely vaccinated status, young age (under four months), high-contact environments like kennels, and exposure to infected wildlife, though studies lack control groups for statistical confirmation; no clear gender or breed preferences emerge, but dolichocephalic breeds may be more susceptible to encephalitis (Freire *et al*., 2025).

Spillover events highlight CDV's threat to wildlife, such as the 1994 outbreak in Serengeti's African lions, causing over 30% population decline, seeded by domestic dogs with prolonged exposure (Weckworth *et al*., 2020). In Namibia, CDV impacts domestic and wild carnivores, but updated data are scarce (Franzo *et al*., 2024). Mutation and recombination in the H gene facilitate adaptation to novel hosts, driving outbreaks in diverse taxa, including 22 families across five orders, with varying suscep-

tibility (Weckworth *et al*., 2020). Understanding transmission dynamics in domestic dogs is crucial for wildlife protection, as vaccination reduces spillover but remains incomplete (Franzo *et al*., 2024; Naveenkumar *et al*., 2025). Molecular epidemiological studies using the H gene reveal strain relationships and dispersal, aiding disease management (Franzo *et al*., 2024; Wang *et al*., 2023).

Transmission and risk factors

CDV is highly contagious and primarily transmitted through close contact among susceptible hosts, including direct interactions such as mating, fighting, grooming, or predation, as well as exposure to respiratory droplets or aerosolized infected bodily fluids, with less common transmission via fomites (Wilkes, 2022).

Figure 4 presents the infection and transmission cycle of CDV, highlighting the primary routes of viral dissemination within and between species. It also demonstrates similarities in transmission patterns among related *Morbillivirus*es, including rinderpest virus and human measles virus, underscoring the cross-species transmission potential of CDV.

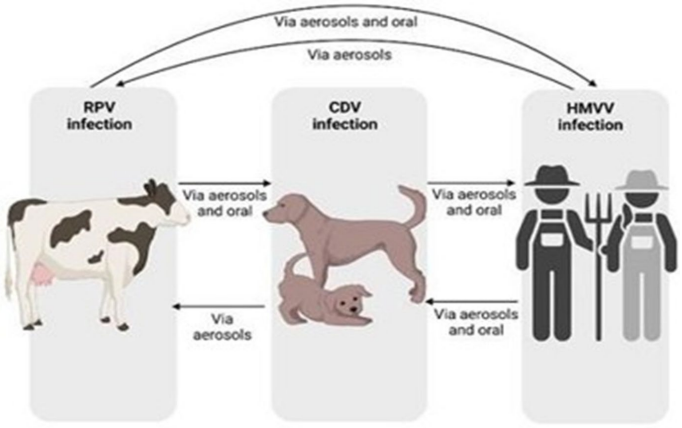

Figure 4. Infection and transmission cycle of CDV.

Virions are transmitted through aerosolized nasal, oral, and ocular fluids, entering primarily via the respiratory system, and are unstable in the environment, necessitating continual infection among susceptible hosts for dispersion (Candela *et al*., 2025). Transmission occurs via direct contact or exposure to aerosolized, oral, respiratory, and ocular secretions, with viral shedding lasting up to 90 days in subclinically infected animals. In dogs, transmission can also occur transplacentally (Sheikh *et al*., 2021). CDV is mainly transmitted via inhalation of infectious aerosols from recently infected animals, whether subclinical or clinically ill, or through contact with contaminated objects such as food and water bowls, clothing, and grooming tools. All dog breeds and ages are susceptible, with unvaccinated animals being particularly at risk (Mohammad *et al*., 2022). Transmission occurs through close contact between susceptible hosts, with infected domestic dogs acting as the primary source of infection and facilitating spillover into wild carnivore populations (Dorji *et al*., 2020). CDV is mainly transmitted via aerosol droplets, with domestic dogs and wild canids being especially susceptible due to their social behavior and reliance on scent communication (Kimpston *et al*., 2022).

Domestic dogs have long been recognized as the primary reservoir for CDV, with no recognized carrier state, and the agent persists through transmission to non-immune offspring or susceptible adults, while infected wildlife species can serve as a source of CDV for domestic dogs, and introduction of novel viruses in improperly vaccinated populations can cause outbreaks, with increased incidence in recent decades, including in vaccinated animals (Wilkes, 2022). Domestic dogs continue to serve as the primary reservoir host, although various wild carnivores can also maintain the virus. Dogs play a crucial epidemiological role because of their susceptibility, generalist ecological habits, and capacity to transmit CDV to carnivores globally (Candela *et al*., 2025). Sources of CDV infection include stray dogs, which constitute a significant free-roaming population capable of transmitting the virus to other animals, as well as wild carnivores from families such as Canidae, Mustelidae, Procyonidae, Ursidae, and Viverridae, emphasizing the potential for interspecies transmission (Mohammad *et al*., 2022). Infected domestic dogs serve as primary sources of infection leading to spillover into wild carnivores, posing risks to endangered species in protected areas (Dorji *et al*., 2020). The appearance of novel CDV lineages, along with incomplete vaccine coverage, has led to outbreaks and spillover events between domestic dogs and wildlife, with interspecies transmission posing a risk across all levels of human settlement (Kimpston *et al*., 2022).

Predisposing factors for CDV include the viral envelope's lability, reducing environmental persistence and influencing spread, alongside a "boom and bust" infection cycle where new variants cause high morbidity in naive populations, followed by fade-outs in small populations lacking susceptible animals (Wilkes, 2022). Host ecology and behavior, including generalist traits, sociality, and frequent use of domestic-wildlife interface areas, elevate the likelihood of transmission, while human-driven factors such as urbanization further increase contact rates in peri-urban regions (Candela *et al*., 2025). In the acute phase, viral shedding occurs through excretions and secretions, resulting in clinical signs such as fever, serous nasal discharge, coughing, respiratory and gastrointestinal symptoms, often complicated by secondary bacterial infections, and pronounced transient immunosuppression (Sheikh *et al*., 2021). Age serves as a significant predisposing factor, with puppies under one year exhibiting higher prevalence due to reduced maternal immunity, although gender does not influence susceptibility, as both sexes are equally at risk, and crowded housing conditions in animal shelters predispose dogs to infection by promoting close contact and viral transmission, with clinical signs such as cough and ocular discharge statistically associated with CDV positivity, while partial immunity can lead to milder or asymptomatic disease, and secondary infections with other viruses and bacteria influence clinical manifestations and severity, particularly in puppies without full immunity (Ulaş *et al*., 2025). Several elements contribute to the risk of infection, starting with geographic location, where urban outskirts displayed notably elevated rates of positive results in contrast to countryside regions—for instance, IgM ELISA tests showed 26.92% versus 3.03%, IgG ELISA indicated 64.15% compared to 14.39%, and RT-PCR revealed 34.62% against 3.79%. Regarding age categories, there were no notable variations across groups such as those under 8 months, between 1 and 3 years, and over 3 years for both IgM ELISA and RT-PCR assays, although IgG ELISA detected a markedly higher rate in the over-3-years bracket at 22.73%. As for gender, results showed no substantial disparities in IgM ELISA and RT-PCR, yet IgG ELISA pointed to considerably greater positivity among females at 25.23% relative to males at 7.84%. Moreover, the absence of vaccination plays a crucial role in amplifying infection vulnerability, given that every stray dog in this investigation remained unvaccinated (Mohammad *et al*., 2022). Predisposing factors include seasonal variation, as dogs sampled in winter are less likely to test seropositive compared to those sampled in summer, and body condition, with healthier dogs exhibiting higher seropositivity. No significant differences were observed regarding sex, breed, age, ownership status, or study location (Dorji *et al*., 2020). Factors such as age and vaccination status influence CDV positivity, with young adult and unvaccinated dogs exhibiting a higher risk of infection (Ariyama *et al*., 2024).

Because CDV is primarily transmitted through direct contact between animals, the relationship between exposure rates and land cover types remains difficult to determine. Most studies focus on individual factors such as age, sex, and vaccination status, while environmental influences are poorly understood. Pasture areas likely facilitate visual contact and interactions among animals, increasing CDV transmission, whereas water bodies are less conducive to such contacts (Fornazari *et al*., 2023). Chilean CDV strains exhibited genetic diversity, clustering into the Europe/South

America 1 and North/South America 4 lineages, with the latter emerging in Chile and potentially carrying antigenic implications (Ariyama *et al*., 2024). Interspecies transmission poses a risk across all levels of human habitation, as wild canids frequently utilize these environments (Kimpston *et al*., 2022).

Pathogenesis

The pathogenesis of CDV begins with infection of dendritic cells or macrophages via the SLAM receptor, leading to viremia and lymphocytic apoptosis that cause immunosuppression. A secondary viremia enables epithelial infection through nectin-4, resulting in systemic shedding and possible invasion of the central nervous system (CNS), where lesions such as demyelination, neuronal necrosis, and nonsuppurative meningoencephalomyelitis may develop, with severity depending on host immunity and viral virulence (Wilkes, 2022). CDV exhibits pantropism by infecting epithelial, lymphoid, and neural cells, with the hemagglutinin (H) protein mediating attachment to SLAM and nectin-4, facilitating hematogenous dissemination, leukopenia, and secondary bacterial infections. Neurological disease such as demyelinating leukoencephalitis arises from CNS spread via infected leukocytes or olfactory pathways, with viral persistence in astrocytes supported by alternative receptors, while V and C proteins suppress interferon responses (Rivera-Martínez *et al*., 2024).

CDV induces severe multisystemic infection—more virulent than measles—through SLAM-mediated lymphoid tropism that causes immunosuppression and systemic involvement of respiratory, gastrointestinal, and nervous systems, producing fever, rash, diarrhea, nasal discharge, conjunctivitis, and high mortality (50–90%) depending on strain. Mutations in the H protein enhance host range, virulence, and immune evasion (Rivera-Martínez *et al*., 2024).

After replication in lymphoid tissues, systemic viremia leads to bone marrow suppression and secondary infections, with clinical signs such as pyrexia, mucopurulent conjunctivitis, cough, anorexia, vomiting, diarrhea, and enamel hypoplasia, progressing to neurological symptoms like myoclonus, seizures, ataxia, paresis, and hyperkeratosis, with variable outcomes from subclinical to fatal (Franzo *et al*., 2024). Infection starts via respiratory inhalation and replication in SLAM-positive immune cells of the upper airways, spreading systemically to nectin-4-expressing epithelial cells in multiple organs, causing pneumonia, diarrhea, and neurologic deficits. The virus spreads through syncytia formation to evade immunity, with disease severity influenced by host age, immunity, and viral strain (Giummole, 2024).

CDV's immunotropic and epitheliotropic nature targets SLAM-expressing lymphocytes, macrophages, and dendritic cells, and nectin-4-positive epithelial cells, resulting in fever, respiratory distress, diarrhea, and neurologic signs (Guimera, 2023). The virus infects respiratory immune cells, causing systemic dissemination, leukopenia, and lymphocyte inhibition, followed by nectin-4-mediated spread to epithelial tissues, producing pneumonia, conjunctivitis, and neurovirulence. CNS invasion occurs hematogenously or via olfactory nerves, leading to demyelinating leukoencephalitis and neurologic disorders such as myoclonus and ataxia, with persistence in astrocytes enabling noncytolytic transmission (Zhao and Ren, 2022).

Overall, CDV spreads from respiratory infection to systemic viremia, causing immunosuppression, multiorgan disease, and high mortality, while vaccination effectively reduces incidence (Bergmann *et al*., 2021). Viral replication in respiratory and lymphoid tissues induces lymphopenia and fever within 3–6 days post-infection, with structural proteins mediating multisystemic effects on the respiratory, gastrointestinal, integumentary, and CNS systems, producing seizures and ataxia in unvaccinated puppies (Mansour and Hasso, 2021). As a highly contagious *Morbillivirus*, CDV affects carnivores—especially unvaccinated dogs—causing up to 50% mortality, with signs including conjunctivitis, nasal and ocular discharge, anorexia, hyperkeratosis, respiratory inflammation, and skin pustules (Joshi *et al*., 2022). Using SLAM and nectin-4 for entry, CDV exhibits lymphoid and epithelial tropism, with H protein features aiding entry and immune evasion (Fukuhara *et al*., 2024).

Pathogenesis begins with H-mediated attachment, replication in lymphoid tissues, and systemic spread to multiple organs, producing respiratory, gastrointestinal, and neurological signs that may progress to fatal multisystemic disease in young or immunocompromised animals. Immunosuppression via lymphopenia impairs immune response, though survivors develop neutralizing antibodies (Di Francesco *et al*., 2022). In domestic dogs, infection mirrors that in wild carnivores; the virus is cleared from most tissues within three weeks except in CNS, lungs, and skin, where persistence and shedding may continue for months (Pranitha *et al*., 2022). The virus's broad host range and variable pathogenicity reflect its adaptability, influenced by age, immunity, and viral lineage (Di Francesco *et al*., 2022).

Clinical manifestasions and pathological features

CDV infection in domestic dogs causes a wide range of clinical signs including fever, lethargy, inappetence, vomiting, diarrhea, respiratory abnormalities, conjunctivitis, neurologic involvement, and hyperkeratosis of the footpads and nasal planum (Johnson *et al*., 2022). The disease occurs in non-neurologic and neurologic forms. Non-neurologic infection is associated with systemic manifestations such as fever, mucopurulent oculo-nasal discharge, cough, dyspnea, depression, anorexia, vomiting, and diarrhea without neurological signs. Neurologic CDV infection presents with behavioral abnormalities, seizures, blindness, paresis or paralysis, imbalance, and head rotation (Mojtahedzadeh *et al*., 2024). Acute disease commonly affects the respiratory, gastrointestinal, and central nervous systems, with signs such as cutaneous rash, secondary bacterial infections, and neurological deficits (Aldujaily *et al*., 2025). Naturally infected dogs may show additional abnormalities including prostration, corneal opacity, tooth enamel hypoplasia, and neurological signs such as paddling and muscle tremors (Aldujaily *et al*., 2025). Dogs with neurologic complications frequently display non-ambulatory tetraparesis, altered mental status, seizures, and extra-neural signs such as dehydration, diarrhea, vomiting, hyperthermia, respiratory issues, and enamel hypoplasia (Freire *et al*., 2025). CD typically features diphasic fever, respiratory discharge, pneumonia, diarrhea, and myoclonus, with seizures characterized by chewing-gum fits, circling, head tilt, nystagmus, and paresis to paralysis (Creevy and Evans, 2025). Post-vaccinal CDV cases may also show predominantly neurological signs including seizures, circling, tremors, hypersalivation, fever, and respiratory and gastrointestinal involvement (Gulliver *et al*., 2025). CDV can present with gastrointestinal disorders such as bloody diarrhea, constipation, and appetite loss, alongside respiratory signs including sneezing and shortness of breath, together with eye inflammation and depression (Shi *et al*., 2024). Clinical outcomes vary widely, from sub-clinical to fatal, involving systemic dissemination and signs such as respiratory distress, anxiety, conjunctivitis, lymphopaenia, encephalitis, rhinorrhoea, and fever (Alfano *et al*., 2025).

CDV infection causes severe tissue damage in lymphoid organs, epithelial cells of the respiratory and gastrointestinal tracts, and the central nervous system, often producing immunosuppression and secondary infections (Shi *et al*., 2024). The virus is a single-stranded RNA *Morbillivirus* with tropism for respiratory and neural tissues, leading to inflammation and demyelination (Mojtahedzadeh *et al*., 2024). Pantropic infection targets mononuclear phagocytes and lymphocytes, transporting the virus to epithelial tissues of multiple organ systems (Aldujaily *et al*., 2025). Neurological disease frequently shows multifocal CNS involvement, particularly in the forebrain and brainstem, with an average interval of 60 days between systemic and neurologic onset (Freire *et al*., 2025). Brain lesions include neuronal degeneration, gliosis, noninflammatory demyelination, perivascular cuffing, nonsuppurative leptomeningitis, and intranuclear

inclusions in glial cells (Creevy and Evans, 2025). Additional findings include thymic atrophy in young puppies, hyperkeratosis of the nose and pads in neurologic cases, bronchopneumonia, enteritis, and skin pustules depending on secondary infections (Creevy and Evans, 2025). Post-vaccinal cases show mononuclear or lymphohistiocytic polioencephalitis, neuronal degeneration, and bronchopneumonia, with necrotizing enteritis or myocarditis in some puppies (Gulliver *et al*., 2025). In wildlife hosts, pathological abnormalities include congested lungs and enteritis, although confirmatory testing remains essential due to overlapping clinical signs with other pathogens (Alfano *et al*., 2025).

Diagnosis of CDV relies on clinical, physical, and neurologic examination findings supported by laboratory testing. RT-PCR is the most common diagnostic tool due to its high sensitivity and compatibility with multiple sample types including blood, urine, respiratory secretions, conjunctival swabs, and tissues (Johnson *et al*., 2022). Histopathology can detect characteristic intracytoplasmic or intranuclear inclusions in affected tissues such as lungs, bladder, lymph nodes, or keratinized footpads and nasal planum. Immunofluorescence may assist early infection detection but is limited to approximately the first three weeks post-infection (Johnson *et al*., 2022). Confirmatory diagnosis is often achieved through immunohistochemistry and necropsy evaluation of neurological and systemic lesions (Aldujaily *et al*., 2025). Due to its wide spectrum of signs resembling other diseases, laboratory confirmation is essential to prevent diagnostic errors in both domestic and wild carnivores (Alfano *et al*., 2025).

Diagnosis

Diagnosis of CD in domestic dogs cannot be based solely on clinical signs and hematological results, requiring supplementary serological and molecular techniques for definitive confirmation. Laboratory evaluations, including complete blood counts, often show neutrophilic leukocytosis, regenerative anemia, and lymphopenia; however, these findings are non-specific and must be distinguished from conditions such as canine parvovirus, canine adenovirus, lead toxicity, Bordetella bronchiseptica infection, and salmonellosis through thorough history, clinical assessment, and additional diagnostic tests. Serological tests, including neutralization antibody assays, are valuable for evaluating immunity but are unreliable for definitive diagnosis due to potential false positives from prior vaccination or exposure. Consequently, antigen- or nucleic acid-based methods are preferred. Reverse transcriptase PCR (RT-PCR) targeting the nucleoprotein (NP) gene, using primers such as PP-I, PP-II, and PP-III, provides high sensitivity and specificity for detecting CDV RNA in cerebrospinal fluid (CSF), whole blood, and mucosal samples, with CSF outperforming blood in neurological cases, yielding 80% positivity versus 55% in whole blood. Rapid immunochromatographic (IC) antigen test kits provide a fast, economical alternative with 93.8% sensitivity and 50% specificity relative to RT-PCR for CSF samples, though less effective in chronic or low-viral-load scenarios. Differential diagnosis involves ruling out analogous neurological disorders, while sequencing of PCR products confirms viral strains, such as those similar to CDV strain HL N, enhancing epidemiological insights. Overall, combining RT-PCR and IC assays on appropriate samples like CSF ensures timely diagnosis, particularly in vaccinated or neurologically symptomatic dogs, facilitating effective management and prevention strategies (Sarchahi *et al*., 2025).

Table 1 summarizes the commonly used diagnostic techniques for detecting CDV in domestic dogs, including their principles, targets, and relative diagnostic performance.

In the diagnosis of CD, laboratory methods are essential, with poly-

Table 1. Commonly used diagnostic techniques for detecting CDV in domestic dogs

Diagnostic method	Detection method	Type of diagnostic method	Target	Notes	Reference
MDCK cells	Virus isolation	Cell culture	Virus	Cytopathic effects observed within 24–72 h	(Desai *et al*., 2021)
MDCK cells + FAT confirmation	Virus isolation	Cell culture + immunofluorescence	Virus antigen	FAT showed apple-green fluorescence	(Saltık and Kale, 2023)
Lateral Flow Assay (LFA)	Antigen detection	Serological	CDV antigen	Rapid point-of-care test; may produce false negatives	Desai *et al*., 2021
Rapid immunochromatographic (IC) test	Antigen detection	Serological	CDV antigen	93.8% sensitivity and 50% specificity relative to RT-PCR	(Sarchahi *et al*., 2025)
Immunofluorescence / FAT	Detection of fluorescently labeled antibodies	Immunofluorescence	Viral antigen	Rapid and accurate antigen detection	(Saltık and Kale, 2023)
RT-PCR	RNA detection	Genomic	Nucleoprotein (NP/N) gene	High sensitivity and specificity; widely used	(Sarchahi *et al*., 2025)
RT-PCR	RNA detection	Genomic	Viral RNA in nasal and conjunctival samples	Reliable early detection	(Baikadamova *et al*., 2022)
One-step RT-PCR	RNA detection	Genomic	Nucleocapsid (N) gene	Molecular confirmation of CDV infection	(Desai *et al*., 2021)
Nested one-step RT-PCR	RNA detection	Genomic	N gene	Amplifies 549 bp and 419 bp fragments	(Desai *et al*., 2021)
One-step real-time RT-PCR	RNA detection	Genomic	N gene	High sensitivity and specificity using TaqMan probes	(Saltık and Kale, 2023)
RT-qPCR (double-check strategy)	RNA detection	Genomic	P gene	Diagnostic sensitivity 98.9% and specifically 100%	(Halecker *et al*., 2021)
Hemagglutinin gene sequencing	Molecular characterization	Genomic	H gene	Used for epidemiological lineage analysis	(Giacinti *et al*., 2022)
Indirect ELISA (i-ELISA)	Detection of specific antibodies	Serological	IgG antibodies	Cost-effective alternative to neutralization tests	(Desai *et al*., 2021)
ELISA	Detection of specific antibodies	Serological	IgM and IgG against N protein	Differentiates infection phases	(Saltık and Kale, 2020)
Virus neutralization (VN) test	Detection of neutralizing antibodies	Serological	Protective antibodies	Reference standard for immunity assessment	(Bergmann *et al*., 2020)
Point-of-care ELISA / lateral flow immunoassays	Detection of antibodies	Serological	Anti-CDV antibodies	Variable sensitivity and specificity	(Bergmann *et al*., 2020)

merase chain reaction (PCR) serving as a highly reliable technique for detecting viral RNA in nasal swabs and conjunctival smears, allowing early identification of the disease at initial clinical signs, as evidenced by amplification cycles confirming positive results in affected animals. Comparative analysis with immunochromatographic assays, such as the Vet-Expert rapid test, demonstrates PCR's superior accuracy at 100% reliability versus 98.3% for the assay, aiding differential diagnosis from similar viral infections like parainfluenza and parvoviral enteritis through antigen detection and antibody titers above pathogenetic thresholds. Clinical observations of symptoms, including fever, lethargy, and neurological signs, further support ruling out other conditions, enabling timely therapeutic interventions in veterinary clinics (Baikadamova *et al*., 2022).

Diagnosis of CDV in domestic dogs relies on a combination of laboratory tests, serological assays, and molecular techniques to ensure accurate identification and differentiation from other canine diseases. Rapid immunochromatography-based lateral flow assays (LFA) provide point-of-care antigen detection, though they may yield false negatives due to low sensitivity, as evidenced by only 4 out of 40 samples testing positive in nasal and ocular swabs from 2 dogs. Serological detection via indirect enzyme-linked immunosorbent assay (i-ELISA) targeting IgG antibodies confirmed CDV infection in 14 out of 17 serum samples from 18 unvaccinated dogs, offering a cost-effective alternative to serum neutralization tests for established infections. Molecular confirmation is performed using one-step reverse transcription PCR (RT-PCR) targeting the nucleocapsid (N) gene, detecting 13 positive samples from 10 dogs. This is followed by nested one-step RT-PCR amplifying 549 bp and 419 bp fragments, and restriction endonuclease analysis with AvaI, yielding characteristic 389 bp and 160 bp bands. Virus isolation in Madin-Darby canine kidney (MDCK) cells produces cytopathic effects, including syncytia and giant cell formation within 24–72 hours, with infection confirmed by RT-PCR of culture supernatants. Differential diagnosis is crucial to distinguish CDV from other diseases with overlapping clinical signs, emphasizing the need for sensitive molecular methods over rapid tests alone, as CDV affects multiple organ systems and is highly immunosuppressive. Overall, these integrated approaches facilitate early detection and characterization of CDV in suspected cases (Desai *et al*., 2021).

Diagnosis of CDV in domestic dogs primarily depends on laboratory confirmation via reverse transcription PCR (RT-PCR) performed on samples such as lung tissue, lymph nodes, or conjunctival swabs, as reported in submissions to Canadian diagnostic laboratories. Nucleic acid extraction and RT-PCR are conducted following standardized protocols at the University of Guelph Animal Health Laboratory. Further molecular analyses, including hemagglutinin gene sequencing, provide epidemiological insights by identifying viral lineages and potential cross-species transmission events (Giacinti *et al*., 2022).

Diagnosis of CDV in domestic dogs involves a combination of laboratory methods, including molecular techniques such as one-step real-time RT-PCR targeting the nucleocapsid (N) gene with TaqMan probes. This approach provides high sensitivity and specificity for detecting viral genomes in clinical specimens, including rectal, nasal, and ocular swabs, urine, and blood, with rectal swabs achieving positivity rates of up to 54%. Serological methods, while useful when combined with clinical symptoms, are less reliable for definitive diagnosis in stray or subclinical cases due to high seroprevalence. CDV can be successfully isolated from naturally infected dogs using unmodified Madin-Darby canine kidney (MDCK) cells, with confirmation through cytopathic effects (CPE) and the fluorescent antibody technique (FAT). Rectal swabs and urine samples exhibited the highest CPE levels (31.62% high, 22.23% medium, 46.15% low), while FAT enabled rapid and accurate detection of viral antigens, indicated by apple-green fluorescence. Differential diagnosis is difficult due to the wide range of non-specific clinical signs, including fever, cough, ocular-nasal discharge, diarrhea, and neurological abnormalities, further complicated by high seroprevalence in subclinical infections. Additional diagnostic approaches include immunohistochemistry for tissue samples and blind passages in cell cultures to enhance isolation efficiency, emphasizing the need for rapid, sensitive methods to facilitate quarantine and treatment in high-risk populations like unvaccinated puppies under 6 months (Saltık and Kale, 2023).

Diagnosis of CDV faces challenges due to global increases in cases, genetic diversity across lineages, and limitations in existing RT-qPCR assays, such as those targeting the nucleocapsid (N) gene by Rivera-Martínez *et al*. (2024) and the phosphoprotein (P) gene by Scagliarini *et al*. (2007) as revealed by an inter-laboratory proficiency test in Germany. To address this, Halecker *et al*. (2021) developed a double-check strategy involving two independent RT-qPCR assays (CDV-Mix 3, an adaptation of the Scagliarini assay, and CDV-Mix 7, a novel system, both on the P gene) equipped with internal controls (heterologous EGFP and endogenous β-Actin), achieving high analytical sensitivity (<10 genome equivalents/μL), diagnostic sensitivity (98.9%), and specificity (100%) through validation on 378 samples from diverse hosts (e.g., foxes, raccoons, dogs) and regions (primarily Germany, with European and African origins). The assays exhibited no cross-reactivity with related *Morbillivirus*es, such as phocine distemper virus and peste des petits ruminants virus, or with paramyxoviruses, including Newcastle disease virus and Nipah virus, ensuring reliable detection across diverse CDV sequences. This molecular approach enhances surveillance in domestic and wildlife populations, mitigating risks from vaccine failures, emerging variants, and interspecies transmission (Halecker *et al*., 2021).

Diagnosis of CDV in domestic dogs relies on serological approaches, with indirect enzyme-linked immunosorbent assay (ELISA) playing a key role in detecting specific antibodies, particularly IgM and IgG against the viral nucleocapsid (N) protein. This enables differentiation of infection phases; acute (4%), early convalescent (54%), and late convalescent (40%) in unvaccinated dogs presenting respiratory, gastrointestinal, neurological, and cutaneous clinical signs. Serological methods, including ELISA, provide a rapid and cost-effective alternative to virus neutralization tests (VNT), which are more time-consuming and expensive, supporting pre-diagnosis when combined with clinical assessment and facilitating differentiation from other infections with similar symptoms. Furthermore, N protein-specific antibody detection is valuable for monitoring outbreak dynamics and evaluating the risk of severe disease in susceptible populations (Saltık and Kale, 2020).

Diagnosis of CDV in domestic dogs involves laboratory methods, including serological and point-of-care (POC) assays for antibody detection, with virus neutralization (VN) serving as the reference standard for assessing protective immunity, typically requiring titres ≥10 for positivity. Serological tests, such as ELISAs (e.g., ImmunoComb, VacciCheck) and lateral flow immunoassays (e.g., TiterCHEK CDV-CPV, FASTest CDV-CPV Ab, CanTi Check), enable rapid on-site evaluation of anti-CDV antibodies, showing variable sensitivity (45–98%) and specificity (8–100%) depending on the assay and dog health status. Specificity is high in pathogen-free dogs but lower in acutely or chronically ill animals, potentially resulting in false positives and warranting caution in clinical interpretation. Overall, POC tests provide convenient alternatives to VN for assessing vaccination status, but their diagnostic accuracy underscores the need for confirmatory testing in symptomatic or immunocompromised dogs to ensure accurate management of this highly contagious disease (Bergmann *et al*., 2020).

Hematology and clinicopathological findings

CDV infection in domestic dogs causes diverse hematological and clinicopathological disturbances that mirror its immunosuppressive impact and systemic spread. During the acute phase, affected animals may exhibit fever, characteristic dermatitis, diarrhea, nasal and ocular discharges, conjunctivitis, and marked immune suppression. The clinical severity ranges from mild to fatal depending on host immunity and viral virulence, yet accurate diagnosis is often hindered by symptom overlap

with other canine viral infections such as parvovirus and adenovirus (Rivera-Martínez *et al*., 2024). Systemic signs include respiratory difficulty, loss of appetite, encephalitis, rhinorrhea, coughing, and fever, accompanied by lymphopenia and other blood irregularities that signal widespread organ involvement through hematogenous dissemination (Alfano *et al*., 2025). Histopathological alterations reveal demyelination of white matter and multifocal neuronal necrosis within the cerebral cortex and ependymal lining of the lateral ventricles, as well as mild interstitial pneumonia characterized by lymphocytic infiltration and macrophage aggregation in alveoli, with CDV antigen detected immunohistochemically in neurons and alveolar macrophages (Ricci *et al*., 2021).

Hematological evaluation of CDV-infected dogs demonstrates pronounced immunosuppression and bone marrow depression, marked by reduced WBC, lymphocytes, granulocytes, RBC, hematocrit, hemoglobin, and platelets, along with lymphopenia, granulocytopenia, and monocytopenia (Batı and Kırmızıgül, 2025). Distemper-positive dogs also exhibit decreased heart rate and hematocrit values, averaging 108.80±30.40 bpm and 31.00±7.40%, respectively. White blood cell counts typically fall within 2–4 days after symptom onset and later normalize, though this fluctuation is influenced by disease stage and age, limiting the diagnostic reliability of CBC findings (Mousafarkhani *et al*., 2023). In terminal cases, hematological data frequently reveal lymphopenia (76.9%), leukocytosis (46.2%), eosinophilia (46.2%), thrombocytopenia (38.5%), mild anemia (38.5%), and thrombocytosis (30.8%), indicating severe immune dysfunction (Silva *et al*., 2022).

Clinicopathological alterations extend to biochemical indices reflecting organ damage. Elevated concentrations of urea, ALP, amylase, and GGT, coupled with reduced glucose levels, suggest hepatic, pancreatic, and gastrointestinal impairment, while biomarkers such as neopterin and procalcitonin indicate inflammatory and immune activation (Batı and Kırmızıgül, 2025). In advanced disease, hypoalbuminemia (76.9%) and hyperproteinemia (23.1%) occur alongside increased globulin, α1-antitrypsin, haptoglobin, IgA, and heavy-chain IgG levels, and decreased creatinine, whereas urea remains unchanged. Proteinuria is common, with urinary protein/creatinine ratios of 0.98±0.93 versus 0.13±0.06 in controls, affecting 65% of dogs with ratios exceeding 0.5, confirming renal involvement (Silva *et al*., 2022). Collectively, these findings demonstrate CDV's progression from initial viremia and immunosuppression to secondary infections and neurologic complications, emphasizing the need for integrated diagnostic approaches in clinical management (Wilkes, 2022).

Treatment and vaccination

Current conventional treatment for CDV infection primarily involves supportive and palliative measures, as there is no specific curative therapy. These protocols include broad-spectrum antibiotics such as cephalosporins to prevent secondary infections, intravenous fluids like Ringer's lactate (RL), dextrose normal saline (DNS), colloids (hetastarch or tetrastarch), and amino acid/protein infusions to address electrolyte imbalances and dehydration from vomiting, diarrhea, and anorexia. Steroids like methylprednisolone or prednisolone are used to reduce brain edema and mitigate the cytopathic effects of cytokine storms. Additional supportive care encompasses antacids (e.g., ranitidine, pantoprazole, omeprazole), anti-emetics (e.g., ondansetron, metoclopramide, maropitant), muscle relaxants/sedatives (e.g., diazepam, midazolam, butorphanol), antiepileptics (e.g., levetiracetam, diazepam, phenobarbitone), pregabalin or gabapentin for neuropathic pain and anxiety, analgesics, nervine tonics (e.g., Vitamin B complex), antioxidants (e.g., Vitamins E and C), immune-modulatory syrups, hematinics, and syrups containing vitamins and minerals. Heterologous immunoglobulin suspensions may be administered at 0.4 ml/kg intravenously or subcutaneously daily for 5-7 days. Dogs with central nervous system (CNS) involvement may occasionally recover, but progression to recumbency often necessitates euthanasia. Conventional therapies alleviate symptoms but lack curative effects, with high mortality rates underscoring the need for novel protocols (Sudibmanna, 2022).

Given the limitations of conventional treatments, alternative approaches have been explored. Ribavirin (1-(β-D-ribofuranosyl)-1,2,4-triazole-3-carboxamide), a broad-spectrum antiviral, has been proposed for use in CDV-infected dogs. In one study, ribavirin was administered at doses of 30 mg/kg body weight (BW) once daily (sid) or 11 mg/kg BW sid, compared to ceftriaxone at 25 mg/kg BW sid, alongside supportive care including fluids, antacids, anti-emetics, sedatives, antiseizure medications, analgesics, nervine tonics, antioxidants, immune-modulatory syrups, and hematinics. However, treatment of neurological manifestations remains generally unrewarding, as it does not cure the disease (Sudibmanna, 2022). Acupuncture (AP), including electroacupuncture (EA), has been investigated for neurological sequelae in CDV-infected dogs, where conventional treatments fail to address chronic deficits. AP modifies sensory, motor, autonomic, visceral, hormonal, immune, and brain functions, promoting neuroplasticity and reducing inflammation via activation of brain areas observed in computed tomography (CT) and functional magnetic resonance imaging (fMRI). Although primarily studied in conditions like intervertebral disk disease (IVDD), preliminary evidence suggests AP combined with EA may offer qualitative and quantitative improvements in CDV-induced neurological deficits, though no specific studies confirm its efficacy in CDV (Santos *et al*., 2022). Anti-Newcastle disease vaccine (NDV) serum has been empirically used to treat distemper, potentially increasing recovery rates even in dogs with neurological signs. The mechanism is unclear but may involve cytokine stimulation triggering rapid immune responses against CDV, rather than antibody production, as antibodies appear only after 10-12 hours post-vaccination. NDV vaccines have also been used to express protective antigens against CDV and modulate cytokine patterns (Arbabi *et al*., 2022). Human measles vaccine has been considered for vaccinating puppies against CDV when maternal-derived antibodies (MDAs) block standard vaccines, though neither measles nor NDV vaccines are used therapeutically for active distemper (Sarchahi *et al*., 2025).

Vaccination is the cornerstone of CDV prevention, as the disease is often lethal without cure. Commercially available modified live vaccines provide long-term immunity and are typically combined with vaccines against canine infectious hepatitis virus, leptospiral organisms, canine parvovirus, canine parainfluenza virus, and occasionally canine coronavirus (e.g., 5-in-1, 7-in-1, 9-in-1, or 11-in-1). The first immunization is given at 45 days or 6 weeks of age, followed by a booster 3 weeks later and annual revaccinations thereafter. Immunity from modified live vaccines persists for about 3 years. In shelters, vaccination at intake is crucial for herd immunity to prevent outbreaks, contrasting with private veterinary practices focused on individuals (Andrukonis *et al*., 2021). Modified live CDV vaccines are safe and effective, though rare cases of suspected vaccine-induced disease have been reported, including fever, anorexia, vomiting, diarrhea, and neurological signs post-vaccination, with vaccine strains confirmed in affected tissues via immunohistochemistry and RNA analysis. These incidents may involve undiagnosed immunodeficiency, affecting multiple puppies in litters (Pekkarinen *et al*., 2024). Despite widespread use, vaccine escape occurs due to genetic diversity in circulating CDV strains, particularly those differing from the America-1 lineage used in most vaccines, leading to infections in vaccinated dogs (Lanszki *et al*., 2021; Zhigang *et al*., 2021).

There are 50 licensed distemper vaccines in the United States, mostly combinations with other pathogens. Inactivated CDV vaccines offer inferior protection and are suited for wildlife. Modified live virus (MLV) vaccines use attenuated strains like Snyder Hill, Rockborn, or Onderstepoort, providing solid immunity but risking disease in related wildlife species, such as nearly wiping out black-footed ferrets. Canarypox-vectored recombinant vaccines, incorporating CDV hemagglutinin (HA) and fusion proteins, overcome maternal immunity earlier, immunizing pup-

pies about 4 weeks sooner without causing post-vaccinal encephalitis. Both recombinant and MLV vaccines offer similar onset and duration of immunity, with serum antibody measurement assessing protection, lasting at least 5 years. Historical strains like Onderstepoort (isolated in the 1930s, attenuated in ferrets and eggs) and Rockborn (isolated in 1950, attenuated in canine cells) have dominated markets, though Rockborn was withdrawn in the 1990s due to encephalitis reports. Ongoing genetic diversity necessitates monitoring for effective prevention (Zhigang *et al*., 2021; Tizard, 2019). Distemper prevalence has declined with vaccination, but infections persist in unvaccinated or immunosuppressed dogs, with subclinical cases common in vaccinated animals. MDAs protect puppies under 12 weeks but hinder vaccination, while severe systemic signs affect unvaccinated pups aged 12-16 weeks (Sarchahi *et al*., 2025).

Control, prevention, and public health importance

CDV presents considerable challenges for control and prevention in domestic dog populations because of its high morbidity and mortality, zoonotic potential, and capacity to spill over into wildlife, including species such as tigers and pandas (Gastelum-Leyva *et al*., 2022). Genomic mutations, especially within the H protein, drive genetic diversity, facilitate infection across multiple host species, and hinder eradication efforts (Rivera-Martínez *et al*., 2024). Sustaining herd immunity is challenged by financial constraints, difficulties in vaccinating feral or semi-owned dogs, and owner misconceptions, rendering complete eradication improbable and highlighting the need for targeted preventive strategies (Parkman, 2023). Vaccination continues to be the primary preventive measure, with core CDV vaccines advised beginning at 6–8 weeks of age, repeated every 3–4 weeks until 16–20 weeks, and subsequently administered annually or every three years, with schedules adapted for high-risk environments such as shelters (Khan *et al*., 2024). In shelter environments, stressors such as overcrowding and inadequate staffing exacerbate CDV transmission, as facilities often lack funding for comprehensive care, leading to prioritization of sterilization over treating infections, and increasing susceptibility through stress-induced immunosuppression (Parkman, 2023). Commercial vaccines, such as Nobivac® DHPPI and Vanguard® Plus 5/CV-L, elicit strong antibody responses peaking around the second month post-vaccination; however, genetic differences between vaccine strains and circulating wild-type viruses can result in field vaccination failures (Nayel *et al*., 2020). Antibody titer measurements using virus neutralization serve as a standard to assess protective immunity and guide revaccination, with any detectable titer in adult dogs indicating long-term protection due to memory cell presence (Bergmann *et al*., 2020).

Building on these prevention strategies, the public health importance of CDV extends beyond domestic dogs, as its bidirectional transmission between domestic dogs and wildlife, including synanthropic species, underscores zoonotic risks, particularly amid waning measles immunity in humans, potentially increasing susceptibility to CDV (Wilson *et al*., 2025). Outbreaks in vaccinated populations underscore the necessity of ongoing surveillance and control measures to prevent cross-species transmission, as genetic variability contributes to vaccine failure (Nayel *et al*., 2020). Genomic sequencing aids in tracking CDV evolution, informing precise prevention strategies (Rivera-Martínez *et al*., 2024). Rapid diagnosis is crucial for managing outbreaks in shelters where infectious diseases historically drive euthanasia (Parkman, 2023). Effective vaccination has mirrored measles control in humans, significantly reducing distemper cases, though incomplete vaccination histories, especially in imported dogs, persist as risks (Bergmann *et al*., 2020). Overall, CDV's impact on companion animals and wildlife necessitates targeted interventions such as vaccination to prevent and control the disease (Khan *et al*., 2024). CDV has been suggested as a potential human health risk, with declining population-level measles immunity possibly increasing susceptibility to CDV infection, underscoring broader zoonotic concerns (Wilson *et al*., 2025).

Economic impact

CDV infection in domestic dogs imposes substantial economic burdens, encompassing veterinary care, preventive measures, and broader community impacts. Socio-economic aspects of dog population management (DPM) highlight the complexities associated with controlling and preventing CDV. A comprehensive scoping review of DPM systems found that only 14 of over 7,200 studies addressed socio-economic factors, reflecting a paucity of economic data to inform effective disease management. Among these studies, sterilization combined with vaccination was the most commonly implemented DPM intervention, with economic assessments reporting metrics such as cost per dog sterilized, cost per dog vaccinated, and cost per disability-adjusted life year (DALY) averted. Methodologies including cost-benefit analysis (CBA) and cost-effectiveness analysis (CEA) yielded benefit-cost ratios ranging from favorable to unfavorable depending on the context, underscoring the necessity of region-specific economic evaluations for domestic dog populations (Ghimire *et al*., 2025).

The economic burden of CDV in domestic dog populations is multifaceted and extends across veterinary care costs, disease prevention programs, and broader community impacts. Studies focusing on domestic dogs revealed that the total costs of DPM services, including vaccination costs, sterilization costs, staff costs, and community education and awareness costs, represent substantial financial investments required for effective disease control. The review highlighted that economic benefits in domestic dog populations stemmed from reductions in dog bites, decreased use of post-exposure prophylaxis (PEP), averted DALYs, and fewer traffic accidents involving dogs, illustrating the wider economic impact of comprehensive disease management strategies. However, gaps in data availability for domestic dog populations remain a major challenge, particularly concerning dog population size, disease frequency, and complete cost estimations that often excluded capital, training, equipment costs, and indirect costs. Moreover, CDV infection in fur-bearing and economically valuable animals has caused considerable financial losses (Liu *et al*., 2024).

Additionally, the interplay between human livelihoods and CDV transmission in domestic dog populations generates complex economic feedback loops. Households reliant on natural resources were more likely to engage in dog-keeping practices that facilitate disease spread ($\beta = 0.54$, $p < 0.001$), while deriving limited economic gains from these resource-dependent activities ($\beta = 0.26$, $p < 0.001$). This pattern highlights how economic constraints in domestic dog-owning households can inadvertently perpetuate disease risk, as owners may lack financial resources for proper veterinary care, vaccination of their domestic dogs, and disease prevention measures. The economic burden is particularly pronounced in rural communities where domestic dog ownership serves functional purposes related to livelihood activities such as guarding farmland (44.9% of owners), guiding mountain hikes, and accompanying owners in grazing or timber product harvest (27.4%), creating situations where economic necessity conflicts with optimal disease management practices in domestic dog populations (Weng *et al*., 2024).

In the study, households maintained an average of 2.1±0.89 domestic dogs, with 76.9% allowed to roam freely or temporarily leave their premises, creating considerable opportunities for disease transmission. Among sampled dogs, only 38.5% had been vaccinated against rabies, while 7.7% displayed detectable antibodies despite no vaccination, indicating natural viral exposure. The economic impact of insufficient vaccination coverage is substantial, as unvaccinated dogs serve as pathogen reservoirs, posing risks to wildlife, other domestic dogs, and potentially humans, thereby elevating overall disease management costs (Weng *et al*., 2024).

Human activities and attitudes toward biological conservation significantly affect the economic impact of CDV in domestic dog populations. Structural equation modeling indicated that increased human ac-

tivity (β = 0.27, p = 0.012) was positively correlated with higher domestic dog numbers, greater contact between dogs and wildlife, and expanded roaming ranges, all of which elevate disease transmission risk and related economic costs. In contrast, enhanced human awareness of conservation (β = -0.51, p = 0.013) was associated with reduced dog populations, wildlife contact, and movement ranges, suggesting that educational interventions for dog owners could serve as cost-effective disease control strategies. Additionally, inadequate dog feeding (β = 0.44) and prior human-wildlife conflicts (β = 0.36) increased the likelihood of practices that negatively affect wildlife and facilitate disease spread, whereas higher education (β = 0.26), income (β = 0.13), and expenditures (β = 0.14) among owners correlated with reduced negative impacts (Weng *et al*., 2024).

The geographic distribution and prevalence of CDV in domestic dogs and wildlife carry significant economic implications for regional disease control initiatives. Studies have shown that CDV prevalence varies significantly across different regions, with some areas experiencing prevalence rates as high as 65.8% in certain species, necessitating region-specific prevention and control strategies for domestic dog populations that require substantial financial investment (Liang *et al*., 2024). The seasonal variation in CDV incidence, with higher prevalence observed during winter months, also impacts the timing and cost-effectiveness of vaccination campaigns for domestic dogs and other preventive measures (Liang *et al*., 2024). Recognizing the significant economic losses from CDV infections in valuable fur animals like foxes and minks is essential for advancing preventive measures that protect endangered wildlife populations, such as giant pandas, and mitigate the spread from domestic dogs to wild species (Liu *et al*., 2024).

Conclusion

Canine Distemper in domestic dogs continues to represent a significant global veterinary concern owing to its broad distribution, high case-fatality rate, and complex pathogenesis. The causative agent, Canine Distemper Virus, exhibits genetic variability that contributes to its adaptability and occasional vaccine failure, posing continuous challenges for disease control. The virus primarily targets epithelial, lymphoid, and nervous tissues, resulting in systemic clinical manifestations ranging from respiratory and gastrointestinal disturbances to neurological disorders. Early and accurate diagnosis through serological and molecular methods is essential for effective management and epidemiological surveillance. Although vaccination has significantly reduced disease incidence, incomplete immunization coverage, waning immunity, and the emergence of new viral lineages continue to sustain outbreaks among domestic dog populations. Strengthening vaccination programs, improving diagnostic tools, and enhancing public awareness are crucial to achieving sustainable control. Future research should emphasize molecular epidemiology, vaccine innovation, and the establishment of integrated control policies to better mitigate the health, welfare, and economic impacts of CD in domestic dogs, as highlighted by previous studies.

Acknowledgement

The authors express their gratitude to the Faculty of Health, Medicine, and Life Sciences, Universitas Airlangga, Indonesia, for providing the essential facilities that supported this study. This research was conducted without any external funding.

Conflict of interest

The authors have declared no conflict of interest.

References

Aldujaily, A.H., Salman, D.B., Hassoon, K.F., Bustani, G.S., 2025. Copper nanoparticles as a novel therapeutic approach for canine distemper virus: Clinical, hematological, and biochemical evidence from naturally infected dogs. Vet. World 18, 2945–2954. doi: 10.14202/vetworld.2025.2945-2954.

Alfano, F., Lucibelli, M.G., D'Alessio, N., Auriemma, C., Rea, S., Sgroi, G., Lucente, M.S., Pellegrini, F., Diakoudi, G., De Carlo, E., Decaro, N., 2025. Detection of canine distemper virus in wildlife in Italy (2022–2024). Front. Vet. Sci. 12, 1527550. doi: 10.3389/fvets.2025.1527550.

Andrukonis, A., Brown, K.M., Hall, N.J., Protopopova, A., 2021. Intake vaccinations reduced signs of canine respiratory disease during an outbreak at an animal shelter. Front. Vet. Sci. 8, 627580. doi: 10.3389/fvets.2021.627580.

Arbabi, M., Sarchahi, A.A., Mohebalian, H., 2022. Evaluation of the anti-Newcastle disease vaccine serum on dogs with canine distemper. Vet. Mex. OA 9, e1044. doi: 10.22201/fmvz.24486760e.2022.1044.

Ariyama, N., Agüero, B., Bennett, B., Urzúa, C., Berrios, F., Verdugo, C., Neira, V., 2024. Genetic characterization of Canine *Morbillivirus* (canine distemper virus) field strains in dogs, Chile, 2022–2023. Transbound. Emerg. Dis. 2024, 9993255. doi: 10.1155/2024/9993255.

Baikadamova, G., Rakhimzhanova, D., Yeszhanova, G., Seitkamzina, D., 2022. Laboratory studies of canine distemper. Vet. Sci. 4, 34–42. doi: 10.52269/22266070_2022_4_34.

Batı, Y.U., Kırmızıgül, A.H., 2025. Investigation of some biochemical parameters, hematological changes, neopterin and procalcitonin levels in dogs with canine distemper virus. J. Hell. Vet. Med. Soc. 76, 9139–9150. doi: 10.12681/jhvms.37942.

Bergmann, M., Freisl, M., Zablotski, Y., Khan, M.A., Speck, S., Truyen, U., Hartmann, K., 2021. Prevalence of neutralizing antibodies to canine distemper virus and response to vaccination in client-owned adult healthy dogs. Viruses 13, 945. doi: 10.3390/v13050945.

Bergmann, M., Holzheu, M., Zablotski, Y., Speck, S., Truyen, U., Straubinger, R.K., Hartmann, K., 2020. Comparison of four commercially available point-of-care tests to detect antibodies against canine parvovirus in dogs. Viruses 13, 18. doi: 10.1016/j.vetmic.2021.109174.

Candela, M.G., Wipf, A., Ortega, N., Huertas-López, A., Martínez-Carrasco, C., Perez-Cutillas, P., 2025. Tracking the spatial and functional dispersion of vaccine-related canine distemper virus genotypes: Insights from a global scoping review. Viruses 17, 1045. doi: 10.3390/v17081045.

Creevy, K.E., Evans, J.B., 2025. Canine distemper – infectious diseases. In: Merck Veterinary Manual. Merck & Co., Rahway, NJ.

Desai, D., Kalyani, I., Solanki, J., Patel, D., Makwana, P., Sharma, K., Vala, J., Muglikar, D., 2021. Serological and nucleocapsid gene-based molecular characterization of canine distemper virus isolated from dogs of southern Gujarat, India. Indian J. Anim. Res. 55, 1224–1232. doi: 10.18805/IJAR.B-1325.

Di Francesco, C.E., Smoglica, C., Di Pirro, V., Cafini, F., Gentile, L., Marsilio, F., 2022. Molecular detection and phylogenetic analysis of canine distemper virus in Marsican brown bear (Ursus arctos marsicanus). Animals 12, 1826. doi: 10.3390/ani12141826.

Dik, I., Hatipoglu, D., Gulersoy, E., 2023. Comparison of some cytokines, acute phase proteins and citrulline levels in healthy and canine distemper infected dogs. J. Vet. Med. Sci. 85, 76–82. doi: 10.1292/jvms.22-0281.

Dorji, T., Tenzin, T., Tenzin, K., Tshering, D., Rinzin, K., Phimpraphai, W., de Garine-Wichatitsky, M., 2020. Seroprevalence and risk factors of canine distemper virus in pet and stray dogs in Haa, western Bhutan. BMC Vet. Res. 16, 135. doi: 10.1186/s12917-020-02355-x.

Echeverry-Bonilla, D.F., Buriticá-Gaviria, E.F., Orjuela-Acosta, D., Chinchilla-Cardenas, D.J., Ruiz-Saenz, J., 2022. The first report and phylogenetic analysis of canine distemper virus in Cerdocyon thous from Colombia. Viruses 14, 1947. doi: 10.3390/v14091947.

Fornazari, F., Sevá, A.D., Oliveira, K.M., Assunção, P.C., Guimarães, V.Y., 2023. Exposure of dogs and wild carnivores to canine distemper virus, canine parvovirus, Leishmania infantum, and Toxoplasma gondii in the Xingu River basin, Brazilian Amazon: Prevalence, spatial distribution, and association with land cover types. Acta Amazon. 53, 325–335. doi: 10.1590/1809-4392202301340.

Franzo, G., de Villiers, L., Coetzee, L.M., de Villiers, M., Nyathi, F.N., Garbade, M., Hansen, C., Berjaoui, S., Ripà, P., Lorusso, A., Molini, U., 2024. Unveiling the molecular epidemiology of canine distemper virus in Namibia: An expected pathogen showing an unexpected origin. Heliyon 10, e34805. doi: 10.1016/j.heliyon.2024.e34805.

Freire, H.L., Iara, Í.H., Ribeiro, L.S., Gonçalves, P.A., Matta, D.H., Torres, B.B., 2025. Neurological manifestation of canine distemper virus: Increased risk in young Shih Tzu and Lhasa Apso with seasonal prevalence in autumn. Viruses 17, 820. doi: 10.3390/v17060820.

Fukuhara, H., Yumoto, K., Sako, M., Kajikawa, M., Ose, T., Kawamura, M., Yoda, M., Chen, S., Ito, Y., Takeda, S., Mwaba, M., 2024. Glycan-shielded homodimer structure and dynamical features of the canine distemper virus hemagglutinin relevant for viral entry and efficient vaccination. Elife 12, RP88929. doi: 10.7554/eLife.88929.3.

Gastelum-Leyva, F., Pena-Jasso, A., Alvarado-Vera, M., Plascencia-López, I., Patrón-Romero, L., Loera-Castañeda, V., Gándara-Mireles, J.A., Lares-Asseff, I., Leal-Ávila, M.Á., Alvelais-Palacios, J.A., Almeida-Pérez, J., 2022. Evaluation of the efficacy and safety of silver nanoparticles in the treatment of non-neurological and neurological distemper in dogs: A randomized clinical trial. Viruses 14, 2329. doi: 10.3390/v14112329.

Ghimire, R., Mohanty, P., Hiby, E., Larkins, A., Dürr, S., Hartnack, S., 2025. Socio-economic assessment of dog population management systems: A scoping review. Front. Vet. Sci. 12, 1519913. doi: 10.3389/fvets.2025.1519913.

Giacinti, J.A., Pearl, D.L., Ojkic, D., Campbell, G.D., Jardine, C.M., 2022. Genetic characterization of canine distemper virus from wild and domestic animal submissions to diagnostic facilities in Canada. Prev. Vet. Med. 198, 105535. doi: 10.1016/j.prevetmed.2021.105535.

Giummole, E., 2024. Canine distemper virus beyond dogs: A comprehensive overview from general pathology to wildlife case studies on Procyonidae. Master's thesis. University of Padua, Padua, pp. 40.

Guimera, A.O., 2023. On the pathogenesis and shifting dynamics of canine distemper infection in dogs and wild carnivores. PhD dissertation. University of California, Davis, pp. 134.

Gulliver, E., Taylor, H., Eames, M., Chernyavtseva, A., Jauregui, R., Wilson, A., Bestbier, M., O'Connell, J., Buckle, K., Castillo-Alcala, F., 2025. Investigation of post-vaccinal canine distemper involving the Rockborn-like strain in nine puppies in New Zealand. N. Z. Vet. J. 73, 278–287. doi: 10.1080/00480169.2025.2481896.

Halecker, S., Bock, S., Beer, M., Hoffmann, B., 2021. A new molecular detection system for canine distemper virus based on a double-check strategy. Viruses 13, 1632. doi: 10.3390/v13081632.

Johnson, K.L., Craig, L.E., Wilson, S., McLarty, E., Hespel, A.M., 2022. Radiographic evidence of metaphyseal sclerosis secondary to canine distemper virus: Four cases in juvenile dogs. J. Vet. Intern. Med. 36, 1303–1311. doi: 10.1111/jvim.16453.

Joshi, V.R., Jhala, M.K., Bhanderi, B.B., Nimavat, V.R., Desai, D.N., 2022. Comparison of lateral flow assay and RT-PCR for detection of canine distemper virus in dogs. Indian J. Vet. Sci. Biotechnol. 18, 79–83. doi: 10.21887/ijvsbt.18.3.18.

Ke, G.M., Ho, C.H., Chiang, M.J., Sanno-Duanda, B., Chung, C.S., Lin, M.Y., Shi, Y.Y., Yang, M.H., Tyan, Y.C., Liao, P.C., Chu, P.Y., 2015. Phylodynamic analysis of the canine distemper virus hemagglutinin gene. BMC Vet. Res. 11, 164. doi: 10.1186/s12917-015-0491-9.

Khan, N., Bhowmik, A., Sandilya, A., 2024. Homeopathic medicines: An alternative approach in therapeutic management of canine distemper in dogs. Sci. World 4, 2951–2954. doi: 10.5281/zenodo.13371603.

Kim, D.Y., Zinn, M.M., Odemuyiwa, S.O., Mitchell, W.J., Johnson, G.C., 2021. Myocarditis caused by naturally acquired canine distemper virus infection in four dogs. J. Vet. Diagn. Invest. 33, 167–169. doi: 10.1177/1040638720971828.

Kimpston, C.N., Hatke, A.L., Castelli, B., Otto, N., Tiffin, H.S., Machtinger, E.T., Brown, J.D., Van Why, K.R., Marconi, R.T., 2022. High prevalence of antibodies against canine parvovirus and canine distemper virus among coyotes and foxes from Pennsylvania: Implications for the intersection of companion animals and wildlife. Microbiol. Spectr. 10, e02532-21. doi: 10.1128/spectrum.02532-21.

Kocatürk, M., Öz, A.D., Muñoz, A., Martinez, J.D., Ceron, J.J., Yilmaz, Z., 2025. Changes in immuno-inflammatory and antioxidant biomarkers in serum and cerebrospinal fluid of dogs with

distemper. Microb. Pathog. 198, 107160. doi: 10.1016/j.micpath.2024.107160.
Krstić, N., Gnjatović, M., Mlađenović, L., Rakin, S., Jovanović, A., Nišavić, J., Lupulović, D., 2025. Canine infectious respiratory disease complex (CIRDC) worldwide: A review of epidemiology and distribution. Vet. Glasnik 2025, 1–22. doi: 10.2298/VETGL2501015K.
Lanszki, Z., Zana, B., Zeghbib, S., Jakab, F., Szabo, N., Kemenesi, G., 2021. Prolonged infection of canine distemper virus in a mixed-breed dog. Vet. Sci. 8, 61. doi: 10.3390/vetsci8040061.
Liang, J., Wang, T., Wang, Q., Wang, X., Fan, X., Hu, T., Leng, X., Shi, K., Li, J., Gong, Q., Du, R., 2024. Prevalence of canine distemper in minks, foxes and raccoon dogs from 1983 to 2023 in Asia, North America, South America and Europe. Front. Vet. Sci. 11, 1394631. doi: 10.3389/fvets.2024.1394631.
Liu, L., Wang, J., Li, R., Wu, J., Zhao, Y., Yan, F., Wang, T., Gao, Y., Zhao, Z., Feng, N., Xia, X., 2024. A bacterium-like particle vaccine displaying envelope proteins of canine distemper virus can induce immune responses in mice and dogs. Viruses 16, 549. doi: 10.3390/v16040549.
Mansour, K.A., Hasso, S.A., 2021. Molecular detection of canine distemper virus in dogs in Baghdad Province, Iraq. Iraqi J. Vet. Med. 45, 46–50. doi: 10.30539/ijvm.v45i2.1267.
Mohammad, H.A., Ajaj, E.A., Gharban, H.A., 2022. The first study on confirmation and risk factors of acute and chronic canine distemper in stray dogs in Wasit Province, Iraq using ELISA and RT-PCR. Vet. World 15, 968–974. doi: 10.14202/vetworld.2022.968-974.
Mojtahedzadeh, S.M., Jamshidi, S., Langroudi, A.G., Vahedi, S.M., Tamai, I.A., Akbarein, H., Moosavian, H., 2024. Molecular detection of canine distemper virus among dogs showing neurologic and non-neurologic forms of disease. Iran. J. Vet. Med. 18, 203–214. doi: 10.32598/ijvm.18.2.1005294.
Mousafarkhani, F., Sarchahi, A.A., Mohebalian, H., Khoshnegah, J., Arbabi, M., 2023. Prevalence of canine distemper in dogs referred to Veterinary Hospital of Ferdowsi University of Mashhad, Iran. Vet. Res. Forum 14, 153–160. doi: 10.30466/vrf.2022.541661.3269.
Naveenkumar, V., Bharathi, M.V., Kannan, P., Selvaraju, G., Nag, B.P., Vijayarani, K., 2025. Unveiling canine distemper epidemiology in association with climatic impacts: Longitudinal analysis and forecasting in Chennai, India. Int. J. Biometeorol. 2025, 1–5. doi: 10.1007/s00484-025-02912-9.
Nayel, M., Zaghawa, A., Zayed, A., Elsify, A., Salama, A., Kamr, A., Mousa, W., Dawood, A., Badr, Y., Altaib, H., Hildreth, B.E., 2020. Phylogenetic analysis and immunohematological response associated with two commercially available vaccines against canine distemper and canine parvovirus. Vet. Med. Public Health J. 1, 5–14. doi: 10.31559/vmph2020.1.1.3.
Parkman, V., 2023. Optimal control applied to a canine distemper outbreak modeled in an animal shelter. PhD dissertation. Florida State University, Florida.
Pekkarinen, H.M., Karkamo, V.K., Vainio-Siukola, K.J., Hautaniemi, M.K., Kinnunen, P.M., Gadd, T.K., Holopainen, R.H., 2024. Post-vaccinal distemper-like disease in two dog litters with confirmed infection of vaccine virus strain. Comp. Immunol. Microbiol. Infect. Dis. 105, 102114. doi: 10.1016/j.cimid.2023.102114.
Pranitha, P., Jhala, M.K., Bhanderi, B.B., 2022. Comparison of lateral flow assay and polymerase chain reaction for diagnosis of canine distemper. VirusDisease 33, 96–101. doi: 10.1007/s13337-022-00763-1.
Quintero-Gil, C., Rendon-Marin, S., Martinez-Gutierrez, M., Ruiz-Saenz, J., 2019. Origin of Canine Distemper Virus: Consolidating Evidence to Understand Potential Zoonoses. Front. Microbiol. 10, 1982. doi: 10.3389/fmicb.2019.01982.
Rendon-Marin, S., da Fontoura Budaszewski, R., Canal, C.W., Ruiz-Saenz, J., 2019. Tropism and molecular pathogenesis of canine distemper virus. Virol. J. 16, 30. doi: 10.1186/s12985-019-1136-6.
Ricci, I., Cersini, A., Manna, G., Marcario, G.A., Conti, R., Brocherel, G., Grifoni, G., Eleni, C., Scicluna, M.T., 2021. A canine distemper virus retrospective study conducted from 2011 to 2019 in central Italy (Latium and Tuscany Regions). Viruses 13, 272. doi: 10.3390/v13020272.
Rivera-Martínez, A., Rodríguez-Alarcón, C.A., Adame-Gallegos, J.R., Laredo-Tiscareño, S.V., de Luna-Santillana, E.D., Hernández-Triana, L.M., Garza-Hernández, J.A., 2024. Canine distemper virus: Origins, mutations, diagnosis, and epidemiology in Mexico. Life 14, 1002. doi: 10.3390/life14081002.
Saaed, M.M., Al-Obaidi, Q.T., 2021. Clinical, hematological and some biochemical changes in dogs infected with canine distemper. J. Agric. Vet. Sci. 14, 26–33. doi: 10.9790/2380-1405022633.
Saltık, H.S., Kale, M., 2020. Evaluation of infection with N protein-specific immunoglobulin M and G in naturally occurring distemper in dogs. Vet. Med. 65, 168–173. doi: 10.17221/31/2019-VETMED.
Saltık, H.S., Kale, M., 2023. Rapid molecular detection and isolation of canine distemper virus in naturally infected dogs. Ankara Univ. Vet. Fak. Derg. 70, 49–56. doi: 10.33988/auvfd.846475.
Santos, B.P., Joaquim, J.G., Cassu, R.N., Pantoja, J.C., Luna, S.P., 2022. Effects of acupuncture in the treatment of dogs with neurological sequels of distemper virus. Innov. Acupunct. Med. 15, 238–246. doi: 10.51507/j.jams.2022.15.4.238.
Sarchahi, A.A., Arbabi, M., Mohebalian, H., 2025. Effects of phenobarbital and prednisolone on neurological signs of canine distemper. Vet. Med. Sci. 11, e70479. doi: 10.1002/vms3.70479.
Scagliarini, A., Dal Pozzo, F., Gallina, L., Vaccari, F., Morganti, L., 2007. TaqMan based real time PCR for the quantification of canine distemper virus. Vet. Res. Commun. 31, 261–263. doi: 10.1007/s11259-007-0020-9.
Sheikh, T., Ranjan, R., Jha, A.K., Kumar, S., 2021. Canine distemper: A fatal disease seeking special intervention. J. Entomol. Zool. Stud. 9, 1411–1418. doi: 10.5455/ijlr.20210102.
Shi, Y., Long, F., Shi, K., He, M., Shi, Y., Feng, S., Yin, Y., Wei, X., Li, Z., 2024. A quadruplex reverse transcription quantitative polymerase chain reaction for detecting canine coronavirus, canine rotavirus, canine parvovirus, and canine distemper virus. Microbiol. Res. 15, 746–761. doi: 10.3390/microbiolres15020049.
Silva, M.D., Silva, G.E., Borin-Crivellenti, S., Alvarenga, A.W., Aldrovani, M., Braz, L.A., Aoki, C., Santana, A.E., Pennacchi, C.S., Crivellenti, L.Z., 2022. Renal abnormalities caused by canine distemper virus infection in terminal patients. Front. Vet. Sci. 9, 822525. doi: 10.3389/fvets.2022.822525.
Sudibmanna, M.S., 2022. Therapeutic management of canine distemper in dogs. Master's thesis. Maharashtra Animal and Fishery Sciences University, Nagpur, pp. 133.
Tizard, I.R., 2019. Vaccines for Veterinarians. Elsevier, Missouri, pp. 336.
Uhl, E.W., Kelderhouse, C., Buikstra, J., Blick, J.P., Bolon, B., Hogan, R.J., 2019. New world origin of canine distemper: Interdisciplinary insights. Int. J. Paleopathol. 24, 266–278. doi: 10.1016/j.ijpp.2018.12.007.
Ulaş, N., Zengin, K., Aydın, H., Timurkan, M.O., Yörü, H.B., 2025. Canine distemper virus infection in shelter dogs presenting clinical signs: Prevalence and risk factors. Van Vet. J. 36, 65–70. doi: 10.36483/vanvetj.1621987.
Van, T.M., Tran, D.T., Nguyen, C.T., Huynh, G.T., Luu, M.T., Le, T.Q., Tran, B.N., 2025. Epidemiological, clinical, and molecular insights into canine distemper virus in the Mekong Delta region of Vietnam. Viruses 17, 781. doi: 10.3390/v17060781.
Wang, H., Guo, H., Hein, V.G., Xu, Y., Yu, S., Wang, X., 2023. The evolutionary dynamics history of canine distemper virus through analysis of the hemagglutinin gene during 1930–2020. Eur. J. Wildl. Res. 69, 56. doi: 10.1007/s10344-023-01685-z.
Weckworth, J.K., Davis, B.W., Dubovi, E., Fountain-Jones, N., Packer, C., Cleaveland, S., Craft, M.E., Eblate, E., Schwartz, M., Mills, L.S., Roelke-Parker, M., 2020. Cross-species transmission and evolutionary dynamics of canine distemper virus during a spillover in African lions of Serengeti National Park. Mol. Ecol. 29, 4308–4321. doi: 10.1111/mec.15449.
Weng, Y., McShea, W.J., Yang, H., Zhang, Z., Lin, W., Wang, F., 2024. Who let the dog out? Dog owner attitudes and economics regulate the potential negative impact of domestic dogs on wildlife in a reserve network. Conserv. Sci. Pract. 6, e13156. doi: 10.1111/csp2.13156.
Wilkes, R.P., 2022. Canine distemper virus in endangered species: Species jump, clinical variations, and vaccination. Pathogens 12, 57. doi: 10.3390/pathogens12010057.
Wilson, J., Rubio, S., Salvador, L.C., Nemeth, N.M., Fishburn, J.D., Gottdenker, N.L., 2025. Canine distemper virus phylogenetic structure and ecological correlates of infection in mesocarnivores across anthropogenic land use gradients. Microbiol. Spectr. 13, e01225. doi: 10.1128/spectrum.01225-24.
Wipf, A., Perez-Cutillas, P., Ortega, N., Huertas-López, A., Martínez-Carrasco, C., Candela, M.G., 2025. Geographical distribution of carnivore hosts and genotypes of Canine Distemper Virus (CDV) worldwide: A scoping review and spatial meta-analysis. Transbound. Emerg. Dis. 2025, 6632068. doi: 10.1155/tbed/6632068.
Zhao, J., Ren, Y., 2022. Multiple receptors involved in invasion and neuropathogenicity of canine distemper virus: A review. Viruses 14, 1520. doi: 10.3390/v14071520.
Zhao, J., Ren, Y., Chen, J., Zheng, J., Sun, D., 2020. Viral pathogenesis, recombinant vaccines, and oncolytic virotherapy: Applications of the canine distemper virus reverse genetics system. Viruses 12, 339. doi: 10.3390/v12030339.
Zhigang, C., Li, Y., Cheng, Y., Shi, P., Wang, J., Feng, E., Cheng, S., 2021. Phylogenetic analysis and biological characteristics identification of a canine distemper virus strain isolated from a vaccinated domestic dog in Northeast China. Res. Square 2021, 1–18. doi: 10.21203/rs.3.rs-349122/v1.