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# Epidemiology, pathogenesis, clinical findings and diagnosis of canine parvo viral infection – a mini review

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Viral enteritis is one of the most common causes of infectious diarrhoea in dogs younger than six months age. Canine parvovirus (CPV)-2 and canine corona virus (CCoV) have been incriminated as primary pathogens (1). It is the number one viral cause of puppy enteritis and mortality (2). Unique properties of CPV make it an emerging and reemerging pathogen of dogs worldwide (3). Since its emergence in 1978, canine parvoviral enteritis remains a common and important cause of morbidity and mortality in young dogs. The continued incidence of parvoviral enteritis is partly due to the virus's capability to "reinvent" itself and evolve into new, more virulent and resistant subspecies (4). This article briefly review about the current knowledge of epidemiology, pathogenesis, clinical findings and diagnosis of canine parvoviral enteritis.

## Epidemiology

### The virus

Parvoviruses (Parvoviridae) are small, non-enveloped, single-stranded DNA viruses that are known to cause disease in a variety of mammalian species, although most parvoviruses are species specific (5, 6). "Parvo" means small (Latin) and CPV belongs to the genus parvovirus, family parvoviridae. Parvoviruses have a single-stranded DNA genome of 5,000 bases with a hairpin structure (7). By means of X-ray crystallography, the parvovirus capsid has been found to be formed by 60 copies of combination of VP1, VP2 and VP3. The VP1 contains the full-length sequence plus an additional N-terminal domain. The VP2, the most abundant structural protein, accounts for 90% of the viral capsid, representing the major determinant of host range and virus-host interactions, and is cleaved to VP3 by host proteases (8). Parvoviruses have exceptional evolutionary ability (9). Canine parvovirus 1 (CPV-1) produces a common subclinical enteric infection in dogs but causes no known disease. Canine parvovirus infection in dogs was first identified in 1978 in the USA (10) and was designated CPV type 2 (CPV-2) to distinguish it from a previously recognized parvovirus of dogs

known as minute virus of canines (11). After its emergence, CPV-2 spread globally, and now CPV viruses are endemic in most populations of domestic and wild canids (12). Analysis of CPV isolates by monoclonal antibodies and restriction enzymes have shown that a new antigenic strain, designated CPV type 2a (CPV-2a), became widespread around 1979 and it replaced the original strain during 1980 to 1981 in the USA (13). Later examination of canine isolates identified another antigenic variant, designated CPV type 2b (CPV- 2b) that emerged around 1984, and after 1986 replaced CPV-2a in many parts of the USA (14). Currently, the antigenic variants have completely replaced the original type 2, which is still used in most commercial vaccines, and are variously distributed in the canine population worldwide (8). Within the past decade a new strain, CPV-2c, has emerged. This strain was first reported in Italy in 2000 (15) and it was soon reported in various countries claimed to be highly virulent, with high morbidity and rapid death (4). This strain known as Glu426, has a substitution of amino acid at the 426 position from aspargine/aspartic acid to glutamic acid and altered the viral capsid antigenic site, epitope A (16). It has rapidly spread more effectively in susceptible dogs in addition to the ability to infect cats. Parvoviruses are extremely stable in the environment and relatively resistant to disinfectants because they are non enveloped viruses (17).

**Host range**

Canine parvo virus causes most dangerous and contagious disease that affect dogs and this infection considered as most threatening to puppies between the time of weaning to six months of age. Adult dogs also contract the disease but it is relatively uncommon (18). Dogs of any breed, age, or sex, but puppies between 6 weeks and 6 months of age appear to be more susceptible (19, 20). Immunity to CPV following infection or vaccination is long lived, and therefore the only susceptible pool of animals is puppies born into the population. For the first few weeks of life, puppies are protected against infection by maternally derived antibody (assuming the bitch has antibodies). Disease is encountered in neonates (5). However, maternal antibody to parvovirus has a half-life of approximately 10 days, and as their maternal antibody titers decline puppies become susceptible to infection (21). The stability of CPV in the kennel environment and excretion of large amounts of CPV by sick puppies can expose susceptible puppies to massive infectious doses of CPV. This CPV susceptibility window coincides with weaning in puppies in the age group of about 6 to 8 weeks old. Eight weeks is the age when the largest number of puppies succumb to CPV. Moreover, there are variations in the decay of

antibodies and induction of active immunity after vaccination directed by the genetic makeup (canine major histocompatibility antigens) of the puppies (22).

**Risk factors**

Factors that predispose to parvoviral infection in puppies are lack of protective immunity, intestinal parasites, overcrowded, unsanitary, and stressful environmental conditions (6, 23). Certain breeds have been shown to be at increased risk for severe CPV enteritis, including the rottweilers, doberman pinscher, American pit bull terrier, labrador retriever, and German shepherd dog (23, 24). Reasons for breed susceptibility are unclear. Besides a genetic component, other factors may also account for increased risk of disease, such as breed popularity and lack of appropriate vaccination protocols (21). Among dogs older than 6 months, sexually intact males appear to be twice as likely to develop CPV enteritis as sexually intact females (24). Stress factors, in particular parasitic and nonspecific factors (eg, weaning), may predispose dogs to clinical disease by increasing mucosal cell activity. During weaning, enterocytes of the intestinal crypts have a higher mitotic index. Because of the changes in bacterial flora and diet during weaning, during this time puppies are more susceptible to the viral tropism (6).

**Pathogenesis**

Canine parvovirus - 2 spreads rapidly among dogs via the fecal-oral route (direct transmission) or through oro nasal exposure to fomites contaminated by feces (indirect transmission) (25). In the kennel environment, the availability of a large number of susceptible puppies, environmental stress, and unique - properties of CPV combine to form an ideal scenario for the rapid spread of CPV. The stability of CPV in the kennel environment and excretion of large amounts of CPV by sick puppies can expose susceptible puppies to massive infectious doses of CPV (22). The virus first replicates in lymphoid tissues, and then disseminates to other rapidly dividing body tissues, notably intestinal crypts, lymphoid tissues, thymus and bone marrow (26). After penetration through the oronasal route, the virus replicates in gastro enteric associated lymphoid tissues and is disseminated by infected leukocytes to the germinal epithelium of the crypts of the small intestine. Intestinal crypt epithelial cells maturing in the small intestine normally migrate from the germinal epithelium of the crypts to the tips of the villi. On reaching the villous tips, they acquire their absorptive capability and aid in assimilating nutrients. This virus multiplies in the rapidly dividing cells of intestinal crypts (7), causing epithelial destruction and villous collapse . As a result, normal cell turnover (usually 1–3 days in the small intestine) is impaired, leading to the characteristic pathologic lesion of shortened and

atrophic villi and during this period of villous atrophy the small intestine loses its absorptive capacity results in diarrhea (27, 28). Infection of leukocytes, mainly circulating and tissue-associated lymphocytes, induces acute lymphopenia (29) often associated with neutropenia (5). In 2–3-week-old sero negative pups, CPV is also able to replicate in cardiac cells inducing a fatal myocarditis. However, this form is no longer observed as almost all young pups are protected by maternally derived antibodies (MDA) (8). Viremia is detected one to five days post-infection. Fecal shedding of viral particles occurs as early as three days post-infection, for as long as ten days (30).The breach in the integrity of the intestinal epithelium with concurrent immunosuppression predisposes dogs to bacterial translocation, bacteremia and sepsis (20).

**Clinical signs**

Enteritis and myocarditis were the two disease entities initially described with CPV-2 infection (4).The most characteristic clinical form induced by CPV is represented by hemorrhagic enteritis, the extent of which is often dependent on the maternally derived antibody titers of the infected pups at the moment of infection. Clinical signs occur after an incubation period of 3–7 days and consist of anorexia, depression, vomiting and mucoid or bloody diarrhea, frequently dehydration and fever. Leukopenia is a constant finding, with white blood cell (WBC) counts dropping below 2000–3000 cells/ml of blood. However, total WBC counts may be even within normal ranges due to concomitant virus-induced lymphopenia, and neutrophilia consequent to infections by opportunistic bacteria. Concurrent pulmonary infections may lead to the onset of respiratory distress. Subclinical and inapparent infections are frequently detected, mainly in pups with intermediate MDA titers and in adult dogs (31). The mortality rates can be high (up to 70%) in pups, but are usually less than 1% in adult dogs (8).

Intestinal tract damage secondary to viral infection increases the risk of bacterial translocation and subsequent coliform septicemia, which may lead to the development of a systemic inflammatory response that can progress to septic shock and ultimately, death. *Escherichia coli* had been recovered from the lungs and liver of infected puppies. Pulmonary lesions similar to those found in humans with adult respiratory distress syndrome have been described (30).

Myocarditis caused by CPV-2 is very rarely seen nowadays, but can develop from infection *in utero* or in puppies less than 8 weeks old born to unvaccinated bitches (19). In this scenario usually all puppies in a litter are affected, often being found dead or succumbing within 24 hours after the appearance of clinical signs. The onset and progression of clinical disease is rapid, and clinical signs include dyspnea, crying, and

retching (31). The myocardial lesion is multifocal necrosis and lysis of myofibers with or without an inflammatory response. Intranuclear inclusion bodies can be found within the myocardial cell nuclei (32).

Primary neurologic disease may be caused by CPV but more commonly occurs as a result of haemorrhage into the central nervous system from disseminated intravascular coagulation or from hypoglycaemia during the disease process or sepsis or acid base electrolyte disturbances. Erythema multiforme with skin lesions of ulceration of footpads, pressure points, mouth and vaginal mucosa, vesicles in the oral cavity and erythematous patches on the abdomen and perivulvuar skin also recorded in parvoviral infection in dogs (1).

**Diagnosis**

Despite the typical presentation seen with CPV infection of acute-onset vomiting and diarrhea, depression, dehydration, fever and leukopenia in an unvaccinated puppy, these findings are nonspecific although this cluster of findings is frequently the legitimate basis of a presumptive diagnosis. Definitive diagnostic tests include demonstration of CPV in the feces of affected dogs, serology, and necropsy with histopathology (33). A near-patient enzyme-linked immunosorbent assay test is available to practitioners to demonstrate CPV in the feces of infected puppies (34). Viral particles are readily detectable at the peak of shedding (4–7 days after infection) (35). False-positive results may occur 3 to 10 days post vaccination with a modified live CPV vaccine, and false-negative results may occur secondary to binding of serum neutralizing antibodies with antigen in diarrhea or cessation of fecal viral shed (12). Slide agglutination test and slide inhibition test was developed and used for detection of all genotypes of CPV by using porcine erythrocytes (22). Other methods available to detect CPV antigen in feces include electron microscopy, viral isolation, fecal hemagglutination, latex agglutination, counterimmunoelectrophoresis, immunochromatography, and polymerase chain reaction (PCR) (36, 37). The PCR based methods, specifically real-time PCR, have been shown to be more sensitive than traditional techniques (38).

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