Canine Parvovirus

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KEYWORDS

• Parvovirus • Canine • Hemorrhagic enteritis • Vaccination

Since its emergence in 1978, canine parvoviral enteritis was and 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. Here the authors review current knowledge about the virus, its epidemiology, clinical manifestation, diagnosis, management, and prevention.

PARVOVIRIDAE

Parvoviruses (Parvoviridae) are small, nonenveloped, single-stranded DNA viruses that are known to cause disease in a variety of mammalian species, although most parvoviruses are species specific.[1–3] Parvovirus requires the host cell for replication, specifically the cell nucleus, and binds the host cell by the double-stranded ends of the genome. Viral replication occurs only in rapidly dividing cells such as intestinal crypt epithelial cells, precursor cells in the bone marrow, and myocardiocytes. Viral replication results in cell death and loss due to failure of mitosis.[2–4] Not all rapidly dividing cell populations are equally affected, suggesting a viral tropism for certain target organs.[4]

EPIDEMIOLOGY

The virus is better known as canine parvovirus type 2 (CPV-2) because it was the second parvovirus described in dogs. In 1967, parvovirus was first discovered as a cause of gastrointestinal and respiratory disease in dogs, and was then called the minute virus of canines.[5] It was later designated CPV-1. Most patients infected with CPV-1 are asymptomatic.[3] In 1978, reports of outbreaks of an unfamiliar contagious enteric disease were reported in the United States. The causal agent was isolated and data showed that it was a new species of the genus Parvoviridae; it was subsequently named CPV-2. Due to the lack of preexisting immunity in the canine population, the virus spread rapidly and by 1980 it was reported to be common worldwide.[1,3]

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Vet Clin Small Anim 40 (2010) 1041–1053
doi:10.1016/j.cvsm.2010.07.007 **vetsmall.theclinics.com**
0195-5616/10/$ – see front matter

The exact origin and evolution of CPV-2 is still a debated issue. Some reports found it to be closely related to feline panleukopenia virus and several publications did suggest that CPV-2 may have originated from this virus.[4] Other research suggests that CPV-2 originated from an antigenically similar ancestor, such as a wild carnivore.[3,6] Initially the infection led to high morbidity and mortality in the naïve canine population, but after the introduction of vaccines, outbreaks were limited to unvaccinated or improperly vaccinated animals and shelter environments. In the 1980s a new CPV-2 strain emerged and was designated CPV-2a. The virus quickly mutated again and a new strain, CPV-2b, emerged in 1984.[3,7] Today, CPV-2a and CPV-2b are still the most common parvovirus species causing disease in canines globally. Within the past decade a new strain, CPV-2c, has emerged. This strain was first reported in Italy in 2000[8] and was soon also reported in Vietnam,[9] Spain,[10] the United States,[11] South America,[12] Portugal,[13] Germany, and the United Kingdom.[14] This strain is claimed to be highly virulent, with high morbidity and rapid death.

Acute CPV-2 enteritis can be seen in dogs of any breed, age, or sex, but puppies between 6 weeks and 6 months of age appear to be more susceptible.[6,15,16] 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 therefore seldom encountered in neonates.[17] 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.[17,18]

Factors that predispose to parvoviral infection in puppies are lack of protective immunity, intestinal parasites, and overcrowded, unsanitary, and stressful environmental conditions.[2,15,19] Certain breeds have been shown to be at increased risk for severe CPV enteritis, including the rottweiler, doberman pinscher, American pit bull terrier, Labrador retriever, and German shepherd dog.[2,19,20] Reasons for breed susceptibility are unclear. Common ancestry in the doberman pinscher and rottweiler, the fact that both breeds have a relatively higher prevalence of von Willebrand's disease (VWD), as well as inherited immunodeficiency in rottweilers have been implicated.[16,20,21] Besides a genetic component, other factors may also account for increased risk of disease, such as breed popularity and lack of appropriate vaccination protocols.[16] Among dogs older than 6 months, sexually intact males appear to be twice as likely to develop CPV enteritis as sexually intact females.[20] A distinct seasonality has also been reported, with peak incidence of disease during summer months and a trough during winter.[20,22]

PATHOGENESIS

CPV-2 spreads rapidly among dogs via the fecal-oral route (direct transmission) or through oronasal exposure to fomites contaminated by feces (indirect transmission).[2,15,23] Fecal excretion of the virus has been shown to be as early as 3 days after experimental inoculation, and shedding may continue for a maximum period of 3 to 4 weeks after clinical or subclinical disease.[23,24] Virus replication begins in the lymphoid tissue of the oropharynx, mesenteric lymph nodes, and thymus, and is disseminated to the intestinal crypts of the small intestine by hematogenous spread (3–4 days after infection).[2,6,15,25,26] Marked plasma viremia is observed 1 to 5 days after infection. Subsequent to the viremia, CPV-2 localizes predominantly in the epithelium lining the tongue, oral cavity, and esophagus; the small intestine; bone marrow; and lymphoid tissue, such as thymus and lymph nodes.[15,24,26,27] Virus has been isolated

from lungs, spleen, liver, kidneys, and myocardium, showing that CPV infection is a systemic disease.[2,15,25]

The rate of lymphoid and intestinal cell turnover appears to be the main factor determining the severity of the disease: higher rates of turnover are directly correlated with virus replication and cell destruction. Stress factors, in particular parasitic and nonspecific factors (eg, weaning), may predispose dogs to clinical disease by increasing mucosal cell activity.[2,6,23,28,29] During weaning, enterocytes of the intestinal crypts have a higher mitotic index because of the changes in bacterial flora and diet, and are therefore more susceptible to the viral tropism for rapidly dividing cells.[20]

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. Parvovirus infects the germinal epithelium of the intestinal crypt, 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.[2,6,15,30,31] During this period of villous atrophy the small intestine loses its absorptive capacity. The changes in the thymus are dramatic. The lesions are usually most obvious in the germinal centers and the thymic cortex, reflecting the tropism of CPV for mitotically active cell populations. The extensive lymphocytolysis in the thymic cortex, as compared with other lymphoid tissues, further reflects the high mitotic rate found in this organ, and it is thus not surprising that infected puppies develop severe lymphopenia.[2,32]

CLINICAL MANIFESTATION

Enteritis and myocarditis were the 2 disease entities initially described with CPV-2 infection. CPV-2 myocarditis is very rarely seen nowadays, but can develop from infection in utero or in puppies less than 8 weeks old born to unvaccinated bitches.[15] 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.[15,33] 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.[34]

Acute enteritis is the most common manifestation of the disease and is mostly seen in puppies up to 6 months of age. Initial clinical signs are nonspecific, and include anorexia, depression, lethargy, and fever. Later typical signs include vomiting and small bowel diarrhea that can range from mucoid to hemorrhagic.[3,16] Due to large fluid and protein losses through the gastrointestinal tract, dehydration and hypovolemic shock often develop rapidly.[16] Marked abdominal pain is often a feature of CPV enteritis and can be caused by either acute gastroenteritis or intestinal intussusception.

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* has 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.[16,31,35] It has also been suggested that the hemorrhagic diarrhea is a consequence of endotoxemia and cytokine production and does not derive directly from viral infection.[36] Research data have shown that

endotoxin and tumor necrosis factor (TNF) are present in measurable quantities in the blood of infected puppies and that a significant association exists between rising TNF activity and mortality.[31] Endotoxin and proinflammatory cytokines are potent mediators of the systemic inflammatory response and activators of the coagulation cascade.[37,38]

No specific radiographic signs are associated with CPV enteritis besides those typically seen in gastroenteritis, that is, fluid- and gas-filled bowel loops. A recent study has examined the ultrasonographic appearance of CPV enteritis in comparison with that of normal puppies.[39,40] Although none of the ultrasonographic changes were pathognomonic for CPV enteritis, the combination of changes was highly suggestive of the disease. Typical changes that were considered indicative of CPV enteritis included fluid-filled, atonic small and large intestines; duodenal and jejunal mucosal layer thinning with or without indistinct wall layers and irregular luminal-mucosal surfaces; extensive duodenal and/or jejunal hyperechoic mucosal speckling; and duodenal and/or jejunal corrugations. The extensive intestinal lesions correlated with the histopathological findings of villous sloughing, mucosal erosion and ulceration, and crypt necrosis. In this study CPV infection did not appear to be associated with sonographically detectable lymphadenopathy. The severity of the sonographic changes did correlate with the clinical condition of the patients.[39,40]

CLINICOPATHOLOGIC FEATURES

The leukocyte count during CPV enteritis is generally characterized as significantly depressed, with a transient lymphopenia being the most consistent finding. The hematological changes are widely accepted to be attributable to destruction of hematopoietic progenitor cells of the various leukocyte types in the bone marrow and other lymphoproliferative organs such as the thymus, lymph nodes, and spleen. This process results in inadequate supply for the massive demand for leukocytes (specifically neutrophils) in the inflamed gastrointestinal tract.[32,41] A recent study showed that a lack of cytopenia, specifically the total leukocyte and lymphocyte counts, had a positive predictive value of 100% for survival 24 hours post admission. A rebound increase in the lymphocyte count 24 hours after admission was seen in the puppies that recovered.[41] Studies have also shown a marked depletion of the granulocytic, erythroid, and megakaryocytic cell lines in the bone marrow followed by hyperplasia of the granulocytic and erythroid elements during convalescence.[42,43] These changes are nonspecific and could reflect the effect of endotoxemia.[43] Despite the severe changes seen in the blood precursor cell lines, it appears that early pluripotent cells are spared.[32] Increased plasma granulocyte colony-stimulating factor (G-CSF) concentration has been observed in CPV enteritis just after the onset of neutropenia, which then decreases to undetectable levels once the neutropenia has resolved.[44]

Anemia is not an uncommon hematological finding in CPV enteritis, especially in the later phases of severe disease. The cause of this is unlikely to be suppression of erythropoiesis, as circulating red blood cells have a long half-life relative to the short period during which the virus suppresses production in the bone marrow.[42] Reduced hematocrit is more likely to be the result of a combination of intestinal hemorrhage and rehydration therapy.[15,28] Increased levels of lipid peroxides and an alteration in antioxidant enzyme concentrations, indicating a state of oxidative stress in these patients, may also play a role in anemia pathogenesis.[45]

Virus-induced thrombocytopenia can occur because of decreased platelet production or as a result of direct action of viruses and/or immunologic components on

platelets or endothelium.[46] Besides hemorrhagic manifestations (which are rare), subclinical thrombocytopenia may affect vascular permeability, which may potentiate extravascular dissemination of the virus.[47] Evidence of hypercoagulability without disseminated intravascular coagulopathy has been documented in puppies with CPV enteritis and is thought to be due to an endotoxin- or cytokine-mediated procoagulant effect on endothelial cells. Loss of antithrombin (AT) through the gastrointestinal tract, as well as consumption of AT as a result of endotoxin-mediated activation of coagulation, and hyperfibrinogenemia are thought to contribute to the hypercoagulable state seen in CPV enteritis.[48]

The response of the adrenal and thyroid glands to critical illness is essential for survival. Similar to critical illness in humans, high serum cortisol and low serum thyroxine (T4) concentrations at 24 and 48 hours after admission are associated with death in puppies with CPV enteritis.[49,50]

Infection-induced serum chemistry abnormalities are nonspecific. Severe hypokalemia due to anorexia, vomiting, and diarrhea may contribute to depression and weakness. Other electrolyte abnormalities (ie, hyponatremia and hypochloremia) may also occur secondary to vomiting and diarrhea.[28,51,52] Although total magnesium concentration has been found to be a prognostic indicator in critically ill humans, total as well as ionized magnesium concentrations were not associated with outcome in CPV enteritis.[53] Hypoalbuminemia may contribute to reduced total blood calcium concentrations.[28] Serum electrophoresis profiles have shown relative and absolute hypoalbuminemia, hypogammaglobulinemia, and hyper–α2-globulinemia.[54] The decrease in plasma proteins through the course of the disease are mostly due to a combination of intestinal hemorrhage followed by rehydration. The increase in α2-globulins are most likely due to the hepatic synthesis of acute phase proteins (APP) stimulated by leukocyte endogenous mediators that are associated with tissue damage and inflammation.[54] Acute-phase protein generation occurs at the expense of albumin generation in critical illness.[55] Unpublished data on serum C-reactive protein (CRP), a major APP in the dog, have shown that higher CRP levels at admission, and 12 and 24 hours after admission are positively associated with an increased risk of mortality (unpublished data from McClure V and colleagues, Faculty of Veterinary Science, University of Pretoria, South Africa, 2010). Elevated blood urea, creatinine, and inorganic phosphate are associated with dehydration. Elevation in alkaline phosphatase and alanine transaminase may occur as a result of hepatic hypoxia secondary to severe hypovolemia or the absorption of toxic substances due to loss of the gut barrier. Elevated alkaline phosphatase activity can also be associated with young age.[28,51] Plasma lipoproteins bind the bioactive portion of the endotoxin (LPS) molecule, preventing it from stimulating monocytes, macrophages, and other LPS-responsive cells thereby providing an important host mechanism for controlling responses to endotoxin. Several reports have shown a strong correlation between low plasma cholesterol and mortality in critically ill and infected human patients. A recent study has shown serum total cholesterol and high-density lipoprotein cholesterol levels to decrease, but serum triglyceride levels to increase in CPV enteritis. Hypocholesterolemia may be used as an index of the severity of CPV enteritis.[56]

Studies on acid-base status in CPV enteritis have shown puppies to develop either acidosis or alkalosis depending on the severity of the vomiting (ie, loss of hydrogen and chloride ions) or the origin of the diarrhea (ie, small versus large intestine).[52] The majority of cases show a decrease in venous blood pH and HCO_3^-, which indicate the development of metabolic acidosis probably caused by excessive loss of HCO_3^- through the intestinal tract.[57,58] The metabolic acidosis seen in CPV enteritis is,

however, readily corrected and is not exacerbated by D-lactate production by the bacterial population within the large intestine.[58]

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.[59] Diagnosis of active CPV infection via serology requires detection of anti-CPV antibody that is of recent origin (ie, IgM class antibodies) in the face of typical clinical signs.[60] A near-patient enzyme-linked immunosorbent assay test is available to practitioners to demonstrate CPV in the feces of infected puppies.[61] Viral particles are readily detectable at the peak of shedding (4–7 days after infection).[59] 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.[6,16,51] 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).[51,59,62,63] PCR-based methods, specifically real-time PCR, have been shown to be more sensitive than traditional techniques.[62]

MANAGEMENT

Canine parvoviral enteritis is associated with a survival rate as low as 9.1% in the absence of treatment, and 64% or higher with treatment.[31] Because no agent-specific treatment exists for CPV enteritis, management of this condition remains supportive care. Mildly affected puppies may be treated on an outpatient basis. Outpatient treatment cannot, however, be recommended, because most of these puppies will deteriorate as owners frequently fail to maintain oral treatment programs in the face of worsening vomiting. Best management requires admission and aggressive treatment with crystalloid fluids, synthetic and natural colloids, correction of hypoglycemia and any electrolyte disturbances, combination antimicrobials, antiemetics, analgesics, enteral nutritional support, and anthelmintics. Fluid therapy to treat dehydration, reestablish effective circulating blood volume, as well as correct electrolyte and acid-base disturbances is the mainstay of managing more severely affected puppies.[16,51] Fluid therapy in these patients can be complex, and careful attention should be paid to physical examination in addition to electrolyte and acid-base status.[64] The preferred route of administration is intravenous, but intraosseus administration, although rarely used, may be useful in patients that need rapid fluid administration when intravenous access is impossible. It is crucial that all intravenous catheterization procedures be aseptic and catheter care be fastidious, as catheter-induced infection (abscessation and cellulites that may extend to septic polyarthritis and discospondylitis) is a serious complication in these immunosuppressed puppies. All intravenous catheters should be replaced after 72 hours of use.[65] Isotonic crystalloid solutions can be administered either subcutaneously or intraperitoneally to treat mild dehydration, but this is contraindicated in the face of circulatory compromise because of inadequate distribution secondary to peripheral vasoconstriction, as well as the risk of infection in severely leukopenic patients.[16,64] The initial fluid of choice is a balanced electrolyte solution that is

isotonic to blood (ie, lactated Ringer solution). The initial rate of fluid administration will depend on the condition of the patient. Fluid deficits should be replaced as soon as possible (within 1–6 hours of presentation).[16,51] Once perfusion is restored the intravenous fluid rate is reduced to a maintenance rate plus estimated ongoing losses. Puppies with CPV enteritis are prone to develop hypokalemia and hypoglycemia (specifically toy breeds) due to ongoing anorexia, vomiting, and diarrhea. Severe hypokalemia can result in profound muscle weakness, gastrointestinal ileus, cardiac arrhythmias, and polyuria.[16,51] Both serum potassium and glucose, together with the packed cell volume (PCV) and total serum protein, should be monitored at least once a day. Potassium chloride should be added to the fluids according to the patient's requirements. The amount of potassium chloride administered should be calculated and the clinician should ensure that the rate does not exceed 0.5 mEq/kg/h, as it may have adverse effects on normal cardiac function.[64] Supplementation of dextrose added to the balanced electrolyte solution to a final concentration of 2.5% to 5% may be necessary to prevent hypoglycemia once the initial critical hypoglycemia has been addressed.[16,51]

Puppies suffering from CPV enteritis often develop a severe protein-losing enteropathy due to the destruction of intestinal villi, and therefore the addition of a nonprotein colloid (ie, hetastarch or dextran 70) should be considered when total protein drops below 35 g/L (albumin <20 g/L) or if the patient shows evidence of loss of fluid into a third space.[16,51] Overzealous colloidal therapy must be avoided to prevent blunting of endogenous hepatic albumin production.[16,55] The role of blood products in the treatment of CPV is controversial. Patients suffering from anemia secondary to hemorrhagic diarrhea or concurrent endoparasitism, and showing clinical signs referable to anemia, can be treated with packed red blood cells or whole blood. Fresh frozen plasma (FFP) transfusion has been recommended in the treatment of CPV enteritis for its ability to provide oncotic components (albumin), immunoglobulins, and serum protease inhibitors, which may help to neutralize circulating virus and control the systemic inflammatory response associated with this disease.[51,55] However, FFP has been shown to be a poor means of supporting patient albumin concentrations, and very large volumes of plasma are required to achieve a small increase in plasma albumin.[55,64] Because of concern about transfusion-related immunomodulation and transfusion reactions, lack of efficacy, and readily available synthetic colloids, FFP is not recommended as a treatment to increase a patient's colloid oncotic pressure or serum albumin concentration.[64] There is a paucity of controlled clinical studies regarding albumin supplementation in veterinary patients, and to the authors' knowledge there have been no studies done to evaluate the efficacy of plasma transfusion for treatment in CPV enteritis. The administration of plasma as a means of providing passive immunization has been reported only anecdotally.[19,51] Despite these cautions and the paucity of studies evaluating the effect of FFP in CPV treatment, it is the experience of the authors that the early use of FFP has a positive effect on outcome.

Nil per os for 24 to 72 hours has been recommended in the past for the treatment of CPV enteritis. Growing evidence, however, supports the use of early enteral nutrition. A recent study has shown that puppies receiving early enteral nutrition via a nasoesophageal tube, when compared with puppies that received nil per os until vomiting ceased, showed earlier clinical improvement, significant weight gain, and improved gut barrier function, which could limit bacterial or endotoxin translocation.[66] Various commercial diets are formulated for animals recovering from gastrointestinal illness, but initial feeding should consist of small amounts of an easily digestible diet fed frequently even in the face of ongoing vomiting. The normal diet should be gradually

introduced. Coinfection with intestinal parasites can exacerbate CPV enteritis by enhancing intestinal cell turnover and subsequent viral replication.[19] Appropriate oral therapy should be initiated as soon as vomiting ceases.

In dogs suffering from CPV enteritis, vomiting is most likely caused by destruction of intestinal crypt cells, abnormal intestinal motility, and endotoxin-induced activation of the cytokine cascade, leading to local irritation and central activation of the emetic center and chemoreceptor trigger zone.[67] Persistent vomiting leads to severe fluid and electrolyte loss, interferes with nutritional support, and precludes oral administration of medication. The most commonly used antiemetic drugs for CPV enteritis are metoclopramide, prochlorperazine, and ondansetron. Metoclopramide is a dopaminergic antagonist that blocks the chemoreceptor trigger zone, stimulates and coordinates motility of the upper intestinal tract, and increases pressure in the lower esophageal sphincter. Metoclopramide must be used with caution in patients at risk of intussusception. Prochlorperazine is a phenothiazine derivative that also limits stimulation of the chemoreceptor trigger zone. Ondansetron is a 5-HT3 receptor antagonist that acts peripherally and centrally to inhibit vomiting.[16,51,67] Of note, a retrospective study showed that in a high number of cases antiemetics did not completely control vomiting, and puppies that received antiemetics generally required longer hospitalization. It was concluded that, although sicker dogs (which have longer hospitalizations anyway) are more likely to require antiemetic drugs, complications of antiemetic drugs, such as hypotension, signs of depression, and immune modulation, could possibly contribute to extended periods of hospitalization. Although this study demonstrated an association between antiemetic use and prolonged hospitalization, a cause-and-effect conclusion cannot be drawn.[67] Antiemetics are definitely indicated in the management of this disease.

Treatment with intravenous, broad-spectrum, bactericidal antibiotics is warranted in puppies suffering from CPV enteritis due to the disruption of the intestinal barrier and severe leukopenia. A combination of a β-lactam antibiotic (ampicillin, 20 mg/kg intravenously [IV] every 8 hours) or a β-lactamase resistant penicillin (amoxicillin clavulanate, 20 mg/kg IV every 8 hours) with an aminoglycoside (amikacin, 20 mg/kg IV, intramuscularly, or subcutaneously every 24 hours once the dog has been rehydrated; used for a maximum of 5 days) will provide effective coverage.[16,51] The possibility does exist, however, that antibiotic therapy may increase the release of endotoxin and exacerbate the systemic inflammatory response.[31] Metronidazole (15–20 mg/kg by mouth every 12 hours for up to 10 days) is indicated in cases where protozoa are found on fecal wet prep.

Lately, more focus has been placed on immunotherapy for puppies suffering from CPV enteritis. The use of recombinant human G-CSF (rhG-CSF) has been investigated in puppies suffering from CPV enteritis with severe leukopenia.[44] To date investigators have not demonstrated benefit in puppies treated with rhG-CSF.[68,69] The ability of recombinant bactericidal/permeability-increasing protein ($rBPI_{21}$) to decrease plasma endotoxin concentration and severity of systemic clinical signs was investigated in CPV enteritis. Current data, however, do not show any benefit with its use.[70] Interferons (IFN) have the ability to modulate several cellular and immune functions, as well as affect virus replication.[71] Despite the lack of canine IFN products, several studies have shown recombinant feline interferon-ω (rFeIFN-ω) to significantly ameliorate severe enteritis caused by CPV and reduce mortality.[71–73] The benefit of oseltamivir, an antiviral drug that inhibits neuraminidase (NA), as a therapeutic agent in CPV was recently investigated. However, CPV does not rely on NA for replication, and the study showed no significant improvement in the days hospitalized or outcome of the patients.[74]

PREVENTION

Effective immunization protocols have been shown to be essential in the prevention of infection in susceptible puppies with CPV. Serum antibody titer is correlated with immunity. In mammals, antibodies are transferred to the neonate through the placenta and colostrum. These maternally derived antibodies play an important role in the protection of the neonate but are also considered one of the most important causes of immunization failures.[17,75] Based on hemagglutination-inhibition (HI) antibody titers, puppies receive approximately 90% of their total maternally derived CPV antibody from colostrum. Despite the low transplacental transfer of antibodies to CPV, the amount is still such that even colostrum-deprived puppies would be refractory to immunization or infection for several weeks. The amount of maternal antibody that puppies receive is proportional to the titer of the dam, and the amount of colostrum available to each puppy is inversely proportional to the size of the litter. Maternally derived antibody titers in puppies declines exponentially with time. The half-life of CPV maternal antibody was reported to be almost 10 days (9.7 days). The amount of maternally derived antibody that interferes with immunization is less than can be detected by the HI method, and the amount of antibody that will block active immunization is less than that necessary to prevent infection with street virus. Recovered animals maintain high antibody titers for at least 16 months after infection.[17]

Attenuated vaccines of canine origin, containing high-titer, low-passage CPV are currently the vaccines of choice. The term high titer refers to the amount of virus in the vaccine dose, and the term low passage refers to the number of times the virus was grown in various tissue cultures. Virus grown by fewer passages retains some of its ability to infect cells but does not cause disease.[2] Complete cross-protection has been reported between CPV-2, CPV-2a, and CPV-2b. The currently accepted vaccination protocol for CPV, based on data generated by vaccine manufacturers and individual researchers, recommends 3 doses of vaccine given at 6, 9, and 12 weeks of age.[75–77] Good protection has also been achieved with the use of a modified live CPV-2b vaccine administered intranasally.[78] Whether annual boosting is needed is controversial. Available data show that 93.7% of vaccinated dogs showed adequate response after more than 2 years following vaccination.[79] Data from dogs that recovered from active infection suggest that immunity following infection is long-lived, perhaps even life-long.[76] Increased risk of immune-mediated disease associated with overvaccination should compel practitioners to base their decision to administer booster annually on serologic results. Skepticism exists on the efficacy of current vaccines as preventive measures for CPV-2c.[80] A recent small study did, however, show cross-protection of 2 modified live vaccines, one containing CPV-2 and the other CPV-2b, against the CPV-2c strain.[81]

Despite the effectiveness of vaccination, good hygienic practices in kennels, including vigilant disinfection of all exposed surfaces and personnel, is extremely important in the prevention of the spread of the disease. Like all parvoviruses, CPV-2 is extremely stable and resistant to adverse environmental influences and can persist on inanimate objects such as clothing, food pans, and cage floors, for 5 months or longer.[6,15,16] Many detergents and disinfectants fail to inactivate canine parvoviruses. Sodium hypochlorite (common household bleach) is an effective viricidal disinfectant if exposure to this disinfectant lasts at least 1 hour.[15]

SUMMARY

Despite ongoing research in CPV enteritis, an agent-specific treatment remains elusive and basic therapeutic principles for gastroenteritis are still applicable. The

identification of several prognosticators has, however, made management of the disease more rewarding. Parvoviral enteritis remains a significant pathogen in canines, especially because of the virus's ability to cause not only local gastrointestinal injury but also a significant systemic inflammatory response. Although effective vaccination has decreased incidence and mortality, the emergence of a new subspecies has led to concern about the efficacy of current vaccination protocols and subsequently about the susceptibility of populations considered to be immune.

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