Canine Parvovirus: Are current vaccines effective against new strains?

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ETIOLOGY

The parvoviruses are small nonenveloped single stranded DNA virus. 3 known to infect dogs:
CPV-1 (minute virus of canines) - uncertain pathogenicity - has been associated with "fading pups" – lethargy, loose stools, respiratory distress, sudden death.
2) Canine adeno-associated virus - apparently non-pathogenic.
3) CPV-2 replicates in dividing cells especially intestinal, lymphoid, bone marrow and fetal tissues and is severely pathogenic. This virus is known simply as canine parvovirus or CPV, and is closely related to feline panleukopenia virus and mink enteritis virus. CPV-2 is a new canine virus appearing about 1977. Current isolates (CPV-2a,b first observed in 1980, 2c reported in Italy in 2000, and widespread in USA and world by 2007) have different antigenic structures, increased pathogenicity, and a shorter incubation period (4-5 days vs 5-8) than CPV-2. These variants also replicate efficiently in cats. MLV vaccines of 2 and 2b protect against 2c.
Of clinical importance are a few features of the virus:-
Parvoviruses- resistant to inactivation; can remain infectious outside the host > 5 months.
Most common detergents and disinfectants fail to inactivate these viruses.
CPV-2 hemagglutinates RBCs from a number of species so hemagglutination assays are useful for diagnosis.

HOST RANGE AND PREDISPOSING FACTORS

Probably all Canidae are susceptible. Within domestic dog populations, Dobermans pinschers, Rottweilers, English Springer Spaniels, and in some studies, American Pit bull terriers and German Shepherds are at higher risk of severe illness.
Intact male dogs seem more predisposed to infection than intact females.
Unvaccinated dogs - about 13 X more likely to become infected than vaccinated dogs.
Concurrent infection with other gastrointestinal pathogens (*Giardia*, hookworms and roundworms, coronavirus) may exacerbate the severity of CPV infection. Stress of overcrowding, poor nutrition, and age at infection can dictate the outcome of infection.

TRANSMISSION

Fecal-oral route. A vast amount of virus is shed in the feces of clinically infected dogs. However, the persistence of virus in the environment is thought to be more important than chronic carriers in perpetuating disease – not clear if carrier state exists?
Active shedding of virus occurs up to the first 2 weeks post inoculation. Generally, dogs that recover from infection do not transmit disease to susceptible kennel mates.

PATHOGENESIS

- After oronasal exposure - primary replication occurs in regional lymph nodes of the pharynx/tonsils followed by plasma-associated viremia (develops even as early as the 1st or 2nd day post-infection (PI) although becomes high 3 to 4 days PI); other lymphoid tissue (thymus, mesenteric nodes, bone marrow) becomes infected by the 3rd day PI; virus can be detected in intestinal epithelial cells by day 4 PI (it is suspected that the virus initially arrives in the GIT by way of plasma or in infected lymphocytes).
- Active excretion of virus in the feces occurs as early as day 3 PI before clinical signs occur.
- Viral fecal shedding increases rapidly to peak at day 4 to 7 PI - coincides with the onset of clinical signs; virus can rarely be found in the feces by 12 to 14 days PI.

CPV-2 depends on dividing cells for replication and cells that become infected die. Thus, cell loss is present in tissues of high multiplication rates – small intestinal crypt cells, lymphatic tissue and bone marrow, and myocardial cells in very young pups.

Myocardial disease.

Age and immunity determine whether CPV infection results in myocardial disease or enteritis.

Cardiac myocyte replication is sufficient enough only to support virus until 2 weeks of age. Although myocarditis is seen in pups at 6 to 8 weeks of age, it is the result of infection several weeks earlier.

Myocardial disease is exceptionally rare in the US these days because most bitches (greater than 85% in one census in 1991 in the USA) are immune and the pups are protected by passive immunity in-utero or during the first weeks of life.

Enteritis.

Commonly seen in pups 6 to 16 weeks of age.

In the intestine, dividing crypts cells are primarily affected, as opposed to the cells at the tip of the villus (as seen in corona virus and rotavirus).

As the enteric cells move up the villus to be lost at the tip they are not replaced from below resulting in the lesion seen in CPV-2 infection.

In severely clinically affected dogs, the crypt cells and lymphoid cells in Peyer's patches are destroyed faster than they can be replaced.

Nearly all signs occur because of crypt cell and lymphoid/bone marrow destruction.

It will take 2 weeks before this damage can be repaired.

Bone Marrow effects.

Of major clinical importance is the effect CPV-2 infection has on bone marrow. CPV-2 infection causes necrolysis of the myeloid and erythroid stem cells in marrow.

Because of the long half-life of RBCs, few effects are seen on RBC indices although anemia may be seen from blood loss from the bowel.

Leukocyte counts reflect both peripheral consumption and myeloid destruction. In severe disease there is progressive reduction in leukocyte numbers from day 3 to 5 PI.

Neutropenia, toxic changes in neutrophils, degenerative left shift and often absolute lymphopenia occurs concurrently with the onset of clinical signs (6 days PI).

In recovery, leukocytosis + left shift often predict a successful treatment outcome.

Recently reported that WBC count > 4.5, lymphocyte count > 1, monocyte count > 0.15, eosinophil count > 0.1 with a left shit are accurate predictors of a good outcome.

Neutrophils: Survivors develop a left shift (usually degenerative): non-survivors don't.

Lymphocytes: Get marked rise in lymphocyte in 1st 24 hrs post-admission in survivors. [more significant than total WBC count]

Monocytes: Quicker production time (3 days compared to 6 days for PMN). So increases in monocytes usually precede those of PMNs.

Eosinophils: Good prognostic indicator when appear especially after 48hrs post-admit.

Neurologic effects.

- Cerebellar hypoplasia (common in kittens infected with feline panleukopenia virus) occurs in dogs (also due to neonatal infection) but is very rare.

CLINICAL SIGNS

Can be extremely variable dependent on age (under 3 months), immunity, co-pathogens (parasites, enteric bacteria, viruses), and infective dose.

Crowding, poor sanitation reduces the chances of successful immunization in kennels but do not enhance disease in individuals.

Signs can vary even within single litters.

Viral dose and antigenic type can influence intensity of illness. Pups infected with CPV-2a or 2b can die acutely even before diarrhea has developed.

Classically:

Depression, **anorexia**, **vomiting**, with or without pyrexia are initial signs.

Dogs vomit repeatedly, sometimes with roundworms in vomitus.

Then **mucoid to then bloody diarrhea** develops. Although many clinicians claim they can "smell" a parvovirus case walk in the door, the character of the vomitus and diarrhea do not distinguish it from other enteritides.

Severe **lymphopenia** even to absolute lymphopenia is common and helps distinguish the disease from other causes of severe diarrhea (Hemorrhagic Gastroenteritis, Salmonellosis).

Neutropenia may also be present.
With diarrhea, severe **dehydration, weight loss, abdominal discomfort and pain** are consistent features.
Dogs may present in endotoxic shock or disseminated intravascular coagulation. These are extremely difficult to save and require 24-hour intensive care.

DIAGNOSIS
Young pups under 16 weeks old, particular breeds affected (Rottweilers, Dobermans, English Springer Spaniels), kennels, acute onset of typical signs with lympho/neutropenia (sometimes absolute).
The progression of leukopenia can help to set a prognosis. When band cells appear in the blood smear, prognosis improves markedly.
Blood chemistry reflects dehydration and electrolyte disturbances (hypokalemia, hypoglycemia).
Virus can be detected in stools for 2-4 days after onset of disease by commercial fecal ELISA tests that appear to be highly specific and sensitive. Blood in the stool may give false negatives due to antibody binding virus in stool.
Again, remember that virus shedding in feces occurs 3-4 days PI, reaching a peak about the time clinical signs first occur, and stops 8-12 days PI.

MANAGEMENT AND TREATMENT
- The most important principle of therapy is to address the tremendous fluid loss associated with diarrhea and vomiting, and prevent secondary bacterial infections.

Replace fluid loss. First, assess dehydration. Dehydration less than 5% is difficult to appreciate clinically. Most dogs with diarrhea and vomiting from CPV infection are 8 to 10% dehydrated as indicated by **sunken eyes** in orbits, **prolonged capillary refill time**, **dry mucous membranes**, **signs of shock** (increased heart rate, weak pulses), **skin tenting**. Simple laboratory tests help: A **PCV** and **Total Plasma Protein** are useful but will be also affected by blood loss (diarrhea). **Urinalysis** should show markedly concentrated urine (> 1.030). It is essential to realize that little or no change can occur in laboratory values in severely dehydrated animals**. Estimate fluid volume to be replaced** (% dehydration X body weight in Kg = liters of fluid to replace). Also add in estimated **ongoing losses** (diarrhea and vomiting) as well as "**normal" (insensible and sensible) losses** (about 15ml/kg/day). Use a balanced fluid, such as Lactated ringers, Plasma-Lyte, Normosol, or 0.9% sodium chloride supplemented with dextrose and potassium. Fluids containing dextrose is usually indicated especially in small puppies (Chihuahuas), and may need to be preceded by a bolus in some cases.

Route of administration. If can, **always** administer fluids to CPV-infected dogs by the IV route. Avoid the subcutaneous route especially in leukopenia animals as can introduce infections. Avoid oral route at least until 24 hours after vomiting has stopped and preferably after diarrhea has stopped.

Replace electrolytes - hypokalemia is not always present but whole body depletion of potassium will occur during the illness due to no oral intake, increased loss in feces, and renal loss. Put in IV fluids not to exceed 0.5 mEq/kg/hr. Use Scott's table to calculate how much K to add. However, generally 20 to 30 mEq/L can be added to fluids. Dogs with severe and persistent diarrhea can suffer from hyponatremia and hypochloremia which will be replaced with balanced fluids.

- Correct acid-based abnormalities. Dogs may be acidemic (due to dehydration and bicarbonate loss and diarrhea if not much vomiting) or alkalotic (loss of gastric acid from vomiting), but rapid IV fluids will usually replace deficit. There is no need to use bicarbonate or ammonium chloride to off set acid-base abnormalities.

Prevent secondary bacterial infection. Use broad spectrum antibiotics against enteric bacteria, especially in leukopenic animals. Enteric *Clostridium perfringens* frequently proliferates in dogs with CPV. Cephalosporins, enrofloxicins, or combinations such as IV ampicillin and gentamicin (NOTE: probably best combination **but** do not give gentamicin to dehydrated dogs unless can monitor urine and BUN). In less severe cases, oral metronidazole has been used. Be aware however that CPV-infected dogs with CPV on extended antibiotic therapy have developed oral and intestinal candidiasis.

Prevent further fluid loss. Antiemetics (not anticholinergic drugs) - metoclopramide and prochlorperazine are most effective in the recovering dog that persists in vomiting. Do not use too early as mask clinical signs. Serotonin receptor antagonists (ondansetron and dolastron) are also very effective. Gut motility modifiers (dephenoxylate or loperamide) are rarely ever needed.

Oral gastric protectants. Once vomiting has stopped carafate and famotidine and even Peptibismol may be indicated.

Withhold food? In fact, the earlier dogs with clinical parvovirus are fed (even by using enteral feeding tubes), the quicker is their recovery and the better they maintain their body weight.

Parenteral nutrition - intravenously. Risk of systemic infection is very high. Only give during the recovery stage when the leukogram is normalizing.

Corticosteroids? Only in severe shock and only one dose. Use is highly questionable.

Non-steroid anti-inflammatory agents (flunixin meglumine) - rarely indicated. Some advocate giving with fluids at 1mg/kg.

Granulocyte colony-stimulating factor. When administered to neutropenic pups with CPV enteritis, it did not change any aspect of clinical outcome.

Recombinant feline interferon-omega. When given (1 mega units/kg/day, IV, for 3 days) to 3-4 mth-old beagles 4 days after experimental infection, the severity of enteritis was improved in some of the dogs.

BPI protein. A recombinant bactericidal-permeability-increasing protein which counteracts endotoxin – not shown to alter the clinical outcome or survival at all, even when plasma endotoxin levels increase in treated animals.

Blood/plasma. Indicated if severe hypoproteinemia. Usually short-lived but may save the dogs life. The administration of antiendotoxin hyperimmune plasma has been shown in one study to decrease both mortality and the length of hospitalization in dogs with CPV enteritis. Hyperimmune serum or immunoglobulin has been tried but few controlled studies have been conducted. In these studies, it has been difficult to separate the beneficial effects of protein as opposed to immunoglobin that binds virus or endotoxins.

Monitor closely: clinical signs (palpate the abdomen daily), dehydration (PCV, TP, urine SpG, body weight), electrolytes (K, Na), renal function (BUN/creatinine), glucose, blood smear for WBC numbers.

Try to avoid doing surgery on recovering dogs as they are at great risk of post-operative wound break down and infections.

CLIENT EDUCAION

Disinfect premises (1:30 solution of 5% sodium hypochlorite is effective in a few minutes). Strict sanitation, isolate pups till reach 3 months of age.

Carrier state has not been demonstrated in the dog. CPV-2 is shed for less than 2 weeks after infection.

Vaccination schedule is essential in at-risk populations.

Even though apparent break down in vaccine efficacy against CPV-2c virus has been reported in a kennel of dogs from Italy, experimental evidence suggests that current vaccines against CPV-2b (MLV vaccine Galaxy DA2PPv; Schering-Plough Animal Health), and CPV-2 (MLV vaccine Continuum DAP, Intervet) protect against CPV-2c. Similar findings from UK.

References

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