

PATHOLOGY: COMMON SHELTER DISEASES

(from AFIP Veterinary Pathology <http://www.afip.org/>)

Canine Distemper Virus (CDV)

General Discussion:

- Canine distemper is an important, ubiquitous infectious disease of dogs, other canidae, wild felidae, mustelidae, and pinnipeds worldwide.
- CDV belongs to the genus *Morbillivirus* in the *Paramyxoviridae* family.
- One recognized serotype; variable strain pathogenicity and tissue tropism
- Closely related to [Rinderpest](#), [peste des petits ruminants](#), [measles](#), and phocine distemper viruses
- Negative-sense, single-stranded, enveloped RNA virus 150-300 nm in diameter
- Pantropic; epitheliotropic
- Natural transmission is usually by inhalation, and the virus is shed in all excretions during the systemic phase of infection.
- **Toxoplasmosis**, [neosporosis](#), coccidiosis, viral enteritis, cryptosporidiosis, giardiasis and [canine adenovirus type 2](#) are **common sequelae to the immunosuppressive effects of CDV.**

Pathogenesis:

- Inhalation > virus replication in tonsils and bronchial lymph nodes > cell associated viremia 2 days PI > spread to all lymphoreticular tissues and blood lymphocytes one week PI > lymphocytolysis and leukopenia > immunosuppression > dissemination to respiratory, GI, urinary, and central nervous systems; skin, endocrine and exocrine glands also affected > secondary infections common, especially *Bordetella bronchiseptica* and *Toxoplasma gondii*

Typical Clinical Signs:

- Biphasic fever, depression, anorexia, lymphopenia, serous to mucopurulent oculonasal discharge, pharyngitis, coughing, vomiting, diarrhea, hyperkeratosis of foot pads and nose, enamel hypoplasia, nervous signs

Additional Diagnostic Tests:

- CDV antigens demonstrated with immunoperoxidase technique
- CDV in epithelial cells by fluorescent antibody test or by virus isolation

Typical Gross Observations:

- Respiratory system:
- Thick, foamy serous to mucopurulent hemorrhagic exudate in the airways
- Edematous and/or consolidated lungs, interstitial pneumonia, and serous pleural effusion
- Lymphoid system: Tonsillar enlargement, thymus atrophy
- Mucopurulent oculonasal discharge
- Hyperkeratosis of the nose and footpad ("hardpad disease")

Canine Parvovirus-2 (CPV-2)

General Discussion:

- Family Parvoviridae: Small (18-26 nm), unenveloped, icosahedral, single-stranded DNA viruses.
- Thought to be a mutation of feline panleukopenia virus.
- Several antigenically different serotypes:
- CPV-1 (minute virus)
- CPV-2, CPV-2a, and CPV-2b
- Replicate in the nucleus of cycling cells (S phase - early G2); therefore, they have a predilection for fetal tissues, bone marrow, lymphoid tissue, and intestinal crypts; produce large intranuclear inclusion bodies.
- Stable in environment and very resistant to disinfection.
- Three forms of disease:
- Enteric form: Most common. Dogs of all ages, most severe in 1-6 month old.
- Cardiac form: Puppies 2-8 weeks.
- Neurologic form

- Myocardial and enteric forms rarely occur together.
- Maternal antibody interference at immunization can cause vaccine breaks.

Pathogenesis:

- Oronasal exposure > uptake of virus by epithelium over tonsils and Peyer's patches > infection of draining lymphoid tissue (1-2 days) > dissemination of infected lymphoblasts > infection of other central and peripheral lymphoid tissues (3-4 days) > lymphocytolysis releases virus, causing viremia > neutralizing antibody appears in circulation, terminating viremia (5-7 days) > Infection of gastrointestinal crypt epithelium and Peyer's patches (5-9 days).
- Occurrence and severity of gastrointestinal signs determined by extent of damage to epithelium in intestinal crypts. Influenced by:
 - Availability of virus (correlated with rate of lymphocyte proliferation and lysis - as more lymphocytes lyse, more virions into the circulation).
 - Rate of cellular proliferation in the crypts of Lieberkuhn: The more cells in S or early G2 phase, the faster the virus can replicate and lyse the enterocytes. Can cause villous atrophy and mucosal erosion/ulceration.
- If the animal survives the acute phase and the crypts have enough undamaged stem cells, regeneration will occur, and the animal can survive.
- Cytolysis of proliferating cells in the bone marrow causes myeloid and erythroid hypoplasia. Megakaryocytes are the least sensitive to lysis.
- Circulating neutropenia is due to failure of recruitment of neutrophils from the damaged marrow, and increased utilization by the small intestine. Transient neutropenia is more common in cats with panleukopenia.
- Lymphopenia results from viral lymphocytolysis in all infected lymphoid tissues. More common in dogs than neutropenia. If animal survives, lymphocytes can be replenished in 2-5 days.

Typical Clinical Signs:

Depression, anorexia, vomiting, dehydration, lethargy, moderate to severe pyrexia, and bloody diarrhea.

Leukopenia, with relative or absolute lymphopenia, hypoproteinemia, and anemia.

Additional Diagnostic Tests:

- Demonstration of virus in feces (PCR)
- In-situ hybridization (for exact localization of virus).

Typical Gross Observations:

- Enteric Form:
 - Segmental to diffuse subserosal hemorrhage in small intestines (+/- colon and stomach).
 - Superficial fibrinous serosal effusion of intestines.
 - Peyer's patches may be dark red. Mucosa is deeply congested, with fibrinous exudate.
 - Mesenteric lymph nodes may be enlarged, congested, and wet.
- Myocardial form:
 - Lungs are wet and heavy with white frothy fluid in trachea and bronchi.
 - Cardiomegaly, with pale streaks and dilated ventricles.
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Differential Diagnosis:

- [Coronavirus](#): Usually self-limiting enteritis, no prominent epithelial or lymphoid necrosis, no leukopenia, affects villus tips.
- [Rotavirus](#): Similar to coronavirus.
- Canine morbillivirus (distemper): Can cause crypt necrosis, gastrointestinal lymphoid involution.
- *Clostridium perfringens* (Canine intestinal hemorrhage syndrome): Often associated with parvovirus infections.
- Intoxication (heavy metals, Warfarin): History, serum chemistry, clotting panel.
- Radiation: Similar lesions to parvovirus, history.

Feline Infectious Peritonitis (FIP)

General Discussion:

- Family *Coronaviridae* - genus - Coronavirus - enveloped, single stranded, positive sense RNA viruses

- [Feline infectious peritonitis \(FIP\)](#) is a worldwide, invariably fatal, sporadic, low prevalence viral disease of domestic and wild felids caused by feline coronavirus. (FCoV).
- Generally, most affected cats are less than two to three years of age and live in multiple-cat situations (shelters, breeding catteries, etc.). Purebred domestic cats and certain species of large cats (e.g. cheetahs) may be genetically predisposed to developing FIP.
- There are two strains of FCoV: feline infectious peritonitis virus (FIPV) and feline enteric virus coronavirus (FECV). It is reported that FIPV is a mutation of FECV that has acquired macrophage tropism.
- FECV infects and replicates only in enterocytes, causing diarrhea or asymptomatic infection; FIPV infects and replicates primarily in macrophages, resulting in systemic infection and FIP.
- There are three clinical forms of FIP: effusive (wet), noneffusive (dry), and a form combining features of both.

Pathogenesis:

- Transmission - **direct (ingestion or inhalation of virus)**, indirect (fomites), transplacental (reported, but uncommon).
- Initially, FIPV replicates in the tonsils or gut > regional lymph nodes > viremia > macrophage infection > widespread dissemination
- Virus is primarily shed in feces, however, early in the infection, virus may also be found in saliva and possibly respiratory secretions and urine. Some cats may shed virus continuously (persistent carriers) or intermittently for prolonged periods of time.
- **The disease is antibody-mediated and complement-dependent.** The clinical outcome is dependent on the levels of cellular and humoral immunity within the host.
 - If **strong** cell-mediated immune (CMI) response > macrophages activated > FIPV replication terminated > no disease
 - If **weak CMI response** > allows FIPV to persist in macrophages > more **prolonged course of disease (1-6 months)**. Local release of cytokines and inflammatory mediators > perivascular pyogranulomas in parenchymatous organs (**non-effusive form**).

- If no CMI response > continuous virus replication and production of non-neutralizing antibodies > **short clinical course** > death in 1-12 weeks. Virus-laden macrophages accumulate around vessels and in interstitium of serous surfaces and tissues throughout body > formation and **deposition of immune complexes in vessel walls** > activation of the complement sequence and generation of chemotactic factors > influx of neutrophils and increased vascular permeability (**vasculitis**) > protein rich pleural and peritoneal effusion (**effusive form**)

Typical Clinical Signs:

- Effusive form - This is the more acute form but can occur in terminal stages of noneffusive FIP. Signs include depression, inappetence, weight loss, dyspnea, tachypnea, and thoracic and/or abdominal effusion (ascites).
- Non-effusive form - This is the more chronic form. Signs may be vague and include weight loss, fever, depression, and signs specific to particular organs affected by vascular lesions (e.g. ocular disease, central nervous disorders, renal failure, hepatic or pancreatic insufficiency).
- Leukocytosis (neutrophilia with left shift), nonregenerative anemia, increased total serum protein, polyclonal hypergammaglobulinemia
- Albumin:globulin ratio (A:G) - decreased; Albumin - normal or slightly Decreased; Globulin markedly increased (d/t IL -6 stimulating B cells).
- The effusion is a modified transudate with a very high protein content (>3.5 g/dl). The fluid is usually viscous, clear (may be flocculent because of fibrin strands), straw-colored to deep yellow, and foams on shaking because of high protein content.

Additional Diagnostic Tests:

- There is no single definitive diagnostic test for FIP because many organ systems may be involved. Histopathology is confirmatory.
- **Serologic tests** (indirect immunofluorescence) may aid in diagnosis but can be **difficult to interpret** and should be used in conjunction with other parameters (e.g. history, clinical signs, bloodwork, examination of the effusion, and virus genetic detection).

- Many cats (healthy and otherwise) are seropositive.
- False positive results can occur because of cross-reaction with feline enteric coronavirus or coronaviruses of other species (e.g. transmissible gastroenteritis virus of swine).
- Virus detection tests include:
 - RT-PCR (reverse transcriptase polymerase chain reaction)
 - Direct FA-
 - Immunohistochemistry
 - Electron microscopy

Typical Gross Observations:

- **Pyogranuloma** - This is the characteristic lesion associated with FIP. Peritoneum, kidney and uvea are the most commonly affected.
- **Effusive form** - The surfaces of abdominal and/or thoracic contents covered with small (1-2 mm) white plaques of fibrin with a granular appearance. Large amounts of fibrin can result in adhesions on visceral and peritoneal surfaces.
- Pleural effusion (40%) and effusive peritonitis (60-70%)
- Orchitis and periorchitis (reported, but uncommon) - scrotal swelling and enlarged testicles
- **Noneffusive form** - Granulomas in various organs (on surface and throughout)
- Colon - thickened - gross appearance similar to alimentary lymphosarcoma
- Abdominal and thoracic lymph nodes - lymphadenopathy
- Kidneys - enlarged with pyogranulomas
- Brain - hydrocephalus possible in cats with neurologic involvement

Feline Calicivirus

General Discussion:

- Small (35 to 40 nm), non-enveloped, single-stranded RNA virus
- Epitheliotropic, replicates in the cytoplasm
- Relatively resistant to heat and lipid solvents, intermediate pH stability
- Worldwide distribution. Many subtypes with varying degrees of cross reactivity
- The virus is transmitted by direct contact or via infected fomites. Persistently infected carrier state occurs in recovered cats.
- **Pneumotropic** form affects upper respiratory tract, occasionally producing pneumonia. The less common **rheumatic** form, "limping kitten syndrome", causes joint pain and lameness. Difference in manifestation is not related to identifiable differences in virus subtype.
- Virulent Systemic form affects skin, lungs, pancreas, liver, mortality ~40-50%

Pathogenesis:

- Virus ingested or inhaled > Replication in oropharyngeal tissues leading to degeneration and necrosis of cells; principal **target cells are the squamous epithelial cells** of the tongue, pharynx, tonsil, and alveoli > Local inflammation with neutrophils, hemorrhage and edema causing vesicle formation > Rupture of vesicles releasing large amounts of infective virus into the environment > Occasional spread to lungs either directly or due to viremia
- Excretion of FCV in oropharyngeal fluids of cats usually persists for 10 to 14 days.

- The site of chronic infection appears to be the tonsils and associated pharyngeal mucosa.

Typical Clinical Signs:

- Fever, anorexia, mucosal vesicles and ulceration affecting the tongue, hard palate, nasal philtrum, lip, or periodontal gingiva, rhinitis, conjunctivitis, and occasionally patchy pneumonia
- Death due to FCV infection is uncommon and is associated with pneumonia chiefly in kittens in catteries or colonies where large infective doses of virus are generated.
- An acute febrile lameness syndrome has been recognized, which may be accompanied by respiratory signs and is characterized by fever, malaise, joint swelling and pain, muscle soreness, hyperesthesia and limping in post-weaning kittens. The pathogenesis of this syndrome is unknown.

Additional Diagnostic Tests:

PCR and virus isolation from oropharyngeal fluids, oral swabbing of the tonsils, urine, feces, blood, and visceral tissues

Typical Gross Observations:

Field strains: oral ulceration

Respiratory form: Pneumonia involves the cranioventral margins of the lungs and other irregular foci. Early lesions are bright red, turning more gray-red at the peak of consolidation (7 to 10 days), then gray-tan as resolution occurs.

Virulent Systemic FCV- ulceration of footpads, oral cavity, pinnae, severe facial and limb edema, variable respiratory and other visceral necrosis (pancreas, liver, GI)

Differential Diagnosis:

- [Feline rhinotracheitis virus \(feline herpesvirus type 1\)](#): usually a more severe disease characterized by purulent oculonasal discharge and corneal ulceration
- Chlamydia psittaci: conjunctivitis and upper respiratory tract disease