



Canine Diseases

Infectious Canine Hepatitis

Infectious canine hepatitis (ICH) is a worldwide, contagious disease of dogs with signs that vary from a slight fever and congestion of the mucous membranes to severe depression, marked leukopenia, and coagulation disorders. It also is seen in foxes, wolves, coyotes, bears, lynx, and some pinnipeds; other carnivores may become infected without developing clinical illness. In recent years, the disease has become uncommon in areas where routine immunization is done, but periodic outbreaks, which may reflect maintenance of the disease in wild and feral hosts, reinforce the need for continued vaccination.

Etiology and Pathogenesis

ICH is caused by a nonenveloped DNA virus, canine adenovirus 1 (CAV-1), which is antigenically related only to CAV-2 (one of the causes of infectious canine tracheobronchitis). CAV-1 is resistant to lipid solvents (such as ether), as well as to acid and formalin. It survives outside the host for weeks or months, but a 1%–3% solution of sodium hypochlorite (household bleach) is an effective disinfectant.

Ingestion of urine, feces, or saliva of infected dogs is the main route of infection. Recovered dogs shed virus in their urine for ≥ 6 mo. Initial infection occurs in the tonsillar crypts and Peyer's patches, followed by viremia and disseminated infection. Vascular endothelial cells are the primary target, with hepatic and renal parenchyma, spleen, and lungs becoming infected as well. Chronic kidney lesions and corneal clouding ("blue eye") result from immune-complex reactions after recovery from acute or subclinical disease.

Clinical and Pathological Findings

Signs vary from a slight fever to death. The mortality rate ranges from 10%–30% and is typically highest in very young dogs. Concurrent parvoviral or distemper infection worsens the prognosis. The incubation period is 4–9 days. The first sign is a fever of $>104^{\circ}\text{F}$ (40°C), which lasts 1–6 days and is usually biphasic. If the fever is of short duration, leukopenia may be the only other sign, but if it persists for >1 day, acute illness develops.

Signs are apathy, anorexia, thirst, conjunctivitis, serous discharge from the eyes and nose, and occasionally abdominal pain and vomiting. Intense hyperemia or petechiae of the oral mucosa, as well as enlarged tonsils, may be seen. Tachycardia out of proportion to the fever may occur. There may be subcutaneous edema of the head, neck, and trunk. Despite hepatic involvement, there is a notable absence of icterus in most acute clinical cases.

Clotting time is directly correlated with the severity of illness and is the result of disseminated intravascular coagulation induced by vascular endothelial compromise, coupled with failure of the liver to rapidly replace consumed clotting factors. It may be difficult to control hemorrhage, which is manifest by bleeding around deciduous teeth and by spontaneous hematomas. CNS involvement is unusual and is typically the result of vascular injury. Severely infected dogs may develop convulsions from forebrain damage. Paresis may result from brain stem hemorrhages, and ataxia and central blindness have also been described.

Clinicopathologic findings reflect the coagulopathy (prolonged prothrombin time, thrombocytopenia, and increased fibrin degradation products). Severely affected dogs show acute hepatocellular injury (increased ALT and AST). Proteinuria is common. Leukopenia typically persists throughout the febrile period. The degree of leukopenia varies and seems to be correlated with the severity of illness.

On recovery, dogs eat well but regain weight slowly. Hepatic transaminase activities peak around day 14 of infection and then decline slowly. In ~25% of recovered dogs, bilateral corneal opacity develops 7–10 days after acute signs disappear and usually resolves spontaneously. In mild cases, transient corneal opacity may be the only sign of disease.

Endothelial damage results in “paint-brush” hemorrhages on the gastric serosa, lymph nodes, thymus, pancreas, and subcutaneous tissues. Hepatic cell necrosis produces a variegated color change in the liver, which may be normal in size or swollen. Histologically, there is centrilobular necrosis, with neutrophilic and monocytic infiltration, and hepatocellular intranuclear inclusions. The gallbladder wall is typically edematous and thickened; edema of the thymus may be found. Grayish white foci may be seen in the kidney cortex.

Diagnosis

Usually, the abrupt onset of illness and bleeding suggest ICH, although clinical evidence is not always sufficient to differentiate ICH from distemper (see Canine Distemper). Definitive antemortem diagnosis is not required before institution of supportive care but can be pursued with commercially available ELISA, serologic, and PCR testing. PCR or restriction fragment length polymorphism is required to definitively distinguish CAV-1 from CAV-2, if clinically necessary. Postmortem gross changes in the liver and gallbladder are more conclusive, and diagnosis is confirmed by virus isolation, immunofluorescence, characteristic intranuclear inclusion bodies in the liver, or PCR or fluorescence in situ hybridization studies of infected tissue.