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Canine hepatozoonosis is a tick-borne disease caused by apicomplexan protozoa. In contrast to most tick-borne pathogens that are transmitted via the tick salivary glands, *Hepatozoon* infects dogs by ingestion of ticks containing infective sporozoites. Two different species of *Hepatozoon* infect dogs, *H. canis* in the Old World and South America, and *H. americanum* in the southern USA. Clinically, *H. canis* infection (HCI) varies between being asymptomatic in dogs with a low parasitaemia, to a severe disease with anemia, profound lethargy and cachexia in dogs with a large number of circulating parasites. *H. americanum* infection (HAI) is manifested mainly by gait abnormalities and musculoskeletal pain due to myositis and periosteal bone lesions. HAI is an emerging disease that is spreading north and east from Texas where it was originally detected in 1978. It has since been reported also from Louisiana, Alabama, Oklahoma, Georgia, Tennessee, and Florida.

The main vector of *H. canis* is the brown dog tick *Rhipicephalus sanguineus* which is found in warm and temperate regions all over the world, making the potential distribution of *H. canis* wide. In addition, a recent study has indicated that *H. canis* in Brazil can be transmitted to dogs by the tick *Amblyomma ovale*. The Gulf Coast tick *Amblyomma maculatum* is the vector of *H. americanum* in North America. *A. maculatum*’s distribution appears to be limited to some parts of America therefore possibly restricting the spread of *H. americanum*. Both of the *Hepatozoon* species that infect dogs are transmitted transstadially from the nymph to the adult stage, in their tick vectors.

**Pathogenesis**

*Hepatozoon* sporozoites release from the oocysts after their ingestion in the dog’s intestine and penetrate the gut wall. The sporozoites invade mononuclear cells and disseminate hematogenously or via the lymph to target organs. Merogony occurs in the dog’s parenchymal tissues and is followed by gamontogony in leukocytes. The tick, which serves as the definitive host, becomes infected when feeding on a parasitemic dog. *Hepatozoon* gamonts release from the dog leukocytes within the tick gut and gametogenesis takes place followed by fertilization and sporogony with the formation of oocysts in the tick’s hemocoel.

*Hepatozoon canis* mainly infects the hemolymphatic tissues and blood-forming organs including the bone marrow, lymph nodes and spleen. *H. americanum* primarily infects skeletal and cardiac muscular tissues and causes myositis and severe lameness. *H. canis* appears to be well adapted to its canine host, and is often detected in necropsy or on a peripheral blood smear as an incidental finding. *H. americanum* induces a violent course of disease in experimentally and naturally occurring infection. It may have
recently crossed the species barrier from the coyote or another wild mammalian host to the domestic dog.

Clinical and laboratory findings

HCl varies from being asymptomatic in apparently healthy dogs to a severe and life-threatening disease in animals with extreme lethargy, cachexia and anemia. An asymptomatic to mild disease is the most common presentation of the infection and it is usually associated with a low level of *H. canis* parasitemia (1-5 %), while a severe illness is found in dogs with a high parasitemia often approaching 100% of the peripheral blood neutrophils. High parasitemia rates are sometimes accompanied by extreme neutrophilia reaching as high as 150,000 leukocytes/µl blood. A seroepidemiological study of HCl in Israel revealed that 33% of the dogs surveyed had been exposed to the parasite as indicated by the presence of anti-*H.canis* antibodies. Only 3% of the seropositive dogs had detectable blood gamonts and only 1% had severe clinical signs associated with the infection. A case-control study of dogs admitted to a veterinary hospital in Israel with *H. canis* parasitemia indicated that 15% had a high number of circulating parasites (> 800 gamonts/µl) accompanied by elevated body temperature, lethargy, weight loss, anemia and hyperglobulinemia. Post-mortem findings from some of the dogs with a high parasitemia revealed hepatitis, pneumonia and glomerulonephritis associated with *H. canis* meronts. Meronts of *H. canis* were also found in the spleen, bone marrow and lymph nodes.

Concurrent HCl and infection with other canine pathogens is common. Co-infections with *H. canis* reported include: parvovirus, *Ehrlichia canis*, *Toxoplasma gondii* and *Leishmania infantum*. Immune suppression induced by an infectious agent, an immature immune system in young animals or immunodeficient conditions, influence the pathogenesis of new *H. canis* infections or the reactivation of pre-existing ones. Treatment with an immunosuppressive dose of prednisolone was followed by the appearance of *H. canis* parasitemia in dogs with experimental HC.

In contrast to the generally mild disease found in HCl, HAI is almost always a severe disease that leads to debilitation and death. Most dogs diagnosed with HAI are presented with fever, gait abnormalities, muscular pain induced by myositis, generalized muscular atrophy and mucopurulent ocular discharge. The pain can be generalized or localized in the lumbar and cervical spine, or joints. Gait abnormalities include stiffness, hind limb paresis, ataxia and inability to rise. A marked neutrophilia is one of the consistent hematoletic findings in HAI. Leukocyte counts range from 30,000 to 200,000/µl blood. Serum biochemical abnormalities include increased alkaline phosphatase activity and hypoalbuminemia.

Diagnosis

1. Microscopy
   
   HCl is usually diagnosed by microscopic detection of intracellular *H. canis* gamonts in stained blood smears. The gamonts are found in the cytoplasm of
neutrophils or monocytes, have an ellipsoidal shape and are about 11 by 4 micrometers. *H. canis* meronts found in infected tissues by histopathology contain elongated micromerozoites arranged in a circle around a clear central core. This form is often referred to as a “wheel spoke” meront.

*H. americanum* parasitemia is rare and usually does not exceed 0.1% of the leukocytes. Confirmation of HAI is commonly carried out by muscle biopsy and demonstration of parasites in cysts or granulomas. Histopathology of skeletal muscles from dogs with HAI reveals pyogranulomatous myositis and large round to oval cysts (250-500 micrometer diameter) containing a central nucleus surrounded by concentric rings of membranes. These cysts are sometimes referred to as having an “onion peel” appearance due to the structure of the membranes surrounding a core mass. Radiography of the long bones or pelvis demonstrating periosteal proliferation can be used for screening suspected animals.

### 2. Serology

An indirect fluorescent antibody test (IFAT) for anti-*H. canis* antibodies was used for epidemiological studies in Israel and Japan. An ELISA for *H. canis* antibodies has also been developed and used for studies in Israel and Greece. A serological test for HAI using sporozoite antigen derived from ticks has been developed for the detection of anti-*H. americanum* antibodies. This assay was found to be as sensitive as the muscle biopsy for the diagnosis of HAI.

### 3. PCR

PCR for *H. canis* in blood has been shown to be a sensitive diagnostic technique. A study from Turkey demonstrated that detection of hepatozoonosis by PCR is by far more sensitive than light microscopy of blood. The prevalence of hepatozoonosis among 349 dogs was 10.6% by blood smear evaluation and 25.8% by blood PCR.

### Feline hepatozoonosis

Hepatozoonosis of domestic cats has been reported from several countries including: India, South Africa, Nigeria, the USA, Brazil, Israel and France. The species of *Hepatozoon* that infect cats has not been definitely identified and it is currently unknown if only a single species is found in cats and whether it is similar to species described in other animals. The vectors of feline hepatozoonosis are also not known. Feline hepatozoonosis is associated with infection of muscle tissues. *Hepatozoon* meronts have been identified in the myocardium and skeletal muscles of cats with hepatozoonosis, and elevated activities of the muscle enzyme CK were found in the majority of cats with hepatozoonosis in a retrospective study of this disease. The level of parasitaemia is usually low in cats with less than 1% of the neutrophils containing gamonts.

### Treatment and prevention
HCl is treated with imidocarb dipropionate at 5-6 mg/kg every 14 days until gamonts are no longer present in blood smears. Oral doxycycline at 10 mg/kg/day for 21 days may also be used in combination with imidocarb dipropionate for treatment of HCl. Elimination of H. canis gamonts from the peripheral blood may require 8 weeks. HAI is treated with a combination oral therapy of trimethoprim/sulfa (15 mg/kg every 12 hours), pyrimethamine (0.25 mg/kg every 24 hours), and clindamycin (10 mg/kg every 8 hours). After remission from clinical signs is obtained, it can be prolonged with the oral administration of the coccidiostat decoquinate at 10-20 mg/kg mixed in the food every 12 hours. Relapse of clinical signs is common following the discontinuation of treatment. Supportive therapy with non-steroidal anti-inflammatory drugs is effective in relieving pain and fever in dogs with HAI. Prevention of exposure of dogs to ticks by the use of acaricides is warranted to control the spread of both forms of canine hepatozoonosis.

References


