

Feline Liver Disease & Management of Inappetence in Cats

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In North America, hepatic lipidosis (50%), inflammatory liver disease (25%), malignant lymphoma (5%), and carcinoma (4%) are the major causes of feline liver disease. Less common feline hepatic disorders include portal vascular anomalies, necrosis, bile duct obstruction, ductal plate malformations and cysts.

Cholangitis describes inflammation of the biliary ducts, and when the inflammation extends into hepatic parenchyma, a diagnosis of cholangiohepatitis is made. The most common type of cholangitis in cats is neutrophilic cholangitis (NC), characterized by infiltration of large numbers of neutrophils into portal areas of the liver and bile ducts. It is believed to result from bacterial infection ascending from the intestine, which is supported by finding common enteric species, including *Escherichia coli*, *Streptococcus* spp., *Clostridium* spp. and *Salmonella typhimurium*. Neutrophilic cholangitis can be further divided into acute and chronic forms that are distinguished by their histopathological appearance.

Lymphocytic cholangitis is another common form liver disease and tends to be more chronic and progressive than the neutrophilic form. This is an immune-mediated disease, causing an infiltration of a different type of white blood cells (lymphocytes) without an underlying infection in the liver or gall bladder. Lymphocytic cholangitis can also occur in cats of any age, breed or sex. Clinical signs associated with inflammatory liver diseases are variable and nonspecific and are frequently similar to those associated with hepatic lipidosis. Partial or complete anorexia is the most common, and sometimes the only, clinical sign. Other less frequently observed clinical signs include weight loss, depression, vomiting, diarrhea, and fever.

Hematology and serum biochemistry will show changes in cats with cholangitis, with neutrophilic cholangitis these include mild to moderate neutrophilia and left shift, normal to slight increase in serum bilirubin and serum alkaline phosphatase (ALP) and a substantial increase in alanine aminotransferase (ALT). This profile tends to differentiate neutrophilic cholangitis from lymphocytic cholangitis, hepatic lipidosis, and hepatic neoplasia. Laboratory changes typical of lymphocytic cholangitis include substantial increases in serum bilirubin, ALP and ALT. Other associated changes may include mild nonregenerative anemia, hyperglobulinemia, lymphocytosis, and hyperglycemia. When cats with inflammatory liver diseases are compared to hepatic lipidosis, hepatic lipidosis cases tend to have higher total bilirubin concentrations, and higher ALT and ALP. Although there are trends that differentiate inflammatory liver diseases from hepatic lipidosis and hepatic neoplasia, liver cytology or histopathology is essential to establish a definitive diagnosis. When the clinical chemistry profile reveals evidence of liver disease, hyperthyroidism should be ruled out. Hyperthyroid cats frequently have changes in ALT and ALP that may be indistinguishable from those associated with inflammatory liver diseases. The increased enzyme concentrations normalize with treatment of hyperthyroidism.

Abdominal ultrasonography is often helpful in evaluation of extrahepatic disorders associated with cholangitis. Most cats with neutrophilic or lymphocytic cholangitis or with lymphocytic portal hepatitis have variable or no detectable alterations in the echogenicity of the hepatic parenchyma. On the other hand, most cats with hepatic lipidosis have hyperechoic hepatic parenchyma. Bile duct abnormalities may be observed in cholangitis. These abnormalities include gall bladder and/or common bile duct distention, cholelithiasis, cholecystitis, and bile sludge. Liver cytology or tissue biopsy is essential in differentiating inflammatory liver diseases from hepatic lipidosis and neoplasia. The diagnostic utility of liver cytology is not helpful for some diseases. Cytologic evaluation is useful in identifying hepatic lipidosis and hepatic lymphoma, however, inflammatory liver diseases are more difficult to identify cytologically. Neutrophilic cholangitis can be diagnosed by cholecystocentesis and cytological evaluation as well as aerobic and anaerobic culture of the

bile. For diagnosis of lymphocytic cholangitis and ductal plate malformations, a liver biopsy needs to be performed; this can be done by laparoscopy or open abdominal surgery.

The therapy for neutrophilic cholangitis is antibiotics. Bacterial culture and sensitivity testing of bile, liver aspirate or biopsy specimens, choleliths, or gall bladder specimens, should be used to select appropriate antimicrobial agents whenever possible. Antibiotics chosen for treatment of cholangiohepatitis should be excreted in the bile in active form, and should be active against aerobic and anaerobic intestinal coliforms. Amoxicillin combined with clavulanic acid or fluoroquinolones to extend the spectrum to anaerobes and more coliforms are often used.

Cats with lymphocytic cholangitis typically require immunomodulatory therapy. An immunosuppressive dose of prednisolone (1.5-2mg/kg q24h) should be used initially. The dosage is slowly tapered to least effective dose for long term maintenance. Chlorambucil or cyclosporine can also be used as an immunomodulator (combined with prednisolone) but infectious causes should be ruled out before immunosuppression. Ursodeoxycholic acid can be used in cats with all types of inflammatory liver disease. It has anti-inflammatory, immunomodulatory, and antifibrotic properties as well as increasing fluidity of biliary secretions. Ursodeoxycholic acid has safely been administered to cats at a dose of 10 to 15 mg/kg q24h PO. Adverse effects in cats are usually limited to mild diarrhea and decrease in appetite. Response of cholangitis cats to therapy should be monitored through use of serial complete blood counts and chemistry profiles.

Feline hepatic lipidosis (HL) is a well-recognized syndrome characterized by accumulation of excess triglycerides in hepatocytes with resulting cholestasis and hepatic dysfunction. Many cats with IHL are obese and often present with a history of prolonged anorexia after a stressful event. The etiopathogenesis of this syndrome is poorly understood, but may relate to protein deficiency, excessive peripheral lipolysis, excessive lipogenesis, inhibition of lipid oxidation or inhibition of the synthesis and secretion of very low-density lipoproteins. The prognosis for this life-threatening disorder has improved dramatically during the past several years as a result of long-term enteral feeding (i.e., three to eight weeks or longer). Initial management should be directed toward correcting complications such as dehydration, electrolyte abnormalities, hepatic encephalopathy, and infection. Any underlying causes for the lipidosis (diabetes mellitus, pancreatitis, neoplasia, cardiac disease, etc.) should be identified and treated whenever possible. Provision of adequate daily energy intake is the cornerstone of successful medical management of cats with HL.

Inappetence may have many origins and, as a presenting sign or observation in cats, is common in feline practice. Nutritional assessment of every patient is encouraged, to identify the need for, and appropriate type of, intervention indicated. The impact of malnutrition may be significant on the feline patient, perpetuating illness, delaying recovery, slowing wound healing and negatively impacting gut health and immunity. Delayed intervention may result in the cat's deterioration; hence prompt control of contributing factors such as the underlying illness, pain, nausea, ileus and stress is vital to optimize voluntary food intake. Management is multimodal, comprising reduction of stress, medications and assisted nutrition in the form of tube feeding or parenteral nutrition. Use of antiemetic, analgesic, prokinetic and appetite stimulant medications may restore appetite, but placement of feeding tubes should not be delayed. Feeding tubes are generally well tolerated and allow provision of food, water and medication with minimal stress, although clinicians must be aware of complications such as stoma site infections and refeeding syndrome.

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