Companion animal liver disease – diagnosis and management

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**ABSTRACT**

This article will review the most common hepatobiliary disorders in cats and dogs and consider their diagnosis and management.

Clinical signs of liver disease can be very variable and include waxing and waning gastrointestinal or neurological signs. A number of animals are identified with a hepatopathy on “routine” blood work taken for other purposes. Unfortunately, given the liver’s large structural and functional reserve, specific clinical signs of liver disease, such as icterus, hypoglycaemia, coagulopathies, ascites or hepatic encephalopathy, are not typically seen until late in disease – when 70% to 80% of the functional liver mass is lost.

Additionally, due to the liver’s dual blood supply, its high blood flow and the connection to other organs drained by portal circulation, the liver is also prone to secondary injury (“reactive hepatopathies”).

Diagnosis can be achieved, in some cases, by a combination of compatible history, clinical signs, clinicopathological abnormalities and diagnostic imaging. However, definitive diagnosis, in most cases, ultimately relies on histological examination of liver tissue (liver biopsy).

Treatment of liver disease depends on the type of hepatobiliary disorder, but, in general, involves the following steps:

- removal of the inciting agent, if present
- specific therapy
- nutrition
- general liver support therapy
Liver diseases are frequently encountered in companion animals, but their diagnosis and management can be challenging.

Clinical signs of liver disease can be variable and are often initially subtle; they may include waxing and waning gastrointestinal or neurological signs. In addition, specific clinical signs of liver disease are not typically seen until late in the disease – when 70% to 80% of the functional liver mass is lost.

Diagnosis can be achieved, in some cases, with a combination of compatible history, clinical signs, clinicopathological abnormalities and diagnostic imaging. However, definitive diagnosis, in most cases, ultimately relies on histological examination of liver tissue (biopsy). Treatment and prognosis will depend on the underlying cause.

Table 1. Liver disorders morphological classification in cats and dogs.

Liver diseases can be categorised into four broad groups: vascular liver disorders, biliary tract disorders, parenchymal disorders and neoplasia (Table 1).

History, clinical signs and physical examination

Cats and dogs with liver disease can have variable clinical signs and, therefore, a thorough and accurate history is the first step in diagnosis. Questions about the previous use of potential hepatotoxic drugs/supplements, exposure to toxins, human medications, recent anaesthesia, travel history, vaccination and worming status should be asked.

The breed, age and onset of clinical signs can also increase the suspicion of certain types of liver disease, such as a puppy with a portosystemic shunt.

Patients can present with a wide range of non-specific clinical signs, including lethargy, inappetence/anorexia, vomiting, diarrhoea, weight loss, polyuria and polydipsia. Other clinical signs include obtundation, jaundice, abdominal pain, hepatomegaly, ascites, pyrexia and ptyalism (cats).
Specific clinical signs of liver disease, such as icterus, ascites, hepatic encephalopathy, hypoglycaemia and coagulopathy, are not evident until more than 70% to 80% of the hepatic function has been lost. Moreover, given the liver’s dual blood supply, its high blood flow and the connection and proximity to other organs drained by portal circulation, the liver is also prone to secondary injury, so called “reactive or secondary hepatopathies” (Figure 1).

**Laboratory evaluation**

Complete blood cell count from animals with liver disease may reveal anaemia that could be either regenerative (due to gastrointestinal bleeding or coagulopathy) or non-regenerative (anaemia of chronic disease), microcytosis (PSS), poikilocytosis and Heinz body formation may be seen on blood smear examination. In addition, there could be concurrent thrombocytopenia (due to consumption or decreased production).

Serum biochemistry often reveals liver enzyme activity elevation. Enzyme activities reflect either the integrity of the hepatocyte membrane – alanine aminotransferase (ALT) and aspartate aminotransferase (AST) – or the patency of the biliary system, gamma glutamyl transpeptidase (GGT) and alkaline phosphatase (ALP). The elevation of hepatic transaminases is usually proportional to the severity of hepatic damage; however, the degree of elevation does not reflect hepatic function or correlate with prognosis.

Moreover, elevated liver enzyme activities have a high sensitivity to detect liver disease, but at poor specificity, meaning, although elevation of liver enzymes is seen with many liver diseases, many other conditions could cause this. Mild elevations should be considered relevant in cats, given the shorter half-life compared to dogs.

On a routine biochemical profile, it is also important to look at the liver function parameters, which
include albumin, glucose, urea and cholesterol, all of which decrease with significant hepatic dysfunction. In addition, prolonged clotting times (activated partial thromboplastin time/prothrombin time) is also seen with significant hepatic dysfunction.

More specific function tests would include the measurement of serum bile acid concentrations, plasma ammonia and bilirubin concentrations. It is important to remember hepatic function can be significantly abnormal despite normal serum activities of hepatic enzymes, such as PSS and end-stage cirrhosis².

**Bile acid stimulation test**

A bile acid stimulation test is not necessary if the patient is clinically jaundiced, as both results will be elevated due to cholestasis. Fasting bile acids greater than 25µmol/L should raise the suspicion of a hepatobiliary disorder and postprandial bile acids greater than 100µmol/L are suggestive of a PSS; a normal concentration does not exclude PSS.

Measurement of bile acid concentrations is, however, not specific for the type of liver disease and diseases that secondarily affect the liver, such as hyperadrenocorticism, pancreatitis and chronic enteropathies, can also increase bile acid concentrations³.

Maltese terriers may have falsely elevated bile acid concentrations due to the presence of a chemical that interferes with spectrophotometry assay²,⁴.
Figure 2. Icteric plasma from a cat (right) and normal plasma (left). The cat was diagnosed with immune-mediated haemolytic anaemia. Notice reduced PCV in comparison to the other tube.

Any diet can be used for the bile acid stimulation test. If the patient is not eating, force-feeding a small amount of food is usually enough. In the case of discordant preprandial and postprandial concentrations, the higher of the two samples is always used as the diagnostic measurement.
**Bilirubin**

Hyperbilirubinaemia appears when there is considerable hepatocellular disease or increased bilirubin load (haemolysis). Icteric plasma is detected when serum bilirubin concentration is between 10.26µmol/L and 17.1µmol/L (**Figure 2**). Icteric mucous membranes are detected with bilirubin concentrations more than 30µmol/L to 35µmol/L.

**Urinalysis**

Hyposthenuria (urine specific gravity