



WELCOME TO ISSUE NO.1 OF THE ADVANCED VETERINARY MEDICINE NEWSLETTER.



SELECTED DIAGNOSTIC AND THERAPEUTIC ASPECTS OF CANINE LIVER DISEASE

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Introduction

The intersection between the art and science of small animal medicine is arguably best illustrated in the diagnosis and treatment of canine liver disease. Practitioners are frequently presented with (1) asymptomatic dogs with abnormal serum liver enzymes, (2) confusing serum bile acid test results, and (3) numerous pharmacologic, nutraceutical, and dietary options for the management of canine liver disease patients. In this brief article, I attempt to address some of these more common clinical problems related to canine liver disease.

The Asymptomatic Dog with Increased Liver Enzymes

Serum alkaline phosphatase (SAP)

concentration – Vacuolar hepatopathy is the most common explanation for this phenomenon in dogs and is generally a diagnosis without a significant medical consequence – i.e. these dogs do not progress to hepatic failure or cirrhosis. Classically, this is the dog that walks around for years with an isolated increase in SAP. Vacuolar hepatopathy is associated with a long list of dietary, infec-

tious, pharmacologic, environmental, genetic, and other causes which cause vacuolar changes in hepatocytes and induction of SAP. The liver is usually normal to increased in size, and pre and postprandial serum bile acids are frequently normal or mildly increased (postprandial results approximately less than 60 $\mu\text{mol/L}$). The liver is sonographically uniform and hyperechoic and adrenal gland size is normal. Differential diagnoses: (1) Although dogs with hyperadrenocorticism (HAC) may initially present similarly, concurrent physical and clinical signs and biochemical changes consistent with HAC almost always develop within weeks or months. Many dogs considered to have “asymptomatic Cushing’s disease” actually have vacuolar hepatopathy. (2) There has been a notable increase in the diagnosis of gall bladder mucocoele, which may also trigger increases in SAP and remain clinically quiet for extended periods. (3) Lastly, geriatric dogs may develop tumors of biliary tract origin that are not initially associated with clinical signs. In all of the above disorders, any increase in ALT will be proportionately far less than that in SAP.

Serum alanine aminotransferase (ALT) – In general, a reactive hepatopathy is present when chronic increases in ALT concentration of approximately three-fold (i.e. 3 times the high end of the reference range) or less are observed. In this disorder, the liver is considered an innocent bystander to an extrahepatic process, most commonly GI disease. This is especially common in puppies with intestinal parasites and may evoke concern for a portosystemic shunt. Differential diagnosis: (1) Asymptomatic adult dogs with chronic increases in ALT greater than 3-fold generally have some form of chronic active hepatitis (CAH), which has the potential to lead to clinically serious disease over months or years. Liver size and serum bile acid results are variable and reflect severity and chronicity of disease. (2) Adverse drug reactions – NSAID’s, immunosuppressive agents (eg azathioprine), and potentiated sulfonamide antibiotics are among the more common causes. (3) Geriatric dogs may develop hepatocellular tumors that cause increases in ALT but are not associated with clinical signs. In all of the above disorders, any increase in SAP will be proportionately less than that in ALT.

Serum bilirubin – Most isolated increases in bilirubin in asymptomatic dogs are mild and artifactual, i.e. they are associated with lipemia or hemolysis. Most dogs with confirmed hyperbilirubinemia are symptomatic but on occasion, an asymptomatic jaundiced dog with a chronic hepatobiliary disorder will be seen.

Summary – (1) Most asymptomatic dogs with persistently increased SAP have a benign vacuolar hepatopathy – careful review of the list of potential triggers may be rewarding (2) Most asymptomatic dogs with persistently increased ALT > 3 fold have chronic active hepatitis – many of these dogs benefit from liver biopsy for sophisticated long-term management if routine testing and empirical therapies are not successful within 6-8 weeks

Canine Liver Disease continued

- (3) Most asymptomatic dogs with increased ALT < 3 fold have extrahepatic diseases, often gastrointestinal or low-grade drug reactions or other relatively benign disorders
- (4) Use caution interpreting serum bilirubin results from lipemic or hemolyzed samples
- (5) Use results of serial physical exams and biochemical profiles, pre and postprandial bile acid testing, radiography, and ultrasound to refine the differential diagnosis and assign a relative risk of future illness to individual patients.

Confusing Serum Bile Acid Test Results

The three most common dilemmas relating to performance of the pre and postprandial serum bile acids test are...

- 1. Presence of hyperbilirubinemia** – The bile acid test will always be moderately to markedly elevated when serum bilirubin is elevated. The clinician will need to rely on other markers of structural and functional hepatic disease in this circumstance.
- 2. Preprandial result higher than the postprandial sample** – Premature gall bladder contraction secondary to the excitement and stress of travel and handling or prolonged fasting are the most likely explanations for this phenomenon. Hemolysis of the fasted sample may also cause this.
- 3. Low bile acid results** – Dogs with severe enteropathies including lymphangiectasia, IBD, and lymphoma may be unable to absorb and recycle bile acids. This is a common dilemma in dogs presenting with hypoalbuminemia, ascites, and hypocholes-

terolemia for which both protein-losing enteropathy and liver disease are both important differential diagnoses.

The Symptomatic Dog with Increased Liver Enzymes

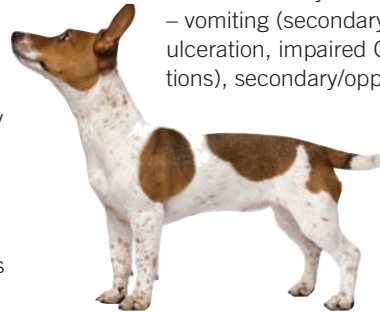
Sick dogs with elevated serum liver enzymes and bilirubin generally fall into one of three categories: (1) acute hepatitis/hepatic necrosis, (2) acute complications of a chronic hepatopathy, or (3) an acute and primarily non-hepatic disease with hepatobiliary involvement or complications.

1. Acute hepatopathy –

Infectious and toxic causes are most common. Leptospirosis and Bilharzia infection are both uncommon but they are specifically hepatotropic. It is the author's impression that the incidence of Leptospirosis may be increasing in our area. Infectious canine hepatitis (canine adenovirus 1) is only a theoretical concern at this time given its extreme rarity in the continental U.S. Cycad (Sago, false Sago) palm ingestion and adverse drug reactions (eg carprofen, potentiated sulfonamides) are the most common toxic hepatopathies in South Florida. Aggressive empirical therapy for presumptive toxicity is almost always warranted in dogs with acute severe hepatopathy, even if hours or days have already passed. This recommendation is based on the observation that cycad toxins cause

decreased motility and therefore facilitate retention of toxic ingesta long after it might otherwise have been expected to pass through the GI tract. Suspicion that cycad toxins (the main toxic principle is cycasin) undergo enterohepatic recycling warrants consideration of actigal (to shorten transit time and displace cycasin from the bile acid pool) and cholestyramine (to potentially facilitate enteric binding and excretion of cycasin).

2. Acute-on-chronic hepatopathy – Acute decompensation and illness in previously stable dogs with chronic liver disease tends to be caused by the same few complications – vomiting (secondary to gastroduodenal ulceration, impaired GI motility, and medications), secondary/opportunistic bacterial hepatitis (usually enteric bacteria from the portal circulation), tense ascites, fluid and electrolyte derangements, and hepatic encephalopathy.



3. Acute non-hepatic disease – Cholecystitis, pancreatitis, enteropathies, zinc toxicity, multicentric lymphoma, and immune-mediated hemolytic anemia are among the more common considerations. In jaundiced patients, the absence of anemia rules out prehepatic jaundice – radiography and ultrasound are generally required to differentiate between hepatic and post-hepatic jaundice and to confirm or refute other differentials. Use of the canine PLI test is most useful to rule out a diagnosis of pancreatitis rather than confirming it.

Summary – (1) Consider leptospirosis in acute cases and act in accordance with its zoonotic potential (2) Consider empirical treatment for toxicity in acute cases even if potential exposures cannot be initially confirmed and even if they are possibly more than 24 hours prior (3) Fluid and electrolyte replacement, GI ulcer treatment (H2 or proton pump inhibitors and carafate), antiemetics, broad-spectrum injectable antibiotics, lactulose, and drainage of tense ascites form the basis for stabilization of most acute and chronic patients (3) Coagulopathy, encephalopathy, ascites, and hemodynamic instability are associated with a much poorer prognosis and the need for intensive care – consider referral in these cases. ~

PRACTICAL ASPECTS OF CLINICAL IMMUNOLOGY

On February 9th, 2011, Dr. Jeff Toll will be the keynote speaker at the BCVMA meeting to be held at the Ft. Lauderdale Country Club. The topic is "Practical Aspects of Clinical Immunology."

Event Information:
Registration: 6:30-7:00pm
Dinner: 7:00pm, Talk: 8:00pm
For more information please contact:
DSchwartz@coralspringsanimalhospital.com

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