Abnormal Liver Enzymes: A Simplified Approach to Diagnosing Liver Disease

ADAPTED FROM A TECHNICAL BULLETIN[1] BY DAVID C. TWEDT, DVM, DACVIM (SAIM)

ABNORMAL LIVER ENZYMES SHOULD NOT BE IGNORED

Abnormal liver enzymes are either identified in the clinically normal patient having screening tests done or during a complete diagnostic work-up of a sick patient

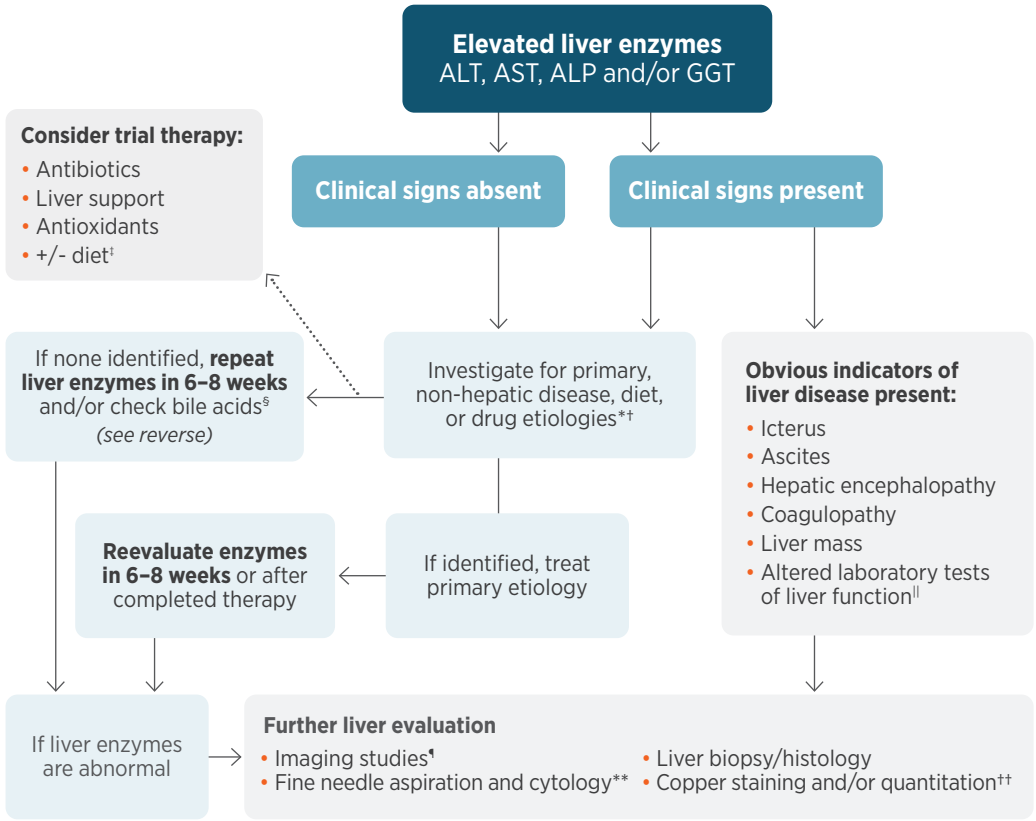
- The ill patient with abnormal liver enzymes may have primary liver disease or, most commonly, disease secondary to non-hepatic disorders

Routine liver-specific chemistry profile tests can be categorized into 3 groups:

- Hepatocellular injury (ALT and AST)[2]
- Cholestasis or enzyme induction (ALP and GGT)[3]
- Tests reflecting impaired metabolic function or synthetic capacity (albumin, bilirubin, cholesterol, bile acids)

A liver biopsy is required for definitive diagnosis in most cases of primary hepatic disease

INTERPRETING ABNORMAL LIVER ENZYME VALUES IN SMALL ANIMALS



ALT, alanine aminotransferase; AST, aspartate aminotransferase; ALP, alkaline phosphatase; GGT, gamma-glutamyl transferase.

*Consider endocrine disease, dental disease, chronic pancreatitis, and gastrointestinal (GI) disease. When investigating drugs, include herbals and nutraceuticals; †Always consider leptospirosis and pancreatitis in the work-up; ‡Trial antibiotic therapy may be indicated if a possibility of infection. Hypoallergenic diet trials if a possibility of GI disease. Antioxidant therapy may decrease oxidative stress in the liver. Consider treatment trials if a comprehensive liver work-up is unlikely to occur; §Identifying both abnormal bile acids and liver enzymes is a strong indication for a complete liver evaluation. Bile acids >100µM/L with normal bilirubin should suggest possibility of portosystemic shunting (congenital or acquired). Performing a fasted and postprandial sample improves diagnostic sensitivity of the test; ‖In some patients the history, signalment, and physical exam indicate primary liver disease. Test results that reflect altered liver function include decreases in albumin, blood urea nitrogen (BUN), glucose, bilirubin, cholesterol, and/or some coagulation factors; ¶Imaging studies include routine abdominal radiographs, ultrasound, and computed tomography (CT) or CT angiograms; **Fine needle aspiration and cytology have poor diagnostic accuracy except for neoplasia and diffuse vacuolar disease; ††Copper evaluation should be considered in all inflammatory liver disorders.

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Total Bile Acids: A Highly Sensitive Marker for Liver Dysfunction in Small Animals

ADAPTED FROM A TECHNICAL BULLETIN[4] BY DAVID C. TWEDT, DVM, DACVIM (SAIM)

TESTING FOR BILE ACIDS SHOULD BE PERFORMED:

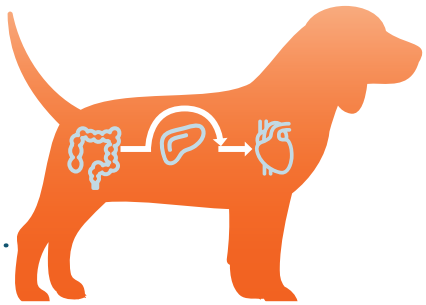
When unexplained liver enzyme elevations are identified[5]

When chemistry profile results are decreased for albumin, glucose, BUN, and/or cholesterol

- All suggest altered liver function

As a screening test for portosystemic shunt (PSS)[6]

- Either congenital or acquired
- Or when clinical signs suggest hepatic encephalopathy



Performing pre– and post–prandial bile acid testing increases sensitivity and specificity of the test[7]

UTILIZING AND INTERPRETING BILE ACID VALUES IN SMALL ANIMALS

PSS suspected* (congenital or acquired)

Hepatobiliary disorder suspected†

Hyperbilirubinemia or obvious primary liver disease

Primary extrahepatic disease identified by other diagnostics

Bile acid testing is not indicated. Continue diagnostics

Perform serum bile acids (fasted and postprandial)

Normal‡ <25 µMol/L	**Grey zone‡** 25–35 µMol/L	**Abnormal‡** >35 µMol/L	**Very high abnormal‡** >100 µMol/L with normal bilirubin
PSS likely ruled out. Consider hepatobiliary or extrahepatic disease	Suggests hepatobiliary dysfunction or PSS *Note: Values do not determine severity or type of disease*		Suggestive of PSS (congenital or acquired)

Continue diagnostics and/or monitor therapy

Normal bile acids following PSS surgery or hepatobiliary disease therapy indicates improvement

How to Perform a Bile Acids Challenge Test[4]

1. Pre-prandial sample is collected after a 12-hour fast
2. Feed a small meal of canned food immediately after the pre-prandial sample collection
   Note: Lipemia will falsely increase bile acid concentration, so avoid a large fatty meal
3. Collect the post-prandial sample 2 hours following the meal

*Hepatic encephalopathy signs may include: cognitive and/or behavioral changes, ataxia, blindness, seizures; †Abnormal tests of liver function include: unexplained low glucose, low albumin, low BUN, and/or low cholesterol; ‡Reference ranges vary by analyzer and those stated in this algorithm pertain to the VETSCAN VS2 canine cut-off and adjusted per author. Please refer to the manufacturer's guidance or reference laboratory for guidance on interpretation.

References: 1. Twedt DC. The approach to abnormal liver enzymes in companion animals. Zoetis Technical Bulletin. 2022. **2.** Webster CRL, Cooper JC: Diagnostic approach to hepatobiliary disease. In Kirk's Current Veterinary Therapy XIV. Bonagura JB and Twedt DC (eds). Saunders Elsevier. St Louis, MO. 2008, 543-549. **3.** Lawrence YA, Steiner JM. Laboratory Evaluation of the Liver. *Vet Clin North Am Small Anim Pract*. 2017;47(3):539-553. **4.** Twedt DC. Bile acids in companion animals. Zoetis Technical Bulletin. 2022. **5.** Hauge JG, Abdelkader SV. Serum bile acids as an indicator of liver disease in dogs. *Acta Vet Scand*. 1984;25(4):495-503. **6.** Johnson SE, Rogers WA, Bonagura JD, et al. Determination of serum bile acids in fasting dogs with hepatobiliary disease. *Am J Vet Res*. 1985;46(10):2048-2053. **7.** Center SA, ManWarren T, Slater MR, et al. Evaluation of twelve-hour preprandial and two-hour postprandial serum bile acids concentrations for diagnosis of hepatobiliary disease in dogs. *J Am Vet Med Assoc*. 1991;199(2):217-226.

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