FEELING GREEN: DIAGNOSING AND MANAGING LIVER DISEASE IN REPTILES

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ABSTRACT

Many reptilian patients with underlying liver disease go undiagnosed. There are many tools available to diagnose liver disease in reptiles. Treating liver disease has some basic principles (nutritional support, optimal thermal environment, hydration) regardless of underlying etiology. Hepatic lipidosis, one of the more common liver diseases in pet reptiles, will be covered in depth.

Diagnostic Tests

A thorough physical examination and medical anamnesis is essential. Veterinarians often omit bloodwork from the initial database or rely on outside labs for blood chemistries. If you’ve got the diagnostic machine, use the machine and your quality of care will improve! In-house bloodwork is available within 30 to 45 minutes. I suggest in-house tests of fecal parasite examination and in-house screening bloodwork (Vetscan® Avian/Reptilian Profile Plus, Abaxis, Inc., Union City, CA) for rapid assessment of an ill reptile. This rapid screening includes aspartate aminotransferase (AST), bile acids (BA), total protein, albumin, indirectly-derived globulin, creatinine kinase (CK), glucose, uric acid, calcium, phosphorus, sodium and potassium. Depending on initial results, outside labwork such as complete blood count, protein electrophoresis, LD, cholesterol, triglycerides, and lipoprotein profiles may be offered.

Major tissue enzymes of the liver in ratsnakes (Elaphe obsoleta) were AST and lactate dehydrogenase (LD). AST was also found at moderate levels in the kidneys along with LD, alanine aminotransferase (ALT), and CK. Striated muscle had high CK. Intestine, lung, and pancreas had low enzyme levels (alkaline phosphatase (ALP), LD, AST, ALT, gamma glutamyltransferase (GGT), CK). GGT was minor or undetectable in any tissues or serum. Green iguanas (Iguana iguana) differed from ratsnakes with CK high in striated muscle and low elsewhere, LD and AST moderate in all tissues analyzed, and GGT also being low or undetectable. Sadly, no other work has been published in this area since 1999! Elevated plasma or serum AST and LD suggest active liver disease while depressed AST and LD suggest cirrhosis or chronic amyloidosis.

Healthy red-eared sliders (Trachemys scripta) do not have significant post-prandial elevations in bile acids at 24 and 48 hr. In my experience, a reptile that has not fed in at least 5 days but maintains elevated bile acids (>35 micromol/L) is significant and suggests biliary obstruction. This may be due to gall stones, infections (including protozoa and metazoan), and neoplasia. Albumin is quantitatively inaccurate using dry film analyzers but taking multiple samples will
reflect overall trends. Low albumin is found with cirrhosis, hepatic lipidosis, myeloidosis, “leaky” kidneys and intestines, and many infections. Protein electrophoresis provides a more accurate and precise albumin level, and can point to liver involvement. Glucose is most often low in anorectic reptiles with liver disease, and will often remain low following an assist-fed meal that lacks glucose. I have yet to diagnose a reptile with true diabetes mellitus and have found underlying granulomatous or inflammatory diseases.

Elevated cholesterol and triglycerides may indicate post-prandial lipemia. In female reptiles it may indicate vitellogenesis. It may herald liver disease if persistently elevated or if markedly elevated.

The liver converts ammonia (derived from protein metabolism) into urea and uric acid. The ornithine cycle producing urea occurs within the mitochondria and cytosol of hepatocytes. The production of uric acid from urea relies on glutamine synthetase (and possibly glutamine dehydrogenase) found within mitochondria of hepatocytes. Ammonia levels are not routinely measured due to the need for rapid transport of the sample to the lab on ice. Increased ammonia levels or decreased blood urea nitrogen (BUN) or uric acid suggest hepatic disease. It may be helpful to measure uric acid on the fasting carnivorous or omnivorous patient and thereafter challenge with a high protein meal. If there is no elevation in uric acid over the next 24 to 48 hr, it supports a diagnosis of hepatic disease. Biliverdin is water soluble, readily excreted, less toxic than bilirubin, and requires less energy to produce. Bilirubin has neuroprotective effects during cerebral ischemia and buffers the brain against decreasing arterial oxygen. Mammals need bilirubin. Reptiles are able to function well with lower arterial oxygen than mammals of the same size. Reptiles lack biliverdin reductase and do not produce bilirubin, a common measure of liver disease in mammals. Measurement of bilirubin is unhelpful in reptiles. Most biliverdin is excreted in the bile. With decreased bile outflow or hepatic regurgitation, biliverdin levels elevate in the blood resulting in green to blue serum and green to blue urine or urates.

Reptiles have low intrinsic thromboplastin activity compared to mammals which greatly lengthens clotting times. I consider a buccosal membrane bleeding time (BMBT) over 120 seconds suggestive for a clotting disorder.

**Complicating Factors**

Interpreting reptilian labworks is complicated due to the lack of published normal blood values. Where there are normal values, they may be incomplete with regard to sex, age, or other classification, and equipment used. There are few retrospective studies correlating labwork with clinical conditions. We do not know the half-life for reptile enzymes in any species which makes the timing of diagnostic or follow-up samples difficult to interpret.

**The Art of Interpretation**

Diagnosing liver disease is an interpretive art that must consider many factors. I consider AST, bile acids, albumin, and glucose as the main indicators of liver function available on the Vet
Scan® Avian Reptilian Profile Plus.

Enzymes may not be elevated depending on the nature of the hepatic insult and the timing of the blood sample. Furthermore, enzyme values may drop with end-stage liver disease, such as cirrhosis and amyloidosis.

I place liver disease high on my differential list with any three of the following: green to blue serum or urine (urates), elevated AST, markedly depressed AST, hypoalbuminemia, elevated bile acids, hyperglycemia, hypoglycemia, low BUN, low uric acid, prolonged clotting time.

Supporting data from outside labwork includes elevated or markedly depressed LD, confirmed hypoalbuminemia on the protein electrophoresis (EPH) particularly with abnormal albumin: globulin, and elevated cholesterol or triglycerides. Leukocytosis or profound leukopenia, toxic heterophils, and elevated globulins suggest an infectious hepatitis. Anemia indicates a chronic illness since reptilian red blood cells may live 90 to more than 300 days.

In-house diagnostic imaging helps refine the diagnosis while outside labwork is pending. Radiographs may confirm cirrhotic (small) liver, hepatomegaly, lipidosis, masses (abscesses, tumors), gall bladder stones, or hydrocoelom, and may reveal other underlying problems such as follicular stasis, bladder stones, etc. An ultrasound exam may reveal all of the above and will provide more detail of organs with hydrocoelom. Celiocentesis is appropriate with hydrocoelom. Chronic liver disease commonly reveals an acellular transudate with total solids under 2.5 g/dl. The aspirate may show inflammatory cells, mesothelial cells, and markedly elevated total solids (3.0 g/dl or higher). Yolk coelomitis may cause all of these inflammatory signs along with visible fat droplets in the fluid sample. Neoplastic cells may be detected. CT / MRI may not reduce your rule-outs over those obtained by radiographs or ultrasound, require anesthesia, and are costly.

Celioscopy with hepatic biopsy is the gold standard to characterize liver disease. It often detects conditions not identified by labwork or other imaging techniques. Unfortunately, the cost, patient risks, turnaround time for results, and sometimes inconclusive histopathology may not alter your treatment plan for “liver disease”. Results, such as cirrhosis, may give a prognosis (poor) but may not answer the client’s question, “Why did my pet get sick?”

**HEPATIC LIPIDOSIS**

Hepatic lipidosis in carnivorous or omnivorous reptiles is linked to obesity and overeating, particularly foods high in cholesterol and other fats. While this can be true for herbivorous reptiles, such as the green iguana fed an inappropriate diet, it is much more common to see these species develop hepatic lipidosis secondary to anorexia from a primary illness.
Carnivorous and Omnivorous Species

Overeating is due to the client either misunderstanding or ignoring the diet recommended for their reptile. A common presentation is an obese adult savannah monitor (with a 5 out of 5 body condition score) consuming one or more “jumbo” mice weekly. Savannah monitors are largely insectivorous in the wild, with dung beetles, grasshoppers, and other invertebrates comprising the majority of their diet. Vertebrate prey is opportunistically consumed and is most likely going to be lean animals with the occasional exception of freshly-nursed mammalian neonates or eggs. Furthermore, the savannah monitor lives in areas where prey abundance varies by season and has to exercise in order to find food. A wild savannah monitor may go weeks without meeting its energetic needs, depleting its fat stores, until the weather changes or it chances upon a patch of high prey density. A wild savannah monitor is generally lean. In approximate order of appearance, signs of hepatic lipidosis are anorexia, lethargy, constipation, diarrhea, flatulence, regurgitation, and death.

Another common presentation is the box turtle fed nothing but canned dog food. A wild box turtle is similar to the savannah monitor, largely insectivorous and opportunistically feeding on fruits, fungi, and rarely vertebrates. It has all of the same demands for survival as the savannah monitor, with the further need of surviving hibernation. They usually have deformed shells, overgrown beaks, flakey skin, overgrown toenails, and deformed tails, all signs consistent with malnutrition. In box turtles, signs of hepatic lipidosis are anorexia, lethargy, diarrhea, and death.

In snakes it is common to see the “power-fed” boa constrictor that the client was trying to get to breeding size within 18 mo. It’s been stuffed with as many rodents as possible, and the rodents have been increased in size as quickly as possible until it is feeding on retired breeder rodents. These retired breeders are higher in fat and lower in protein than young adults, and are not optimal to sustain healthy growth. The snakes are often held in small rack systems with no ability to exercise. Many of these power-fed snakes are found dead. Signs of hepatic lipidosis in these power-fed snakes include anorexia, regurgitation, gastrointestinal gas (“bloat”) and flatulence, and diarrhea or constipation.

Herbivorous Species

I see this most commonly in desert tortoises and sulcata tortoises that have failed to eat for more than 10 days. As mentioned, it is almost always secondary to some other primary illness that has created anorexia, such as infections, bladder stones, toxicosis, etc.

Presumptive Diagnosis of Hepatic Lipidosis

Hepatic lipidosis should be suspected based on weight history, the diet history, possessing one or more of the listed signs, AND ruling out other primary disease. Green to blue urates may be reported, and clay-like, tan, or watery feces may also be noted. Blood is often noticeably lipemic. Cholesterol and triglycerides may reach 30 times the normal values! Liver enzymes and bile acids may be normal. Ultrasound may reveal a brightly reflective enlarged
rounded liver and confirm the ubiquity of fat throughout the coelom. An endoscopically-guided liver biopsy may confirm your presumptive diagnosis, but rarely alters your treatment plan unless it confirms another disease process.

**Treatment of Hepatic Lipidosis**

Hepatic lipidosis management is better documented in cats (obligate carnivores), humans (omnivores), and horses (obligate herbivores) than reptiles, and that research serves as a foundation for treating reptiles. A major difference is the need to provide a high quality thermal environment that provides the reptile’s preferred operating temperature zone (POTZ) so that its metabolism is optimized.

The carnivorous reptile with hepatic lipidosis requires: POTZ; exercise; caloric reduction with a nutritionally complete, low fat, high quality protein liquid diet (such as an elemental diet low in fat, e.g., LaFeber’s Emeraid for Carnivores (www.lafebervet.com, Lafeber Company, Cornell, IL); proper hydration; and nutriceuticals such as milk thistle, S-Adenosyl methionine (SAMe), and possibly lactulose. The value of these nutriceuticals in reptiles is uncertain but I feel it does no harm and may provide benefit; these are commonly used in as well as cats, humans, and horses.

Herbal remedies provide additional nutriceutical options. Hyperlipidemic rats given an herbal remedy had reduced total cholesterol total, triglycerides, Low-density lipoprotein (LDL), coronary index, and atherosclerotic index with a concomitant increase in High-density lipoprotein (HDL) and antioxidants. Several herbs lower cholesterol and LDL in humans. These may be considered as additional nutriceutical options but there are no guidelines published for reptiles and safety and efficacy of these herbal remedies in humans is still under review.

The omnivorous reptiles and herbivorous reptile follow the same overall guidelines, but it is important to use an elemental diet initially, e.g., LaFebers Emeraid for Omnivores or Herbivores (Lafeber Company, Cornell, IL). The elemental diet will help herbivorous reptiles minimize the role of the liver in metabolizing fatty acids, the main energy source from hindgut fermentation, but ultimately the herbivorous reptile’s survival depends on the liver being able to resume its role converting the volatile fatty acid. After 3 to 7 days, herbivores need to transition to a diet designed to sustain hindgut fermentation, such as Oxbow’s Critical Care for Herbivores (www.oxbowanimalhealth.com, Oxbow Animal Health, Murdock, NE). Some herbivores may need transfaunation from healthy reptiles of the same species in order to re-establish normal gut flora for fermentation. In herbivores, it is important to “jump start” fermentation in order to instigate more normal digestion.

I believe frequent feedings of small amounts of the liquid diets is more helpful than less frequent feedings of a larger volume UNLESS you are treating a very fractious or dangerous patient. I don’t calculate the reptile’s basal metabolic rate (BMR) and instead offer a total volume of formula of 2 to 3% of the reptile’s current bodyweight at the initial daily feeding. After 96 hr, and assuming the reptile shows minimal signs of abnormal digestion, I’ll increase the volume to be 2 to 3% of the reptile’s estimated ideal body weight. When the reptile begins to
self-feed, or show interest in food, the transition to a more normal diet can begin. Unfortunately, the outlook for a patient with hepatic lipidosis is guarded. If a patient does not begin to show more activity and an interest in its normal diet within 7 days, the outlook declines.

**Conclusion**

Once a reptile is self-feeding, the treatment regimen should be continued until it reaches a healthy body condition score. Periodic ultrasounds and bloodwork should be performed to monitor progress.

**LITERATURE CITED**