LIVER DISEASE — DIAGNOSIS AND MANAGEMENT

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The avian liver is the bird’s central station for metabolic processing. Its numerous functions tie the liver to several body systems including digestive, reproductive, hematopoietic and endocrine. With all of its responsibilities, the avian liver has multiple ‘opportunities’ to develop problems. Hepatic ‘disease’ in birds is rarely a single entity and usually involves numerous different pathologic processes. The intent of this discussion is to help the reader understand basic avian hepatic anatomy and physiology and to diagnose liver disease in birds. Management of avian liver disease will be briefly discussed but should be based on the patient’s needs and the form(s) of hepatic pathologic change(s) present.

BASIC ANATOMY

The avian liver is divided into a left and, typically larger, right lobe. The two hepatic lobes meet cranially at the midline and the combined cranoventral portion surrounds the cardiac apex. It is because of this close association with the heart that hepatomegaly and/or cardiomegaly can result in a palpable abdominal pulse and may cause an audible ‘friction rub’ that resembles a murmur. A single bile duct drains each hepatic lobe. The gall bladder (not present in most psittacines, pigeons and the ostrich) is found in the right hepatic lobe. The celiac artery (giving rise to right and left hepatic arteries) and portal veins (which go to the sinusoids and then to the hepatic veins) supply blood to the liver. Young altricial species (psittacines, passerines, etc) normally have a red-purple liver at hatching while precocial chicks (chickens, turkeys, etc) have yellow hepatic tissue up to 8-14 days post hatch.

HEPATIC PHYSIOLOGY

The avian liver has numerous vital body functions including digestion, metabolism, selective storage, red blood cell production and detoxification. Bile production activates pancreatic lipase, emulsifies fats and contains some amylase that aids in carbohydrate metabolism. Avian bile contains mainly Na+ and K+ salts of taurocholic acid and glycocholic acid, while deoxycholic acid may be absent in birds. Avian livers contain little or no biliverdin reductase, so biliverdin, not bilirubin, is the primary bile pigment. As a result, clinical ‘icterus’ is rare and arguably absent in birds, but biliverdinuria (bright green urine and urates) is seen associated with avian liver disease.

The avian liver is responsible for many metabolic functions. The gluconeogenic pathway is considered similar in birds when compared with mammals. Gluconeogenesis is vital for young birds utilizing their low carbohydrate dense yolk lipid for energy. Carnivorous (birds of prey) birds require gluconeogenesis to produce carbohydrates during fasting and tend to have more stable blood glucose levels when compared to granivorous species (psittacines). In many birds, de novo lipogenesis is mainly hepatic and tends to be enhanced by dietary carbohydrates. Avian protein metabolism is quite different from mammals with the main difference being a poorly developed ornithine cycle (urea synthesis) and the end product being water-insoluble uric acid (nitrogenous waste). Plasma proteins are synthesized in the liver and are involved in structural protein formation (hormones, antibodies, neuromodulators and hemostatic components) and preserving blood volume. The avian liver is the major site for production of fatty acids, cholesterol and (in ovulating females) blood lipids that are transported to the ovary by lipoprotein complexes. The avian liver plays a role in blood cell synthesis during embryogenesis. Vitamin D is also metabolized in the liver and can be stored along with iron (as ferritin) and vitamins A and B12.

The avian liver biotransforms many biologically active substances. Biotransformation occurs on several levels within the hepatic smooth endoplasmic reticulum, mitochondria and cytosol. The end result is to (usually) reduce a substance’s toxicity/activity and facilitate elimination by increasing a compound’s water solubility and polarity. Additional non-synthetic hepatic reactions include oxidation, reduction and hydrolysis.

HISTORICAL AND PHYSICAL FINDINGS ASSOCIATED WITH AVIAN HEPATOPATHIES

Attending veterinarians should collect accurate information describing the bird’s diet, egg laying history (when applicable), exposure to known toxins, source, exposure to other birds and any other information that may seem pertinent. Understanding the bird’s nutritional background may quickly point to a problem such as a high fat diet and probable hepatic lipidosis or vitamin A oversupplementation and liver toxicosis. Knowledge of certain species (toucans, mynahs, lories) prone to a specific liver disease (hemochromatosis) is also helpful when evaluating a bird’s health. Active egg laying causes estrogen-stimulated lipogenesis and oftentimes results in slight hepatomegaly and elevated total solids, plasma proteins and cholesterol that should all return to normal once the ovary is quiescent. Chronic egg laying and underlying liver disease can make various diagnostics difficult to interpret. Mycotoxin exposure from moldy food is commonly implicated as a cause of vacuolar fibrosing hepatopathy but the avian liver is potentially sensitive to any of numerous toxins. Understanding the bird’s source and exposure to other avian species is very important and may help narrow your differential list, especially when infectious diseases are suspected. Also, knowledge of non-infectious diseases present within a certain ‘line’ of birds may help to identify liver disorders with a genetic predisposition such as seen with certain large-bodied ‘show’ cockatiels that seem to have an increased incidence of hepatic lipidosis.
Although birds with fulminate hepatic disorders may have the classically described biliverdinuria (bright green urates/urine), hepatic encephalopathy (clinically rare), and polyuria/polydipsia, most liver disease patients have more subtle signs such as weight loss, lethargy and anorexia. Occasionally, birds with liver disease develop an overgrown rhinotheca (upper beak). The true cause of this phenomenon is unknown but seems to be a fairly accurate clinical indicator of liver disease, especially when other forms of beak overgrowth (normal occlusion, use of chew toys and no obvious facial trauma or parasitic infestation) are ruled out. *Amazona spp.* parrots occasionally develop a foot mutilation syndrome that may be associated with hepatic inflammation. This association is not clearly defined and is relatively uncommonly seen, but worth noting. There is, however, a fairly well defined association in psittacines between hepato-cellular neoplasia and concurrent cloacal papillomas and herpesvirus infection. All birds with cloacal papillomas should be periodically monitored for signs of hepatic neoplasia (routine physical examinations, coelomic ultrasound, selected enzymes, etc). Rarely, avian hepatic disease patients will develop ascites and is usually only noted with concurrent heart disease. Excessive subcutaneous fat deposits are often associated with varying degrees of hepatic lipidosis. Although discussed in the literature, birds with acute weight loss rarely, if ever, develop a secondary hepatic lipidosis (as noted in cats).

### Laboratory Evaluation and Association with Avian Liver Disease

Because of the many functions the liver performs, several laboratory diagnostics are available to assess the status of the liver. Albumin, glucose, cholesterol, triglycerides and uric acid are either entirely or partly produced within the liver and their decreased values may be associated with hepatic disease. Conversely, cholesterol is frequently elevated in birds with fatty liver disease. Globulin may be increased especially with chronic hepatitis, which is possible with any extended inflammatory process. (Plasma protein electrophoresis should be utilized to best protein levels in birds.) Bile acids may be poorly reabsorbed from the blood (resulting in elevated bile acids) in birds with hepatic disease, especially with fatty liver syndrome and severe necrosis. Chronic hepatitis, fibrosis and atrophy may result in decreased bile acid levels.

Several enzymes can have clinical use in identifying avian liver disease. Always consider sample collection artifact and hemolysis during evaluation. Aspartate aminotransferase (AST or SGOT) is probably the most sensitive indicator of psittacine liver disease. AST is found in both liver and all muscle types and should be interpreted concurrently with creatine kinase, which is only found in muscle. Glutamate dehydrogenase (GDH) is highly specific but poorly sensitive for liver disease. GDH is mitochondrially bound and is usually only elevated with certain forms of severe hepatocyte damage. Specifically in racing penguins, GDH is considered the most sensitive ‘liver specific’ enzyme. Gamma glutamyl transferase (GGT) is also poorly sensitive, but highly specific for liver disease and elevation has been associated with hepatic carcinomas in psittacines with papillomatosis. Lactate dehydrogenase (LDH) and alkaline phosphatase are infrequently elevated with hepatic disease, but liver-specific isoenzymes may have some use. LDH has been shown to be a sensitive indicator of liver damage in laying chickens with fatty-liver hemorrhagic syndrome. Despite being present in high amounts in avian liver tissue, alanine aminotransferase is rarely elevated, even with well-documented hepatocellular disease. In some cases of severe liver dysfunction (noted in chronic fibrosis), many or all of the above listed enzymes can be within normal limits or slightly decreased. So, ‘normal’ enzyme levels do not necessarily indicate a healthy liver.

Other diagnostics can be useful in evaluating the liver in avian patients. Screening radiographs give an indication as to liver size and shape. In general, the avian liver should not extend beyond a line drawn from the coracoid to the acetabulum (ventro-dorsal view) or caudally past the sternum (lateral view). Contrast radiographs are sometimes helpful to visually separate the intestinal tract from the liver. A dorsally or (left) laterally displaced but normally sized proventriculus or caudally depressed ventriculus may indicate hepatomegally. A very narrow cardiohepatic ‘waist’ may subjectively indicate microhepatia. Ultrasound has proven useful in many cases for detecting hepatic lipidosis (diffuse, hypechoic liver) and neoplastic masses (especially metastatic disease and bile duct/hepatic carcinomas). A complete blood count can give non-specific indications as to inflammation and may also be a useful monitoring tool post-treatment, especially with active inflammatory hepatic diseases. Many serologic diagnostics are currently available to help identify specific infectious agents (such as polyomavirus, adenovirus, circovirus, *Chlamydia psittaci*, etc) that may be associated with or directly causing liver disease.

When all signs point to liver disease, a definitive etiology and/or the pathologic process(es) is(are) not known, hepatic biopsy (in stable patients) offers the best diagnostic tool. Liver biopsies are fairly easy to perform (via laparoscopy or laparotomy) and often provide the most valuable information in cases of suspected liver disease. Ultrasound guided liver biopsies have also been described and can be successfully used with practice-especially in the larger birds. Many hepatic histopathologic changes are not pathognomonic for a single specific disease process. The author encourages attending clinicians to work with pathologists familiar with avian histologic anatomy to help correlate histopathologic with patient clinical findings to better define the disease process and set a treatment plan.

### Treatment

Treating avian liver disease should focus on decreasing clinical signs (anorexia, weight loss, bleeding) while addressing the hepatic pathologic
changes (inflammation, fibrosis, neoplasia). Acutely ill and anorexic liver disease patients should be provided appropriate supportive care including fluid therapy and readily digestible food. Offering diets high in complex carbohydrates and foods pretreated with pancreatic enzyme preparations should be considered. Birds with hemochromatosis should be offered low iron (less than 20-50 ppm) diets. More immediate needs of birds suffering from hemochromatosis may be managed with phlebotomy for hyperviscosity (remove blood equal to 1% of the bird’s body weight weekly) and furosemide for ascites (0.15-2 mg/kg SID-BID). Lactulose (0.3-1.0 ml/kg PO BID) has generally been recommended for ‘liver disease’ but its use has not been proven beneficial in birds. Decreased protein intake has questionable efficacy in birds with hepatic encephalopathy but is mentioned in the literature. Severely hypoproteinemic birds may benefit from hetastarch (10-15 ml/kg IV TID for 1-4 treatments). Birds with coagulopathies and concurrent liver disease can be given parenteral vitamin K (0.2-2.2 mg/kg IM q 4-8 hours until bleeding is controlled). Obese birds with hepatic lipidosis may simply respond to diet and exercise but should be monitored through the treatment course. In cases of infectious hepatitis or concerns of upper gastrointestinal inflammation, choose antibiotics based on fecal and/or liver biopsy culture and sensitivity results or when specific organisms are otherwise identified (Chlamydia psittaci). Colchicine (0.04 mg/kg PO SID-BID) may help to decrease collagen formation and has been used (subjectively) successfully in some cases of hepatic fibrosis. Silymarin (bioactive extract from Silybum marianum or milk thistle) has been used in both human and veterinary medicine for managing hepatic diseases. The mechanism of silymarin action is poorly understood but is generally believed to act as antioxidant, cell membrane stabilizer, permeability regulator and promoter of DNA, RNA and protein synthesis. The dose of silymarin is highly variable but has been based off the human dose of 4-15 mg/kg PO SID-BID. Rely on clinical signs, physical re-evaluations and monitor laboratory abnormalities to help gauge treatment.

References available from the author upon request.