

## **A Review of the Avian Liver**

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**Abstract.** The liver is frequently involved in pet bird diseases, either as the primary organ or secondarily to other diseases. A description of the anatomy, the common clinical signs of liver disease, the diagnostic tests used to evaluate the liver, and some general treatment guidelines are discussed. The more common specific diseases involving the liver are covered.

### **Introduction**

The liver maintains the body's metabolic homeostasis. It is an important organ, responsible for proper digestion, metabolite detoxification, phagocytosis of particulate material in the splanchnic circulation, and metabolism of proteins, fats, and carbohydrates. The liver produces and secretes bile, which is vital for digestion. The primary function of bile is to emulsify fats, which aids in their absorption. Bile aids in carbohydrate digestion through one of its components, amylase. It also activates pancreatic lipase. The liver has enormous functional reserve which can mask the signs of early damage from disease (1).

### **Anatomy**

The liver is a bilobed organ that lies in the mid-coelomic cavity of avian species (2,3). The left and right lobes join at the midline (2,3). In most avian species the left lobe is slightly smaller (2,3). Each lobe is drained by separate bile ducts into the distal ascending loop of duodenum (2,3). The cranioventral portion of the liver surrounds the heart (3). A gallbladder is an inconsistent finding (2,3). No gall bladder is identified in pigeons, many parrots (such as Amazons and Indian ringneck parakeets), and the ostrich (3). In those species with gallbladders (chickens, ducks, and geese), it is found on the visceral surface of the right lobe (3). Woodpeckers, toucans, and barbets have very long gallbladders (3). The major bile pigment is biliverdin (most

mammals produce bilirubin) and chenodeoxycholic acid is the primary bile acid (4,5).

#### Clinical signs of disease

Many diseases of the liver produce non-specific clinical signs. In the early stages, or with mild disease, there are periodic bouts of anorexia, lethargy, ruffled feathers, and watery yellow or green urates (2,6). As the liver pathology progresses, there is vomiting, weight loss, dyspnea from hepatic enlargement or ascites, bruising of the beak and nails, and neurological signs such as tremors, ataxia, paresis, circling, and seizures (2,6). In the larger psittacines, a color change of the feathers can be associated with liver disease (6). Frequently, budgies develop an overgrown beak with chronic hepatic disease (2,6).

#### Diagnostics

The diagnosis of a primary liver disease can be difficult because of the many non-specific laboratory and physical findings. There are many disease processes not specific to the liver which will involve it secondarily.

On physical examination, an enlarged liver can be visualized by moistening the skin over the liver as it extends beyond the caudal border of the sternum (2,6). An enlarged liver will displace other organs in the coelomic cavity and this may be recognized on palpation.

Radiographically, the margins of the liver should not extend past the sternum on the lateral view (2). With enlargement there will be a dorsal deflection of the proventriculus and caudodorsal displacement of ventriculus (to level of acetabulum) (2). The normal proventricular angle on a lateral view is 45 degrees (2). There is a loss of the hourglass cardiac-hepatic silhouette on the dorsoventral view and the liver will extend beyond an imaginary line drawn from the scapula to acetabulum (2,6). Contrast studies are useful in determining the extent of liver changes, as ascites or an enlarged fluid-filled proventriculus can produce the appearance of hepatomegaly. Radiographs are indicated before endoscopic or surgical evaluations are considered to rule-out concurrent disease processes and determine the size and location of the liver.

Ultrasound can be a useful diagnostic tool in many liver diseases. Even the livers in birds as small as budgerigars can be imaged with a small probe (7.5

MHz finger probe). The air sacs are avoided by keeping the probe on the ventral midline along the caudal rim of the sternum. Ultrasound-guided fine needle aspirates can be considered for birds presenting as anesthetic risks.

Elevations in serum aspartate aminotransferase (AST, SGOT) and lactate dehydrogenase (LDH) can occur in liver disease, but are not specific for the liver (2,7). The best use of these tests is to evaluate them in combination with the results of other more specific tests, such as creatinine kinase (CK), a muscle specific enzyme, to exclude muscle damage as a cause of the elevations (7). SGOT is found in kidney, spleen, heart, skeletal muscle, small intestine, lung, brain, as well as the liver (4,7). The most common causes of serum elevation are with liver disease and muscle damage (4). Elevations of this enzyme have been reported with vitamin E and selenium deficiencies, and intoxication from pesticides and carbon tetrachlorides (4). Lactic dehydrogenase (LDH) is a highly labile enzyme that rises and falls more quickly than AST (4,7). Large amounts of this enzyme are found in myocardium, kidney, liver, and muscle (7). Hemolysis of the serum and hepatic diseases in psittacines can result in elevated levels of LDH(4).

Serum bile acid measurement is a liver function test because extraction, conjugation, and secretion of bile acids are all functions of the liver (7,6). When liver function is impaired, bile acids are not properly reabsorbed from the blood, and the proportion of excreted bile acids reaching the peripheral circulation increases (5,6). Elevations have correlated well with liver disease in many avian species (6,7). It is recommended to submit a single, fasted (3 to 4 hours) sample for bile acids determinations in birds (5,7). Bile acids are labile in plasma and samples should be run within 48 to 72 hours of collection.

Cholesterol is a major lipid that is a precursor of all steroid hormones and bile acids. The source is animal proteins in the diet and it is synthesized in the liver. Increased serum levels can be associated with high fat diets, hypothyroidism, liver disease, starvation, budgies with xanthomatosis, obese birds, and very high levels usually accompany lipemia, especially in Amazons (4).

Decreases in albumin can be a non-specific indicator of chronic liver disease, as albumin is manufactured by the liver (4,6). This decrease will occur very late in the course of the disease (6). A yellow appearance of the avian plasma or serum should not be mistaken for jaundice, as birds do not

produce appreciable amounts of bilirubin. The yellow color is suspected to be due to carotene pigments from the diet. Most chronic diseases, including hepatic diseases can induce a depression anemia .

The definitive diagnosis of liver disease is obtained by a liver biopsy and histopathology (2,6). This not only describes the pathological process, but also provides information about the degree of change, which is important for prognosis. The liver can be biopsied from three approaches; percutaneous, endoscopic, and by laparotomy (6). With suspected liver disease, pretreatment with vitamin K<sup>a</sup> is warranted. The liver is the site of vitamin K-dependent coagulation factor synthesis (1). Excessive hemorrhage can accompany chronic hepatic diseases (6). The indications for a biopsy are persistently elevated liver enzymes, radiographic changes, and a limited or absent response to therapy.

### General Therapy

Although the best treatment plan should include a specific therapy directed at the causative agent, this is frequently not possible. In many liver diseases the specific etiology is unknown, or is an agent that is non-responsive to current treatments (viruses, amyloid), or is no longer present (toxins). Supportive care is important, especially with acutely ill birds. If the bird can be supported through an acute episode and then maintained on a regimen designed to minimize liver insults, the bird can enjoy varying intervals of good health. Oxygen therapy is helpful for birds with anemia, ascites, and hepatomegaly which results in respiratory compromise. Excessive ascitic fluid can be aspirated to provide immediate respiratory relief as long as appropriate precautions are taken to prevent severe albumin depletion and hypovolemia. Diuretics such as furosemide<sup>b</sup> can be used to control ascites.

Fluid therapy is important as many of these birds are not eating or drinking enough to meet their needs. With severely compromised birds, subcutaneous fluids may be safer initially, until a catheter (IV or IO) can be placed if needed. For hepatic diseases, an easily digested, low-residue diet is recommended. Vitamin supplementation is also important. Lactulose<sup>c</sup> given orally changes the intestinal pH and prevents the absorption of ammonia (8).

### Select disease conditions

Diseases of the liver include: bacteremia with subsequent colonization of liver; chlamydia which is the most common cause of hepatitis in psittacines; viral infection from Pacheco's, polyomavirus, reovirus, and adenovirus (6); internal parasitism by liver flukes, microsporidia, plasmodium, and atoxoplasma (6,9,10,11); neoplasia (6); toxins such as mycotoxins (aflatoxins) (6); and metabolic disorders (hepatic lipidosis and iron storage disease) (6,11).

Iron storage disease: Iron storage disease is the excessive deposition of iron in parenchymal cells with resultant cellular damage (12). Hemosiderosis is the excessive deposition of iron without resulting cellular damage (12). Iron absorption in mammals, which is an active process, occurs in the small intestines (13). The majority of the iron is bound as ferritin (1,13). Ferritin is the primary iron storage form in tissues (1,13). The other iron pigment is hemosiderin, a less available storage form composed of native and denatured ferritin and protein (1,13). Iron storage disease results when ferritin and hemosiderin accumulate in the tissues due to prolonged iron overload (13).

In avian species, the exact etiology of the iron overload is not known. With Rothschild mynahs there is an age-related increase in the amount of iron pigments within the hepatocytes where dietary iron intake has only a minor influence on the iron accumulation (14). In Indian hill mynahs, a viral or metabolic abnormality is suspected (12). A dietary cause of iron overload is possible in tanagers (12). Toucans may have an inherited genetic defect that results in this disorder (12). Other species described with this condition include greater and lesser Indian hill mynahs, greater and lesser birds of paradise, Quetzals, crows, common starlings, North American wood ducks, Virginia rails, Rothschild mynah, casqued hornbill, tanagers, and twelve species of Ramphastidae, of which the most frequently affected is the keel-billed (sulfur-breasted) toucan (12,15).

The clinical signs of iron storage disease include a cachexic body condition, abdominal swelling due to ascites and/or hepatomegaly, dyspnea, listlessness, and death (12,15). In one case, an elevation in blood ammonia and neurological signs (ataxia and seizures) were felt to be due to hepatic encephalopathy (16).

The definitive diagnosis is made by a liver biopsy (13,12). Upon visual inspection, the liver will appear to have an orange pigmentary discoloration (15).

Therapy is palliative at best. Weekly phlebotomies with the removal of 1% of body weight until borderline anemia is reached, the use of daily iron chelating drugs such as deferoxamine<sup>d</sup>, and dietary modification (low iron foods) have all been recommended in the literature (6,12,15,17).

**Chlamydia:** *Chlamydia psittaci* is an energy-dependent, obligate intracellular-parasitic agent. The organism has a gram negative cell envelope, contains both DNA and RNA, possesses prokaryotic ribosomes, synthesizes its own proteins, nucleic acids, and lipids, and is susceptible to antibiotics. It has a biphasic life cycle. The elementary body (EB) is the small dense infectious form which attaches to a host cell. Once in the cell it makes the transition from the metabolically inert EB to the metabolically active reticulate body (RB). The RB grows and divides by binary fission. In the cell, the RB matures into the infectious EB. The EB completes the cycle when the cell ruptures to release the infectious particles (18,19, 20).

Aerosol inhalation and ingestion are the primary routes of transmission (19). Egg transmission is believed to be rare, but has been reported (19). In some species, parent to young transmission via feeding is thought to be important, although contamination of the nesting site may play a larger role. Carriers can excrete the organism intermittently over several months (19). In cockatiels chlamydia can be shed 16 days after inoculation (21). Immunity is usually short lived in recovered cases, permitting rapid reinfection.

Clinical signs vary tremendously and are affected by management factors, immune competence of the bird, pathogenicity of the particular strain, and the presence of coexisting organisms (bacterial, viral, fungal) (18,22,23). Young birds are more susceptible than mature birds (19). The large South American parrots (macaws and Amazons) are more susceptible than ones from South Asia, Australia, and related islands (cockatoos, lorries, and king parrot) (19). Canaries, finches, and mynahs are susceptible and may die acutely without clinical signs (19). The signs in pigeons, in which the organism is widespread, rarely extend beyond a mild conjunctivitis (19). There appears to be no serious disease among wild bird populations possibly due to host adapted strains of chlamydia (24).

The incubation period of *Chlamydia psittaci* ranges from five days to several weeks (22,25). The signs of disease include sinusitis, dyspnea, conjunctivitis, polyuria, diarrhea, lethargy, anorexia, yellow to dark green droppings, poor feathering, flaccid paralysis of the legs, chronic weight loss, and central nervous system signs such as opisthotonos, tremors, and convulsive movements (19,22,26,27). Adult breeding birds may have decreases in hatchability of eggs, decrease fertility, and early death of embryos or chicks (28).

Hematology, radiography, and serum biochemistries are all procedures that can provide a rapid clinical diagnosis of chlamydiosis (19,22,27,28). It is important to remember that no antemortem test will certify a bird is free of chlamydia. If the disease is suspected (by history, clinical signs, non-specific laboratory tests) and yet the definitive tests such as enzyme-linked immunosorbent assay (ELISA) (29,30,31), elementary body agglutination (EBA) (21,32), or cell culture are negative, it is prudent to start treatment and monitor the response.

Tetracyclines are the most effective antibiotics but only when chlamydia are actively replicating (19,27,33). They interfere with the synthesis of proteins and the growth and fission of reticulate bodies (19). A prolonged treatment of 30-45 days is recommended, because chlamydia can persist in cells without activity (19).

Fatty liver disease: Fatty liver disease (hepatic lipidosis) is an insidious condition that is poorly understood. It is a common hepatic lesion seen in budgies, cockatiels, and Amazons (2). The typical presentation is an acutely ill bird. The clinical signs include sudden and complete anorexia, depression, dyspnea, and ataxia (2). Commonly the birds are obese and most have been on all-seed diets for the major part of their lives (6). The liver is usually palpably enlarged and yellow in color. The probable pathogenesis is by an excessive lipid accumulation in the liver caused by fatty acid synthesis exceeding their utilization (11). Some possible etiologies include endocrine diseases (hypothyroidism or diabetes mellitus), any disease condition interfering with nutrient digestion or absorption, or a primary defect in fat metabolism (34). Often these birds will have elevated bile acids and commonly the other liver enzymes may be normal. A liver biopsy is important for prognosis. Therapy is supportive (6) .

**Chronic Liver Disease:** This is a not uncommon presentation of liver disease in psittacines. The liver on gross appearance is often discolored, may be atrophied or enlarged, and have a smooth or nodular surface (35). The exact pathogenesis is unknown, however, chronic inflammation, toxins, and nutritional problems may contribute. Histologically there is variable inflammation, fibrosis, bile duct hyperplasia, and hepatocellular degeneration (35). The definitive diagnosis and prognosis depends on a liver biopsy.

**Neoplasia:** The most common primary neoplasm of the liver is the bile duct carcinoma (cholangiocarcinoma) which may be associated with internal papillomatosis (35). The common presenting clinical signs are a prolapsing cloaca and weight loss (36). The majority of reported cases involve Amazon parrots (36).

Tumors of the hepatocytes include adenomas and carcinomas. These primary hepatic neoplasms grow by infiltration. Some may develop foci of necrosis within the tumor, which if biopsied, may result in a missed diagnosis. Other neoplasms involving the liver include; fibrosarcoma (37), lymphosarcoma (34), myelolipomas (38), and hemangiomas (34).

**Pacheco's:** The Pacheco's herpesvirus is a double-stranded enveloped DNA virus. It is one of several types of herpes virus known to infect avian species (25). The clinical signs generally are non-specific and the birds frequently present unexpectedly dead (39). Transmission is by fecal and oral viral shedding from dying, infected birds or from asymptomatic carriers (25,39). Stress from cold, shipping, socialization, or courtship induces viral shedding in carriers (39). Incubation is from five days to several weeks (39). The findings on gross postmortem range from hepatomegaly and splenomegaly to no lesions (39). The diagnosis is commonly obtained on histopathology (39). Treatment in exposed birds has been attempted with acyclovir<sup>e</sup>, an acyclic purine nucleoside, with variable success (39).

- a. Furosemide, Lasix, Hoescht-Roussel, Somerville, NJ.
- b. Lactulose, Cephulac, Marion Merrell Dow, Kansas City, MO.
- c. Vitamin K, AquaMephyton, Marck Sharp & Dohne, West Point, PA.
- d. Deferoxaminemesilate, Desferal, Ciba-Geigy, The Netherlands
- e. Acyclovir, Zovirax, Burroughs Wellcome, Research Triangle Park, NC.

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