

CHAPTER

20

HEPATOLOGY

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The avian liver is bilobed and relatively large in comparison to the size of the bird. The left hepatic duct connects to the duodenum. The right hepatic duct connects to the gall bladder in those species that have this organ (gallinaceous birds, ducks, geese). If the gall bladder is absent (pigeons, parrots, ostriches), the right hepatic duct drains directly into the duodenum. If this duct dilates, it may appear as though a gall bladder is present (see Color 14). Birds have no mesenteric lymph nodes, and patients with chronic enteritis may also have periportal hepatitis. The liver in a normal Psittaciforme rests ventrally against the sternum, wraps cranially around the base of the heart and wraps dorsally along the lateral margins of the proventriculus (see Anatomy Overlay). The size of the liver varies among species. In Galliformes, the liver lobes are of similar size while in Psittaciformes, the right lobe is generally larger. Bile acids secreted by the liver function to emulsify fats and activate pancreatic lipase and amylase, all of which aid in digestion. The liver also metabolizes fats, proteins and carbohydrates and detoxifies metabolites and ingested toxins.

Diagnostic Considerations²²

Physical findings associated with liver disease are often nonspecific, and are generally not sufficiently diagnostic to establish a clinical diagnosis. A green coloration of the urine and urate fractions in the excreta is a strong indication of liver disease (Color 20.4). Dyspnea is a common finding in birds with hepatomegaly or ascites. Occasionally, an enlarged liver can be palpated and in the smaller Passeriformes, an enlarged liver may be visible through the transparent abdominal wall. Abnormal coloration of the liver is also sometimes visible, particularly in small species and neonates. Polydipsia and vomiting are sometimes associated with liver disease. Pruritus occurs commonly in icteric humans and is thought to be caused by the deposition of irritant bile salts in the skin. Clinical signs suggestive of pruritus and feather picking have been reported in birds with liver disease. Other integumentary disorders that are loosely discussed in association with liver disease include pigment changes of feathers (Color 20.2), abnormal molting and softening, flaking and overgrowth of beak and nails (Figure 20.1).

Because liver diseases may be associated with many physical findings and may even be asymptomatic, fecal examination, hematologic examination (PCV,



FIG 20.1 Liver disease should always be considered in the differential diagnosis list for birds with beaks and nails that consistently overgrow.

WBC and differentiation, buffy coat for parasites), total protein, plasma protein electrophoresis (A:G ratio), AST, LDH, bile acids and a total body radiograph are considered the ideal database for evaluating a sick bird. The history should involve questions concerning contact with birds outside the premises, which might indicate exposure to infectious diseases that cause hepatitis like Pacheco's disease virus or chlamydia.

Clinical Pathology

Bile Pigments

Green-colored urates are suggestive of liver disease.^{5,20,38} This discoloration is the result of increased excretion of biliverdin (biliverdinuria), which is the most important bile pigment in birds. Icterus or jaundice, which is caused by a hyperbilirubinemia, is seen very infrequently in birds. In chickens, if both bile ducts are ligated, the concentration of plasma bile pigments rises immediately but stabilizes after two weeks at about 85 $\mu\text{mol/l}$. This is a much lower concentration than is found in mammals with total biliary obstruction. In sera of healthy ducks, low levels of bilirubin may be detected, and significantly elevated levels have been reported after experimental infection with duck hepatitis virus; however, the observed levels of about 17 $\mu\text{mol/l}$ were well below the serum concentration of 34-51 $\mu\text{mol/l}$, which is considered the level above which jaundice becomes apparent in man. The infrequent occurrence of icterus in birds may also be explained by the fact that the enzyme biliverdin reductase, which converts biliverdin to bilirubin, is absent in the bird species that have been tested.^{18,19,39} It has been suggested that in birds, some biliverdin may be converted to bilirubin by bacteria or nonspecific reducing enzymes.¹⁷

Avian plasma may be colored yellow because of the presence of carotenoids, and this normal color should not be misinterpreted as icteric plasma. Some avian species, such as Hyacinth Macaws, have a normal yellow coloration of the skin that could be misinterpreted as icterus (see Color 8). A few hours after birds have received an intramuscular multivitamin injection, the urate fraction can be yellow-brown in color, which should not be confused with liver-induced changes in the urates (see Color 8).

Clinical Enzymology

The application of clinical enzymology in human and veterinary medicine is a common method for estab-

lishing a diagnosis in certain disease conditions. Increases in plasma enzyme activities are usually related to leakage of enzymes from damaged cells, but sometimes there may be increased production in affected tissues. The increased concentration of a particular enzyme in plasma depends on factors such as the activity of enzyme in the cells, the rate of leakage and the rate of clearance of the enzyme from the plasma. Rational interpretation of elevated plasma activity of intracellular enzymes due to cellular damage can be performed only if the enzyme profiles of the various organs of the species under investigation and the elimination half-lives of these enzymes are known. The most reliable way to investigate the specificity and sensitivity of various plasma enzymes for detecting liver disease is to establish reference intervals in healthy individuals, and to monitor plasma enzyme changes after selective experimental liver damage. These data are compared to changes associated with diseases of other organs.

Enzyme profiles of the various organs have been investigated in chickens, Mallard ducks, turkeys, racing pigeons, budgerigars and African Grey Parrots.

The elimination half-life of an enzyme can be calculated from the exponential decline in activity during recovery from acute tissue damage. Alternately, it can be determined by measuring the decline in activity after intravenous administration of purified enzymes. After intravenous injection, most enzymes follow a biphasic exponential decline. The rapid primary phase is related to distribution of enzymes by diffusion from plasma into other extracellular body fluids, and the slower secondary phase is related to the actual clearance of enzyme from the body fluids. During the secondary phase, a constant fraction of the enzyme present is eliminated per unit of time, making the decline linear on a logarithmic scale (first order kinetics). The time required for 50 percent completion of the latter process is defined as the elimination half-life ($t_{1/2\beta}$).

Plasma enzyme profiles have been studied in a number of avian species following experimentally induced or spontaneously occurring liver disease. Unfortunately, there is a large interspecies variation in data and the type of liver disease. Additionally, the presence of concomitant injury to other organs that could alter the results of enzyme activity measurements may occur. The results of experimental studies of liver-specific enzymes in racing pigeons are listed in Table 20.1.^{22,27,28} Information on enzyme activity in

other tissues may be found in Chapter 11 and in the Appendix.

Glutamate dehydrogenase (GLDH) is the most liver-specific enzyme in the racing pigeon. Since GLDH is localized within the mitochondria of the liver cells, elevated plasma GLDH activities are seen only after severe liver cell damage (necrosis). Liver cell degeneration without necrosis will not cause elevated GLDH activities. In the budgerigar, GLDH activity in liver tissue is relatively low when compared to man and most other birds tested, including cockerel, duck, turkey and pigeon.³¹ However, increased GLDH activities were observed in Amazon parrots with extensive liver necrosis due to Pacheco's disease virus, suggesting that this enzyme may be useful for the detection of liver necrosis in at least some psittacine species.

Aspartate aminotransferase (AST, formerly GOT) is the most sensitive indicator of liver disease in the pigeon. This variable, however, is not specific because elevated AST activities can also be seen with muscle damage.

Despite relatively low alanine aminotransferase (ALT, formerly GPT) activities in liver tissue of racing pigeons, this enzyme is useful for detecting liver cell damage because the elimination half-life in plasma is relatively long.

Lactate dehydrogenase (LDH) disappears rapidly from plasma, making it a poor indicator of liver damage, despite relatively high concentrations of this enzyme in liver tissue. Neither ALT nor LDH is specific for the liver because these enzymes, like AST, also occur in muscle.

Gamma glutamyl transferase (τ -GT), has been found to be a specific indicator of liver disease in the racing pigeon. The fact that no activity of this enzyme can be found in supernatants of liver tissue homogenates may be due to the synthesis of τ -GT during cholestatic liver disease, as has been reported in mammals. This enzyme is not as sensitive as AST.

Alkaline phosphatase (AP) and creatine kinase (CK) are never elevated after liver cell damage, while activities of these enzymes in liver tissue are negligible.

It should be emphasized that elevated activities of "liver enzymes" in plasma may indicate recent damage to liver cells and does not give information on liver function.

Intramuscular injections given within one to five days before collection of a blood sample may cause an elevation of some plasma enzyme activities due to damage of muscle tissue. This can lead to an erroneous diagnosis of liver disease.

TABLE 20.1 Plasma Chemical Variables in Liver and Muscle Disease Based on Experimental Studies in Pigeons.²²

Variable	Liver Disease		Muscle Disease	
	Specificity	Sensitivity	Specificity	Sensitivity
Bile acids	+++	+++	–	–
τ-GT	+++	+	–	–
AST	–	+++	–	+++
ALT	–	+	–	+++
AP	–	–	–	–
GLDH	+++	+*	–	–
CK	–	–	+++	+++
LDH	–	+	–	+

– low, + some, ++ moderate, +++ high
*Only with liver and kidney cell necrosis.

Bile Salts

Plasma bile acids and bile salts are formed in the liver from cholesterol. It is likely that there is a continuous secretion of bile into the intestine in birds, with or without a gall bladder. A slight increase in secretions would be expected postprandially due to the intrahepatic effects of intestinal hormones like secretin, avian vasoactive intestinal peptide (VIP) and cholecystokinin (CCK). These hormones are released after the consumption of food.

The exact site responsible for increased bile secretion and the regulatory mechanisms involved are presently unknown.²⁴ Bile acids secreted by the liver enter the small intestines, are absorbed in the lower small intestines, enter the portal vein and are extracted from the blood by the liver. Enterohepatic recirculation accounts for over 90% of the secreted bile acids being reabsorbed in the jejunum and ileum.⁹ Plasma bile acid concentrations (PBAC), including their salts and corresponding glycine and taurine conjugates, are a reflection of the clearing capacity for bile acids by the liver. All liver functions (extraction, conjugation and excretion) are involved in this process, and determination of plasma bile acid concentration provides information on the combined effectiveness of these functions.

Due to the development of specific and sensitive enzymatic assays for bile acids, bile salts and their corresponding glycine and taurine conjugates, there

has been substantial progress with respect to the use of PBAC for the diagnosis of hepatobiliary disease. Circulatory levels of bile acids increase if the liver is damaged and cannot extract bile from the portal vein or if the enterohepatic cycle is blocked and blood from the portal vein does not reach the liver. PBAC should be considered a sensitive and specific variable for testing liver function in birds as it is in mammals.^{3,12,23,36} Reference intervals for PBAC have been established for the racing pigeon and the most common psittacine species found in captivity (see Appendix). Experimental studies²² indicate that PBAC is the single most useful, available test for determining liver dysfunction in the racing pigeon. In experimentally induced liver disease, five- to ten-fold increases of PBAC over the upper limit of the reference interval are common.

Food consumption significantly increased PBAC in granivorous birds with a gall bladder (Mallard Duck) and granivorous birds without a gall bladder (racing pigeon).²⁴ The same effect was seen in carnivorous birds.³⁰ Although up to a 4.5-fold postprandial increase of PBAC was seen in individual birds, the concentrations were never elevated more than 1.65-fold over the upper limit of the reference range. In hepatobiliary disease, five- to ten-fold increases over the upper limit of the reference range were common.²⁷ Although postprandial increase might complicate interpretation of PBAC, differentiation between postprandial elevations and elevations due to hepatobiliary disease is possible. Experimental findings suggest that values >70 μmol/l in fasted racing pigeons and most psittacine species, and values >100 μmol/l postprandially should be considered elevated, and therefore suggestive for hepatobiliary disease. In Amazon parrots, PBAC values >145 μmol/l are considered elevated.^{24,28,29}

Hepatic Encephalopathy

A tentative diagnosis of hepatic encephalopathy is often made when neurologic signs are seen in birds with documented liver disease; however, this syndrome has not been well documented in avian species. In man and other mammals, hepatic encephalopathy and hepatic coma are mostly seen in portosystemic shunting as a result of a portocaval anastomosis. It is not a disease in itself but a medical condition characterized by neurologic symptoms caused by intoxication of the brain by products of protein digestion, which enter the portal circulation and are not detoxified in the liver. It is believed that degradation products from protein catabolism act as false neurotransmitters. For this reason, protein-rich

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Color 20.1

A mature Blue and Gold Macaw was presented with a history of developing necrotic lesions in the beak. The bird was severely obese (1300 g) and had thick, white serum. The bird's cholesterol level was 1700 mg/dl. A biopsy of the liver indicated severe fatty degeneration. The obesity and lipemia were controlled by switching the bird to a formulated diet supplemented with fresh fruits and vegetables. The formulated portion of the diet was offered on a limited basis and the bird's exercise was increased. The beak lesion was theorized to have occurred secondary to a vascular accident that caused an area of ischemic necrosis.

Color 20.2

The occurrence of black discolored feathers in Amazon parrots and macaws is frequently discussed as a clinical change indicative of hepatitis. While a connection between the appearance of black feathers and hepatitis has not been confirmed, clinical experience suggests that hepatitis should be included in the differential diagnosis list.

Color 20.3

An obese Amazon parrot was presented for exercise intolerance (dyspnea) and intermittent depression. The bird weighed 700 g and had difficulty ambulating because of fat in the inguinal and abdominal regions. The bird's blood was yellow; a normal Amazon parrot's blood is provided for comparison. The bird's cholesterol level was 2300 mg/dl. Most other blood parameters were considered non-diagnostic because of the lipemia. Radiographs indicated severe hepatomegaly. Histopathology of a liver biopsy confirmed fatty liver degeneration.

Color 20.4

Yellow-to-green urates are suggestive of biliverdinuria and are most commonly associated with hepatitis.

Color 20.5

Normal liver of an adult Umbrella Cockatoo hen with PBFV virus. Note the reddish-brown color, smooth consistency of the surface and sharp defined margins of the normal liver lobes. In Psittaciformes, the right liver (rl) lobe is slightly larger than the left liver (ll) lobe. The lung (lu) can be seen lying under the transparent, contiguous wall of the cranial and caudal thoracic air sacs (open arrow). The transparent ventral hepatic peritoneal membrane can also be seen (arrows). Other organs that should be noted include the heart (h), proventriculus (p) and ventriculus (v).

Color 20.6

A breeding toucanette was found dead in its enclosure. The abdomen was severely distended. Characteristics of fluid collected by abdominocentesis at necropsy were consistent with a transudate. The enlarged liver was orange and rough in appearance. Histopathology was suggestive of hemochromatosis, and the disease was confirmed using a Prussian blue stain to demonstrate iron-laden hepatocytes.

Color 20.7

Swollen, pale-yellow liver from an Amazon parrot with severe hepatic lipidosis. Neonates that are mobilizing egg yolk will have a similarly appearing liver for the first two to three weeks of life. Note that the heart is also pale and rotund.

Color 20.8

A Blue and Gold Macaw chick was presented for evaluation. The bird was in a comatose state and was the sixth baby from a psittacine nursery to die acutely. The bird had subcutaneous hemorrhages, hepatomegaly and swollen, hemorrhagic kidneys, all suggestive of avian polyomavirus. A polyomavirus infection was suspected by identifying basophilic intranuclear inclusion bodies in the liver, spleen, kidneys and heart, and was confirmed by DNA probe detection of viral nucleic acid on a swab taken of the cut surface of the liver and

spleen. Note the petechial to ecchymotic hemorrhages in the liver and heart.

Color 20.9

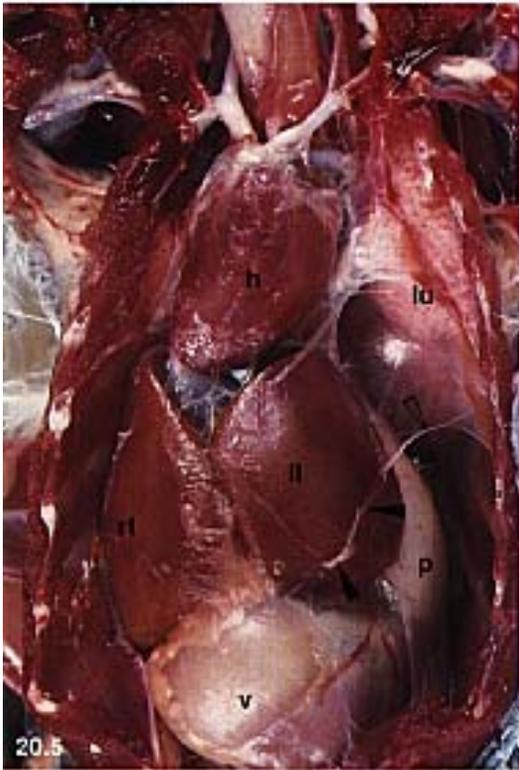
An Amazon parrot with severe dyspnea was found on the bottom of its enclosure. The bird died while en route to the emergency clinic. At necropsy, the bird's muscle tissue was extremely pale. Exsanguination had occurred secondary to a tear in the liver capsule. Note the pale heart and left liver below the blood clot.

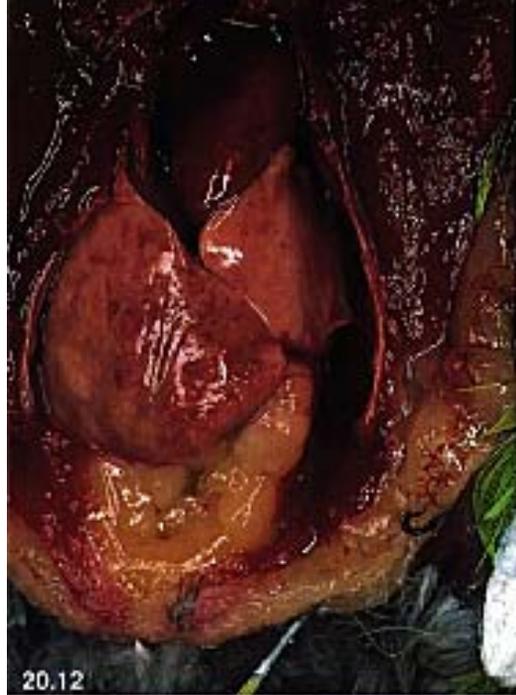
Color 20.10

A Blue and Gold Macaw that was being treated for aspergillosis air sacculitis was presented with an acute onset of anorexia, depression and abdominal swelling. Radiographs indicated a soft tissue density filling most of the abdominal cavity. Abdominocentesis was unproductive. An exploratory laparotomy was performed. When the abdominal cavity was opened, unclotted blood flowed from the incision with each breath. The bleeding originated from a tear in the right lateral liver lobe (arrow). The hemorrhage was controlled with pressure. Both liver lobes had multiple, raised, white lesions that were suspected to be fungal granulomas. The client elected euthanasia. At necropsy, the liver was firm and had multiple, granulomatous-like lesions. Similar lesions were noted in the lungs, and the right caudal thoracic air sac was thickened and necrotic. Histopathology confirmed *Aspergillus* sp. in the lung and air sac. The liver lesions were characterized by massive hepatocellular necrosis and biliary hyperplasia. These lesions are suggestive of aflatoxicosis. Interestingly, the LDH=397, AST=141 and bile acids=1.9, determined two weeks before surgery, did not reflect the severity of the liver damage.

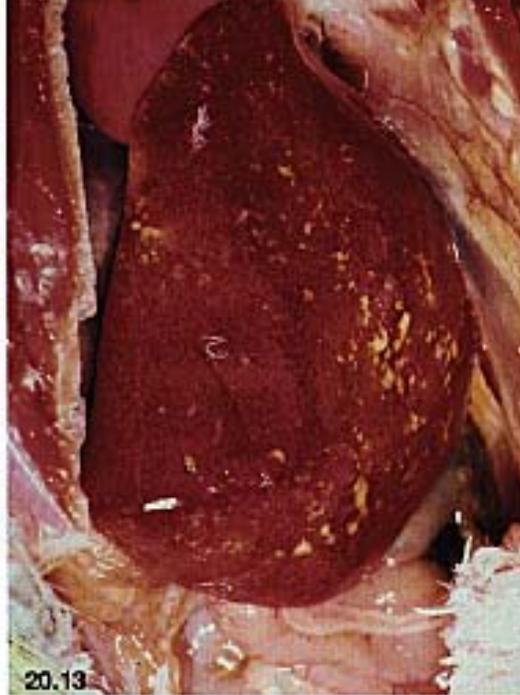
Color 20.11

Cut surface of the liver from the Blue and Gold Macaw in Color 20.10. Note the substantial involvement of the liver and the scarcity of normal-appearing liver tissue.

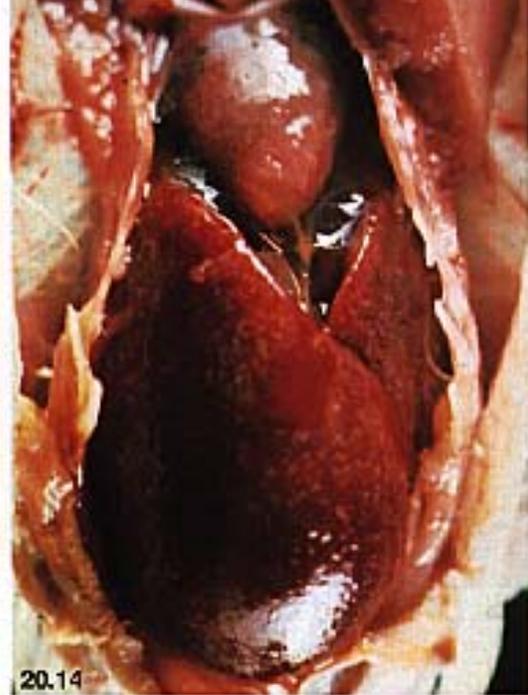




20.12



20.13



20.14



20.15



20.16



20.17



20.18



20.19



20.20

Hepatology

Color 20.12

Severe fatty liver degeneration and bacterial hepatitis in a 23-year-old Amazon parrot hen with ovarian cysts.

Color 20.13

Multifocal, white-to-yellow discoloration of the liver is characteristic of hepatocellular necrosis. The lesions in this African Grey Parrot were caused by *Chlamydia* sp. Bacterial and viral infections can cause similarly appearing lesions.

Color 20.14

Hepatomegaly and multifocal, white-to-yellow foci in the liver and heart of a mynah bird that died from toxoplasmosis (courtesy of Carol Partington).

Color 20.15

Iron storage hepatopathy in a mynah bird. Small brown-black foci were clearly visible throughout the liver parenchyma. The lesions can be more clearly visualized using a magnifying glass (courtesy of Robert E. Schmidt).

Color 20.16

Histomonas meleagridis (blackhead) lesions in the liver of a gallinaceous bird. Multiple round foci with central depressions extending into the liver parenchyma are considered pathognomonic (courtesy of R. Korbel).

Color 20.17

Mycobacteriosis hepatitis in a Sandhill Crane. *Mycobacterium* spp. infections frequently affect the liver and gastrointestinal tract in birds. Unlike in mammals, infec-

tions rarely occur in the lungs. Mycobacteriosis should be considered in any bird with granulomatous hepatitis. A quick diagnosis can be achieved by acid-fast staining of an impression smear of the cut surface of the liver (courtesy of Robert E. Schmidt).

Color 20.18

An Amazon parrot was presented with anorexia, dyspnea, depression and weight loss of three days' duration. Radiographs indicated severe hepatomegaly. Abnormal clinicopathologic findings included WBC=25,000, LDH=700, AST=600 and bile acids=150. A fecal antigen test for *Chlamydia* sp. was positive. Doxycycline therapy was initiated, but the bird did not respond and died the following day. Necropsy indicated a severely enlarged, firm, irregular yellow liver. The histopathologic diagnosis was lymphosarcoma. Chlamydia was not detected in any tissues, suggesting that the fecal antigen test result was a false positive.

Color 20.19

Multiple, disseminated granulomas in the liver of a gallinaceous bird. These lesions were caused by *Mycobacterium tuberculosis* (courtesy of R. Korbel).

Color 20.20

Plasmodium sp. infection in a Peregrine Falcon. The liver (l) and spleen (s) are both enlarged, but the characteristic change is the black discoloration of both organs. Other easily distinguishable organs include the lung (lu), proventriculus (p), ventriculus (v), heart (h) and intestines (i) (courtesy of Robert E. Schmidt).

diets in patients with liver disease frequently trigger neurologic symptoms.

Fasting plasma ammonia levels and plasma ammonia levels 30 minutes after oral loading with NH_4Cl (100 mg/kg in a gelatine capsule) have been used in dogs to establish the ability of the liver to convert ammonia into urea. Fasting plasma ammonia concentrations in healthy psittacines have shown values ranging from 36 to 274 $\mu\text{mol/l}$, which are well above the fasting concentrations described in dogs. Furthermore, some avian species will normally show up to an eight-fold increase of plasma ammonia concentration on oral ammonia tolerance test (ATT) using the canine protocol, and therefore an abnormal ATT is not diagnostic for portosystemic shunting in these species.²⁶ Further work is needed to properly diagnose and document the occurrence of hepatic encephalopathy in birds.

Avian Hemochromatosis

Limited work has been done on the clinical pathology associated with avian hemochromatosis. The iron status of an individual bird is determined by measuring three main areas of iron: storage iron, transport iron and erythrocyte iron. Storage iron can be semiquantitated by histologic examination of liver biopsies for stainable iron. In humans with hemochromatosis, urinary iron excretion in the six hours following injection of an iron chelating agent, desferrioxamine or diethylenetriamine pentacetic acid (DTPA) is significantly higher compared to normal individuals. Serum concentration of the iron storage protein ferritin is directly related to the available storage iron in the body and is clinically the most useful method for assessing iron stores.¹⁴

Transport iron in man is determined by measuring serum iron concentration and the total iron binding capacity (TIBC). The latter estimation is performed by determining the amount of iron required to saturate fully the iron-binding protein present in the serum sample. Reference values for serum or plasma iron concentration and TIBC in man are 10-34 $\mu\text{mol/l}$ and 45-72 $\mu\text{mol/l}$, respectively.³⁷ In pigeons these values are 11-33 $\mu\text{mol/l}$ and 30-45 $\mu\text{mol/l}$, respectively.²⁵ In Ramphastidae, total serum iron concentrations should be below 63 $\mu\text{mol/l}$, while TIBC should fall below 100 $\mu\text{mol/l}$.⁴² Total serum iron in a mynah bird with confirmed hemochromatosis exceeded 360 $\mu\text{mol/l}$, while control birds had values that were about 36 $\mu\text{mol/l}$.³² (See update on need for biopsy in Chapter 47.)

Erythrocyte iron can be evaluated by determining the red blood cell morphology and the various red cell parameters, such as PCV, hemoglobin concentration, mean corpuscular volume, mean corpuscular hemoglobin and mean corpuscular hemoglobin concentration. Low erythrocyte iron will be reflected by abnormalities in these parameters. Treatments of patients with hemochromatosis using repeated phlebotomies require frequent evaluation of red cell parameters to detect excessive iron depletion.

Plasma Chemistry and Liver Disease

To facilitate interpretation of plasma chemistry, it is advisable to include specific and sensitive indicators of both liver and muscle disease in the plasma chemistry panel (eg, GLDH, AST, CPK, bile acids). It should be stressed that elevated plasma enzyme activities are a sign of recent cell damage and not necessarily of impaired organ function. Most enzymes are not specific for one particular organ. Furthermore, in chronic conditions, extensive damage occurring in the past may have led to major dysfunction of an organ while enzyme activities may have returned to normal. This is a common finding in birds with liver fibrosis (normal AST, but elevated bile acids and extremely low protein and albumin) (Figure 20.2). When periodic blood chemistry is performed in a bird with liver disease, fluctuation of plasma enzymes and bile acids are often noted. Enzymes may be elevated while bile acids are not, and vice versa. Occasionally both variables may be found to be within established reference intervals. Repeated plasma chemistries are recommended when evaluating liver disease to prevent misinterpretation of results.

Radiology

Both hepatomegaly and ascites due to liver disease may be diagnosed radiographically. Hepatomegaly and microhepatia are common findings in birds (see Chapter 12). It is important to differentiate between hepatomegaly and cardio-hepatomegaly, because the latter indicates the presence of cardiac failure and secondary congestion of the liver. Caudal displacement of the ventriculus on a lateral radiograph is often caused by enlargement of the liver or associated structures (eg, bile duct or gallbladder in those species that possess one). Loss of the hourglass appearance between the heart and the liver on a ventrodorsal radiograph and widening of the liver beyond a line between the scapula and the acetabulum indicate hepatomegaly. Caudodorsal displacement of the ventriculus is also possible with hepatomegaly.

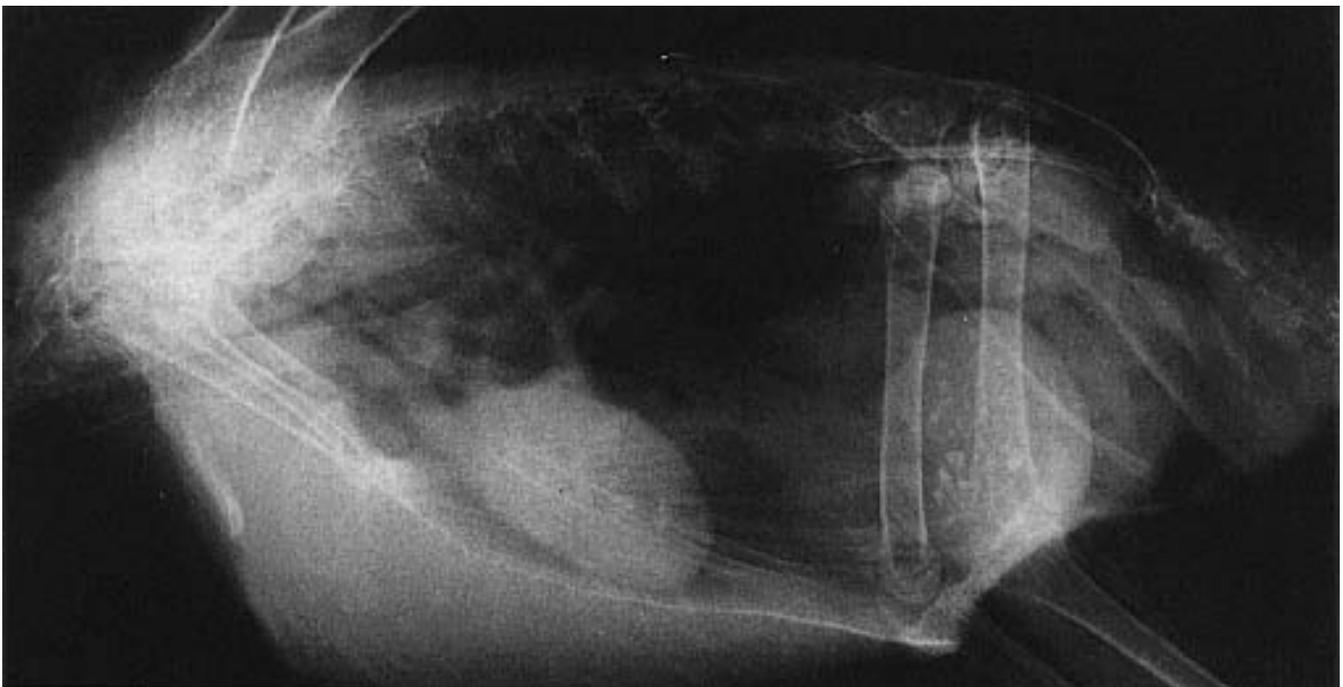


Ascites and peritonitis may complicate radiographic interpretation and obscure hepatic enlargement by overshadowing the liver. Repeat radiography of the abdomen after removal of peritoneal effusion fluid by paracentesis or diuretic treatment may be needed to visualize an enlarged liver and heart.

■ Liver Biopsy

In order for the clinician to establish a definitive diagnosis of liver disease, it is essential to take biopsies for histologic examination. Indications for liver biopsy include biochemical and radiographic changes suggestive of liver disease. Laparoscopic examination and biopsy of the liver through a midline ventral approach just caudal to the sternum is the method of choice to confirm a diagnosis of liver disease (see Chapter 13).^{8,16,22} Alternatively, the liver can be exposed through a ventral laparotomy incision and a small wedge of liver tissue can be excised with small surgical scissors. The possibility of severe, life-threatening hemorrhage secondary to liver congestion should be considered prior to biopsy in cases

FIG 20.2 A one-year-old Scarlet Macaw was presented with blood-tinged feces two days after destroying a plastic bowl. Radiographs indicated severe microhepatia (arrows). Abnormal clinicopathologic findings included WBC=18,500, TP=3.1 and bile acids=130. AST=50 and LDH=130 were both normal. High bile acid levels with normal AST and LDH activities suggest liver dysfunction in the absence of ongoing cellular injury. Histopathologic evaluation of a liver biopsy indicated severe hepatic fibrosis of unknown etiology.



showing radiographic signs of congestive heart failure or electrocardiographic abnormalities indicative of cardiac disease. A liver biopsy site will usually clot without complication, but caution should be exercised when performing biopsies in birds that have prolonged bleeding times after blood collection. Routine tests to determine the efficiency of the avian clotting mechanism are presently not available. In birds with ascites, it is important to perform a biopsy by entering just caudal to the carina to avoid damaging the air sacs and asphyxiating the bird with its own ascitic fluid.⁴ Liver biopsies should be examined histologically and cultured for bacteria. Acid-fast staining is of importance for the detection of mycobacteria.

Liver Diseases

Liver disease occurs frequently in companion birds. Clinical and clinicopathologic signs may indicate liver disease that can be confirmed by histologic examination of a liver biopsy. The following liver diseases discussed below have been documented in gallinaceous, companion or aviary birds.^{1,2,6,7,10,13,15,33,34,40} This review is based on known etiologies of avian liver disease, but it should be stressed that an etiologic diagnosis for many hepatopathies cannot be determined.

Infectious Diseases

Bacteria

Many bacterial species can cause hepatitis in birds (Color 20.12). A diagnosis can be made by culturing the organisms from a biopsy specimen. If bacteremia occurs, the same organisms can be isolated by blood culture. Elevated white blood cell counts and monocytosis are common with hepatitis caused by *Mycobacterium avium*. Bacteria that have been associated with hepatitis in birds include: *Borrelia*, *Escherichia coli*, *Salmonella typhimurium*, *Yersinia pseudotuberculosis*, *Acinetobacter*, *Serratia marcescens*, *Staphylococcus*, *Campylobacter*, *Corynebacterium*, *Streptococcus zooepidemicus*, *Pseudomonas*, *Citrobacter*, *Pasteurella haemolytica*, *P. multocida*, *Mycobacterium avium*, *M. bovis*, *M. tuberculosis* (Colors 20.17 and 20.19). In gallinaceous birds, bacterial cholecystitis has been reported. *Eubacterium tortuosum* has

been associated with hepatic granulomas and ulceration of the lower intestines in turkeys.

Chlamydiosis

Chlamydia psittaci is an extremely common cause of hepatitis in psittacine birds (Color 20.13). Hepatosplenomegaly on radiographs of a bird that has been in recent contact with infected birds is a characteristic clinical presentation (Figure 20.3). A tentative diagnosis can be made by using an ELISA-type antigen capture test for the detection of chlamydial organisms in a fecal swab. Liver biopsies can be screened for chlamydiosis with a Stamp, Giemsa or Macchiavello's stain, or by fluorescent antibody IFA or ELISA.

Viruses

Many viruses that infect birds can cause hepatitis alone or in combination with other systemic changes. Elevated plasma GLDH activity has been shown to occur with Pacheco's disease virus infections and should alert the practitioner to extensive liver necrosis. Other herpesviruses are known in other avian species. Pacheco's disease virus, adenovirus, polyomavirus, reovirus, coronavirus and avian serositis virus have all been associated with hepatitis in companion birds (Color 20.8).

Duck virus hepatitis is a highly fatal, rapidly spreading viral disease of young ducklings that can be caused by either of one of the three known duck hepatitis viruses: DHV types 1 (worldwide distribution, classified as a picornavirus), 2 (only in England, classified as astrovirus), or 3 (only in USA, classified as picornavirus, unrelated to type 1). The sudden onset, rapid spread and acute course of this disease, in combination with hemorrhagic lesions in livers of ducklings up to three weeks of age, are practically pathognomonic.

Turkey viral hepatitis is a highly contagious, often subclinical disease of turkeys that produces lesions only in the liver and pancreas (hence the suggested name hepatopancreatitis). The presence of stress factors is considered to be essential for manifestation of the disease. Mortality is usually very low and does not occur over six weeks of age.

Helminths

Trematode infections have been reported in the liver and bile ducts of cockatoos (*Platynosomum proxilliensis*), penguins (*Renicola* sp.), cormorants (*Amphimerus elongatus*), ducks and turkeys. A diagnosis can be made by examination of the feces for trematode eggs.

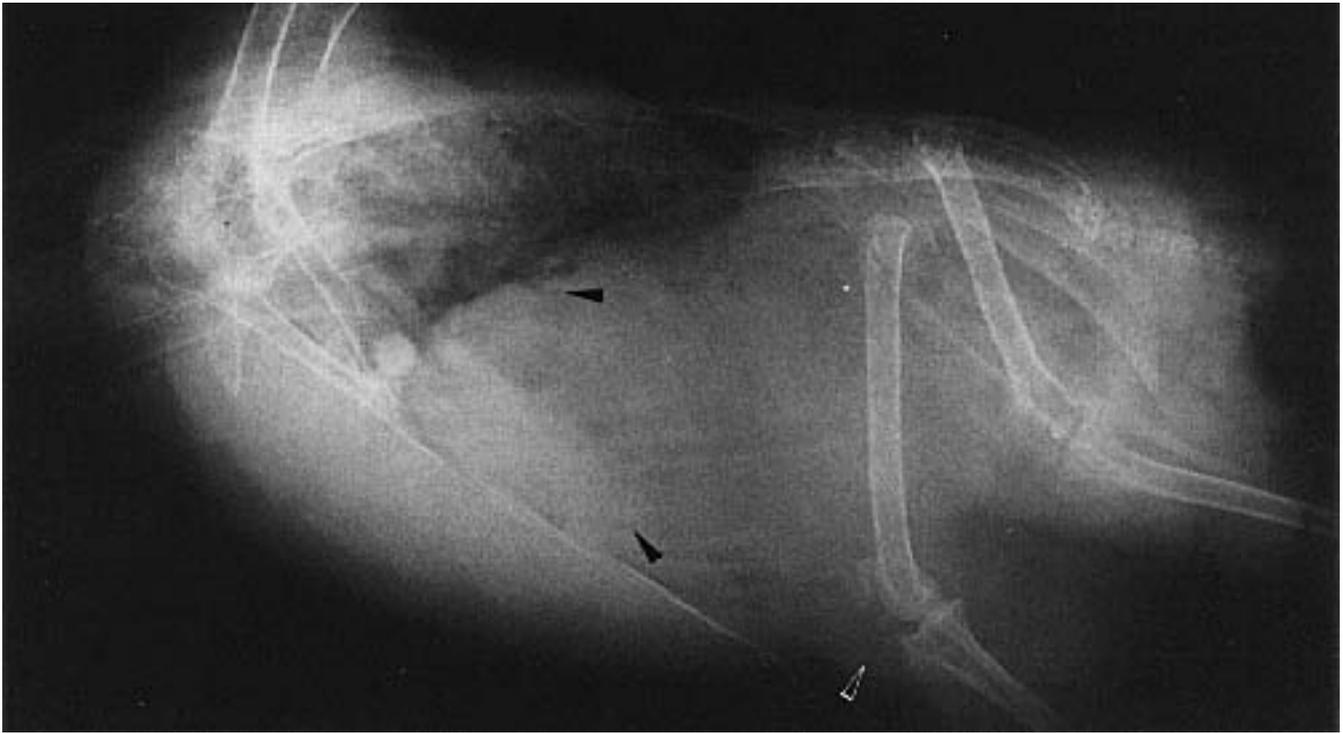


FIG 20.3 A young Double Yellow-headed Amazon Parrot was presented with lethargy, dyspnea and lime-green excrement. Radiographs indicated massive hepatomegaly causing cranial displacement of the heart (arrows), abdominal swelling (open arrow) and compression of the abdominal air sacs. The bird was positive for chlamydiosis by serology and responded to doxycycline therapy (courtesy of Marjorie McMillan).

It should be noted that in birds, trematode eggs in the feces do not always originate from parasites in the liver. In pigeons and ducks, trematodes can also be found in the alimentary tract (*Echinoparyphium* and *Echinostoma* spp.) or the kidney (*Tamerlania bragai* in the pigeon). In various avian species (including chickens, Passeriformes and Anseriformes), trematodes can be found in the oviduct (*Prosthogonimus ovatus*). Pancreatic trematodes have also been reported in birds.

Protozoa

A variety of protozoa can cause hepatopathies. *Trichomonas gallinae*-induced hepatic necrosis has been reported in Columbiformes, Falconiformes and Passeriformes.

Histomonas meleagridis is a common cause of hepatitis in captive Galliformes (Color 20.16). Sulfur-colored feces in turkeys, bloody cecal discharge in chickens, leucocytosis with heterophilia, a decreased albumin/globulin ratio and elevated liver enzymes are all suggestive of histomoniasis.

Leucocytozoon simondi is a well known cause of mortality in ducks and geese; however, the infection can also occur in other species. Hepatosplenomegaly is

common, and parasites can often be detected in a peripheral blood smear.

Atoxoplasma (*Lancesterella* sp.) and toxoplasma infections are common in Passeriformes, but the latter also occurs in Psittaciformes (Color 20.14). An enlarged liver can often be seen through the transparent abdominal wall in Passeriformes with atoxoplasmosis. Sporozoites may be seen in small lymphocytes in a peripheral blood smear.

Microsporidian infections have been associated with hepatitis in lovebirds.

Noninfectious Diseases

Metabolic Disorders

In zoological collections, Psittaciformes show a high prevalence of fatty infiltration of the liver (Color 20.7). Hepatic steatosis, hepatic lipidosis and fatty degeneration have all been used to describe the condition. It has been well established that an unbalanced diet (biotin, choline and methionine deficiencies) or excessive consumption of high-energy diets with restricted exercise may lead to fatty degeneration. It should be stressed that many companion

psittacine birds are fed high-energy, multi-nutrient-deficient, all-seed diets that predispose them to fatty liver degeneration.

Fatty liver hemorrhagic syndrome in laying hens has been associated with high-energy diets fed to birds with restricted exercise. The dramatic estrogen-induced increase in liver lipogenesis to supply the developing ova has been suggested as the etiology of this condition. Reticulolysis and fibrosis of hepatic parenchyma is sometimes associated with a fatty liver. Reticulolysis is associated with rupture of intrahepatic portal veins and liver hemorrhage. Affected chickens have greatly elevated serum calcium and cholesterol concentrations. The condition can be artificially induced with estrogen injections.

Fatty liver and kidney syndrome of young broilers or layer pullets is associated with diets with a marginal biotin content. Extensive fatty infiltration occurs in the heart, liver and kidney without inflammatory or degenerative changes. There is a failure of hepatic gluconeogenesis which may lead to an acute hypoglycemia in biotin-deficient, otherwise healthy birds, if normal food intake is interrupted for a short time.

Iron Storage Disease

Hemosiderosis has been defined as an accumulation of an increased amount of hemosiderin in tissues without alteration of tissue morphology, while hemochromatosis is associated with pathologic lesions in hemosiderin-containing tissues (Color 20.6).²¹ Hemosiderin is an iron-containing pigment derived from hemoglobin. The abnormal storage of iron is most frequently seen in the liver, but other organs may be involved. It has been suggested that excessive iron in the diet may be the cause of iron storage disease but this hypothesis has not been confirmed.

Hemochromatosis is most frequently described in Rampastidae (see Chapter 47), Sturnidae (birds of paradise), mynahs and quetzals, but has also been reported in Psittaciformes. Rampastidae are generally clinically normal prior to death, but occasionally affected birds are listless 24 hours prior to dying. Cardiac disease has been reported in mynahs due to iron storage in the myocardium. Electrocardiographic changes are possible due to cardiomegaly. In mynahs, generalized weakness, dyspnea and ascites are common. Radiography may reveal (cardio)hepatomegaly and ascites, and blood chemistry may indicate a liver function disorder (Figure 20.4). A specific diagnosis can be made by histologic examination of a



FIG 20.4 A four-year-old mynah bird fed predominately a seed-based diet was presented for severe dyspnea, lethargy and abdominal swelling. Radiographs indicated a diffuse soft tissue opacity in the abdomen suggestive of hepatomegaly and ascites. The heart was displaced cranially (arrows). Fluid collected by abdominocentesis was characterized as a transudate (low cellularity, SpGr=1.012 and TP=2 gm/dl). These findings are typical for iron storage disease.

liver biopsy after specific staining for iron (see Chapter 10). Total serum or plasma iron and TIBC may not be helpful in evaluating the iron status of the animal.

Circulatory Disorders

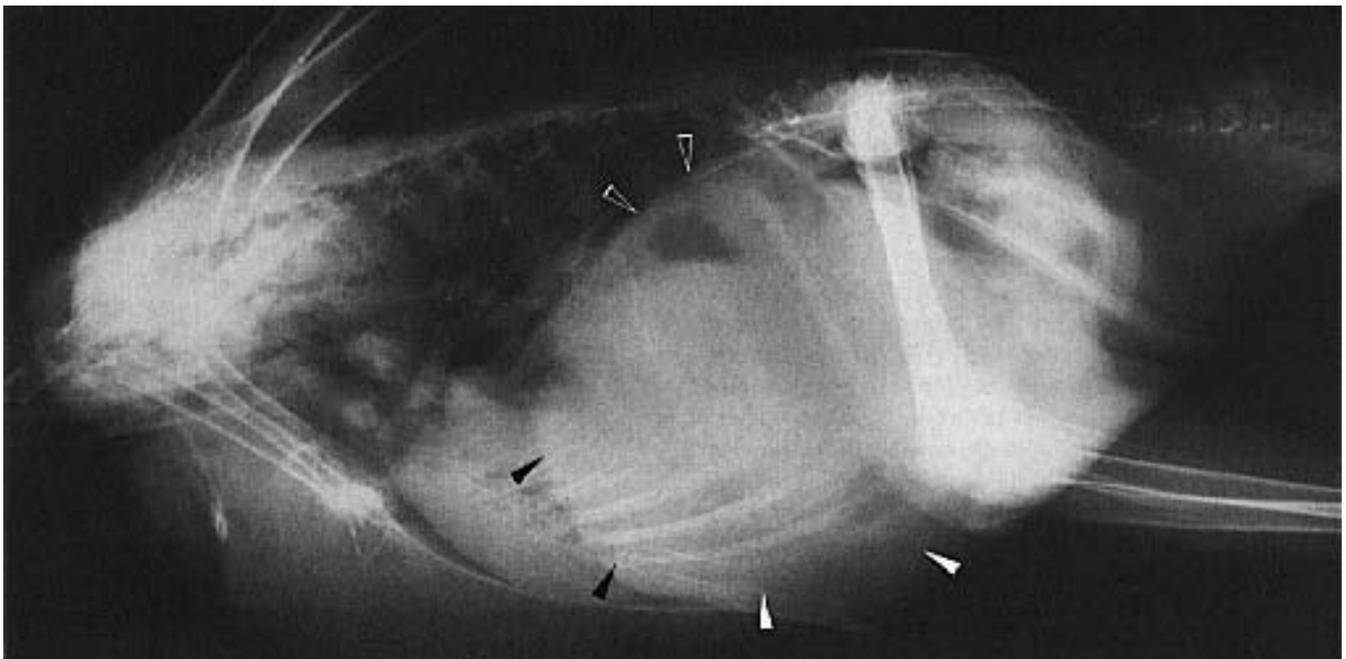
Portal hypertension can occur as the result of right atrioventricular valvular insufficiency. Portal hypertension may cause hepatic congestion. In the acute stage, the liver is swollen; as the disease progresses, the organ may be fibrotic and have a shrunken appearance. When liver enlargement is caused by congestion, a liver biopsy may result in fatal hemorrhage. The use of an artificial substrate (eg, Gelfoam) at the biopsy site to facilitate clotting may help control bleeding.

Anemic infarctions of the liver, especially of the caudal margins, can be seen as a result of bacterial endocarditis. Streptococci or staphylococci are often involved, but other bacteria like *Erysipelothrix rhusiopathiae* (formerly *E. insidiosa*) and *Pasteurella* spp. have also been associated with these lesions.

Hepatotoxins

Many plants are known to be hepatotoxic in some birds including: rapeseed (*Brassica napus*), ragwort (*Senecio jacobea*), castor bean (*Ricinus communis*),

FIG 20.5 A mature Blue and Gold Macaw with a history of aspergillosis air sacculitis that was being treated with systemic antifungals became depressed and anorectic (see Color 20.10). Radiographs indicated a diffuse soft tissue opacity throughout the abdomen (arrows). Gas is seen in the dorsally displaced proventriculus (open arrows).



hemlock (*Conium maculatum*), oleander (*Nerium oleander*), *Oxalis* spp., *Grantia* spp., *Crotalaria* spp., *Daubentonia* seed and cotton seed (*Gossypium* spp.). Interestingly, canaries are routinely fed rapeseed and do not appear to be affected by its toxins.

The following substances are hepatotoxic: arsenic, phosphorus, carbon tetrachloride, toxins from certain blue-green algae, halothane, methoxyflurane and mycotoxins (especially aflatoxin from *Aspergillus flavus*, *A. parasiticus* and *Penicillium puberulum*) (Figure 20.5). Degeneration and necrosis of hepatocytes are typical with aflatoxicosis. Bile duct proliferation and fibrosis leaving only islands of hepatocytes are common in chronic cases (Colors 20.10 and 20.11).

Fatty degeneration and the feeding of feeds contaminated with mycotoxins causing aflatoxin hepatitis are likely to be involved in the high incidence of liver disease in birds. Peanuts and Brazil nuts are notorious sources of aflatoxins, but many other seed mixtures can be contaminated. Chemical analysis of food for aflatoxin is possible (see Chapter 37).

Neoplasia

Liver tumors can be classed as primary and multicentric (metastatic) (see Chapter 25). Examples of the former are hepatoma, hepatocellular carcinoma, cholangioma, cholangiocarcinoma, lipoma, fibroma, fibrosarcoma, hemangioma, and hemangiosarcoma. Examples of metastatic tumors are leukosis/lymphosarcoma, rhabdomyosarcoma, renal carcinoma, and pancreatic carcinoma (Color 20.18).

It has been suggested that there is an association between cholangiocarcinoma and the presence of cloacal papillomatosis in Amazon parrots (see Chapter 19). Likewise, it has been suggested that hemochromatosis in mynah birds and aflatoxicosis in ducks are associated with hepatomas.

Amyloidosis

Amyloidosis is commonly seen in Anseriformes, gulls and shorebirds. It is caused by deposition of amyloid A (a waxy, translucent substance) in various organs, including liver and kidney (see Chapter 21). Amyloid A is a degradation product of an acute phase, reactant protein. Amyloidosis is often seen in birds with chronic infections (bumblefoot, tuberculosis and aspergillosis). Severe hypoalbuminemia caused by glomerular and hepatic damage can cause ascites and peripheral edema of the feet and legs.

Traumatic Rupture

Rupture of the liver is most likely to occur secondary to liver diseases, such as fatty degeneration, amyloidosis, mycobacteriosis and neoplasia, but can also occur as a result of trauma (Color 20.9). The reticulolysis that is associated with some liver diseases makes the liver more sensitive to traumatic insult. When the bleeding is limited or confined to a subcapsular hematoma, survival is possible. Birds can also survive liver hemorrhage confined to one of the hepatic peritoneal cavities. This is based on clinical cases and the documentation of blood clots in these cavities during laparotomies.

In the acute phase, bleeding birds may show signs of shock. Radiographically, liver enlargement is indistinguishable from perihepatic hematoma (Color 20.10). A diagnosis is usually made during endoscopy or exploratory laparotomy. Ultrasonography is a useful diagnostic tool in these cases.



Treatment of Liver Disorders

Generalities about treating avian liver disease can be extracted from known etiologies. The single most important treatment seems to be the administration of a well balanced diet free of hepatotoxins. Moldy foods and seed-based diets, particularly those containing peanuts (unless certified mycotoxin-free), should be avoided. The use of lactulose, hemicellulose and supportive care including IV fluids and assisted feeding are indicated in many cases of hepatitis. Special attention should be given to known causes of fatty degeneration or fatty infiltration of the liver (biotin, choline and methionine deficiencies or excessive consumption of high-energy diets in birds with restricted exercise). A multivitamin injection is indicated when malnutrition is suspected. In birds with hemochromatosis, the iron content of the diet should be drastically reduced (<100 ppm), although high iron content of the diet may not be the only cause of excessive iron storage in the body.

The treatment of choice for hemochromatosis in man is to remove excess iron from the body by phlebotomy (one percent of body weight once a week for six months, then twice a month for two years). Frequent

monitoring of hemoglobin and serum iron level is essential.³⁵ A few birds with hemochromatosis have responded to phlebotomy therapy (see Chapter 47).^{32,41}

When a microbiologic cause of liver disease can be diagnosed, a specific treatment against the causative organism is possible. Doxycycline is the treatment of choice for chlamydiosis (see Chapter 34). Pacheco's disease virus infections can be treated with acyclovir. Liver flukes may be susceptible to praziquantel.

Outbreaks of duck hepatitis virus can be controlled by IM injection of DHV antiserum into each duckling at the time the first deaths are noted.

Ascitic fluid should not be removed from birds with liver disease. Removal of this fluid will further deplete body stores of protein in a bird with an already compromised liver function. The author's preference

for treating ascites is to use a potent diuretic, such as furosemide, to effect, and to take only a small amount of ascitic fluid for diagnostic purposes.

Corticosteroids are occasionally used for the treatment of hepatopathies in man (eg, viral hepatitis, chronic active hepatitis) and may result in a dramatic clinical improvement. Limited experience with prednisolone in cases of chronic active hepatitis of unknown etiology in African Grey Parrots suggests that this drug may also be beneficial for treating some avian liver disorders. The use of corticosteroids in mycotoxicosis may limit the formation of fibrosis; however, corticosteroids may exacerbate an underlying infection and may be contraindicated in cases of infectious hepatitis. Colchicine has been used to prevent the progression of hepatic fibrosis in a conure.¹¹

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