THE ICTERIC DOG AND CAT

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The detection of icterus in the dog and cat poses a diagnostic challenge to the veterinary practitioner. Because icterus has several very different etiologies, it is best to pursue the cause initially by attempting to answer the question: Is the icterus due to a prehepatic, hepatic or posthepatic disorder?

PREHEPATIC

This particular cause of icterus accompanies a hemolytic condition that allows for the accumulation of unconjugated bilirubin. Some of the causes of hemolysis in the cat are hemobartonellosis (*Mycoplasma haemofelis)*, adverse drug reactions (acetaminophen, methylene blue), autoimmune hemolytic anemia (often FeLV positive), transfusion reactions, and hemolytic disease of the newborn. The main causes of hemolysis-induced icterus in the dog include immune hemolytic anemia, adverse drug reactions, and infectious disease such as babesiosis. The history and the physical examination findings will often help to differentiate the causes of prehepatic icterus.

The laboratory findings will support the prehepatic origin of icterus based on the presence of a regenerative anemia and other features depending on the particular etiology as shown with RBC Heinz body formation with certain drug toxicities such as acetaminophen and methylene blue. Hemobartonella (Mycoplasma) should be searched for. In the cat, it should be noted that most positive cases of *Mycoplasma haemofelis* or the Coombs positive hemolytic anemia are also FeLV positive. Hemoglobinuria and hemoglobinemia usually accompany an intravascular hemolysis.

The classic laboratory signs of intravascular hemolysis in the dog with immune hemolytic anemia (IMHA) include a regenerative anemia (macrocytosis, reticulocytes, NRBC's), hemoglobinuria, hemoglobinemia, macroagglutination, spherocytes, bilirubinemia and bilirubin-uria.

Treatment depends on the particular etiology. Acceptable cross-matched blood should be given if the patient is weak and depressed or if it has a packed cell volume of < 15%. Discontinuing the offending drug should be immediate if the hemolysis is drug related. In the case of IMHA, immunosuppressive doses of glucocorticoid (prednisone 1-2 mg/kg once or twice daily) are begun immediately. Other immunosuppressive or immune modifying drugs can be given depending on the patient's status and its initial response to treatment. Persistently FeLV positive cats usually have a very guarded to grave prognosis.

HEPATIC

This includes both primary and secondary causes of hepatic disease (Table 1). Only the primary and more common types will be discussed here.

Feline Primary Idiopathic Hepatic Lipidosis. This is a common syndrome in the indoor cat. The history often provides a stressful event that triggered the inappetence. Anorexia and its effects on

protein and lipid metabolism may play an important pathogenetic role. Abnormal triglyceride metabolism is thought to reflect other derangements in hepatocyte functions that contribute to hepatic failure.

There is no age, breed or sex predisposition, but obesity is considered a contributing factor. The common clinical features include anorexia of several days to weeks duration, lethargy and depression. Intermittent vomiting and diarrhea can also occur. The physical examination often detects a palpably enlarged smooth surfaced liver, icterus, varying degrees of dehydration, and evidence of weight loss.

The clinical pathological abnormalities include a nonregenerative anemia and elevated serum transaminase, alkaline phosphatase, and bilirubin levels. The GGT is normal or mildly elevated in cats with hepatic lipidosis. Bilirubinuria is common and indicative of liver disease in the cat in the absence of hemolysis. Coagulation abnormalities occur with the advanced form of disease. The presence of hepatic fat deposits found on cytology specimens obtained by fine needle aspiration or histopathologically on a liver biopsy specimen are confirmative.

Treatment for idiopathic hepatic lipidosis entails restoring hydration along with the provision of nutritionally balanced feedings. The latter can be accomplished with "finger feeding" baby food (without onion powder) for a short term or more efficiently through nasogastric, pharyngostomy, or gastrostomy tubes using a more nutritionally balanced ration.

Ursodeoxycholic acid (Ursodiol) is a choleretic agent that increases bile flow and decreases bile toxicity. It is dosed at 10-15 mg/kg once daily orally.

S-Adenosylmethionine (SAM e) is a product that can increases hepatic glutathione levels thereby providing a protective antioxidant effort for the liver. The dose is 18 mg/kg once daily orally.

Milk thistle also has protective effects on the liver. The usual capsule dose for a large dog is 250 mg/day. Cats will get fractions of this amount of the capsule form. The compounded form (250 mg/ml?) containing silymarin extract is dosed at 0.25 ml for small breed dogs, 0.5 ml for medium-sized dogs, and 1.0 ml for large breed dogs, and be given q8-12h. Cats should receive 0.25 ml q8-12h.

B vitamins are generally administered. This author prefers not to use benzodiazepine tranquilizers to stimulate the appetite because of sedative side effects and their potential for hepatotoxicity in the cat.

The prognosis is fair to guarded depending on whether or not the anorexia disappears and the appetite returns. Predisposing psychological stressors might be difficult to reverse.

Hepatic lipidosis in the dog is generally a secondary disease associated with diabetic ketoacidosis. It will resolve once the primary disorder is cured.

Cholangiohepatitis. This is an inflammatory disorder of the hepatobiliary tree. In the cat it has 2 main types: 1) suppurative (neutrophilic) cholangitis/cholangiohepatitis and 2) nonsuppurative cholangio-hepatitis. Advanced inflammatory disease can progress to cirrhosis. These syndromes can be associated with other conditions such as duodenitis, pancreatitis, and cholecystitis. In the

tropics, cholangiohepatitis can be caused by the liver fluke, *Platynosum concinnum*. Cholangiohepatitis in the dog and cat can occur with cholecystitis with the latter often becoming a surgical disorder when it becomes emphysematous or if it is associated with biliary outflow obstruction.

The clinical signs include varying degrees of anorexia, weight loss, dehydration, vomiting, diarrhea, hepatomegaly, and jaundice. Fever is sometimes present especially in the cat with suppurative cholangiohepatitis and the dog with emphysematous cholecystitis. Anterior right-sided abdominal discomfort might be evident on palpation. The clinical pathologic features include elevated serum transaminases, GGT, alkaline phosphatase, serum globulins, and bilirubin levels and bilirubinuria. A neutrophilia is common with the suppurative type. Eosinophilia is occasionally present with fluke infections in the cat. A liver biopsy is necessary for a definitive diagnosis. Some advocate ultrasound guided percutaneous gall bladder aspiration for culture and cytology, but this procedure in a diseased gall bladder might cause leakage and bile peritonitis.

Fluid therapy and B vitamins are important for both types of cholangiohepatitis. Vitamin K_1 should be given when there is obstruction to bile flow. Antibiotics (ampicillin, ampicillin-clavulanic acid, cephalosporins, and metronidazole) are strongly recommended for the suppurative form; those commonly used include those effective against gram negative and anaerobic bacteria. SAM e and milk thistle are also used as liver support drugs. Ursodeoxycholic acid (Ursodiol) is a hydrophilic bile acid that has a choleretic effect and promotes the formation of nontoxic bile acids. It has to be prepared by a compounding pharmacist for a dosage of 10-15 mg/kg/day. It should not be used when there is a bile duct obstruction.

For nonsuppurative cholangiohepatitis in the cat, prednisone is recommended at a daily dose 2.2 mg/kg for 1-2 weeks and then slowly tapered to an alternate day regimen over a 4-6 week period.

Feline liver flukes are treated with praziquantel at 20 mg/kg once daily for 3 consecutive days. Fenbendazole at 50 mg/kg PO can also be given for 5 consecutive days. The prognosis is fair to good if the condition is treated before biliary fibrosis becomes established.

Cholestasis. Cholestatic hepatopathy is characterized by bile stasis within the canaliculi. It can occur with cholangitis, cholangiohepatitis, or it can be due to adverse drug reactions on the liver. Other causes include various enterotoxins, sepsis, and certain inflammatory disorders such as acute pancreatitis. These conditions are managed medically along with the discontinuation of any predisposing medications, herbs, or other hepatotoxins and the treatment of the primary underlying disorder. Liver supportive measures include can include the administration of Ursodiol, SAM e, milk thistle, and adequate nutrition and vitamins.

POSTHEPATIC

The posthepatic causes of jaundice in the dog and cat include those disorders that cause common bile duct obstruction. These conditions are listed in Table 2.

The clinical pathological features of this group of disorders include remarkably elevated serum alkaline phosphatase, cholesterol, and bilirubin levels. Serum transaminase levels will vary

from mild to moderately elevated. The hemogram is seldom contributory, except for prolonged coagulation times due to the inactive vitamin K dependent factors II, VII, IX, and X. Parenteral vitamin K_1 treatment is recommended.

Radiographs and abdominal ultrasound examinations might suggest masses or markedly dilated bile ducts. Surgical exploratory is essential for an absolute diagnosis and the determination of the treatment plan and prognosis.

Critical Care for the Dog and Cat in Liver Failure

The main concerns in treating the dog and cat with severe liver disease are nutrition, fluid and electrolyte balance, hepatic encephalopathy, and coagulation disorders.

Nutrition

Oral feeding or feeding with the assistance of a pharyngostomy, esophagostomy or gastrostomy tube would be the ideal way to maintaining the patient so long as it is not vomiting. In the case of significant vomiting (more than twice/day), parenteral nutrition will have to be instituted. It is essential to provide an adequate caloric base to allow the patient to be maintained in an anabolic state. The required amount of calories needed per day (RER) can be computed using the formula where

$$RER = 70 \times (\text{Body weight in kg})^{0.75} \text{ or}$$
$$RER = 30 \times (\text{Body weight in kg}) + 70$$

This formula has to be adjusted for catabolism, dietary thermogenesis, and the presence of sepsis. The diet should contain good quality protein and must not be restricted unless hepatic encephalopathy, hyperammonemia, or ammonium biurate crystalluria are present. In the absence of vomiting the protein requirement can be met with most available prescription diets that contain high quality protein, adequate fat and carbohydrate along with adequate vitamins and minerals to meet the cat's daily requirements. If the cat is being tube fed the use of a blender will greatly facilitate its administration. Those on enteral nutrition will be fed commercially available liquid diets that are made of the right consistency for enteral tube administration. It is important to start such diets slowly so that osmotic diarrhea is avoided.

Sodium intake should be limited to 100 mg/100 kcal energy requirement in hypoalbuminemia and in those with ascites. The palatability from such a diet will probably suffer, and in the patient that is already anorectic, tube feeding will probably be essential.

The critically ill cat can very likely become depleted of thiamine and vitamin B_{12}. Thiamine deficiency can cause a severe polioencephalomalacia and is best avoided by providing normal daily needs. Thiamine hydrochloride injection (50-100 mg IM or SQ) should be given in any cat that is showing signs compatible with thiamine deficiency (starry-eyed gaze, fixed mid-position or dilated pupils, ataxia, dementia, and dysequilibrium. Fifty milligrams can be given daily for the next few

days followed by normal dietary amounts. Vitamin B_{12} (cobalamine) supplementation might help cats with co-existing pancreatic and small intestinal disease. Blood cobalamine levels can be sent to a commercial laboratory and treatment can be provided with 0.5 to 1.0 mg of B_{12} IM or SQ every 7-21 days.

Vitamin E and Vitamin K_1 are also important nutrients that should be provided for their activity against cellular oxidative injury and coagulation disorders, respectively. A recommended dose for Vitamin E is 10 units/ kg/day. Vitamin K_1 is necessary for the facilitation of Factors II, VII, IX and X and is dosed at 0.5 to 1.5 mg/kg sid-bid. **It is important to remember that no vitamin injection should be given by IV push because it will likely cause an anaphylactoid reaction.**

Fluid Therapy

Fluid therapy and meticulous protocols for its administration is an essential part of caring of critical care medicine. Patients with hypoalbuminemia are very susceptible to intravenous fluid overload and should therefore be monitored closely. The special considerations concerning fluid therapy for dogs and cats with liver disease include hypovolemia, hypoalbuminemia, blood loss, predisposition to edema and body cavity effusions, and sepsis caused by breaks in sterile procedure. The tendency for sensitivity to fluid overload is because the patient with chronic liver disease can have an active renin-angiotensin-aldosterone system because of the ineffective blood volume they might have. One good way to administer parenteral fluids to such patients is to infuse a slow infusion of both crystalloids and colloids. This can be done with alternating or combined delivery methods. The increased plasma oncotic pressure delivered with this fluid formulation will help restore intravascular Starling's forces to normal by expanding intracellular volume, limiting the requirement of crystalloid, and allowing for a more prolonged lasting effect of the volume expansion efforts. It is recommended that only one third of the normal amount of crystalloid be given if a colloid is given at a dose of 10/ml/kg which is the 24 hour recommendation of Hetastarch for the cat. If either Hetastarch or Dextran 70 is used, it is important to consider their effect on the patient's coagulation status because of their known tendency to antagonize blood clotting which is already a concern in a cat whose liver disease is already compromising hemostasis.

Albumin infusions will benefit the patient with hypoproteinemia and when combined with rapid paracentesis in the ascitic patient, the procedure might avoid being complicated by life-threatening hypovolemia. Although human albumin has been given to several dogs without allergic complications, it is safer to use same species plasma. Any foreign protein carries the threat of anaphylaxis with it thereby calling for much diligence during its administration. All allergic reactions must be met with immediate discontinuation of the plasma or albumin infusion. If necessary, parenteral epinephrine must be given at a dosage of 0.01 mg/kg IM and repeated in 20 minutes if anaphylaxis occurs.

Dextrose-containing solutions should be used whenever the blood glucose concentration cannot be maintained within normal limits of 70-125 mg/dl. Hyperglycemia can cause several complications including immune compromise thus predisposing to infection, osmotic diuresis with its attending loss of important electrolytes and water soluble vitamins, and a contributing factor to the formation of respiratory acidosis. However if hypoglycemia is present it should be countered with dextrose administration. Hypoglycemic encephalopathy should be treated immediately with dextrose injection at a dose of 0.5 gm/kg which is met with 1.0 ml of 50% dextrose IV or 2 ml/kg 25% dextrose solutions. Intravenous injections of such hypertonic solutions must not be allowed to extravasate because of the extensive tissue sloughing that can occur.

Treating Anemia

The anemia that occurs with liver disease can be uni- or multifactorial. Blood loss can occur from slow bleeding gastric ulcers, especially if mast cell cancer is the cause of the liver disease. Liver disease alone has been associated with gastric ulcers. Other causes can be the anemia of chronic disease or that due to any co-existing disease such as feline leukemia virus. Lastly and by no means least, iatrogenic blood loss will occur from too frequent phlebotomies. When anemia is expected, a donor should be identified, cross-matched, and be readily available when needed. The anemia of chronic disease might even benefit from Epogen treatment, but here again judicious use is important in order to avoid autoimmune destruction of the patient's red blood cells.

Hepatic Encephalopathy

This is a critical part of treating any dog and cat with severe liver disease. The major strategies include avoiding the onset of hypokalemia or metabolic alkalosis; treating GI bleeding vigorously and expediently; maintaining normal blood pressure; avoid protein administration; and maintain normal fluid, pH and serum electrolyte balance.

Adjusting enteric bacterial flora is sometimes necessary and this can be brought about by several different methods. Neomycin or metronidazole can be given orally in order to remove the bacteria that are producing ammonia within the intestinal lumen. Retention enemas containing neomycin and saline in a proportion of 7:1 can also be used if the cat is comatose or where oral medication is otherwise restricted as occurs with severe vomiting. Lactulose solution can also be used to adjust the bacterial flora through its ability to maintain an acidic environment within the lumen of the colon thereby preventing the conversion of ammonium to the more absorbable ammonia.

General Patient Care

Any care delivered should always include measures that consider their species requirements for gentle handling, minimal restraint, and measures taken to keep them as clean as possible. Baths should be given to remove any soiling from feces or urine. All catheters should be inspected for potential sites of contamination or underlying skin inflammation and any such occurrences should be managed as soon and as appropriately as possible. Any medications that are not necessary should be omitted and care should be taken to avoid drug interactions. Intravenous catheter sites should be ideally rotated every 3-4 days, but because of the logistical difficulties encountered with a small animal, many intravenous catheters can be retained for as long as 7 days without

consequence, but under such conditions extremely meticulous catheter care is essential.

TABLE 1
SOME OF THE CAUSES OF LIVER DISEASES IN THE DOG AND CAT

Primary	1.	Lipidosis - dog and cat
	2.	Lymphocytic cholangiohepatitis - cat
	3.	Suppurative cholangiohepatitis – dog and cat
	4.	Parasitic cholangiohepatitis - cat
	5.	Primary neoplasia – dog and cat
	6.	Congenital portosystemic anomalies – dog, cat
	7.	Infections (FIP(cat), toxoplasmosis, hepatitis) – cat and dog
Secondary	1.	Toxins
	2.	Drugs
	3.	Metastatic neoplasia
	4.	Metabolic
	5.	Sepsis

TABLE 2
CAUSES OF POSTHEPATIC JAUNDICE IN THE DOG AND CAT

	Pathologic Process	Cause
1.	Inflammatory stricture	Acute pancreatitis
2.	Bile duct tumors	Adenocarcinoma
3.	Duodenal tumors	Lymphosarcoma, carcinoma, leiomyosarcoma, leiomyoma
4.	(ampullary)	Liver flukes
5.	Parasites	Cholecystitis
	Slugged bile	