Biliary Anatomy

Bile is formed in the hepatocytes and drains into canaliculi, to interlobular ducts, then lobar ducts. Once the lobar ducts exit the individual liver lobes they are called hepatic ducts. The hepatic ducts converge to form the common bile duct which enters the duodenum at the major duodenal papilla. The cystic duct connects the gall bladder, which stores and concentrates bile, to the common bile duct. In the dog, the common bile duct enters the duodenum separately from the major pancreatic duct. In cats, the common bile duct and the pancreatic ducts join just before the major duodenal papilla.

Extrahepatic Biliary Obstruction.

Extrahepatic biliary obstruction (EHBO) occurs infrequently in dogs and cats. However the animal with EHBO is often systemically unwell and requires a thorough diagnostic evaluation to determine the underlying cause of the obstruction and the severity of associated problems including coagulopathies.

The most common causes of biliary obstruction in dogs include pancreatitis, neoplasia, biliary mucocoeles, cholangitis and cholelithiasis. However it is important to note that in some dogs and cats choleliths (stones in the biliary system) may be incidental findings and not associated with disease. The most common causes of biliary obstructions in cats include neoplasia, cholangitis/cholangiohepatitis, pancreatitis and cholelithiasis.

There are several fairly immediate consequences from EHBO regardless of the underlying cause. A lack of bile salts prevents emulsification, and subsequently digestion and absorption of fat and fat soluble vitamins, including Vitamin K. Vitamin K is an essential factor for the synthesis of clotting factors II, VII, IX, and X. As factor VII has a short half life (approximately 6 hours), biliary obstruction can rapidly lead to a surgically significant coagulopathy. EHBO can also be associated with gall bladder rupture and bile peritonitis.

Cholecystolithiasis

In humans, choleliths and cholecystoliths are primarily composed of cholesterol. Unlike humans, the majority of choleliths in dogs are composed of calcium bilirubinate. Mixed choleliths (comprised of cholesterol, bile acids, pigments, calcium, and protein) and cholesterol stones are reported less commonly. Although many dogs may have choleliths as incidental findings, they can obstruct the common bile duct or cystic duct in some cases.

Gall Bladder Mucocoeles

Gall bladder mucocoeles are being diagnosed with increasing frequency in dogs. They have not been diagnosed in cats. A thick, gelatinous bile accumulates in the gall bladder. Affected dogs may show no clinical signs, or may be lethargic, anorexic, and have episodes of vomiting or diarrhea. In some cases the thickened bile may cause obstruction of the common
bile duct; in others the gall bladder may rupture and result in bile peritonitis. The underlying cause of gall bladder mucocoeles is not clear. It is not clear if the initiating event is cystic mucinous hyperplasia of the gall bladder mucosa, obstruction of the cystic duct, or decreased contractility of gall bladder smooth muscle leading to inspissations of bile. It is clear that dogs with hyperthyroidism and hyperadrenocorticism have an increased incidence of gall bladder mucocoeles compared to the remaining canine population.

Bile Peritonitis

Bile peritonitis occurs when the common bile duct, hepatic duct, or gall bladder ruptures and bile leaks into the peritoneal cavity. In dogs this may be associated with blunt or penetrating trauma or rupture of the gall bladder seen in association with gall bladder inflammation (cholecystitis) or gall bladder infarction and necrosis. Bile causes severe inflammation within the peritoneal cavity. Bile peritonitis may be sterile or associated with secondary infection (septic) which has a worse prognosis. The most reliable diagnostic test for bile peritonitis is comparison of the bilirubin concentration in the abdominal effusion with that of the serum. A bile concentration in the effusion two or more times greater than the serum concentration is diagnostic for bile peritonitis and an indication for immediate aggressive stabilization and exploratory laparotomy.

Gall Bladder Infarction

Gall bladder infarction has been described in a group of dogs with either gall bladder Distension or rupture treated at surgery by cholecystectomy. In each of these dogs the gall bladder wall was necrotic with minimal inflammation seen on histopathology. In several cases organized thrombi were seen in blood vessels supplying the gall bladder. Several dogs in this report were also hyperthyroid or had hyperadrenocorticism. Thrombosis and infarction were also present in the spleen in two dogs, suggesting that a more generalized hypercoagulable or thrombotic state in these cases.

Etiology of Feline Biliary Diseases

In a recent study of feline biliary obstruction, many cats with non-neoplastic biliary obstructions either had concurrent pancreatitis, cholangiohepatitis, inflammatory bowel disease (IBD), cholelithiasis, or some combination of these conditions. In some of these cases, the cholangitis/cholangiohepatitis appeared to be a primary problem, and in others it appeared to be secondary to cholelithiasis. Cholelithiasis has been associated with biliary stasis, cholecystitis, bacterial or parasitic biliary infections, and diet.

An association between feline cholangiohepatitis, pancreatitis, and IBD has also been documented in a previous study. There are several factors that probably contribute to this association. Unlike the dog, the sphincter of Oddi is a common anatomic and physiologic point of entry for the common bile duct and major pancreatic duct into the descending duodenum. IBD, one of the most common gastrointestinal conditions in the cats, is most often associated with vomiting, which raises intra-abdominal pressure. This predisposes cats to duodenal reflux
into the pancreatic and biliary duct systems. Feline duodenal contents also have a much higher bacterial concentration than that of dogs ($10^8$ bacteria/ml Vs $10^4$ bacteria/ml fluid). Speculatively, reflux of duodenal contents into the biliary and pancreatic duct systems may initiate pancreatitis and cholangitis/cholangiohepatitis in many cases.

Is It Really Biliary Disease in Cats?

Many non-hepatic diseases can affect serum liver enzyme and bilirubin levels. Pancreatitis, sepsis, diabetes mellitus, hyperthyroidism, and severe enteritis can all cause elevations in either serum liver enzymes and/or bilirubin. As mentioned previously, some of these conditions, such as pancreatitis and enteritis, appear to be linked to the hepatic disease. However in other diseases, such as sepsis, the primary condition is not directly related to the liver. The condition does, however, mimic primary hepatic or biliary disease and this mimicry often diverts attention from the underlying primary problem.

Further discussion of sepsis-associated cholestasis is particularly important when considering feline biliary disease. Extrahepatic infection can impair bile flow significantly and result in clinical signs of jaundice. In these cats a marked elevation of serum bilirubin is often accompanied by a somewhat milder rise in hepatic enzyme levels. Histopathological changes in the liver are generally minimal other than bile accumulation and canalicular plugs. There is a mild periportal lymphocytic infiltrate with occasional hepatocyte necrosis. This is probably a secondary change as bile stasis has been demonstrated to cause hepatocyte apoptosis. The mechanisms of bile stasis in these diseases are incompletely understood, but thought to be related to the effects of bacterial toxins on the canalicular membrane and bile acid transport systems. Successful treatment of the primary infectious or septic focus resolves the cholestasis.

Investigation and Indications for Surgery

Many hepatic and non-hepatic diseases can cause elevations in hepatic enzyme and bilirubin levels. An accurate diagnosis is vital when considering surgical intervention given the potential overlap in laboratory findings between cases with primary and “secondary” biliary disease. An elevated serum bilirubin is the most sensitive laboratory finding in extrahepatic biliary obstruction (EHBO), but is not necessarily specific for this condition. Serum ALP, ALT, AST, GGT, and amylase and lipase are less sensitive than bilirubin. Ultrasound is useful for imaging the liver, gall bladder, common bile duct, pancreas, intestine and peritoneal cavity. Ultrasound will often confirm suspected biliary obstruction, with a distended common bile duct and gall bladder visible in a vast majority of the cases reported. It will also allow visualization of gall bladder mucocoeles and visualization and sampling of peritoneal effusion. The common bile duct is reported to be less than 4mm in normal cats and at least 5mm in most cats with EHBO. Even in the presence of gallbladder and common bile duct dilation, ultrasound cannot always confirm biliary obstruction without stimulation of gallbladder emptying with a fatty meal or cholecystokinin.

Cholecystitis is commonly associated with feline EHBO and cholelithiasis. Gallbladder wall thickening can be seen ultrasonographically but is a non-specific sign of EHBO. Choleliths are often visible on plain abdominal radiographs and ultrasound, but they can also be seen in
asymptomatic, unobstructed dogs and cats. In some cases feline EHBO is caused by pancreatic or biliary adenocarcinoma. Preoperative evaluation of the abdomen for neoplasia is vital in cats with EHBO as these diseases invariably carry a poor prognosis.

The indications for exploratory laparotomy in animals with suspected EHBO include an increasingly elevated serum bilirubin in the absence of hemolytic or primary hepatic disease, clinical signs compatible with EHBO, and ultrasonographic evidence of biliary obstruction. The indications for exploratory laparotomy in animals with choleliths include clinical signs that are not responding to medical management, including vomiting, anorexia, and icterus, elevated serum liver enzymes and bilirubin, and radiographic or ultrasonographic evidence of obstructive cholelithiasis.

Preoperative Considerations

Animals should have a complete coagulation profile performed as one study showed abnormally prolonged PT or PTTs in 50% of EHBO cats. A blood type is obtained and whole blood should be available to treat intraoperative anemia and/or hypotension. Many animals with EHBO or cholelithiasis have positive bacterial cultures obtained from either bile, liver or gall bladder wall, hence surgery in these areas should be viewed as potentially contaminated, and perioperative antibiotics should be administered. The affect of perioperative antibiotics on the results of bile or liver culture results is unknown in cats. Bacteria cultured in reported studies include Staphlococcus, Enterococcus, Streptococcus, E. coli, Acinetobacter, Clostridium, and Bacteroides. The majority of aerobic bacteria cultured are sensitive to aminoglycosides or fluroquinolones.

Management of Choleliths

A complete exploratory laparotomy is performed before detailed evaluation of the liver and biliary system. Particular attention should be given to the intestines, pancreas, and abdominal lymph nodes for evidence of inflammatory or neoplastic disease. Each lobe of the liver is evaluated and the gall bladder and extrahepatic biliary system carefully examined. The proximal descending duodenum is opened and the patency of common bile duct assessed by catheterization. An attempt should be made to clear any choleliths from the common bile duct by flushing. The most successful long term results reported in cats with cholelithiasis were obtained when the biliary tree was patent at surgery and a cholecystectomy was performed. When the common bile duct remains blocked by a cholelith in spite of repeated flushing attempts, bile is diverted by a cholecystoduodenostomy or –jejunostomy. Biopsies and cultures of the liver are obtained. Many cats have concurrent cholecystitis or cholangiohepatitis. A minority of cats have concurrent hepatic lipidosis; in two reports hepatic lipidosis appeared to be associated with a poor clinical outcome. Biopsies of the small intestine should also be obtained.

Management of Biliary Obstruction

Reported non-lithogenic causes of EHBO in dogs and cats include cholangitis/cholangiohepatitis, pancreatitis, and pancreatic or biliary neoplasia. Cats with EHBO secondary to neoplasia had a very poor prognosis in one report. Neoplasia can sometimes be
confirmed at surgery by cytology or frozen sections; in these cases owners should make an informed decision on proceeding before a biliary diversion procedure is performed. Cases of EHBO secondary to pancreatitis can be managed by placement of a tube from the duodenum into the common bile duct or by cholecystoduodenostomy.

Perioperative morbidity and mortality were high in one study that reported surgical treatment of 19 cats with EHBO. Six cats were euthanized because of a poor prognosis (neoplasia n=4; poor recovery n=2). Six additional cases suffered cardiopulmonary arrest in the immediate postoperative period. This emphasizes the severity and chronicity of the disease processes in many of these cats. Intraoperative hypotension was common in spite of careful anesthetic management and necessitated discontinuation of inhalant anesthetic agents and blood products or vasopressors for blood pressure support. A high mortality rate, hypotension and poor response to vasopressors are among the complications reported in humans with EHBO. The cause of these complications is uncertain, but the absence of bile salts in the intestine may lead to intestinal bacterial overgrowth and endotoxin absorption. Obstructive jaundice impairs reticuloendothelial function and promotes bacterial translocation in the rat, and similar processes may be occurring in cats with EHBO.

Other Considerations

Given the association between feline cholangiohepatitis, cholelithiasis, pancreatitis, and IBD, and the small but significant incidence of concurrent hepatic lipidosis in these cats, biopsies of the liver, pancreas, and small intestine are obtained at surgery. Cultures of the liver or bile are also obtained. A gastrostomy or jejunostomy feeding tube is placed. A minimal amount of dissection is used to tunnel the tube through the subcutaneous tissue and body wall and the tube is securely fastened to not only the skin but underlying musculature to prevent migration and subcutaneous leakage of either food or enteral contents. This complication has been described in several reports and can be fatal.

Immediate postoperative management goals include maintaining adequate blood pressure, hemoglobin levels, and tissue perfusion, and normalizing serum electrolytes and acid/base balance. Hypokalemia is common in anorectic cats and potassium supplementation of parenteral fluids is often required. Low serum phosphorus levels (<2.5 mg/dl) are sometimes seen in cats with hepatic lipidosis and can result in hemolytic anemia. Potassium phosphate is added to either 0.9% saline or 5% dextrose and infused at between 0.011 to 0.017 mmol phosphate/kg/hr for 6 to 12 hours.

Medium term postoperative management is guided by the results from surgical biopsies and cultures. Antibiotics are often required to treat bacterial infections associated with cholangitis/cholangiohepatitis. Nutritional management is vital in anorectic, debilitated cats. Initially only small amounts of water are flushed through the gastrostomy or jejunostomy tube. Energy requirements can be estimated using the following formula:

\[ 1.5 \times [30 \times \text{body weight (kg)} = 70] \]

In cats with gastrostomy tubes, commercial diets are mixed with equal volumes of water and blenderized. In cats with jejunostomy tubes, a liquid enteral diet is used. Approximately 50% of the calculated caloric requirement is fed on the first day either in 4 feedings with a gastrostomy.
tube or ideally by constant rate infusion with a jejunostomy tube. If this is well tolerated, 100% of the calculated caloric requirement is fed on the second day.

There are many theoretical benefits to bile acid (ursodeoxycholic acid) therapy although no controlled clinical trials have been performed in dogs and cats with EHBO. Administration of ursodeoxycholic acid may increase bile flow, bind endotoxin in the intestinal lumen, replace more hepatotoxic bile acids in the circulating bile acid pool, and inhibit ileal uptake of toxic bile acids formed by bacterial modification in the intestinal lumen. One concern with ursodeoxycholic acid therapy in cats is the possibility of increased taurine conjugation and subsequent taurine deficiency. The recommended dose of ursodeoxycholic acid, 10-15 mg/kg/day, is extrapolated from human medicine. Ursodeoxycholic acid available in a 300 mg capsule for oral administration.