



# Feline Cholangiohepatitis

Michelle Edwards, DVM

Michigan Veterinary Specialists  
Southfield, Michigan

## ABSTRACT:

Cholangiohepatitis is a common hepatic disorder in cats that is second only to hepatic lipidosis in frequency. There are two forms of cholangiohepatitis: acute and chronic. There has been speculation on the exact cause; however, it remains unknown. A definitive diagnosis can be made only with hepatic biopsy. A complete diagnostic workup is recommended to determine the presence of concurrent disease. Treatment is variable and often long-term. The prognosis depends on the form, presence of concurrent disease, and response to treatment.

Inflammatory liver disease is a common feline hepatic disorder that is second only to hepatic lipidosis in frequency.<sup>1,2</sup> Other disorders that affect the liver less often include neoplasia, feline infectious peritonitis (FIP), and toxoplasmosis. Inflammatory diseases of the liver have various names. However, based on a recent review of histologic lesions, inflammatory liver disease can be divided into two types of histologically distinct patterns: cholangiohepatitis and lymphocytic portal hepatitis.<sup>1,3,4</sup> Cholangiohepatitis involves neutrophilic or mixed inflammation pertaining to the biliary system, with secondary hepatocyte involvement. Periportal necrosis and bile duct degeneration may also be seen.<sup>1,3,4</sup> Lymphocytic portal hepatitis differs in that the bile ducts are not primarily involved and the hepatic lobules are not invaded.<sup>1,3,4</sup>

Cholangiohepatitis can be further divided into two types: acute (suppurative) and chronic (nonsuppurative). Acute cholangiohepatitis is histologically characterized by infiltration of a large number of neutrophils into the portal areas of the liver as well as walls and lumens of the bile ducts. Periportal necrosis, disruption of the periportal limiting plate, and invasion into

the hepatic lobules may also be seen. The acute form has been associated with (and is believed to be caused by) an ascending bacterial infection. Many enteric organisms have been isolated from cultures of bile or liver tissue (see box on page 856). Pretreatment with antibiotics as well as the bacteriostatic properties of bile can lead to negative cultures.

Chronic cholangiohepatitis may be characterized histologically by a mixed inflammatory infiltrate in portal areas and bile ducts consisting of neutrophils, lymphocytes, and plasma cells. Bile duct hypertrophy and fibrosis are present with chronic cholangiohepatitis but are not seen with acute disease.<sup>1</sup> It is speculated that the chronic form is a progression of the acute form. However, there are currently no studies demonstrating this progression. Chronic disease may progress to biliary cirrhosis.<sup>1,4,5</sup>

Some authors believe that anatomic abnormalities of the gallbladder may predispose cats to cholangiohepatitis<sup>3,4,6</sup> (Figure 1). The box on page 857 lists the diseases that have reportedly been associated with cholangiohepatitis. Concurrent inflammation of the pancreas and intestinal tract is often found in cats with cholangiohepatitis. A recent study found that 80% of cats had concurrent inflammatory bowel disease and 50% had at least mild inflammation of the pan-

Email comments/questions to  
[compendium@medimedia.com](mailto:compendium@medimedia.com),  
fax 800-556-3288, or log on to  
[www.VetLearn.com](http://www.VetLearn.com)

## Bacteria Associated with Cholangiohepatitis<sup>3,7</sup>

*Escherichia coli*  
*Actinomyces* spp  
*Clostridium* spp  
*Fusobacterium* spp  
*Bacteroides* spp  
*Staphylococcus* spp  
 $\alpha$ -Hemolytic *Streptococcus* spp

creas.<sup>7</sup> These findings suggest a strong relationship between these diseases.

## CLINICAL SIGNS AND FINDINGS

There is no specific signalment for cats with cholangiohepatitis. They can be young to very old. In one report, affected cats were 3 months to 16 years of age.<sup>8</sup> Some discrepancies regarding the age and sex predilection associated with each form of the disease have been reported. One report found that the average age of cats with chronic disease was higher than that of those with acute disease.<sup>4</sup> Another study reported that cats with chronic disease were younger.<sup>9</sup> However, most cats are middle aged at presentation. One study reported that 69% of all cats diagnosed with cholangiohepatitis were males.<sup>3</sup> Another report found that male cats predominately had the acute form but not the chronic form.<sup>8</sup> Other reports have not found a sex predilection. There is no known breed predilection.

Clinical findings can be vague, making this disease impossible to diagnose based on clinical signs alone. With the acute form, the duration of signs is shorter (usually less than 1 week), with anorexia and lethargy commonly noted. Fever and abdominal pain are more commonly associated with the acute form.<sup>10</sup> Abdominal pain can be found if a secondary obstructive liver disease is present. Vomiting is a frequent complaint; more than 50% of affected cats reportedly present with this sign.<sup>8</sup> Icterus and hepatomegaly are not commonly associated with the acute form.

In the chronic form, signs are usually present for more than 2 weeks. The signs are often vague and can be intermittent, suggesting a chronic disease process. Cats with the chronic form may have periods of good appetite and attitude.<sup>10</sup> Icterus and hepatomegaly are commonly found with the chronic form. Vomiting is also found with this form. Diarrhea is not commonly associated with either form. Hepatic encephalopathy,



**Figure 1.** Ultrasonogram of a gallbladder stone in a cat with cholangiohepatitis.

ascites, and excessive bleeding are uncommon unless severe end-stage liver disease is present.<sup>10</sup>

## DIAGNOSTIC EVALUATION

Liver biopsy is the only diagnostic tool that can substantiate a definitive diagnosis of cholangiohepatitis. However, a variety of tests can help evaluate patients before and after a diagnosis has been made. Initial evaluation of these patients should begin with a complete blood count, comprehensive serum chemistry profile, and urinalysis. Hematologic findings are often normal; however, approximately 25% to 30% of acute cases have neutrophilia with a mild left shift.<sup>3,8</sup> Mild nonregenerative anemia may be present in association with chronic disease. No consistent biochemical pattern is associated with either form of the disease. Alanine transaminase, aspartate transaminase, and alkaline phosphatase are usually mildly to moderately elevated. Hyperbilirubinemia is most often present; it appears to be more marked with chronic disease.<sup>4</sup> Hyperglobulinemia is found in approximately 50% of cats with chronic cholangiohepatitis.<sup>10</sup> Hypoalbuminemia and decreased blood urea nitrogen are found with end-stage liver disease. Bilirubinuria is the most consistent urinalysis finding. Because hyperthyroidism is a common cause of elevated liver enzymes, a thyroid profile, total thyroxine ( $T_4$ ) level, and free  $T_4$  level determined by equilibrium dialysis should be obtained for cats 7 years of age or older. Blood work (e.g., FeLV and FIV tests, *Toxoplasma* titers) should be obtained to rule out infectious diseases. FIP and toxoplasmosis have been implicated as causes of cholangiohepatitis.

Liver function can be biochemically evaluated. A serum bile acids test is helpful in assessing hepatic function when bilirubinemia is not present. Fasting and/or postprandial bile acids are usually abnormal in cats with cholangiohepatitis. In one study, fasting serum bile acids were normal in 50% of affected cats, but postprandial serum bile acids were usually abnormal.<sup>9</sup> If bilirubinemia is present, an increase in serum bile acids should be expected. Blood ammonia levels can also be checked; however, technical limitations with this test can make blood ammonia levels difficult to obtain.

A coagulation profile or at least prothrombin time (PT) and partial thromboplastin time (PTT) should be obtained from any cat suspected of having coagulopathy secondary to hepatic disease or undergoing a liver biopsy. Coagulopathy may occur in chronic inflammatory liver disease because of vitamin K malabsorption, hepatocyte deficiency, or disseminated intravascular coagulation. Hepatocytes are responsible for synthesiz-

### Diseases, Conditions, and Procedures Associated with Cholangiohepatitis<sup>4,7</sup>

- Inflammatory bowel disease
- Chronic bacterial infections within other organs
- Pancreatitis
- Toxoplasmosis
- Anatomic abnormalities of the gallbladder
- FIP
- FeLV
- Cholelithiasis
- Extrahepatic bile duct obstruction
- Biliary reconstructive surgery
- Septicemia
- Neoplasia
- Liver fluke infestation

ing liver size. Diffuse hepatomegaly is indicated by extension of the hepatic shadow beyond the costal arch, rounding of the caudal edges of the liver, and caudodor-

## ***Cholangiohepatitis is the second most commonly diagnosed hepatic disorder in cats.***

ing the coagulation factors, except factor VIII; therefore, PT and PTT may be prolonged. Alternatively, the proteins induced by vitamin K absence (PIVKA) clotting time can be used. A recent study demonstrated increased sensitivity of Thrombotest (Oslo, Norway; PIVKA) compared with routine PT and PTT.<sup>11</sup> A thrombotest may be able to identify cats with bleeding tendencies while they are clinically asymptomatic.<sup>11</sup> A recent study suggested that approximately 75% of cats that present with a liver problem had at least one coagulation abnormality.<sup>12</sup> However, it is unclear whether these abnormalities represented a problem in obtaining diagnostic samples without life-threatening consequences. A study of 124 cats indicated that complications were infrequent in cats in which liver biopsies were performed in the face of increased coagulation times.<sup>13</sup> Bleeding is more likely if significant thrombocytopenia is present.<sup>13</sup> If disseminated intravascular coagulation is a concern, a full coagulation profile, including fibrin degradation products and D-dimer, in addition to complete blood and platelet counts should be obtained for diagnosis.

Diagnostic imaging is very useful in assessing hepatic disease. Abdominal radiography can be useful in assess-

sal displacement of the pylorus caudally.<sup>14</sup> Cholelithiasis has been associated with cholangiohepatitis. In some instances, a cholelith can be identified on an abdominal radiograph as a small, often circular opacity in the cranial right abdomen within the liver shadow.

Abdominal ultrasonography can help differentiate between focal hepatic disease and diffuse disease. This is also useful in determining a biopsy location if using a percutaneous technique. Many cats with cholangiohepatitis may have no detectable parenchymal abnormalities or changes in echogenicity via ultrasonography.<sup>15</sup> The biliary system and portal vessels can also be assessed with ultrasonography. Extrahepatic biliary obstructions, including choleliths, neoplasia, and pancreatitis, can be identified using ultrasonography. Ultrasonography is the most sensitive and specific method of detecting choleliths.<sup>8</sup>

Hepatobiliary scintigraphy is a noninvasive way to differentiate obstructive from nonobstructive disease. One study suggested that scintigraphy can be used to assess the severity of hepatobiliary disease in cats.<sup>16</sup> Because a special facility is required for scintigraphy, this technique is not currently a practical approach in routine veterinary practices.



**Figure 2.** Bile can be obtained via percutaneous ultrasound-guided cholecystocentesis.

Liver biopsy is required to definitively diagnose cholangiohepatitis and differentiate between acute and chronic disease. Fine-needle aspiration of the liver is a mildly invasive and relatively easy way to obtain cells for examination. However, this technique does not provide samples that allow examination of hepatic architecture. It is important to evaluate hepatic architecture to differentiate acute from chronic disease. Percutaneous liver biopsy is an appropriate diagnostic tool if there is no evidence of extrahepatic obstruction and cholelithiasis via ultrasonography. Percutaneous biopsies are best performed with ultrasonographic guidance but can be done without it. Aerobic and anaerobic cultures of liver tissue should also be conducted when a biopsy specimen is obtained. Previous antibiotic therapy may impair culture results. Cytologic preparations of the tissue allow easier visualization of bacterial organisms than does histologic evaluation.<sup>8</sup> Limitations with this approach include size of the tissue

via percutaneous ultrasound-guided cholecystocentesis<sup>8</sup> (Figure 2). This procedure has an increased risk of gallbladder rupture and bile peritonitis if the gallbladder is diseased, as may be found with cholangiohepatitis. Laparoscopy can also be used to perform hepatic biopsies. This procedure allows visualization of the liver, larger samples, and hemostasis. Special equipment and training are required to perform this procedure.

Surgical biopsy is indicated if one of the following exists:

- Biliary decompression is required because of extrahepatic obstruction
- Cholelithiasis
- Removal of inspissated bile is indicated
- Necrotizing cholecystitis
- Needle biopsy is inconclusive

Surgery also allows evaluation and biopsy of the pancreas, biliary system, and small intestinal tract to determine whether there is concurrent inflammatory disease in these systems. Cultures should be obtained during biopsy. This method is more invasive and expensive than is the percutaneous technique.

## TREATMENT

An appropriate treatment plan for cats with cholangiohepatitis includes antibiotic therapy, fluid therapy to restore and maintain normal fluid balance as necessary, nutritional support, surgical intervention as already indicated, and choleric therapy.

Long-term (i.e., 3 months or longer) antibiotic therapy is central to treating the acute form of cholangiohepatitis. Antibiotics should also be used with the chronic form, but usually for a shorter period (i.e., 4 to 6 weeks). While culture and sensitivity results are

## ***A liver biopsy is required to definitively diagnose feline cholangiohepatitis.***

sample obtained and inability to apply hemostasis. Because of the small size of the tissue obtained, an accurate diagnosis is not always possible. Therefore, several biopsy samples should be obtained as long as ongoing hemorrhage is not seen with ultrasonography. Bile samples as well as anaerobic and aerobic cultures can also be submitted for cytologic evaluation. Bile can be obtained

pending, a broad-spectrum antibiotic should be administered. This antibiotic should be able to achieve therapeutic concentrations within the bile. Potentially hepatotoxic drugs should be avoided. Ampicillin, amoxicillin, and cephalixin are good initial choices. Metronidazole has a good anaerobic spectrum. Because metronidazole is metabolized by the liver, it should be administered at

**Table 1. Commonly Used Drugs for Treating Cholangiohepatitis<sup>9</sup>**

Drug	Dose
Ampicillin	10–20 mg/kg IV, IM, or SC q6–8h
Amoxicillin	11–22 mg/kg IM, SC, or PO q8–12h
Cephalexin (gram +)	22 mg/kg PO q8–12h
(gram –)	30 mg/kg PO q8h
Cefazolin (gram +)	22 mg/kg IV, IM, or SC q6–8h
(gram –)	30 mg/kg IV, IM, or SC q6–8h
Metronidazole	7.5–10 mg/kg PO q12h
Prednisolone	2.2 mg/kg PO q12–24h
Ursodiol	10–15 mg/kg PO q24h
Vitamin K <sub>1</sub>	2.5 mg/kg once, then 1 mg/kg PO or IM q24h
Chlorambucil	2 mg/m <sup>2</sup> PO q24–48h

a lower dose if severe hepatic disease is present.<sup>8,9</sup> Although there are reports that metronidazole can be hepatotoxic in dogs, this has not been reported in cats. This drug may be used in combination with penicillin. These drugs are excreted into the bile in the active form. Other antibiotics and their dosages are listed in Table 1. Antibiotic therapy is often continued for 3 to 6 months. The risk of long-term antibiotic therapy is low; however, antibiotic resistance can occur and is potentially the most harmful side effect. Bio-

### ***Long-term treatment is often needed for both forms of cholangiohepatitis.***

chemical and leukocyte parameters should be followed and correlated with improved clinical signs.

Nutritional support is important in treating many disorders. In cholangiohepatitis, dietary protein restriction is not indicated unless overt signs of encephalopathy are present.<sup>8,10</sup> A feeding tube, such as a percutaneous gastric feeding tube, may be needed if anorexia is prolonged, hepatic lipidosis or pancreatitis is present, or severe weight loss is noted. If concurrent inflammatory bowel disease is present, an easily digestible diet can be used. However, novel protein diets have also been found to be beneficial to many cats with inflammatory bowel disease. These diets can be diluted to be used with a percutaneous endoscopic gastrostomy tube. In patients with concurrent pancreatitis or hepatic lipidosis, a high-calorie diet can be used to provide appropriate nutrition in small amounts. Appetite stimulants such as cyproheptadine can also be tried. However, we have had greater success with nutritional support via a gastrostomy tube. Vitamin K<sub>1</sub> therapy may be indicated if a deficiency is suspected or proven. Because vitamin K is fat soluble, deficiency of it is common in cats with severe malabsorption. Parenteral vitamin K<sub>1</sub> therapy may be indicated instead of oral therapy if severe gastrointestinal malabsorption is suspected.

A choleric is a drug that alters biliary consistency to prevent sludging of bile. A choleric such as ursodeoxycholic acid (ursodiol) is strongly recom-

mended for all cats with cholangiohepatitis, provided there is no evidence of extrahepatic biliary obstruction. Ursodiol has also been found to have antiinflammatory, immunomodulatory, and antifibrotic effects on the liver.<sup>3,8</sup> No adverse effects have been reported in cats. A compounding pharmacist must specially formulate the drug in smaller strengths as either a liquid or capsule, depending on the needs and temperament of the patient. Other supplements such as *S*-adenosylmethionine have not been evaluated specifically for cholangiohepatitis. However, because of the effectiveness of *S*-adenosylmethionine in treating other hepatic diseases, it should be considered for supplemental treatment.

Long-term immunosuppressive therapy should be used to treat chronic cholangiohepatitis and lymphocytic portal hepatitis. Glucocorticoids are the mainstay of this treatment. Prednisolone is preferred over prednisone because of the inability of a subset of cats to metabolize prednisone to prednisolone. The dose should be decreased gradually based on improvement in clinical signs and biochemical parameters. In most cases, prednisolone therapy cannot be discontinued and is maintained at the lowest possible dose to achieve clinical remission.<sup>8</sup> Metronidazole should be considered because of its immunomodulatory properties. Chlorambucil has been found to be effective in some cases. Other drugs have been suggested; however, their success has been limited. Because cats are very sensitive to azathioprine (they frequently become anorectic or leukopenic), this drug should be used with caution. Combination pulse therapy with methotrexate, prednisolone, metronidazole, and ursodiol has reportedly been effective in some cats with chronic cholangiohepatitis.<sup>8</sup> Side effects of this therapy include hepatotoxicity, vomiting, diarrhea, and leukopenia.<sup>10</sup>

## PROGNOSIS

The prognosis for cats with cholangiohepatitis varies with the form of the disease. Patients with acute cholangiohepatitis have a good prognosis with appropriate long-term antibiotic therapy. One report suggested that the prognosis was good, provided that the patient survived the initial 48 hours of therapy.<sup>8</sup> Patients with chronic cholangiohepatitis have a variable prognosis. Most patients that survive require long-term medication. One study reported that 47% of cats survived 1 year or less, with only 13% living longer than 5 years.<sup>4,5</sup> There is often an initial response to medical therapy, but relapses have been noted.

## CONCLUSION

Inflammatory liver disease is the second most commonly diagnosed liver disease in cats. Cholangiohepatitis is one of two recognized types of inflammatory liver disease and is further subdivided into acute and chronic disease. Acute disease is thought to be associated with ascending bacterial infection and requires long-term antibiotic therapy. Chronic disease may be the progression of the acute form or secondary to an immune-mediated response. Cholangiohepatitis has been shown to be associated with other conditions, including inflammatory bowel disease and pancreatitis. A liver biopsy is needed to provide a definitive diagnosis. The prognosis for patients with this disease is variable and depends on the type and response to therapy.

## REFERENCES

- Gagne JM, Weiss DJ, Armstrong PJ: Histopathologic evaluation of feline inflammatory liver disease. *Vet Pathol* 33(5):521-526, 1996.
- Zawie DA, Garvey MS: Feline hepatic disease. *Vet Clin North Am Small Anim Pract* 14(6):1201-1230, 1984.
- Armstrong PJ, Weiss DJ, Gagne JM: Inflammatory liver disease, in August JR (ed): *Consultations in Feline Internal Medicine*. Philadelphia, WB Saunders, 1997, pp 68-78.
- Weiss DJ, Armstrong PJ, Gagne JM: Feline cholangiohepatitis, in Bonagura JD (ed): *Kirk's Current Veterinary Therapy XIII*. Philadelphia, WB Saunders, 2000, pp 672-674.
- Weiss DJ, Armstrong PJ, Gagne JM: Inflammatory liver disease. *Semin Vet Med Surg (Small Anim)* 12(1):22-27, 1997.
- Hirsch VM, Doige CE: Suppurative cholangitis in cats. *JAVMA* 182:1223-1226, 1983.
- Bunch SE: Hepatobiliary diseases in the cat, in Couto CG, Nelson RW (eds): *Small Animal Internal Medicine*. St Louis, Mosby, 1998, pp 510-528.
- Guilford WG, Center SA, Strombeck DR, Williams DA, Meyer DJ: Diseases of the gallbladder and biliary tree, in *Strombeck's Small Animal Gastroenterology*, ed 3. Philadelphia, WB Saunders, 1996, pp 860-888.
- Day D: Feline cholangiohepatitis complex. *Vet Clin North Am Small Anim Pract* 25(2):375-385, 1995.
- Johnson SE: Chronic hepatic disorders, in Ettinger SJ, Feldman EC (eds): *Textbook of Veterinary Internal Medicine: Diseases of the Dog and Cat*. Philadelphia, WB Saunders, 2000, pp 1298-1325.
- Center SA, Warner K, Corbett J, et al: Proteins invoked by vitamin K absence and clotting times in clinically ill cats. *J Vet Intern Med* 14(3):292-297, 2000.
- Lisciandro SC, Hohenhaus A, Brooks M: Coagulation abnormalities in 22 cats with naturally occurring liver disease. *J Vet Intern Med* 12(2):71-75, 1998.
- Bigge LA, Brown DJ, Penninck DG: Correlation between coagulation profile findings and bleeding complications after ultrasound guided biopsies: 434 cases (1993-1996). *JAAHA* 37(3):228-233, 2001.
- Pechman RD: The liver and spleen, in Thrall DE (ed): *Textbook of Veterinary Diagnostic Radiology*. Philadelphia, WB Saunders, 1998, pp 458-464.
- Newell SM: Correlations between ultrasonographic findings and specific hepatic diseases in cats: 72 cases. *JAVMA* 213(1):94-98, 1998.
- Newell SM, Selcer BA, Roberts RE, et al: Hepatobiliary scintigraphy in the evaluation of feline liver disease. *J Vet Intern Med* 10(5):308-315, 1996.

## ARTICLE #2 CE TEST

This article qualifies for 2 contact hours of continuing education credit from the Auburn University College of Veterinary Medicine. Subscribers who wish to apply this credit to fulfill state relicensure requirements should consult their respective state authorities regarding the applicability of this program. To participate, fill out the test form inserted at the end of this issue. To take CE tests online and get real-time scores, log on to [www.VetLearn.com](http://www.VetLearn.com).

### 1. Which disease does not affect the liver in cats?

- a. hepatic lipidosis
- b. lung worm infection
- c. neoplasia
- d. cholangiohepatitis

### 2. What are the histopathologic differences between cholangiohepatitis and lymphocytic portal hepatitis?

- a. There are no differences; they are the same disease.
- b. Lymphocytic portal hepatitis involves the bile ducts and adjacent hepatocytes, whereas cholangiohepatitis does not.
- c. Cholangiohepatitis involves the bile ducts and adjacent hepatocytes, whereas lymphocytic portal hepatitis does not.
- d. Lymphocytes are not found in cholangiohepatitis lesions.

### 3. Which disease is not commonly associated with cholangiohepatitis?

- a. inflammatory bowel disease
- b. FIV
- c. pancreatitis
- d. toxoplasmosis

### 4. Cholangiohepatitis is often found in \_\_\_\_\_ cats.

- a. Siamese
- b. female
- c. male
- d. Himalayan

### 5. The most definitive diagnostic test for inflammatory hepatic disease is

- a. liver biopsy.
- b. fine-needle aspiration of the liver.

- c. a serum bile acids test.
- d. hepatobiliary scintigraphy.

### 6. Which of the following is not an indication for surgical biopsy?

- a. the presence of a cholelith
- b. inconclusive needle biopsy results
- c. extrahepatic obstruction
- d. an elevated  $T_4$  level

### 7. What are the histopathologic differences between acute and chronic cholangiohepatitis?

- a. Bile duct hypertrophy and fibrosis are often found with the chronic form.
- b. Bile duct atrophy is often associated with the acute form.
- c. Lymphocytes are the predominant cell type in the acute form, whereas macrophages dominate the chronic form.
- d. Periportal necrosis is found only in the chronic form.

### 8. A complete diagnostic workup should include

- a. cardiac ultrasonography.
- b. bacterial cultures of bile and hepatic tissue.
- c. renal biopsy.
- d. a therapeutic trial with prednisolone.

### 9. If immunosuppressive therapy is needed, an appropriate drug to begin with is

- a. prednisone.
- b. azathioprine.
- c. prednisolone.
- d. cyclophosphamide.

### 10. Which antibiotic should not be used as an initial choice?

- a. cephalexin
- b. amoxicillin
- c. metronidazole
- d. amikacin