The terms feline cholangitis/cholangiohepatitis and cholangitis/cholangiohepatitis complex describe a spectrum of inflammatory hepatobiliary diseases that can share similar clinical presentations but have different histopathologic hallmarks (see box on page 7). Inflammatory diseases of the liver are the second most common cause of feline liver disease (hepatic lipidosis is first). The terminology of these diseases can be confusing and is currently under review by a working group of international veterinarians. This article focuses on suppurative (acute and chronic) and nonsuppurative (lymphocytic/plasmacytic or lymphocytic) cholangitis/cholangiohepatitis (CH), which is the traditional way these diseases have been classified; we have included cases described more recently by some authors as lymphocytic portal hepatitis in the nonsuppurative CH group. Other associated conditions found in the veterinary literature, such as biliary cirrhosis and sclerosing cholangitis, may represent a continuum in the progression of chronic hepatobiliary inflammation or may be entirely separate diseases.

In cats, there is a unique relationship between the common bile duct, the major pancreatic duct, and the duodenum. The major pancreatic duct and the common bile duct intersect just before emptying into the duodenum. It is postulated that this anatomic conformation predisposes cats to cholangitis from extension of duodenal bacteria, reflux of pancreatic secretions, or both. In fact, one study has shown that 83% of cats with CH had concurrent inflammatory bowel disease, 50% of cats with CH had concurrent pancreatitis, and 39% of cats with CH had evidence of both inflammatory bowel disease and pancreatitis.

Because suppurative and nonsuppurative CH have very similar clinical presentations, diagnosis is ultimately made by interpretation of hepatic biopsy specimens in conjunction with aerobic and anaerobic bile and/or hepatic tissue culture. A complete blood count, serum biochemistry profile, urinalysis, coagulation profile, and abdominal ultrasonography are indicated in any cat with evidence of hepatobiliary disease. The diagnosis of suppurative or nonsuppurative CH, obtained from histopathologic evaluation of liver biopsy specimens, is predominantly based on the presence, type, and distribution of inflammatory cells as well as the amount of inflammation, proliferation, and fibrosis of the bile ducts. Biopsy specimens can be obtained via ultrasound guidance, laparoscopy, or abdominal exploratory surgery. Ultrasound-guided biopsy is minimally invasive, but there is a risk of hemorrhage due to hepatic laceration and leakage of bile following gallbladder aspiration; furthermore, sample quality can be poor (the morphologic diagnosis with hepatic needle biopsy samples correlates with larger wedge biopsy samples only 48% of the time). Hepatic biopsies obtained by laparoscopy offer several advantages, including the ability to visualize the gallbladder and areas to be sampled, apply pressure to control hemorrhage if needed, and obtain larger tissue samples than is possible with needle biopsy techniques; also, postoperative recovery time is reduced compared with exploratory surgery. Abdominal exploratory surgery is invasive and may subject patients to prolonged periods of anesthesia, but bile duct patency can be assessed, bile leakage can be minimized, and biopsy specimens are generally of superior quality.

DIAGNOSTIC CRITERIA

**Historical Information**

**Acute Suppurative Cholangitis/Cholangiohepatitis**

**Gender Predisposition:** Males.

**Age Predisposition:** Young and middle-aged cats (mean age, 5.7 years; median age, 3.3 years).

**Breed Predisposition:** None.

**Chronic Suppurative Cholangitis/Cholangiohepatitis**

**Gender Predisposition:** Males.

**Age Predisposition:** Older cats (mean age, 9.7 years; median age, 9.0 years).

**Breed Predisposition:** None.
Nonsuppurative Cholangitis/Cholangiohepatitis

Gender Predisposition: None identified.

Age Predisposition: The reported age range is wide (6 months to >10 years) because various retrospective studies have used different categorization schemes.

Breed Predisposition: Reports vary; Persians were overrepresented in one study.

All Three Diseases

Owner Observations (in order of frequency)

• Anorexia.
• Lethargy.
• Weight loss.
• Vomiting.

Other Historical Considerations/Predispositions

• Clinical signs of acute suppurative CH are nonspecific but are almost always less than 1 month in duration.
• Clinical signs of chronic suppurative and nonsuppurative CH generally are noted for longer than 1 month.
• Many cats with nonsuppurative CH can have an unremarkable history and a normal appetite.

Physical Examination Findings

Acute Suppurative Cholangitis/Cholangiohepatitis

• Fever (present in >70% of affected cats).

Chronic Suppurative Cholangitis/Cholangiohepatitis

• Nonspecific physical examination findings.

Nonsuppurative Cholangitis/Cholangiohepatitis

• Nonspecific physical examination findings, although ascites has been described in some cases.

All Three Diseases

• Icterus may or may not be present.
• Hepatomegaly may or may not be present.

Laboratory Findings

Acute Suppurative Cholangitis/Cholangiohepatitis

• Neutrophilia.
• Increased band neutrophils (left shift).
• Serum bilirubin concentration tends to be the highest (>3 mg/dl in many cases).

Chronic Suppurative Cholangitis/Cholangiohepatitis

• Neutrophilia.
Other Diagnostic Findings

All Three Diseases

- Serum pre- and postprandial bile acid concentrations are usually abnormal.
- Coagulopathies (increased prothrombin time, partial thromboplastin time, activated clotting time, and abnormal Thrombotest [see Resource List]) can be present because of impaired absorption of vitamin K and/or poor hepatic function.
- Ultrasonographic findings used to separate cholangiohepatitis from other types of liver disease include prominent hepatic portal veins, an abnormal biliary tract, normal splenic appearance, and normal abdominal lymph node size and appearance.
- A definitive diagnosis can be made only by histopathologic evaluation of liver biopsy specimen(s).
- Clinicians should be aware that the risk of hemorrhage following liver biopsy has little association with normal coagulation parameters; however, liver biopsy should be avoided in cats that already have evidence of a coagulopathy.
- Bile fluid sampling for cytology with bacterial culture and sensitivity is highly recommended during diagnostic evaluation.
- Enteric bacteria, such as Escherichia coli, are the most commonly isolated bacteria from affected cats, although other aerobic and anaerobic species have been isolated.
- Bile cytology should ideally be used in combination with histopathology to more accurately assess the inflammatory cell population.
- Protozoal organisms and liver flukes have also been sporadically identified as causes of the different forms of CH.

Summary of Diagnostic Criteria

Acute Suppurative Cholangiohepatitis

- Clinical signs present for less than 1 month.
- Fever.

Chronic Suppurative Cholangiohepatitis

- Clinical signs present for more than 1 month.
- Mature neutrophilia.
- Hyperbilirubinemia and hyperglobulinemia.
- Variably increased activity of ALT and ALP.

Nonsuppurative Cholangiohepatitis

- Clinical signs present for more than 1 month or an unremarkable history.
- Hyperbilirubinemia and hyperglobulinemia.
- If present, abdominal effusion will have a high protein concentration (>5 g/dl).
- Neutrophilia is less common.
- Variably increased activity of ALT and ALP.

Diagnostic Differentials

- Hepatic lipidosis is the most common hepatic disease in cats; the history (obesity followed by rapid weight loss), radiographic and ultrasonographic findings (hepatomegaly and hyperechogenicity), and aspiration cytology findings (minimal inflammatory cells with lipid vacuolization of hepatocytes) typically differ from those seen in cats with cholangiohepatitis. It is important to note, however, that some cats with cholangiohepatitis could also develop hepatic lipidosis as a result of the anorexia and weight loss associated with this condition.

- Extrahepatic biliary obstruction is usually ruled in by abdominal ultrasonography or during abdominal exploratory surgery; it can occur as a separate entity or may initiate cholangiohepatitis by causing intrahepatic biliary stasis. Biliary or pancreatic adenocarcinoma, pancreatitis, cholelithiasis, and cholecystitis have all been reported to cause extrahepatic biliary obstruction.

- Neoplasia, including primary hepatic or biliary neoplasia, lymphoma, or metastatic neoplasia, is usually confirmed by evaluation of liver biopsy but may be diagnosed by fine needle aspiration and cytology in some cases. It is important to note that...
well-differentiated lymphoma may be difficult to
distinguish from nonsuppurative CH.

**TREATMENT RECOMMENDATIONS**

**Initial Treatment**

*For All Three Diseases*

Empiric antibiotic therapy (see below) should be initiated while awaiting histopathology and bile or hepatic tissue culture and sensitivity results.

**Suppurative Cholangitis/Cholangiohepatitis (Acute and Chronic)**

- Antibiotics that achieve high biliary concentrations, are minimally hepatotoxic, and do not require hepatic excretion should be used. Long-term (6 to 8 weeks) antibiotic therapy using one of the following regimens is recommended for cats with confirmed (culture-positive) disease.
  - Ampicillin–sulbactam (Unasyn, Pfizer): 22 mg/kg IV q8h (if the cat is vomiting or anorectic).
  - Cefazolin: 10–20 mg/kg IV q8h (if the cat is vomiting or anorectic).
  - Amoxicillin–clavulanic acid (Clavamox, Pfizer Animal Health): 11–22 mg/kg PO q8–12h.
  - Cephalexin: 11–22 mg/kg PO q8h.

- Ursodeoxycholic acid (ursodiol): 10–15 mg/kg PO q24h until clinical and laboratory abnormalities (hyperbilirubinemia, increased ALP) have resolved.

- Ursodiol promotes bile flow and reduces biliary inflammation but should not be used if extrahepatic biliary duct obstruction is present or suspected.

- Vitamin K: 2.5–5.0 mg/cat PO or SC q24–72h as needed for coagulopathy. Coagulopathy associated with vitamin K malabsorption generally resolves within several days of initiating therapy; care must be taken to avoid an overdose.

- For patients with chronic suppurative CH, if no improvement is seen with the above recommendations, corticosteroid therapy (as described for nonsuppurative CH) is recommended.

**Nonsuppurative Cholangitis/Cholangiohepatitis**

- Immunosuppressive therapy is recommended to reduce the amount of lymphocytic/plasmacytic infiltration within the hepatic and biliary system. Various antiinflammatory and immunosuppressive dosages of corticosteroids have been recommended:
  - Prednisone: 2.2 mg/kg PO q24h for 2–3 weeks, then tapering, is the traditionally recommended dosage. For cats that fail to respond to this regimen, a dosage of 4.0 mg/kg PO q24h for 2–3 weeks, then tapering, may be beneficial.
  - Metronidazole: 7.5 mg/kg PO q12h for 2–3 weeks in conjunction with corticosteroid therapy. Metronidazole has both anaerobic antibacterial activity and immunomodulatory properties.

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**TABLE 1**

*Summary of Clinical Data from Cats with Suppurative Cholangiohepatitis and Hepatic Lipidosis*

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Acute CH</th>
<th>Chronic CH</th>
<th>Hepatic Lipidosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (yr)</td>
<td>5.7</td>
<td>9.7</td>
<td>6.2</td>
</tr>
<tr>
<td>Male/Female (%)</td>
<td>86/14</td>
<td>56/44</td>
<td>55/45</td>
</tr>
<tr>
<td>Anorexia (%)</td>
<td>81</td>
<td>78</td>
<td>100</td>
</tr>
<tr>
<td>Weight loss (%)</td>
<td>56</td>
<td>33</td>
<td>84</td>
</tr>
<tr>
<td>Lethargy (%)</td>
<td>75</td>
<td>78</td>
<td>80</td>
</tr>
<tr>
<td>Vomiting (%)</td>
<td>43</td>
<td>67</td>
<td>70</td>
</tr>
<tr>
<td>Diarrhea (%)</td>
<td>0</td>
<td>11</td>
<td>10</td>
</tr>
<tr>
<td>Fever (%)</td>
<td>71</td>
<td>11</td>
<td>6</td>
</tr>
<tr>
<td>Poikilocytosis (%)</td>
<td>28</td>
<td>44</td>
<td>85</td>
</tr>
<tr>
<td>Neutrophilia (%)</td>
<td>80</td>
<td>54</td>
<td>15</td>
</tr>
<tr>
<td>Leuk shift (%)</td>
<td>40</td>
<td>23</td>
<td>2</td>
</tr>
<tr>
<td>Increased ALT (%)</td>
<td>71</td>
<td>78</td>
<td>95</td>
</tr>
<tr>
<td>Increased ALP (%)</td>
<td>14</td>
<td>56</td>
<td>95</td>
</tr>
<tr>
<td>Increased bilirubin (%)</td>
<td>57</td>
<td>78</td>
<td>85</td>
</tr>
</tbody>
</table>


---

STANDARDS of CARE: EMERGENCY AND CRITICAL CARE MEDICINE
**Ursodeoxycholic acid (ursodiol):** 10–15 mg/kg PO q24h until clinical and laboratory abnormalities (hyperbilirubinemia, increased ALP) have resolved.

**Alternative/Optional Treatments/Therapy**

- **Chlorambucil:** 0.25–0.5 mg/kg q48h in conjunction with corticosteroid therapy to reduce lymphocytic/plasmacytic hepatic infiltration is likely a safer choice than azathioprine. Myelosuppression can occur with chlorambucil administration. Monitoring complete blood count every 3 to 4 weeks is essential to look for evidence of leukopenia, anemia, or thrombocytopenia.

- **Azathioprine:** 0.3 mg/kg q24h at a tapering dosage has been tried in cats but should be used with extreme caution because of the potential for serious side effects, including profound anorexia and bone marrow toxicity.

**Supportive Treatment**

- Intravenous fluid therapy is recommended for cats that exhibit anorexia and/or vomiting.
- Nutritional support, ideally via enteral feeding, should be initiated for any cat with anorexia lasting more than 72 hours.
- Appetite stimulants such as diazepam, midazolam, or cyproheptadine can be attempted but should be discontinued if not successful within 12 to 24 hours. If appetite stimulation does not work, it is very important to initiate nasoesophageal, esophageal, or gastric tube feeding.
- Calculate the daily caloric requirement (40 to 60 kcal/kg depending on degree of activity) to ensure an appropriate volume of food is fed.

**Patient Monitoring**

- The frequency of monitoring laboratory parameters should be reduced as the patient continues to improve: generally every 1 to 2 days for hospitalized patients and weekly to every 2 weeks for non-hospitalized patients.
- A follow-up hepatic biopsy is ideal in the weeks to months following treatment to help evaluate therapeutic outcome.

**Home Management**

- Owners should quantitate food intake to ensure that adequate nutritional support is maintained at home.
- Owners need to understand how, when, and for how long to administer oral medications.

**Milestones/Recovery Time Frames**

- Attitude and appetite should improve within 1 to 2 days of initiating appropriate therapy for acute suppurative CH but may take days to weeks for the chronic forms.
- Improvement in abnormal laboratory parameters (neutrophil count, serum bilirubin concentration, and liver enzyme activity) generally occurs within several days after initiating therapy for acute suppurative CH but may take weeks to months for the chronic forms.
- Abnormal liver enzyme activity may take months to completely resolve.
- In general, cats that are eating, drinking, and able to take oral medications can be managed at home.

**Treatment Contraindications**

- Drugs that require extensive hepatic metabolism or biliary excretion or that have known hepatotoxic capabilities should generally be avoided.
• The liver is the primary site of lactate metabolism. Intravenous fluids containing lactate are traditionally considered a poor choice for patients with compromised hepatic function. The clinical significance of this in dogs and cats is somewhat uncertain, and many clinicians use these fluids in patients with hepatic disease.
• The use of prednisone is contraindicated in feline patients that exhibit signs of hepatic encephalopathy. Therapy to reduce hyperammonemia should be initiated in such cats. Because protein catabolism resulting from glucocorticoid therapy could worsen hyperammonemia, administration of prednisone should be considered only after signs of hepatic encephalopathy have resolved.

**PROGNOSIS**

**Favorable Criteria**
- Cats with acute suppurative CH that survive the initial treatment period.
- Cats that maintain their appetite and body condition.
- Resolution of abnormal laboratory criteria.

**Unfavorable Criteria**
- Cats with chronic suppurative CH and nonsuppurative CH may not respond to therapy but can still have a reasonable quality of life for months to years in some cases.
- Cats with evidence of sepsis resulting from extension of hepatobiliary infection may be more difficult to manage.
- Microorganisms that exhibit multiple drug resistance may be harder to eliminate from the bile.
- Worsening of laboratory findings in the face of appropriate treatment is a poor prognostic sign.
- Progressive anorexia is a poor prognostic sign.

**RECOMMENDED READING**


