Bacterial cholangitis is reported rarely in the dog, with previous reports comprising a few case reports and one small case series.1–6 Reports of bacterial cholecystitis in dogs are also not common, but this disease has been described more frequently than cholangitis.7–10 The pathogenesis of these conditions is poorly understood with little information available to determine the relationship, if any, between them. There are also few data available about the clinical implications of and rate of occurrence of bactibilia. A retrospective study of biliary culture results from both dogs and cats demonstrated that (13/46) bile samples from dogs yielded positive bacterial cultures.11 However, the clinical consequences of positive bile cultures were not evaluated.11 A more recent study looked at the occurrence of bactibilia and cholecystitis in a retrospective case series, showing (10/40) bile samples were positive and that (6/6) dogs evaluated had cholecystitis.10

It has been suggested that canine bacterial cholangitis might occur with a greater frequency than is currently reflected in the literature.3,10,12 The aim of this study was to conduct a large multicenter retrospective survey to characterize both the frequency of presentation in dogs with hepatitis and the clinical characteristics of bacterial cholangitis and cholecystitis in dogs.

**Materials and Methods**

Case records of all dogs presented to 4 veterinary college referral hospitals in the United Kingdom and Ireland (University College Dublin Veterinary Hospital, Cambridge Veterinary School Queen’s Veterinary Hospital, University of Bristol Small Animal Hospital, and the Royal Veterinary College Queen Mother Hospital) between January 2000 and June 2011 were reviewed retrospectively. The inclusion criteria for cases of bacterial biliary tract disease were the combination of a positive bile/gallbladder wall culture or a bile cytology/Gram stain, demonstrating bactibilia, with contemporaneous histopathological evidence of cholangitis.
cholangitis, or both. Cholangitis was defined by the demonstra-
tion of neutrophil infiltration of portal areas, with or without
extension into the hepatic parenchyma. Cholangitis was defined
as infiltration of neutrophils into the gallbladder wall. The data
collected from each case meeting the inclusion criteria included sig-
nalment, clinical history, information on previous treatments,
physical examination findings, hematology and biochemistry
results (pre- and postreferral if available), abdominal ultrasound
findings, bacteriology results, bile cytology or Gram stain results,
where available, along with treatment and outcome information.
In addition, the clinical histopathology database (as appropriate
for each location) were interrogated at each university to quantify
the number of histopathologically confirmed cases of hepatitis pre-
sented at each institution during the same time period for compar-
ison. The study received ethical approval from the University
College Dublin, Animal Research Ethics Committee.

In each center, board-certified specialists in veterinary diagnos-
tic imaging oversaw ultrasound examinations. The ultrasound
reports were evaluated (where available); however, they were not
systematically reviewed for predefined criteria by 1 ultrasonogra-
pher. Gallbladder wall thickening was defined by a thickness of
≥ 3 mm and bile duct distension by a diameter of >3 mm.

Liver and extrahepatic biliary system biopsy samples were
obtained by ultrasound-guided needle biopsy technique or during
a laparotomy. After fixation in 10% neutral buffered formalin,
biopsy samples were embedded in paraffin wax, sectioned (4 μm),
and stained with Gill 2 Hematoxylin and Eosin (HE). Biopsy
samples from each case were evaluated by 1 pathologist (Jahns)
using specific predetermined criteria. Inflammation in the adventi-
tia of the portal tracts was graded using a semiquantative score:
mild = few inflammatory cells with inconsistent involvement of
portal triads, moderate = intermediate numbers of inflammatory
cells affecting the majority of portal triads, severe = large numbers
of inflammatory infiltrate with diffuse involvement of portal triads.
Biopsy samples were obtained by cholecystocentesis, either by percu-
taneous ultrasound-guided sampling or directly during the course
of a laparotomy. For all bacterial culture samples, both standard
anaerobic and aerobic techniques were performed. If a positive
culture was found, antibiotic susceptibility testing was then per-
formed in the majority of cases. Cytology was performed on a
proportion of the samples of bile which were stained with Giemsa
and evaluated by a boarded clinical pathologist.

Results

Twenty-seven dogs fulfilled the inclusion criteria including 2 previously reported cases. These cases comprised 12 males (6 neutered) and 15 females (14 neutered) with a mean age of 8.9 years (range 0.5–14 years). The median body weight was 15.4 kg (2.3–38.6 kg); weight was not recorded in 8 cases. The number of cases of hepatitis identified from databases during the study period was 378. However, the number of cases of hepatitis from Cambridge was only available between January 2007 and June 2011. Hence, the true overall hepatitis case numbers were likely to be closer to 490 (based on extrapolation from 4.5 to 11.5 years for Cambridge). This would equate to an approximate preva-
ience of 6% for confirmed cases of bacterial cholangitis or cholecystitis within the hepatitis group.

The most frequent presenting complaints and physical examination findings (referring veterinarian history or
at the time of referral) were vomiting (24/27), anorexia (19/27), lethargy (18/27), jaundice (15/27; described in
history or noted in addition where hyperbilirubinemia
[25 μmol/L] was recorded in the history), abdominal
discomfort/pain (15/27), diarrhea (12/27), and pyrexia
(9/27). Additional signs such as ascites (5 identified clini-
cally and 9 ultrasonographically/27), weight loss, and
polyuria/polydipsia were also reported in several cases.

The duration of clinical signs prior to referral ranged
from 1 day to several months. Nineteen dogs presented
with an acute history (< 3 weeks) and 8 with chronic
waxing and waning signs. Within the group with an
apparently acute presentation 21 cases, combined with
signs suggestive of an acute flare-up on a background of chronic
disease. Approximately 2/3 of dogs had received antimicro-
bial treatment prior to referral. Summarized signal-
ment, clinical presentation and clinical pathology
findings are available in Table S1 presented as support-
ing information not appearing in the parent article.

The most frequently reported clinical pathology
abnormalities, either prior to referral or at the time of
referral, were increases in serum ALT (25/26 cases) and
ALP activities (20/26 cases), hyperbilirubinemia (20/26
cases), hypercholesterolemia (19/22 cases), and an
inflammatory leukogram (21/24 cases). Cholangitis (19
cases, band/toxic changes in 7 cases, and monocytosis
in 8 cases). Concurrent band neutrophils/toxic changes
and neutrophilia were apparent in 7 cases and monocytos-
istosis and neutrophilia in 7 cases. Globulin was
increased in 4 cases; 2 of which had an inflammatory
leukogram. Prothrombin time and activated partial
thromboplastin time were elevated in 16 of the 19 cases
evaluated.

The 19 cases with an acute presentation had either
hyperbilirubinemia (15/18) or signs suggestive of an
acute abdomen (8/19) or in a few cases, both abnor-
malities (4/18). Abdominal pain and pyrexia were com-
monly observed and were present in all except 2 of the
acutely presenting cases. Neutrophilia was recorded
in 15/19 of these acute cases, hyperglobulinemia in 4/19 of
the cases, and in 2 cases both abnormalities were pre-
ent. When considering the 8 cases with a chronic pre-
sentation, hyperbilirubinemia was documented in 4/8 cases,
and 2/8 cases presented with both abnormalities, leaving 2/8 cases presenting
with neither change. All except 3 of the chronic cases had either abdominal pain or pyrexia.

Abdominal ultrasound reports were available in 26/27
cases. One case immediately underwent surgery having had
been referred with a known gallbladder rupture. No
abnormalities were found in 1 case. The most frequent
findings were distended common bile duct (10/26),
thickened gallbladder wall (9/26; Fig 1), distended gall-
bladder (9/26), gallbladder sludge (9/26), free abdominal
fluid (8/26), heterogeneous hepatic parenchyma (7/26),
hyperecoic hepatic parenchyma (6/26), and gallbladder
mucocele (6/26). In cases where thick or sludge was
noted, there was at least one other abnormal finding reported.
Choleliths (4/26), enlarged liver (3/26), gas in the gall-
bladder (3/26), thickened common bile duct wall (2/26),
and ruptured gallbladder (2/26) were less commonly
reported. In 3 cases, changes in echogenicity or size of
portions of the pancreas were noted; however, reports
of pancreatic findings were not available in the majority


of cases, so it was not possible to comment on the frequency of these abnormalities overall. Summarized ultrasound findings and clinical follow-up data are available in Table S2 presented as supporting information not appearing in the parent article.

Ascites was identified at presentation in 9 cases, either detected by clinical examination or by ultrasoundography. In 5/9 cases, it was confirmed to be biliious. A further 3 cases were recorded as having an exudate, although bilirubin had not been measured in the fluid. In one of these 3 cases, an orange fluid was described at postmortem examination, and in another case, a small perforation was noted in the gallbladder at surgery and this dog developed postsurgical bile peritonitis. Of the 9 cases had previously undergone cholecystectomy for a mucocele at the referring veterinary practice and then subsequently developed ascites. At the time of referral, surgery revealed multiple acquired shunts and portal hyperension with common bile obstruction caused by stricture of the duodenal papilla.

Overall, there were 23 bile cultures (22/23 positive), 9 gallbladder wall cultures (9/9 positive), and 10 liver cultures (3/10 positive). Antimicrobial sensitivity testing was available in 24 cases. In 3 cases, bile was resampled, in 2 cases on 1 occasion and in 1 case on 2 occasions. The second samples were taken 3, 4, and 6 weeks after the first sample and antimicrobial treatment and were all positive (3/3 positive, n = 2 recultured Enterococcus spp., n = 1 cultured a different bacterium). The second resample culture, performed after 8 weeks of treatment, was negative. Concurrent cultures from different sites were available in a proportion of cases, as follows: bile and gallbladder wall cultures (n = 5, all the same isolates), gallbladder wall and liver culture (n = 1, same isolate), liver and bile cultures (n = 8, all bile culture positive and n = 2 liver cultures positive, same isolates), and liver, bile, and gallbladder wall cultures (n = 1, only gallbladder wall positive). Bile was obtained percutaneously using ultrasound guidance in 5 cases with no reported complications associated with this procedure. One additional case had bactibilia evidenced by a Gram stain (performed on histological sections taken from the common bile duct), but unconfirmed on culture. Cytological examination of the bile was performed in 4 cases, all of which had positive culture results. In 3 of these cases, the cytological examination confirmed bactibilia; 2 cases had rods (Fig 2) and one had cocci identified on the smear. In 1 case, there was no bactibilia on cytology. None of the samples had cytological evidence of inflammation.

Overall, there were 40 separate bacterial isolates from 26 dogs. The most frequent isolates from bile, gallbladder wall, or liver were Escherichia coli (n = 17 isolates in 16 cases), Enterococcus spp. (n = 8 isolates in 6 cases of which 4 were specifically speciated as Enterococcus faecalis), and Clostridium spp. (n = 5 in 5 cases of which 4 were specifically speciated as Clostridium perfringens). Other isolates included untyped coliforms (4), Enterobacter cloacae (1), Klebsiella sp. (1), Proteus sp. (1), Bacteroides sp. (1), a Gram-negative bacillus, and an untyped anaerobe. More than one bacterial species was isolated in 7/27 cases. In 10 of the cases from which E. coli was isolated, this was the sole bacterial isolate. In 31/32 aerobic isolates tested, antimicrobial resistance was identified (Table 1). Sixteen of these isolates were E. coli, of which 10/16 showed resistance to 3 or more classes of antimicrobials. All of the Enterococcus spp. isolates showed resistance to several agents. Resistance to amoxicillin clavulanate was noted in 2 Enterococcus spp. isolates. Four of 6 first isolates showed sensitivity to fluoroquinolones; although in 2 of these cases, a repeat culture 4–6 weeks later grew an isolate with enrofloxacine resistance.

After referral, 21 animals underwent surgery with cholecystectomy performed in 18 of these dogs. One additional dog had a cholecystectomy 3 weeks after a Tru-cut liver biopsy due to confirmation of cholelithiasis following a previously equivocal ultrasound examination. Overall, the indications for cholecystectomy were various: mucocele (8/19), gallbladder rupture (7/19), suspected cholecystitis due to gallbladder wall thickening, irregularity or gas in the bile duct.

**Fig 1.** Ultrasound of gall bladder. This picture shows a thickened gall bladder wall, defined as ≥3 mm. This was a common finding (9/26) in the study.

**Fig 2.** Cytology of the bile. This picture shows rod-shaped bacteria, as identified in 2 cases. Bar 10 μm.
Antimicrobial sensitivity testing was performed in 36 isolates using the Kirby-Bauer method according to the standard procedures of individual laboratories. All anaerobes tested (4/4) were sensitive to metronidazole; *Clostridium* spp. isolates (2), *Bacteroides* sp. (1), and an untyped anaerobe (1). The sensitivity results from 31 aerobic isolates are summarized in the table, 1 additional case (not included in the table) was reported as a profuse growth of a Gram-negative bacillus, sensitive to aminopenicillin and clavulanic acid with no further sensitivity testing reported. 3 *Clostridium* spp. isolates and 1 Coliform isolate were not sensitivity tested.

<table>
<thead>
<tr>
<th>Isolate Type</th>
<th>Number</th>
<th>N</th>
<th>A</th>
<th>+C</th>
<th>Carb</th>
<th>1st</th>
<th>2nd</th>
<th>3rd</th>
<th>Fluoroquinolone</th>
<th>Aminoglycoside</th>
<th>Tetracycline</th>
<th>TMP</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>E. coli</em></td>
<td>17</td>
<td>7/7 R</td>
<td>13/15 R</td>
<td>10/16 R + 1 I</td>
<td>2/2 R</td>
<td>12/16 R</td>
<td>8/11 R</td>
<td>4/9 R</td>
<td>3/16 R</td>
<td>3/5 R (1 S Amikacin R Gentamicin)</td>
<td>9/16 R</td>
<td>6/16 R</td>
</tr>
<tr>
<td>Other</td>
<td>6</td>
<td>2/3 R</td>
<td>4/6 R</td>
<td>1/6 R</td>
<td>1/1 R</td>
<td>1/6 R</td>
<td>1/4 R</td>
<td>0/2 R</td>
<td>2/6 R</td>
<td>0/2 R (1 I Streptomycin)</td>
<td>5/6 R</td>
<td>1/6 R</td>
</tr>
<tr>
<td>Coliforms/</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proteus sp.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Enterococcus sp.</td>
<td>8</td>
<td>4/5 R</td>
<td>4/8 R</td>
<td>2/8 R</td>
<td>–</td>
<td>7/8 R</td>
<td>1/3 R</td>
<td>2/2 R</td>
<td>4/8 R</td>
<td>1/1 R</td>
<td>6/8 R</td>
<td>5/8 R</td>
</tr>
</tbody>
</table>

This table shows the proportion of those isolates tested that was resistant to given antimicrobial classes. In total, there were 40 bacterial isolates in 26 cases. One additional case was diagnosed on a Gram stain with no culture. Seven dogs had multiple isolates and 3 cases had positive culture results on a second sample taken after antimicrobial treatment. Antimicrobial sensitivity testing was performed in 36 isolates using the Kirby-Bauer method according to the standard procedures of individual laboratories. All anaerobes tested (4/4) were sensitive to metronidazole; *Clostridium* spp. isolates (2), *Bacteroides* sp. (1), and an untyped anaerobe (1). The sensitivity results from 31 aerobic isolates are summarized in the table, 1 additional case (not included in the table) was reported as a profuse growth of a Gram-negative bacillus, sensitive to aminopenicillin and clavulanic acid with no further sensitivity testing reported. 3 *Clostridium* spp. isolates and 1 Coliform isolate were not sensitivity tested.

Treatment with antimicrobials prior to referral was reported in 18 cases, and no antimicrobial medication was recorded in 7 cases and was unknown in 2 cases. The most commonly prescribed antimicrobial prior to referral was amoxicillin clavulanate.

Key: R, resistant; S, sensitive; I, intermediate sensitivity; N, natural penicillin; A, aminopenicillin; +C, aminopenicillin +clavulanic acid; Carb, carboxypenicillin; 1st, 2nd, 3rd, generation cephalosporin; TMP, trimethoprim sulfonamide.

gallbladder (or combination of these) (5/19), cholelithiasis (3/19), and 1 case with a distended gallbladder and solid-appearing contents at ultrasound (1/19). In 6 cases, the gallbladder rupture occurred concurrently with lithiasis, a mucocele, or emphysematous cholecystitis. Surgery was performed in the other 3 noncholecystectomy cases for duodenal stenosis at a previous surgical site (n = 1), surgical liver biopsies (n = 1) and persistent jaundice, distended common bile duct, and ascites in a dog with a history of previous mucocele excision (n = 1).

Liver histopathology was available in 26/27 cases (20 surgical, 5 Tru-cut biopsies, and 1 postmortem) and gallbladder histopathology in 20/27 cases, including 1 case that did not have liver histopathology (Table 2). All liver biopsy samples revealed cholangitis (Fig 3). This was mild in 11/26 cases, moderate in 14/26 cases, and severe in 1 case. Histopathological examination of the gallbladders (Fig 4) showed cholecystitis in 14/20 cases, gallbladder infarction in 5/20, and mucocele in 2/20 cases, although a greater number were noted on examination at surgery, giving a total number of 8. In 1 case, both cholecystitis and infarction were noted.

Overall, 21/27 dogs were discharged. Five dogs died or were euthanased perioperatively, and 1 additional dog was euthanased without treatment. Three of these dogs had bile peritonitis, I developed SIRS postoperatively, and the other died perioperatively following cholecystectomy and stenting of the common bile duct. Four of these 6 patients that died presented with signs of an acute abdomen and were confirmed to have gallbladder rupture. The culture of multiple isolates on biliary culture did not correlate with a poorer prognosis. Short-term outcome (1–2 months) was available in 18 of the discharged cases: 10 cases were clinically well, 5 showed persistent clinical signs, in 2 dogs the serum activities of liver enzymes remained elevated but no other clinical information is available, and 1 dog died. Long-term outcome (1–3 years) was available in 11 cases with 6 alive at 3 years. Treatment information was available for 19/21 discharged dogs, although this was incomplete in several cases. The overall duration of treatment was difficult to discern clearly due to the retrospective nature of the study, but ranged from 4 to 12 weeks for antibiotic administration. Overall, 10 dogs received ursodeoxycholic acid, 13 received amoxicillin clavulanate, 7 received fluoroquinolones (typically enrofloxacin), 4 received metronidazole, and 3 received other antibiotics.

Concurrent conditions/relevant drug exposures identified in the cases included gallbladder mucocele in 8 dogs, cholelithiasis in 5 dogs, endogenous or exogenous glucocorticoid exposure in 4 dogs, the latter including treatment for immune-mediated thrombocytopenia, lymphoplasmacytic gastritis (also treated with Azathioprine), and long-term skin disease. Two dogs had previous surgery that could have predisposed them to biliary infection; one had duodenal stenosis and the other stricture of the duodenal papilla following previous cholecystectomy for a gallbladder mucocele. One additional dog had mild lymphoplasmacytic enteritis, 1 dog had a calcified gallbladder wall (which could have been an incidental finding), and 3 dogs had ultrasonographic signs suggestive of pancreatitis.

**Discussion**

This study presents data from a large number of confirmed cases of bacterial cholangitis, cholecystitis, or both in dogs and suggests that this disease might be...
Table 2. Summarized histopathology findings and final diagnosis for 27 dogs with concurrent bactibilia and cholangitis, cholecystitis, or both.

<table>
<thead>
<tr>
<th>Groups of Cases</th>
<th>Number of Cases</th>
<th>Liver Histopathology</th>
<th>Gallbladder Histopathology</th>
<th>Final Diagnosis and Potential Predisposing Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>A/C</td>
<td>+</td>
<td>Cholecystitis Infarction Mucocele</td>
</tr>
<tr>
<td>Acute presentation</td>
<td>11 Clinical cases</td>
<td>8/11 Acute</td>
<td>3/11</td>
<td>5/7 2/7 3/7 11/11 Cholangitis</td>
</tr>
<tr>
<td></td>
<td>7 Gallbladder histopathology</td>
<td>3/11 Chronic</td>
<td></td>
<td>11/11 Cholangitis 5 Confirmed cholecystitis (incl. 2 with cholelithiasis and 1 with mucocele) 2 Thickened gallbladder wall (ultrasound) 3 Gallbladder mucocele (incl. 1 with Hypothyroidism) 2 Cholelithiasis 1 Receiving corticosteroids 1 Previous surgery (altered anatomy)</td>
</tr>
<tr>
<td>Acute presentation</td>
<td>8 Clinical cases</td>
<td>7/7 Acute</td>
<td>3/7 3/7 1/7</td>
<td>6/8 3/8 2/8 7/7 Cholangitis</td>
</tr>
<tr>
<td>with signs of acute abdomen</td>
<td>7 Liver histopathology</td>
<td></td>
<td>6/8 Cholecystitis (incl. 2 with cholelithiasis and 1 with mucocele) 2 Gallbladder mucocele 3 Cholelithiasis</td>
<td></td>
</tr>
<tr>
<td></td>
<td>8 Gallbladder histopathology</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chronic presentation</td>
<td>8 Clinical cases</td>
<td>6/8 Acute</td>
<td>2/8</td>
<td>3/5 0/5 3/5 (1 Mucocele previously removed)</td>
</tr>
<tr>
<td></td>
<td>8 Liver histopathology</td>
<td>6/8 2/8 0/8</td>
<td>8/8 Cholangitis</td>
<td>3/5 Confirmed cholecystitis (incl. 1 with mucocele, 1 partial calcification of gallbladder wall) 3 Gallbladder mucocele (incl. 1 with IBD receiving corticosteroids) 1 Previous surgery (altered anatomy—duodenal papilla stricture and previous mucocele removed) 2 Receiving corticosteroids 1 Hyperadrenocorticism 3 Inflammatory bowel disease</td>
</tr>
<tr>
<td></td>
<td>5 Gallbladder histopathology</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

This table summarizes the liver and gall bladder histopathology findings of the 27 cases meeting the inclusion criteria. Cases are divided within the table into those that presented acutely and those that presented more chronically (>3 weeks history). The acute cases are further divided, with those in the shaded section all having presented with signs of an acute abdomen (acute presentation and free abdominal fluid).

Cholangitis was subjectively defined as +: mild, ++: moderate, +++: severe. A denotes acute and C denotes more chronic classification of the lesion.

IBD, inflammatory bowel disease; Incl., Including.
The most frequent presenting complaints and physical examination findings in this study were vomiting, anorexia, lethargy, jaundice, abdominal discomfort, and diarrhea. In addition, pyrexia was noted in 9/27 of the dogs, with 20/27 cases presenting with either pyrexia or abdominal pain. These are reported to be common findings in animals with inflammatory or obstructive biliary tract disease.18,19 The duration of clinical signs prior to presentation was variable, 19 cases presented acutely (signs present <3 weeks), and 8 dogs had a more chronic course, typically with signs waxing and waning over this period. At least 18 cases had received antibiotic treatment prior to referral. In several cases, the clinical signs were reported to have improved with this treatment, although the data available from referring veterinarians were incomplete in many cases. In view of this, when figures were reported for the number of cases with clinical, such as jaundice or vomiting, they included cases that had the signs reported either in the referral history or at presentation, as it was thought to be more representative of the data, particularly when the signs wax and wane.

The main clinical pathology abnormalities noted in the present case series were liver enzyme elevation, hyperbilirubinemia, hypercholesterolemia, an inflammatory leukogram, and in a few cases, hyperglobulinemia, findings consistent with cholestasis and an inflammatory process.1–6 These findings are broadly similar to those reported in previous cases; however, 10/10 cases in previous reports had been jaundiced and 8/8 had an inflammatory leukogram (2 others not reported) at some point in their history. When the cases in this study are considered based on their presentation, 15/18 of the acute cases presented with hyperbilirubinemia (one additional acutely presenting case had no serum biochemistry performed) and 17/19 had at least one of neutrophilia, monocytosis, or hyperglobulinemia. This suggests that finding increased bilirubin and an inflammatory leukogram should increase the index of suspicion for cholangitis and/or cholecystitis. The cases presenting with acute signs had predominantly either hyperbilirubinemia or an acute abdomen with biliary tract rupture, with a few cases showing both signs. The 3 cases without hyperbilirubinemia in this group of acute cases all had gallbladder rupture when investigated further. In the cases with chronic presentation, 5/8 dogs presented with hyperbilirubinemia and 4 had a mature neutrophilia with/without a concurrent monocytosis.

The ultrasound findings in the cases were variable and nonspecific, with almost all cases having abnormalities identified. Abnormalities relating to the biliary tract, such as gallbladder wall thickening and distension of the common bile duct, were identified in a number of cases. More specific abnormalities included choledoliths, mucocoeles, and free abdominal fluid. Gallbladder sludge has been reported to occur in normal animals, although its clinical significance is debated.10,20 In addition, distension of the gallbladder is a subjective finding that was not clearly quantified. In view of this,
these latter 2 findings alone were not considered sufficient to warrant the description of an abnormal ultrasound. In each case, when present, the change was in addition to at least one other abnormal finding. One exception with respect the gallbladder size was that of a small gallbladder, noted in 2 cases, which were then found to have gallbladder rupture.

Although overall many of the ultrasound findings were nonspecific, they were generally helpful in case management. In 19 cases, abnormalities indicated a potential requirement for surgical intervention; these included free abdominal fluid and suspected ruptured gallbladder, choleliths, gas in the gallbladder, and biliary mucocoeles. In 4 additional cases, the presence of thickening, irregularity, or abnormal echogenicity of the gallbladder wall raised suspicion of cholecystitis and directed bile sampling and culture. In 1 case, the presence of a gallbladder mass/cholelith and ascites led to the decision for euthanasia. In 1 case, increasing quantities of gallbladder sludge with persistent liver enzyme elevation led to a decision to resample bile for culture and 1 case was the unintended result of an instrumental in the management decision. However, at this point, it is worth acknowledging the inherent bias of a study such as this; dogs with ultrasonographic abnormalities of the gallbladder, gallbladder wall, or bile duct are more likely to have gallbladder aspirates, culture, and/or histology and be included in this study. Without normal ultrasound findings it is not possible to determine the sensitivity of ultrasound for the confirmation of the presence of mucocoele in these cases, as in several cases known to have a mucocoele at surgery, the full ultrasound report was not available.

It is generally accepted that the human gallbladder and bile are normally sterile, but whether this is the case in dogs and cats is unclear. Older studies suggested that organisms could readily be isolated from the normal canine liver. More recently, it has been proposed that bile from dogs and cats is sterile in the absence of biliary defense mechanisms, for example, biliary stasis and increased mucus, aiding prevention of bacterial adhesion and colonization. Factors that predispose to biliary infection are likely to impair these natural defense mechanisms, for example, biliary stasis and increased

The literature available regarding bile or gallbladder wall culture in dogs with cholangitis is limited, with more information available for cholecystitis and cholelithiasis in this species. There has been 1 large retrospective study looking at the prevalence and identity of bacterial isolates in canine and feline hepatobiliary cultures, and 1 smaller case series looking at cholecystitis and bactibilia, but the current report describes the largest reported series of positive bile/gallbladder wall cultures to date, and in the current report to examine liver histopathology concurrently in the majority of cases. Overall, the results are in broad agreement with the findings from the previous report; the predominant bacterial isolates from the hepatobiliary system were enteric isolates. E. coli was the most frequent bacterium isolated with Enterococcus spp. and Clostridium spp. also frequently cultured. In just under one third of dogs, more than 1 bacterial isolate was cultured; a lower figure than previously reported: 11/21 dogs in 1 previous study and 6/10 in another. In agreement with previous reports, anaerobic organisms were cultured in the majority of cases in the current study, but still represented an important group. An important finding in this report was the frequency with which antimicrobial resistance occurred. Resistance occurred frequently in E. coli isolates, with just under two thirds of resistant isolates showing resistance to 3 or more classes of antimicrobials. Two thirds of the E. coli isolates were resistant to amoxicillin clavulenate and 3 of these resistant isolates were also resistant to fluoroquinolones and 1st-generation cephalosporins. As would be expected, 1 of the Enterococcus spp. isolates showed resistance to several antimicrobial agents; however, an important finding was the development of fluoroquinolone resistance over time in the 2 cases that were resampled. Overall, the bacteriology and antimicrobial sensitivity results underline the importance of obtaining multiple isolates and repeat sampling of the number of animals that had been referred with ongoing disease despite antibiotic treatment. They would also suggest that repeat sampling is important both to confirm or refute resolution of bactibilia, as has been previously suggested, and to ensure there is continued antimicrobial sensitivity screening.

There is little known about the etiopathogenesis of bacterial cholangitis in dogs. The 2 main routes by which bacteria can invade the biliary tract are by ascending infection from the duodenum or hematogenously via the hepatic portal venous blood. Normal biliary defense mechanisms comprise a number of components: a mechanical barrier provided in part by the sphincter of Oddi, the flushing action of bile and bacterial action of bile salts, and potent local immunological defense mechanisms (Kupffer cells, secretory IgA and mucus), aiding prevention of bacterial adhesion and colonization. Factors that predispose to biliary infection are likely to impair these natural defense mechanisms, for example, biliary stasis and increased

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biliary pressure or overwhelm the hepatobiliary-enteric circulation of bacteria, for example, large portal vein inocula or cholestasis. Concurrent clinical conditions or exposure to immunosuppressant agents that could have predisposed to biliary infection were identified in 22/27 of the cases in this report. These conditions included gallbladder abnormalities, such as mucoceles, cholelithiasis, and a calcified gallbladder wall, which could cause cholestasis or provide a nidus for infection; surgical manipulations or anatomical abnormalities, such as biliary denal stenosis and stricture of the duodenal papilla, which could affect biliary pressure and the potential for reflux into the biliary tree; and finally pancreatitis and lymphoplasmacytic enteropathy, which could again affect biliary pressure, biliary defenses, and in addition the gut microflora and the enterohepatic circulation of bacteria.

The potential interrelationship between bacterial cholangitis and cholecystitis has not been clearly defined, although it would seem likely that their etiology is inter-related due to similar predisposing factors. Concurrent cholecystitis has been observed in several cases within a series of cholecystitis, although not evaluated systematically and of the 4 cases in a case series of bacterial cholangitis had evidence of cholecystitis. The inclusion criteria for the study were deliberately designed to be wide, including cases of confirmed bactibilia with histopathological evidence of cholangitis, cholecystitis, or both. The authors acknowledge that when biliary disease occurs, inflammation and infection become established in the gallbladder and then may progress to involve the biliary tree and liver. The confounding problem with this approach is that mild cases of cholecystitis are likely to be excluded due to lack of histopathological confirmation; or that the management would not entail cholecystectomy. In this study, 26 dogs had confirmed cholangitis, 20 had confirmed gallbladder pathology, a further 3 had gallbladder changes suggested by ultrasound findings, and 1 case had previous removal of a gallbladder mucocoele. This shows a very large proportion of the cases had concurrent liver and gallbladder pathology; indeed as gallbladder evaluation was not performed in all cases, it is difficult to exclude the possibility of an even greater proportion having gallbladder pathology, particularly as it is well recognized in humans that ultrasound is not 100% sensitive for the detection of cholecystitis. This concurrent presentation would tend to support a link between bacterial cholangitis and gallbladder pathology in dogs.

Cholecystitis was identified in 14 of the 20 cases in which gallbladder histopathology was performed, suggesting that cholecystitis and cholangitis share similar predisposing causes or that one predisposes to the other. The inclusion of gallbladder pathology in the other 6 cases is potentially of more significance, as one interpretation would be that a variety of gallbladder pathologies might predispose to cholangitis or that these conditions are also predisposed to by similar factors. Five of these 6 cases had biliary mucocele and 1 dog had gallbladder infarction and cholelithiasis. The presence of gallbladder pathology might disrupt the hepatobiliary-enteric circulation of bacteria, with any abnormal tissue acting as a potential nidus of infection, a situation shown experimentally. Once there is any cholestasis or further perturbation of biliary defense mechanisms, the dogs would be likely to become symptomatic for cholangitis, as seen in the experimentally manipulated cats. This situation is likely to further exacerbate cholecystitis, develop, as bacterial infection has been shown to result in proliferative activities in bacteria, and several of the chronic cases in this report. Antibiotics only provided a temporary resolution of clinical signs, which then resolved with cholecystectomy suggesting a continued focus of infection. It is noteworthy that bile or gallbladder wall cultures yielded a far higher proportion of positive culture results than liver cultures, in agreement with Wagner et al.

The overall management of the cases was variable reflecting the diverse clinical presentations, different participating institutions, and the retrospective nature of the study. This type of study is not an appropriate design to allow clear recommendations on the appropriate management of these cases. However, treatment with a broad-spectrum antibiotic is indicated for bacterial hepatobiliary disease with coverage for Gram-positive and Gram-negative aerobes and anaerobes, as evidenced by the bacteriological culture results. These findings, along with the results of antimicrobial sensitivities testing, underscore the importance of this type of evaluation. While empirical coverage with either a fluoroquinolone and amoxicillin clavulanate or a fluoroquinolone, metronidazole, and an amino penicillin could be suggested based on the likely organisms involved, resistance remains a potential problem. Significant resistance to both amoxicillin clavulanate and fluoroquinolones among E. coli and Enterococcus spp. isolates, along with examples of changing resistance over time in isolates from individual cases, highlights that an empirical approach to antimicrobial treatment should be used with caution. This is particularly pertinent where a medical approach is taken with the gallbladder left in situ, as a clinical response does not always equate to resolution of bactibilia. Ursodeoxycholic acid would seem an appropriate choice to promote choleresis once biliary obstruction is relieved, although again the evidence base for this approach is currently limited. The main limitations of this study reflect its retrospective nature. All clinical records were not complete, hindering the ability to make clear interpretations about the sensitivity of investigations such as ultrasound for predicting particular clinical abnormalities. The analysis of treatment and outcomes was also limited by this approach and the variable histological examinations of institutions. The inclusion criteria of histopathologically proven cholangitis, cholecystitis, or both were deliberately strict as little is known about these conditions and only clearly defined cases were included. This type of approach is likely to bias toward the inclusion of more severe cases that had samples taken for histopathology. This is particularly the case for cholecystitis cases where
tissue samples were available following cholecystectomy. In addition, cases with a histopathological diagnosis of neutrophilic cholangitis and an unproven bacterial etiology did not meet the inclusion criteria, likely to result in an underestimate of the true case numbers due to some of these cases being culture negative following antimicrobial treatment. However, despite these limitations, by virtue of the number of cases presented against a sparse literature in this area, this study offers important information about the rate of occurrence, clinical presentation, and features of canine cholangitis and cholecystitis.

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Supporting Information

Additional Supporting Information may be found online in the supporting information tab for this article:

Table S1. Summarized signalment, clinical presentation, and clinical pathology findings for 27 cases with concurrent bactibilia and cholangitis, cholecystitis, or both.

Table S2. Summarized ultrasound findings and clinical follow-up data for 27 cases with concurrent bactibilia and cholangitis, cholecystitis, or both.