



Canine Gallbladder Mucoceles

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ABSTRACT: Gallbladder mucoceles occur when the gallbladder distends abnormally from excessive accumulation of mucus within the lumen. Mucoceles have become an important cause of extrahepatic biliary tract disease in dogs. The clinical presentation is variable, and signs may even be absent. Gallbladder rupture can occur and lead to significant morbidity in affected dogs. Cystic mucinous hyperplasia of the gallbladder epithelial cells represents the key histologic feature in this disease. The pathogenesis of mucocele formation is unknown. Surgical cholecystectomy is an effective treatment of affected patients. The long-term prognosis is excellent in patients that survive the postoperative hospitalization period.

A gallbladder mucocele is an enlarged gallbladder containing an excessive amount of mucus. The word *cele* is derived from the Greek word *kele* for tumor. A mucocele therefore describes a solid accumulation of mucus that may resemble a tumor or mass. For many years, pathologists have noted gross accumulation of excess mucus in the gallbladder of many older dogs during necropsy and have considered it an age-related incidental lesion.¹ Recently, a series of reports²⁻⁷ have shown that not all gallbladder mucoceles are clinically silent and that they can be associated with extrahepatic bile duct obstruction (EHBDO), cholecystitis, and gallbladder wall rupture. This article reviews normal gallbladder structure and function and discusses what is currently known about the pathogenesis, diagnosis, and treatment of gallbladder mucoceles.

The cystic duct extends from the neck of the gallbladder until it empties into the common bile duct (Figure 1). The last part of the common bile duct lies embedded in the duodenal musculature as it courses to its exit site at the major duodenal papilla. This intramural part behaves like a sphincter and is therefore referred to as the *sphincter of Oddi* in humans. In dogs, the pancreatic duct also exits at or near the major papilla. The accessory pancreatic duct, which is the larger of the two pancreatic ducts in dogs, opens about 2.5 cm caudal to this at the minor duodenal papilla.^{8,9}

The gallbladder is a thin-walled, muscular sac that can distend to accommodate bile for storage during interdigestive periods. Histologically, the gallbladder wall is composed of an innermost mucosal epithelial cell layer, a submucosal layer containing the lamina propria, a middle smooth muscle layer, a layer of connective tissue, and an outermost serosa¹⁰ (Figure 2). The lamina propria contains the vascular supply, which originates from the cystic artery, a branch of the left branch of the hepatic artery.¹¹

NORMAL ANATOMY

The gallbladder is a pear-shaped sac that lies on the visceral surface of the liver between the quadrate lobe medially and the right medial

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NORMAL GALLBLADDER FUNCTION

Bile is the secretory product of hepatocytes and primarily consists of water, bile acids, bile pigments, cholesterol, and other inorganic salts.¹²⁻¹⁴ Certain drugs and antimicrobials may also enter bile. Bile is secreted continuously by the liver.¹⁵ It eventually enters the gallbladder, where it is stored and modified. After a meal, the gallbladder contracts and discharges bile through the cystic duct and common bile duct into the duodenum. At the same time, the sphincter of Oddi opens to facilitate bile flow through the common bile duct into the duodenum.

Between meals, most bile is diverted into the gallbladder, where bile can be stored, acidified, and concentrated. The primary changes that occur in bile composition include transport of sodium, chloride, water, and other small electrolytes across the mucosal lining and out of the gallbladder lumen.^{10,16-18} Secretion of hydrogen ions by the gallbladder mucosal epithelial cells acidifies the gallbladder contents. At mealtimes, the gallbladder mucosa secretes a mucinous, bicarbonate-rich fluid into its lumen that mixes with the modified stored hepatic bile. Secretion of this fluid is facilitated by the action of the gastrointestinal peptides secretin and vasoactive intestinal polypeptide on gallbladder epithelial cells.^{17,18} Following secretion of this fluid, the gallbladder contracts and discharges its contents into the cystic duct and common bile duct.

The strongest stimulus for postprandial gallbladder contraction is the hormone cholecystikinin (CCK), which is released by enterocytes when fat from a meal enters the duodenum. CCK also causes relaxation of the sphincter of Oddi, which facilitates bile flow into the duodenum.^{19,20} Parasympathetic stimulation (vagus) and

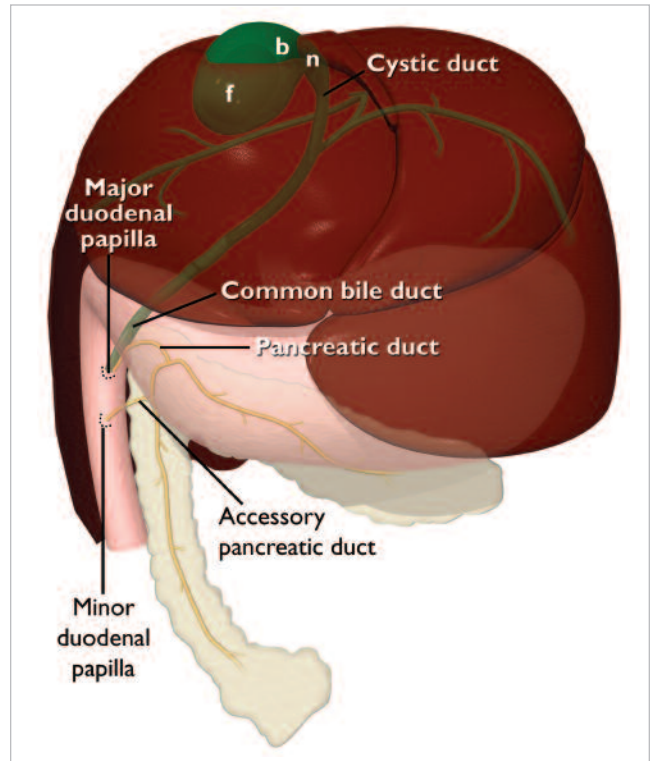


Figure 1. Schematic drawing of the anatomy of the intra- and extrahepatic biliary tree showing the gallbladder fundus (f), body (b), and neck (n). (Illustration by Felecia Paras)

hypertrophy, and *mucinous cholecystitis*, have appeared in the veterinary literature.^{1-4,23} The principal gross abnormality associated with gallbladder mucoceles is gallbladder enlargement secondary to buildup of excessive amounts of mucus within the lumen. The predominant

The appearance of a characteristic stellate or finely striated immobile gallbladder bile pattern on an ultrasonogram accurately identifies a gallbladder mucocele.

sympathetic inhibition (greater splanchnic nerve) have milder effects on gallbladder contraction.^{20,21} Other gastrointestinal hormones may enhance contraction (e.g., neurotensin, substance P, neuropeptide Y) or gallbladder relaxation (e.g., somatostatin, vasoactive intestinal polypeptide, nitric oxide, pancreatic polypeptide) but generally have only mild effects.²⁰⁻²²

GALLBLADDER MUCOCELE

Several synonyms for canine gallbladder mucoceles, including *cystic mucinous hyperplasia*, *cystic mucinous*

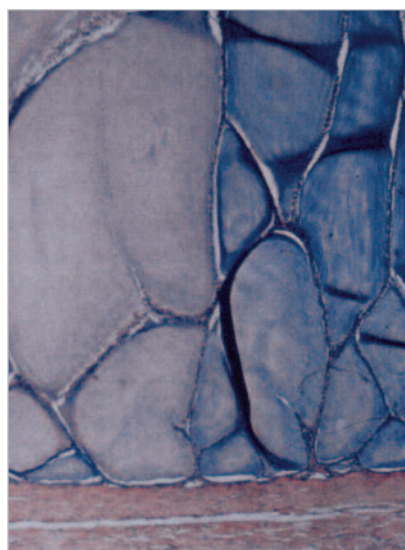
histologic feature of gallbladder mucoceles is cystic mucinous hyperplasia. Mucocele formation has been reported as an incidental lesion on necropsy¹ but can be associated with extrahepatic biliary tract disease.²⁻⁷

Pathogenesis

Little is known about the pathogenesis and potential causative factors that can lead to gallbladder mucocele formation in animals. The pathogenesis and cause of mucoceles in humans are equally uncertain. Mucoceles are an infrequent cause of human noninflammatory

Figure 2. Normal gallbladder histology and mucinous cystic hyperplasia.

Photomicrograph of a normal gallbladder. The gallbladder consists of columnar epithelium (arrow), lamina propria (LP), and smooth muscle (SM). (Hematoxylin–eosin, original magnification $\times 40$)



Photomicrograph of mucinous cystic hyperplasia of the gallbladder from an old male golden retriever characterized by the presence of large cysts filled with mucinous material. The cysts are lined by low cuboidal epithelium. (Hematoxylin–eosin, original magnification $\times 100$; courtesy of Dr. Joseph Alroy, Tufts Cummings School of Veterinary Medicine)

gallbladder disease but can occur as a result of obstruction of the neck of the gallbladder (i.e., usually by stones, and occasionally by neoplasia). Mucoceles can occur with or without concurrent cholecystitis.

The factors that promote mucocele development in dogs remain poorly understood. Extrahepatic bile duct obstruction may accompany this disorder, and some authors had previously considered obstruction of the common bile duct or cystic duct to be a potential inciting factor in mucocele development.^{4,7} In studies with dogs,^{1,24} experimental ligation of either duct failed to consistently lead to gallbladder mucocele development even after weeks of duct ligation. Although experimental ligation of the cystic duct in dogs resulted in increased amounts of mucus within the gallbladder in one study,²⁴ cystic mucinous hyperplasia did not develop in any of these dogs and intraluminal gallbladder pressure did not change significantly during the experiment. In a separate study²⁵ in which the cystic duct of dogs was obliterated using electrocoagulation, gallbladder mucocele formation did result in dogs not immediately treated with tetracycline. In two large retrospective

studies of dogs with mucoceles, EHBDO was not present in all the subjects. EHBDO (as defined by nonexpressible bile from the gallbladder or cystic duct) was present in only 17 of 33 cases at surgery.^{2,3} This suggests that EHBDO may be a secondary event to mucocele development.

Choleliths have also been implicated in the pathogenesis of canine mucocele formation.^{7,24} However, choleliths have been reported in only one dog with a gallbladder mucocele.⁷

In one case report,²³ a gallbladder mucocele occurred in a dog during progestational therapy, which led the authors to speculate on a relationship between progestational compounds and gallbladder mucocele formation. However, gallbladder abnormalities were not reproducible in a subsequent study in which dogs received a similar progestational compound.²⁶ In addition, previous use of a progestational drug did not occur in any of the gallbladder mucocele cases reported in the veterinary literature.

Interestingly, in one study,² glucocorticoid excess (endogenous and exogenous) accompanied gallbladder mucocele development in nine of 30 dogs. It remains to be established whether corticosteroids played a causative or perpetuating role in the gallbladder pathology of these patients.

Cystic mucinous hyperplasia has concurrently been identified with other gallbladder diseases, such as cholecystitis^{3,5} and, in one dog, a “porcelain” gallbladder.²⁷ Whether cholecystitis precipitated mucocele formation in some patients or inflammatory changes developed secondarily to the presence of mucoceles remains unanswered. Because mucoceles can occur in the absence of inflammatory lesions, the presence of inflammation does not appear to be a prerequisite for abnormal mucus buildup and gallbladder distention.

The very limited information available to date in the veterinary literature suggests that mucocele development may result from an abnormality of the mucosal cells within the gallbladder, resulting in hyperplasia of mucus-secreting cells and excessive mucus production by these cells. The abnormality of the mucosal cells may be a primary defect or may result secondarily from

Table 1. Prevalence of Common Clinical Signs, Physical Examination Findings, and Biochemical Abnormalities in 48 Reported Cases of Canine Gallbladder Mucocoeles^{2-4,6,7}

Clinical Signs	Incidence
None	23%
Vomiting	70%
Anorexia	65%
Lethargy	65%
Polyuria/polydipsia	27%
Diarrhea	12.5%
Physical Examination	
Abdominal pain	60%
Icterus	46%
Fever (>102.7°F [39.3°C])	22%
Biochemical Abnormalities	
Elevated alkaline phosphatase	81%
Elevated alanine aminotransferase	79%
Elevated γ -glutamyl transferase	67%
Increased total bilirubin	69%

endogenous or exogenous substances acting on gallbladder epithelial cells.

Gallbladder mucocoeles might also occur secondary to a defect in gallbladder motility. Gallbladder hypomotility could contribute to impaired egress of accumulated mucus from the gallbladder. Gallbladders in patients with mucocoeles may have decreased sensitivity to normal hormonal or neural stimuli that control gallbladder emptying.

In dogs, gallbladder mucocoele development may eventually lead to the development of clinical signs associated with necrosis or rupture of the gallbladder wall, secondary inflammation within the gallbladder wall, or EHBDO. Chronic overdistention of the gallbladder lumen with inspissated bile and mucus in mucocoele cases can promote pressure and ischemic necrosis of the wall and ultimately result in gallbladder rupture. In the literature, 51% of patients have gallbladder rupture when they present for evaluation.²⁻⁷ Furthermore, one study³ showed that 71% of patients without overt gallbladder rupture during surgery had microscopic mural necrosis. This suggests that a large proportion of patients with clinical signs of gallbladder mucocoele disease have some

degree of compromise of the gallbladder wall at presentation. Secondary inflammatory events in the gallbladder wall may be the result of wall ischemia from overdistention, noxious effects of retained bile acids, and/or bacterial overgrowth.³ Gallbladder stasis and distention are recognized predisposing factors for cholecystitis in humans.²² However, cholecystitis alone may precipitate gallbladder stasis and distention. Gallbladder mucocoeles are accompanied by EHBDO, when inspissated bile and mucus block gallbladder outflow, but also arise from the obstructive effects of congealed mucus that extends outward from the gallbladder into the biliary ducts.

Signalment, Clinical Signs, and Physical Examination Findings

Gallbladder mucocoeles occur most frequently in older dogs. The reported median age is 9 years (range: 3 to 17 years of age).¹⁻⁷ Mucocoele formation is more common in small to medium-sized dogs, but there appears to be no sex predilection.¹⁻⁷ A possible breed predilection for the cocker spaniel has been suggested by two authors.^{2,3}

Clinical signs are often nonspecific and include vomiting, anorexia, and lethargy. There is a relatively short period (i.e., ≤ 1 week) of illness in most cases. A more chronic course with short-lived responses to antibiotic therapy is occasionally described. In some dogs (i.e., 23% of reported cases), gallbladder mucocoeles have occurred in the absence of clinical signs.

Abdominal pain and icterus are the most common physical examination abnormalities (Table 1). Palpation of the cranial abdomen elicits pain in as many as 60% of affected dogs.^{2-4,6} Patients may also be febrile. In one study,² abdominal distention due to ascites reportedly occurred in 11% of cases. Evidence of shock (e.g., tachycardia, pale mucous membranes, slow capillary refill time) may be present in some patients if the gallbladder has ruptured and either bile or bacterial peritonitis has developed.

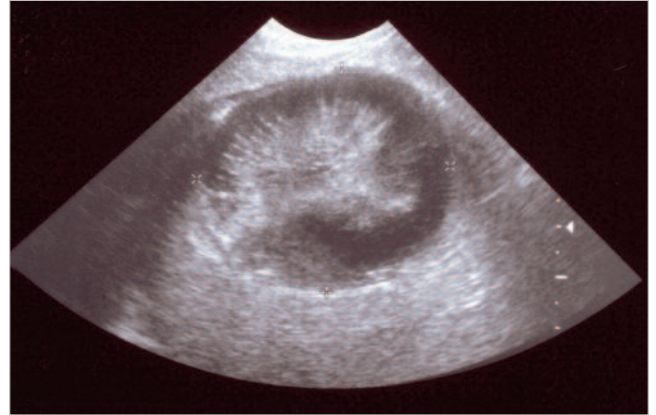
Diagnostics

Laboratory Evaluation

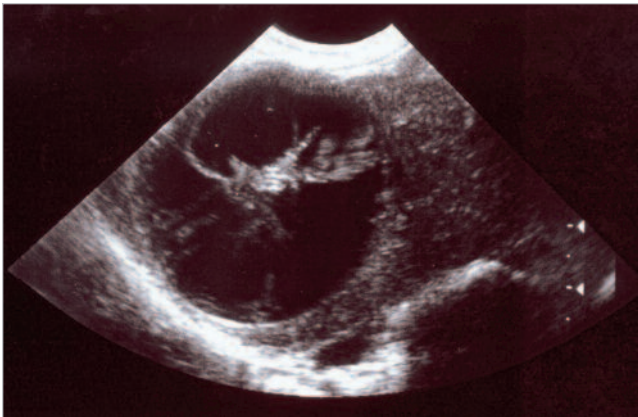
Clinicopathologic abnormalities are not specific for the presence of a gallbladder mucocoele and are indistinguishable from those seen with other hepatobiliary disorders. The most common laboratory alterations reported are hyperbilirubinemia and variable increases in liver enzymes (Table 1). Neutrophilic leukocytosis may be documented but is an inconsistent finding on the leukogram of these patients. Urinalysis may show bilirubinuria.

Figure 3. Ultrasonograms of gallbladder mucocoeles.

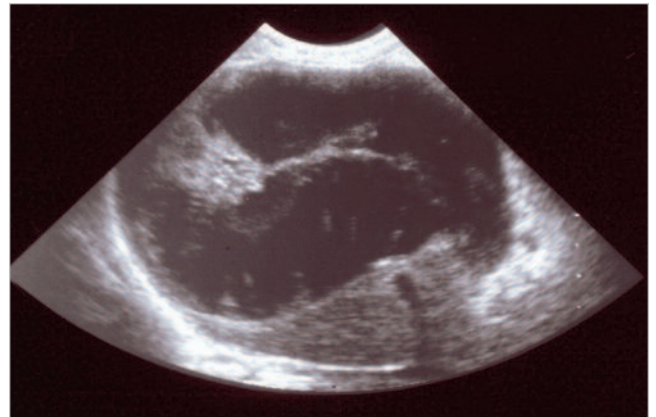
Transverse ultrasonogram. The central echogenic bile forms a stellate pattern, whereas bile at the periphery is anechoic. Bile did not move with changes in the patient's position.



Transverse ultrasonogram. Both central echogenic bile and a finely striated bile pattern (at the periphery) are identified.



Transverse ultrasonogram. Central echogenic bile has a loosely stellate pattern. An unevenly striated pattern can just be discerned at the periphery of the gallbladder.



Longitudinal ultrasonogram. Echogenic immobile bile is present in the center, and an unevenly striated pattern can be appreciated at the periphery.

The remainder of the diagnostic assessment in affected patients should be approached in the same way as in animals with liver enzyme elevations caused by other hepatobiliary diseases.

Imaging

Because affected patients may present with signs of acute abdomen, survey radiography is indicated. This allows clinicians to rule out other intraabdominal causes of acute abdomen, such as pancreatitis, small intestinal obstruction, and peritonitis. Survey radiography may help identify the presence of biliary tree calculi, gas within the gallbladder wall, or bile leakage. Abdominal ultrasonography, however, is the most helpful imaging tool to deter-

mine whether a mucocoele is present.²⁻⁴ Diagnosis of gallbladder mucocoele is made by finding an enlarged gallbladder filled with immobile, echogenic bile via ultrasonographic examination of the abdomen. The echogenic bile found in affected patients differs from normal biliary sludge in that it fails to gravitate to dependent areas when the patient's position is changed.²⁻⁴ An enlarged gallbladder with or without mobile sludge can be a common occurrence in anorectic or normal, fasted dogs and must not be mistaken for a mucocoele.^{28,29}

In patients with gallbladder mucocoeles, the gallbladder contents often have a striated and/or stellate pattern (Figure 3). The ultrasonographic appearance of gallbladder mucocoeles has often been likened to cut

fruit, such as kiwifruit. The precise pathway by which normal bile progresses to echogenic sludge with a kiwifruit-like appearance has not been determined. However, Besso et al³ proposed a possible continuum (Figure 4) in which ultrasonographic changes might reflect progressive increases in inspissation or the mucus content of bile within the gallbladder lumen. The stellate pattern is characterized by central echogenic bile with a stellate appearance surrounded by a cast of hypoechoic bile peripherally. Striations within the hypoechoic bile are either absent or barely visible. When the fine striations within the hypoechoic bile become more obvious, the pattern is referred to as a *finely striated bile pattern*. The resemblance to kiwifruit has been described when an ultrasonogram shows a small amount of echogenic bile in the center surrounded by a finely striated pattern in the periphery. Variations of these patterns can exist.

Additional ultrasonographic features of gallbladder mucoceles have been described. The gallbladder wall may appear to be normal in width, thickened, or discontinuous (i.e., ruptured). Increased echogenicity of the wall has been noted in a few cases. Ultrasonographic signs that suggest gallbladder rupture include a discon-

Pain may be detected in some patients as the ultrasound probe is moved over the gallbladder area. In humans, this is referred to as a *positive Murphy sign* and is highly suggestive of cholecystitis.^{3,22,29} The specificity of this finding in determining cholecystitis in veterinary patients has not been determined.

If peritoneal effusion is confirmed on ultrasonographic evaluation or when it is suspected based on physical examination or survey radiographic findings, clinicians must establish whether rupture of the biliary tree has occurred. Diagnostic abdominal paracentesis should be performed. A diagnosis of bile and/or septic peritonitis is confirmed if bile pigment and bacteria are observed via cytology. With bile leakage, the abdominal fluid has a disproportionately higher total bilirubin concentration than does serum.³⁰

Microbiologic Sampling

Because cholecystitis may accompany canine gallbladder mucoceles, aerobic and anaerobic bile cultures should be obtained. Bile from normal dogs is sterile.^{29,30} Bacterial cholecystitis is typically associated with enteric bacteria that gain entry to the bile duct either by ascending infection via the common bile duct or

In dogs with biochemical evidence of hepatobiliary disease, gallbladder mucoceles can be associated with gallbladder wall necrosis and/or cholecystitis.

tinuous gallbladder wall, the presence of hyperechoic pericholecystic bright fat, a hypoechoic ring of fluid surrounding the gallbladder, and/or the presence of free abdominal fluid.³ If rupture has already occurred, the gallbladder may not be visible, and its contents may instead be found free within the abdominal cavity.³ The sensitivity and specificity of ultrasonographic findings for detecting gallbladder rupture were reported by one author to be 85.7% and 100%, respectively.²

In the literature, bile duct obstruction was visible via ultrasonography in 29% of cases but was present in 54% of patients at surgery.²⁻⁴ Obstruction of the bile ducts by congealed mucus is thus a common feature of this disease. One author reported² the finding of a dilated intrahepatic biliary tree in 23% of cases.

Ultrasonographic changes in the liver may accompany gallbladder mucoceles. Reported hepatic abnormalities include hepatomegaly (56%) and inhomogenous hepatic parenchyma (27%).²⁻⁴

through hematogenous delivery by the hepatic vasculature.^{29,30} The former seems a more likely source of bacterial contamination in dogs with gallbladder mucoceles. A variety of enteric organisms (e.g., *Escherichia coli*, *Enterobacter* spp, *Enterococcus* spp, *Staphylococcus* spp, *Micrococcus* spp, *Streptococcus* spp) have been isolated from gallbladder mucoceles.^{2,3} In one study,³ six of 14 dogs had positive bacterial cultures, whereas another study² reported only two of 23 positive cultures. This discordance in culture results may be partly due to frequent use of antibiotics before acquisition of cultures in the second study. In the first study, there was also a larger proportion of cases with histologically confirmed cholecystitis compared with the second study, confirming the much lower incidence of inflammation or infection in the latter group.

In animals undergoing exploratory surgery, bile samples should be obtained at surgery. In medically managed patients, bile can be collected by percutaneous

transhepatic ultrasound-guided fine-needle aspiration of the gallbladder with the patient under heavy sedation or anesthesia.^{3,29,31,32} To reduce the risk of iatrogenic leakage, removing as much bile as possible during aspiration has been recommended. Complications of ultrasound-guided gallbladder aspiration are reportedly rare but could include leakage of bile into the peritoneum or circulation, decreased appetite, mild abdominal pain, vasovagal reactions, bacteremia, or local hemorrhage.^{29,32}

Pathology

During gross examination, the gallbladder is enlarged or ruptured.^{2-4,6} The lumen is completely filled with gelatinous material, consisting of congealed mucus and inspissated bile, or a semifirm mucus cast that conforms to the internal contour of the gallbladder.¹⁻⁷ The characteristic histologic finding in dogs with gallbladder mucocoeles is mucosal hyperplasia of the gallbladder epithelium (Figure 2). Concurrent inflammatory infiltrates or mural necrosis may be seen in 28% and 34% of patients, respectively.²⁻⁴

Because of the gallbladder's intimate association with the liver, inflammatory changes can extend into adjacent liver tissue. Hepatic histopathologic abnormalities seen in 76% of cases reported in the literature include inflammatory portal infiltrates, bile duct hyperplasia, hepatocyte vacuolation, or varying degrees of fibrosis.²⁻⁴ The hepatic changes observed in affected patients may be a consequence of one or more insults, including bile stasis from partial or complete EHBDO, extension of the inflammatory process from gallbladder to adjacent liver tissue, injurious effects of retained bile acids on liver tissue, or sepsis. Alternatively, they may represent a concurrent disease process (e.g., hyperadrenocorticism, diabetes mellitus, preexisting hepatopathy).^{2,3,33} In one study² involving 30 dogs, pituitary-dependent hyperadrenocorticism was concurrently present in seven patients.

Treatment

The approach to treating gallbladder mucocoeles must be individualized to each patient; however, some general guidelines can be applied. One of the most important decisions is whether the mucocoeles should be treated surgically or medically. Depending on the patient, surgery may be needed on an emergency basis, delayed for up to 24 hours, or performed as an elective procedure.

Patients with bile leakage, septic peritonitis, or suspected recent or impending gallbladder perforation

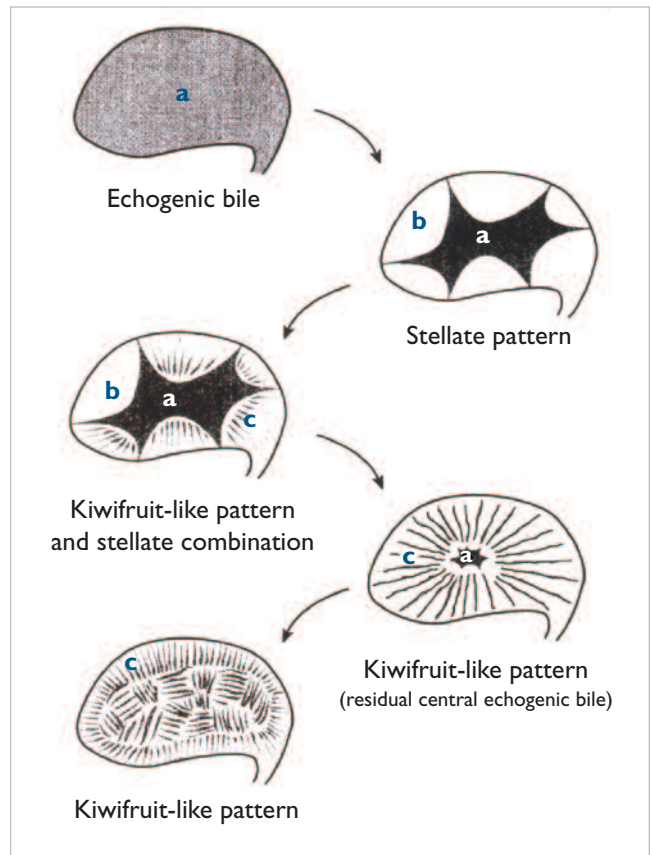


Figure 4. Schematic drawing of the proposed continuum between ultrasonographic bile patterns with gallbladder mucocoele: immobile echogenic bile (a), immobile anechoic bile (b), immobile finely striated bile (c). (Reprinted with permission from Besso JG, Wrigley RH, Gliatto JM, Webster CRL: Ultrasonographic appearance and clinical findings in 14 dogs with gallbladder mucocoele. *Vet Radiol Ultrasound* 41[3]:261–271, 2000.)

are candidates for emergency surgery. Gallbladder rupture should be suspected if the gallbladder wall is discontinuous, there is hyperechoic pericholecystic bright fat, a hypoechoic ring of fluid surrounds the gallbladder, or free abdominal fluid is present.^{2,3} It should also be suspected in patients presenting with signs of shock.

It is our clinical impression that dogs with ultrasonographic results suggestive of mucocoeles, compatible clinical signs, and biochemical alterations consistent with hepatobiliary disease should undergo cholecystectomy. Stable patients with signs of EHBDO detected via ultrasonography but no evidence of gallbladder rupture should undergo surgery soon after the mucocoele is detected (i.e., within 24 hours), but these patients do

not require emergency surgery as long as they remain clinically stable. Because the risk of imminent rupture always exists and gallbladder rupture is associated with increased perioperative morbidity, it is strongly recommended that surgery not be delayed for an extended period in stable patients that have clinical and biochemical abnormalities. In addition, it may be difficult to determine the presence of gallbladder rupture because the most sensitive tool available (i.e., ultrasonography) was reportedly able to detect rupture in only 85% of dogs in one study.²

Asymptomatic patients with mucoceles with or without biochemical alterations on blood work can be managed medically or surgically, a decision that rests with the individual clinician. Because mucocele formation is suspected to result from an abnormality of the gallbladder itself and the possibility of eventual progression to potentially life-threatening complications exists in any patient with this disorder, it is our opinion that all patients with gallbladder mucoceles should undergo cholecystectomy. However, the risk of this surgery must

be weighed for each patient. Because gallbladder mucocele is primarily a disease of middle-aged and older dogs, concurrent disease may put some patients at a very high anesthetic risk; therefore, medical therapy may be most appropriate in these patients.

At surgery, a full abdominal exploratory examination and cholecystectomy should be performed. The presence of a mucocele can be confirmed if a distended mucus-filled gallbladder is found (Figure 5). The biliary tree and gallbladder should be examined to confirm whether a rupture is present. If biliary tree rupture has occurred preoperatively, bile-stained fluid may be observed free within the peritoneal cavity. In animals in which rupture occurred weeks or months earlier but was sealed off, omental (or falciform) adhesions to the gallbladder may be found.³ The most common site of biliary rupture in dogs with mucoceles is the gallbladder fundus.^{2,3} In a gallbladder that grossly appears normal, accurate assessment of gallbladder wall integrity cannot be made by visual inspection alone because, in one study,³ microscopic mural necrosis was noted in 71% of cases in which the gallbladder grossly appeared normal at surgery.

The surgeon must then determine whether EHBDO is present. If the bile duct is patent, gentle pressure applied to the gallbladder should result in the flow of bile through the cystic duct and common bile duct and into the duodenum. In dogs with gallbladder mucoceles, the gallblad-

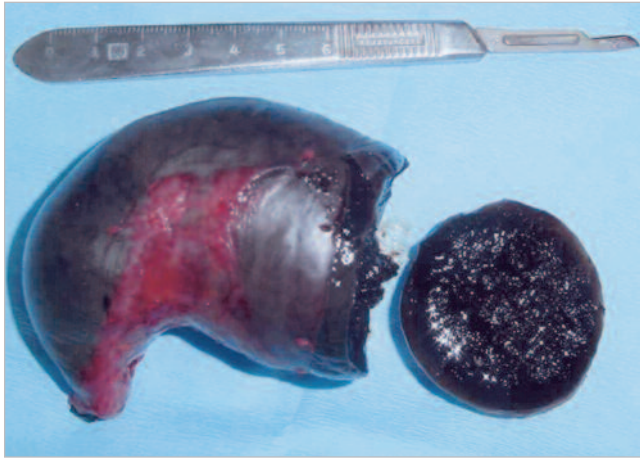
Dogs with gallbladder mucoceles that are clinically or biochemically affected should undergo cholecystectomy.

Before being anesthetized, the patient should be stabilized as best as possible by correcting fluid and electrolyte deficits. If significant cholestasis is present (which might interfere with intestinal absorption of vitamin K, which is fat soluble), a coagulopathy may develop. Coagulation parameters (i.e., one-stage prothrombin time and activated partial thromboplastin time) and a platelet count should be assessed in all surgical patients. If available, the PIVKA (i.e., proteins induced by vitamin K antagonism) test may be more sensitive in evaluating the vitamin K status of animals.³⁴ If abnormalities in coagulation parameters are identified, treatment with vitamin K (0.5 mg/kg SC q12h) is indicated. Vitamin K therapy should also be started in all patients with documented EHBDO because coagu-

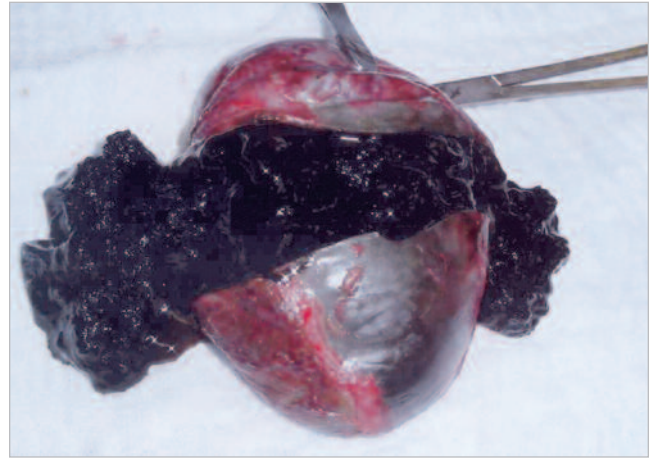
Surgery

lation testing is not 100% accurate in determining vitamin K deficiency. If surgery is delayed for 1 to 2 days, one-stage prothrombin time and activated partial thromboplastin time should be rechecked to determine whether improved coagulation status with vitamin K can be documented. If the previously noted abnormalities fail to correct, fresh-frozen plasma should be administered to replace deficient clotting factors.

Figure 5. Gallbladder mucoceles removed at surgery and opened to reveal their contents.



Gallbladder contents have solidified into a mucinous mass (tumefacient sludge).



Gallbladder contents consist of thick, congealed mucus and bile.

der lumen often contains very thick, gelatinous mucus that may, in some patients, have finger-like extensions that extend outward into ducts and cause variable degrees of EHBDO. It may be possible to gently milk bile from the cystic duct and common bile duct into the duodenum in patients that do not have bile duct obstruction. In many cases, surgeons have to cannulate the bile duct to ensure patency. In gallbladder mucoceles, it may be diffi-

be performed in all surgically treated dogs, even when the gross appearance of the liver is normal. The gallbladder and its contents should be submitted for histopathology. A surgical text should be consulted for more detailed information regarding surgical technique.

Before closure, the peritoneal cavity should be flushed extensively with crystalloid solutions. This is particularly important in patients with septic biliary effusion

The presence of bright fat around the gallbladder on an ultrasonogram is a warning sign of gallbladder wall rupture or necrosis and should warrant emergency surgery.

cult or impossible to express the inspissated contents of the gallbladder into and through the bile ducts. If EHBDO is present, the biliary tree should be carefully examined by visual and digital inspection and through cannulation to avoid missing other potential causes of obstruction (e.g., choleliths, neoplasms, pancreatitis).

Cholecystectomy should be performed in dogs with gallbladder mucoceles. Attempts at repairing the gallbladder after rupture or following removal of congealed mucus should not be made because signs of mural compromise can be present without gross evidence of rupture.³ A bile sample should be collected for aerobic and anaerobic culture and sensitivity testing. If rupture has occurred, cultures of the site of rupture and/or abdominal fluid should be submitted. Because hepatic histopathologic changes are common in patients with mucoceles, a liver biopsy should

be performed in all surgically treated dogs, even when the gross appearance of the liver is normal. The gallbladder and its contents should be submitted for histopathology. A surgical text should be consulted for more detailed information regarding surgical technique.

After surgery, vital signs should be monitored frequently and fluid and electrolyte needs addressed. Standard supportive care consists of intravenous fluid therapy, antimicrobial therapy, analgesia, and nutritional support. Septic patients should be considered critical and require frequent monitoring and reassessment. Colloid therapy may be required in patients with bacterial bile peritonitis that develop severe hypoalbuminemia. Factors previously determined to negatively impact survival in dogs with bile peritonitis include fluid and electrolyte loss, marked hemoconcentration, and bacterial peritoni-

Table 2. Postoperative Complications Following Cholecystectomy in 35 Dogs with Gallbladder Mucoceles²⁻⁴

Postoperative Complications	Number of Patients
Bile peritonitis	5
Cardiac arrest on anesthetic recovery	3
Pneumonia	2
Pulmonary edema	1 ^a
Pulmonary thromboembolism	1
Pancreatitis	1
Return of clinical signs months later	1

^aThe patient also had pneumonia.

tis.^{5,30} Reported postoperative complications following cholecystectomy in dogs with gallbladder mucoceles include bile and septic peritonitis, sepsis, pneumonia, and thromboembolic events^{2,3} (Table 2).

Antibiotic therapy should be continued for a minimum of 4 to 6 weeks in patients with positive culture results. Many patients may already be receiving antibiotics by the time a surgical bile sample has been collected. There-

Bile peritonitis from gallbladder rupture and bacterial peritonitis are indications for emergency surgery in patients with mucoceles.

fore, a similar course of antibiotics may be appropriate in dogs in which cultures fail to identify microbial growth but in which there is microscopic evidence of cholecystitis.

Medical Management

It is unknown whether medical management can result in resolution of gallbladder mucoceles. Medical management of asymptomatic gallbladder mucoceles involves use of antibiotics and choleretics. Selection of antibiotics should be based on culture results, when possible, or the ability of an antimicrobial to reliably achieve good liver, gallbladder, and bile penetration while providing coverage against common isolates.

Choleretics increase secretion of bile. Ursodeoxycholic acid (ursodiol) is a commercially available natural bile acid that stimulates bile flow. The recommended dose is 15 mg/kg PO q24h. Ursodeoxycholic acid might provide some benefit to affected patients because of its “thinning” effect on biliary secretions, theoretically making it easier for sludgy bile to exit the gallbladder and bile ducts. Other potential beneficial effects of ursodeoxycholate include replacement of injurious bile acids in the bile acid pool and hepatoprotective activities.^{37,38} Use of choleretics is contraindicated in patients with EHBDO.

In medically managed patients, ultrasonography and biochemical parameters should be closely monitored (approximately every 6 weeks or sooner). In patients in which infection has been confirmed by culture, antibiotic treatment should continue for at least 6 to 8 weeks. The ideal duration of ursodeoxycholate treatment is unknown, and the treatment may need to be given indefinitely in some patients. Clinical, clinicopathologic, and ultrasonographic evidence of improvement should indicate control of the disease. Progression of ultrasonographic abnormalities, continued increases in liver enzymes or bilirubin, and development of clinical signs all suggest failure of medical management and imply the need for cholecystectomy. Whether ultrasonographic changes of the gallbladder ever regress in medically managed dogs or in untreated asymptomatic dogs is still unknown. Cholecystectomy patients in which bile duct distention was present before surgery may have persistent ultrasonographic bile duct enlargement.^{2,19,28,31}

Outcome

The prognosis in patients with gallbladder mucoceles varies greatly with the clinicopathologic presentation of the patient. Bile peritonitis can be a life-threatening sequela to gallbladder rupture, particularly with concurrent bacterial infection.³⁰ When hypovolemic shock and bacterial sepsis are present, signs may progress very rapidly and patients may die acutely before surgery can be performed.^{3,7} In patients requiring surgery, perioperative mortality has reportedly been as high as 22%² to 40%.³ However, the long-term outcome for dogs that survive postoperative hospitalization is excellent.²

Future Directions

Gallbladder mucoceles have reportedly been a common incidental necropsy finding in older dogs.¹ However, the true incidence of gallbladder mucocele in dogs that lack clinical signs is unknown. Determination of the true incidence of gallbladder mucosal disease would require examination of necropsy records in which the gallbladder and its contents were routinely examined in all dogs.

The incidence of gallbladder mucoceles is being recognized with increasing frequency in veterinary practice. This may be due to a true increase in incidence or a result of improved recognition attributable to use of more advanced ultrasonographic equipment.

Prospective clinical trials are needed to determine whether conservative medical management has a role in managing asymptomatic or mildly ill patients without gallbladder rupture or EHBDO. Studies aimed at determining the cause and risk factors associated with development of gallbladder mucoceles are necessary. Determining the chemical composition of gallbladder contents may provide clues. To date, gallbladder motor function has not been investigated in dogs with gallbladder mucoceles, and additional research in this area may elucidate what role, if any, impaired gallbladder motility plays in the pathogenesis of this disease. It would be equally interesting to determine whether neurohormonal alterations exist in affected patients and how these alterations might contribute to gallbladder hypomotility or to hypersecretion of mucus by mucosal epithelial cells. It is possible that environmental or nutritional factors may also play a role in the development of gallbladder mucoceles.²

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ARTICLE #2 CE TEST



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I. Which statement regarding biliary tree structure and function is correct?

- a. Bile secretion originates in biliary ductule cells.
- b. Secretin and vasoactive intestinal polypeptide exert an inhibitory influence on gallbladder mucosal cell secretion.
- c. During a meal, the gallbladder mucosa secretes mucinous, bicarbonate-rich fluid into its lumen.
- d. The sphincter of Oddi at the minor duodenal papilla facilitates bile flow into the duodenum.
- e. The accessory pancreatic duct is absent in dogs.

2. Which statement concerning gallbladder physiology is correct?

- a. Hepatic bile is concentrated compared with gallbladder bile and is secreted by hepatocytes in response to a meal.
- b. The major stimulus for gallbladder contraction is CCK.
- c. The sphincter of Oddi is open during interdigestive periods.
- d. Gallbladder bile is secreted continuously.
- e. Gallbladder secretion occurs independently of hormonal or neural influence.

3. The gallbladder is not able to perform

- a. acidification.
- b. storage.
- c. secretion.
- d. concentration of hepatic bile.
- e. bile acid conjugation.

4. Which statement regarding the clinical presentation and physical examination findings in dogs with gallbladder mucoceles is correct?

- a. Senior female dogs are most commonly affected.
- b. Abdominal pain is infrequently detected.
- c. Fever occurs in all affected dogs.
- d. Anorexia and vomiting are often reported.
- e. Clinical signs are usually present for longer than 1 month before presentation.

5. Which statement regarding the diagnosis of mucoceles is incorrect?

- a. Mucocele development is associated with gallbladder enlargement and excessive intraluminal mucus buildup.
- b. Microscopic inflammatory changes are absent when cholecystitis is concurrently present.
- c. Documentation of cystic mucinous hyperplasia provides a definitive diagnosis.
- d. Ultrasonography can show an enlarged gallbladder containing immobile echogenic bile with a striated or stellate appearance.
- e. Ultrasonographic evaluation or surgical exploration may detect concurrent bile duct obstruction.

6. Which is(are) an indication for emergency surgery in patients with gallbladder mucoceles?

- a. septic peritonitis
- b. lack of clinical signs or biochemical abnormalities
- c. the presence of pericholecystic fluid or bright fat on an ultrasonogram
- d. hyperbilirubinemia
- e. a and c

7. In which situation can medical therapy be attempted in dogs with mucocele formation?

- a. septic peritonitis
- b. lack of clinical signs or biochemical abnormalities
- c. the presence of pericholecystic fluid or bright fat on an ultrasonogram
- d. bile duct obstruction
- e. a discontinuous gallbladder wall on an ultrasonogram

8. Which ultrasonographic finding is a contraindication of ursodeoxycholate use?

- a. gallbladder enlargement
- b. evidence of extrahepatic bile duct obstruction
- c. the presence of gallbladder sludge
- d. a thickened gallbladder wall
- e. mucocele development

9. During exploratory laparotomy in patients with gallbladder mucoceles, the surgeon should not

- a. attempt primary repair of the gallbladder.
- b. culture the bile.
- c. perform a biopsy of the liver.
- d. scrutinize the biliary tree for evidence of other potential causes of bile duct obstruction.
- e. perform a cholecystectomy.

10. Following cholecystectomy in dogs with gallbladder mucoceles, long-term outcome has reportedly been excellent if

- a. there is no evidence of bile duct obstruction before surgery.
- b. the patient survives surgery.
- c. abdominal pain is absent at initial evaluation.
- d. the patient does not develop bile peritonitis.
- e. the patient survives hospitalization.