

The Gallbladder

Anatomy of the gallbladder

Location:

- Right cranial abdominal quadrant.
- In the gallbladder fossa of the liver.
 - Between the quadrate and right medial liver lobes.

Macroscopic:

- Pear-shaped organ
- Fundus, body and neck.
 - Neck attaches, via a short cystic duct, to the common bile duct.
 - Opens into the duodenum via sphincter of Oddi at the major duodenal papilla.
 - Found on the mesenteric margin of oral duodenum.
 - 3-6 cm aboral to pylorus.

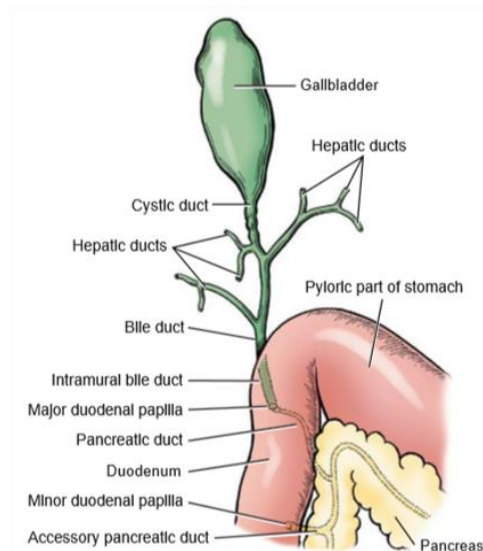


Figure 95-2 Anatomic arrangement of the hepatic ducts, common bile duct, and pancreatic ducts. (From Evans HE, de Lahunta A: Miller's anatomy of the dog, ed 4, St Louis, in press, Saunders/Elsevier.)

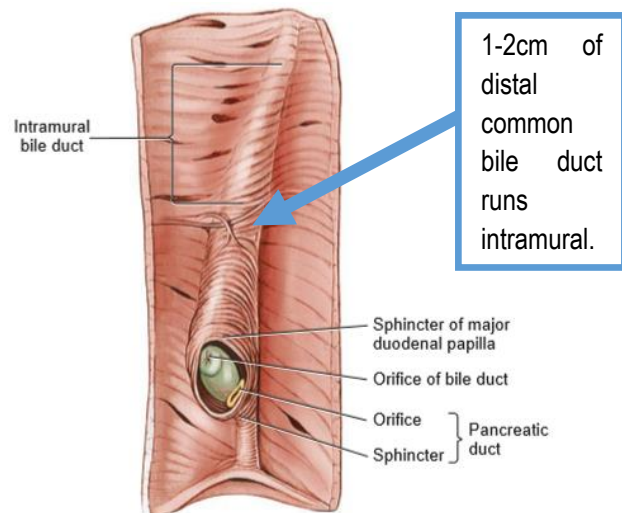


Figure 95-3 View from the interior of the duodenum (mucosa removed). Note that the pancreatic ducts open separately from the common bile duct in dogs. (From Evans HE: The digestive apparatus and abdomen. In Evans HE, de Lahunta A: Miller's anatomy of the dog, ed 4, St Louis, 2013, Saunders/Elsevier.)

Species differences:

- Dogs:
 - Common bile duct enters at major duodenal papilla.
 - Adjacent to pancreatic duct (no confluence prior to entrance).
 - Accessory pancreatic duct enters at minor duodenal papilla.
 - \pm 2 cm aboral to major duodenal papilla.
 - MAJOR conduit for pancreatic secretions.
- Cats:
 - Common bile duct and pancreatic duct converge before opening at major duodenal papilla.
 - Thus, any surgical procedure that affects the major duodenal papilla can affect the exocrine pancreatic secretions in cats.
 - Accessory pancreatic duct only seen in 20% of cats.

Gallbladder wall:

- 5 histologically distinct layers. From innermost these include:
 - Epithelium,
 - Submucosa (consisting of the lamina propria and tunica submucosa),
 - Tunica muscularis externa,
 - Tunica serosa (outermost layer covers gallbladder facing away from the liver),
 - Tunica adventitia (outermost layer covers gallbladder facing towards the liver).

Blood supply:

- Solely by the cystic artery (derived from the left branch of the hepatic artery).
 - Susceptible to ischaemic necrosis should its vascular supply become compromised.

Function:

- Storage reservoir for bile
 - Concentrated (up to 10-fold), acidified (through epithelial acid secretions) and modified (by the addition of mucin and immunoglobulins) before being released into the gastrointestinal tract at the major duodenal.
- Not essential and cholecystectomy is well-tolerated in numerous species.

Specific disease processes: Gallbladder

1. Gallbladder mucocoele

What is it?

- An abnormal, intraluminal accumulation of inspissated bile and/or mucous within the gallbladder.
 - The result is macroscopic distension with a green-black gelatinous material which may extend throughout the biliary tree causing variable degrees of extrahepatic biliary (EHB) obstruction.
 - May cause necrosis of the gallbladder wall and eventual rupture with subsequent peritonitis.

Why is it important?

- Becoming an increasingly common cause of extrahepatic biliary disease in dogs.
 - Emerging disease in veterinary science.

Predisposing factors and aetiopathogenesis

Aetiology:

- Incompletely understood...
 - complex and multifactorial.

Predisposing factors:

- Certain endocrinopathies.
 - Hyperadrenocorticism.
 - Up to 29 times more likely to have findings of GBM.
 - Why?
 - Alterations in bile acid cytotoxicity in the hypercortisolaemic state.

- Increased concentration of hydrophobic, unconjugated bile acids.
 - Increased risk for development of bacterial cholecystitis (as a result of concurrent immunosuppression)?
 - Alterations in gall bladder motility?
 - Hypothyroidism.
 - 3 times more likely to have GBM compared to euthyroid animals.
 - Why?
 - Thyroxine allows relaxation of the sphincter of Oddi (major duodenal papilla) in humans and pigs.
 - May cause biliary stasis from increased tonicity if deficient/absent?
 - Allows concentration of bile leading to irritation.
 - Effect of thyroxine on bile acid composition?
 - NOT diabetes mellitus
- Dyslipidaemias
 - Due to:
 - Hypothyroidism, hyperadrenocorticism and idiopathic hyperlipidaemia.
 - Why?
 - Increased conversion of cholesterol into bile acids.
 - Catabolic escape pathway.
- An insertion mutation.
 - Exon 12 of canine adenosine triphosphate-binding cassette (ABCB4).
 - Seen in:
 - Shelties.
 - Heritable.
 - Why?
 - ABCB4 is a phospholipid translocator.
 - In its absence, the concentration of phospholipids in the biliary lumen decreases.
 - Increasing the cytotoxicity of bile salts.
- Other steroid hormones (e.g. progesterone).
 - Why?
 - Concentration-dependent inhibition of gall bladder motility.
- Cholestasis.
 - Why?
 - Bile becomes more concentrated.
 - Irritation of the gallbladder wall and increased mucous production.
- Biliary sludge.
 - Why?
 - Not sure of connection.
 - One would expect there is an intermediate microprecipitate formation.

Diagnosis

Signalment

- Older, small- to medium-breed dogs.
 - Breeds:
 - Shetland sheepdogs, Cocker spaniels and miniature schnauzers.
- Average age of 9.1 years.
- No sex-predilection.

Clinical signs

- Non-specific
 - Vomiting, lethargy, anorexia, abdominal pain, icterus and polyuria-polydipsia.
 - Duration of signs \pm 5 days prior to presentation.
 - \pm 71.3% of cases displaying clinical signs.

Clinicopathologic findings

- Complete blood count:
 - Usually unremarkable.
 - Possibly leukocytosis.
 - Left shift neutrophilia.
- Serum biochemistry:
 - Increased liver enzymes:
 - Alkaline phosphatase, alanine aminotransferase, gamma-glutamyltransferase, and aspartate aminotransferase.
 - Hyperbilirubinaemia.
 - With EHB obstruction it increases within 24-48 hours.
 - Amylase and lipase are also elevated in some cases.
 - Cholesterol is often elevated.
- Most significant biomarkers associated with outcome:
 - Elevated mean serum lactate concentration.
 - Decreased packed cell volume.

Ultrasonography

- Classic appearance:
 - Finely striated stellate pattern.
 - “Kiwi fruit”.
 - Differs from biliary sludge in that it is non-dependent.
- Abdominal ultrasonographic findings:
 - Echogenic peritoneal fluid (often confined to the gallbladder fossa).
 - Thickened or laminated gallbladder wall.
 - Echogenic reaction in the gallbladder fossa.
- Ultrasonographic signs of gall bladder rupture:
 - Discontinuity of the gallbladder wall.
 - Hyperechogenicity of the cranial abdominal fat.



- Free peritoneal fluid.
- Free well-organised mucocoele within the peritoneal cavity.
- The ultrasonographic pattern not associated with the clinical signs.
 - Not a valid tool for grading disease.
- Gallbladder motility can be evaluated ultrasonographically.

Scintigraphy

- Useful to determine bile duct patency.
 - Hepatic extraction fraction (portion of the radiopharmaceutical removed from the plasma on each pass through the liver).
 - Clearance half-life.
 - Ability to view the biliary tree.
 - Presence of radioactivity in the intestine.
- Disadvantages:
 - Registered facilities.
 - Health and safety risk.
 - Accuracies do not compete with ultrasound.

Bacteriology

- 9 - 43% of GBM have concurrent bacterial colonisation of the gallbladder.
- Ultrasound-guided cholecystocentesis for medical managed cases.
 - USE CAUTION!
 - Complications:
 - Bile leakage, bradycardia due to vagal stimulation, bacteraemia and local haemorrhage.

Histopathology

- Cystic mucosal hyperplasia.
- Transmural ischaemic necrosis possible in the fundic region
- Advised to submit ALL gallbladders post cholecystectomy.

Treatment

Medical management

- Cannot be recommended as the first line of treatment in dogs.
- Owners must be aware:
 - Asymptomatic cases may develop into an acute clinical emergency.
- How?
 - Ursodeoxycholic acid.
 - Natural hydrophilic bile acid.
 - Acts as a choleric and hepatoprotectant.
 - Dose at 10-15mg/kg, PO, as a single dose/divided into 2 doses per day.
 - S-adenosylmethionine.
 - Essential for production of the antioxidant glutathione.
 - Acts as a hepatoprotectant.
 - Dose at 18-20mg/kg, PO, administered once daily on an empty stomach.
 - Tablets must not be split.

- A low-fat diet is encouraged.
- Concurrent ENDOCRINOPATHIES must be treated appropriately.
- Regular monitoring:
 - Follow-up visits every 2-4 weeks.
 - Abdominal ultrasound, haematology and serum biochemistry.
 - Surgical intervention if progresses.

Surgical intervention

- Therapeutic gold standard.
- Pre-operative:
 - haematology, serum biochemistry, urinalysis and coagulation profiles.
 - Vitamin K₁ (even if normal coagulation profiles).
 - How?
 - 3 doses of vitamin K₁ at 0.5mg/kg, SC, every 12 hours, prior to surgery.
 - No studies to support this recommendation.
- Cholecystectomy recommended
 - Gallbladder wall diseased thus advised to remove.
 - PATENCY OF COMMON BILE DUCT MUST BE CONFIRMED!
 - Manual normograde expression of the gallbladder.
 - Retrograde catheterization.
 - Duodenal enterotomy.
 - Flush biliary tree prior to ligation of cystic duct.
 - Removes residual thick, inspissated bile and/or small choleliths.
 - Histopathology:
 - Resected gallbladder.
 - Liver biopsy.
 - For histopathology, copper, iron and zinc concentrations.
- Laproscopic cholecystectomy is best.
 - If:
 - Biliary tract obstruction or rupture excluded.
- Cholecystotomy NOT recommended!
 - Why?
 - Microscopic mural necrosis may be present.
 - Recurrence of GBM formation.
 - THERE ARE ACTUALLY VERY FEW INDICATIONS FOR THIS PROCEDURE.
- Cholecystoenterostomy rarely if:
 - If common bile duct not patent.
 - Procedure has a higher complication rate.
 - Size of stoma should be large (2.5-4cm) to prevent recurrent bacterial cholecystitis.
- Peri-operative care:
 - Low-fat diet.
 - Broad-spectrum antimicrobial.
 - Hepatoprotectant therapy.

Prognosis

- Short- and long-term survival for biliary surgery is 66%.
 - Worst outcome for cholecystoenterostomy.
 - Mortality rate of 21.7% to 40% if cholecystectomy for GBM.
 - Most within the first 2 weeks.
 - Especially if:
 - Older (mean age 11.8 ± 1.5 years).
 - Higher white cell counts ($46,600 \pm 11,912$ / μ L).
- Most common complications:
 - Bile peritonitis, sepsis, DIC and surgical-site dehiscence.
- Prognostic factors:
 - Poor prognosis:
 - Concurrent pancreatitis.
 - Post-operative serum lactate concentration elevation.
 - Post-operative hypotension.
 - Survival rate NOT affected by:
 - Bile leakage from gallbladder rupture.
 - Concurrent bacterial colonisation of the bile.

2. Cholelithiasis

- Infrequently results in clinical disease.
 - Accounts for < than 1% of dogs with EHB tract disease.
 - More often an incidental finding.

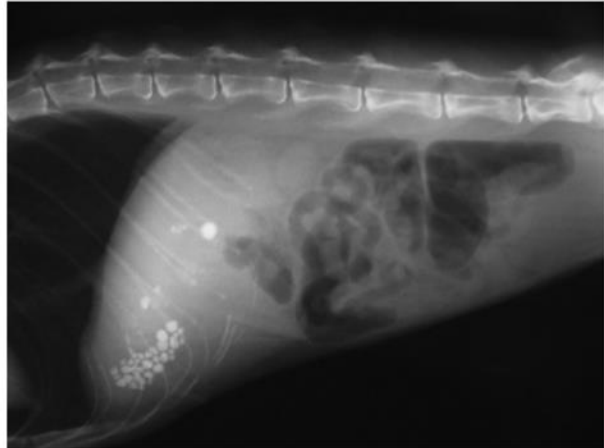
Predisposing factors and aetiopathogenesis

Aetiology:

- The aetiopathogenesis, in dogs, poorly understood.
 - Significantly different than in humans, where:
 - Supersaturation of bile with cholesterol and decreased bile salt secretion.
 - Basically, for formation of spontaneous cholelithiasis it requires:
 - An initial nidus formation,
 - Retention of particles within the gall bladder and,
 - Growth of the cholelith.
- Canine choleliths divided into three types according to composition:
 - Pure cholesterol-,
 - Mixed- and,
 - Pigment-choleliths.
- Dogs:
 - Less saturated with cholesterol.
 - Usually “pigment stones”.
 - Dogs: mainly consist of calcium bilirubinate.
 - Cats: mainly consist of calcium carbonate.
 - Poorly responsive to medical dissolution.

Predisposing factors:

- Cholestasis.
- Increased mucin production.
- Bacterial cholecystitis.
 - Some bacteria produce β -glucuronidase.
 - Deconjugates soluble bilirubin glucuronide to insoluble unconjugated bilirubin.
 - Precipitates out as calcium bilirubinate.
 - 70% of animals with cholelithiasis have positive aerobic cultures.
 - 55% have positive anaerobic cultures.
 - Most frequently:
 - *E. coli*, *Streptococcus* spp., *Enterococcus* spp., *Klebsiella* spp.
- Haemolysis.
 - Leads to an overproduction of bilirubin.
- Trauma.
- Dietary alterations.



Diagnosis

Signalment

- Aged female small breed dogs.
- Middle-aged to older male cats.

Clinical signs and clinicopathologic findings

- Often asymptomatic, unless:
 - Complicated by bacterial infection.
 - EHB tract obstruction.
 - Bile peritonitis.
- See gallbladder mucocoele.
- May see sign of "Triaditis" in cats.

Radiography

- Dogs:
 - 50% of choleliths are radio-opaque.
- Cats:
 - Up to 80% of choleliths are radio-opaque.

Ultrasonography

- Very effective.
- Focal hyperechoic structures (choleliths) with distal acoustic shadowing.
- Mostly within the gallbladder.
 - Rarely formation in the intrahepatic and extrahepatic ductal system.
- Signs of EHB obstruction:

- Distension of the common bile duct.
 - Usually evident within 1st 48hours.
 - Normal is 3-4mm in diameter.
- Distension of hepatic ducts and intrahepatic ducts.
 - Usually seen within 1st week.
- Remember that you get extraluminal (e.g.. pancreatitis) and intraluminal causes of obstruction.

Treatment

Medical management

- Medical dissolution is not considered successful.

Surgical intervention

- Cholecystectomy is the treatment of choice.
 - If associated with EHB obstruction.
 - When to operate?
 - If serum bilirubin ↑ over 7-10 days in absence of defined hepatic disease or pancreatitis and,
 - Supportive radiographic/ultrasonographic evidence of obstruction.
 - Or if rapidly, progressive haemodynamic compromise.
 - Emergency surgery.
 - No recurrence has been reported when the gallbladder is removed.
 - First flush choledochal choleliths back into the gallbladder.
 - If patency can't be confirmed:
 - Choledochotomy/cholecystoenterostomy.
 - Bile and cholelith samples submitted for:
 - Aerobic and anaerobic culture.
 - More likely to culture positive than hepatic tissue.

3. Trauma to the gallbladder

Confirmation of bile peritonitis

- Compare [total bilirubin] of free peritoneal fluid with that of serum.
 - If $\geq 2x$ that of serum = bile peritonitis
- If bacterial infection:
 - Higher mortality rate than if sterile.

Where to look?

- If due to blunt trauma:
 - Usually common bile duct or hepatic ducts.
 - Most commonly just distal to the insertion of the last hepatic duct.
 - Remember to check the distal insertion of the common bile duct as could avulse.
 - Rarely from the gallbladder.
- If due to ruptured mucocoele:
 - Usually the fundic region of the gallbladder.

4. Neoplasia of the gallbladder

- Rare.
 - Comprise only 2% of all canine hepatic tumours.
- Cholangiocellular adenomas.
 - Benign tumours of the bile duct.
 - 12% of all primary hepatic tumours in dogs.
- Cholangiocellular carcinomas.
 - 22% of all primary hepatic tumours in dogs.
 - 4-21% are extrahepatic.
 - 1-4% confined to the gallbladder.

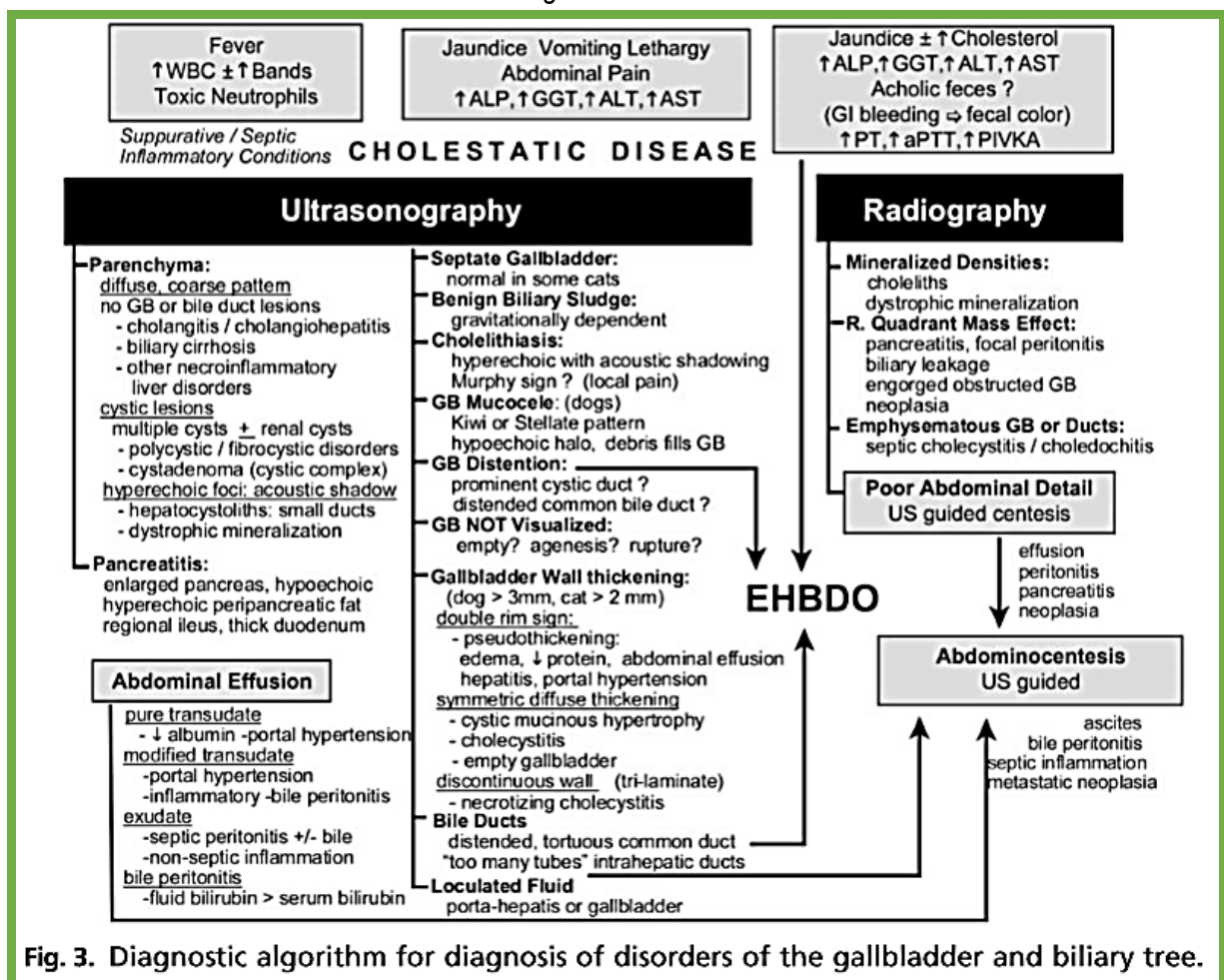


Fig. 3. Diagnostic algorithm for diagnosis of disorders of the gallbladder and biliary tree.

Center, S.A., 2009, 'Diseases of the gallbladder and biliary tree', *Veterinary Clinics of North America: Small Animal Practice* 39, 543-598.