Canine Gallbladder Disease: A Surgeon's Perspective

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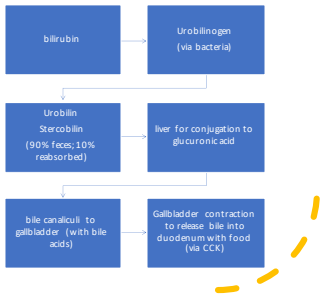
Objectives:

- Bile — Components, Physiology, Function
- Anatomy
- Mucocele Formation — Various etiopathologies
- Diagnosis and Clinical Signs
- Current Therapies — Medical Management, Surgical Intervention

Bile

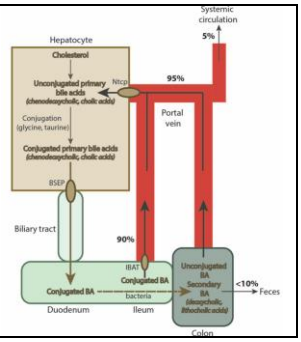
- Composition
  - **Bile acids**, bilirubin, cholesterol, phospholipids, water, bicarbonate, other ions
    - Bile acids are synthesized in liver from cholesterol
    - Bilirubin is bound to albumin when transported to liver
- Bile salt functions
  - Emulsify fats → digestion and absorption
  - Bind endotoxin in SI → prevents absorption into portal circulation
- Sterile
- pH 6.2 or higher
- Heavily recycled via enterohepatic circulation

Bile



Enterohepatic Circulation

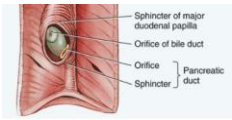
1. 1° BA produced in liver
2. BA excreted into bile → SI
3. CBA in SI aids fat absorption
4. 90% BA reabsorbed in ileum → portal supply
5. BA enters liver → 95% extracted by hepatocyte transporters
6. Other 5% → systemic circulation
7. Small amount lost in feces

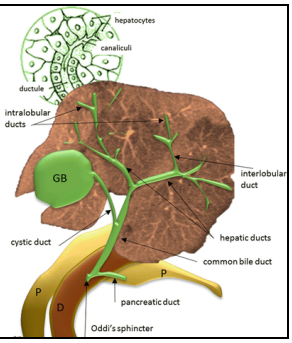


https://eclinpath.com/chemistry/liver/liver-function-tests/bile-acids/

Biliary Tree Anatomy

- Portal triad (bile duct) → canaliculi → intralobular ducts → interlobular ducts → lobar ducts → hepatic ducts → common bile duct
- Dogs have 2-8 hepatic ducts
- Insertion- major duodenal papilla





Species Differences

Canine- CBD and pancreatic duct do not join together

- They are side-by-side, wrapped in muscular conduit (sphincter of oddi)
- Accessory pancreatic duct = majority of pancreatic secretions @ minor duodenal papilla (2cm aborad to major)

Feline- CBD and pancreatic ducts joint into single lumen at major duodenal papilla

- May result in increased pancreatic and hepatobiliary disease in cats
- ~20% cats have smaller accessory pancreatic duct which exits at minor duodenal papilla

Gallbladder Anatomy and Function

- Hepatic fossa
- Limited vascular supply
  - Cystic artery
- Low pressure flow - passive filling
  - ~15mL capacity medium-sized dogs
- Functions
  - Store and concentrate bile
  - Excrete bile into the intestinal tract
- Mucosa - columnar epithelial cells
- Contraction stimulated via CCK

http://www.vivocolostate.edu/hbooks/pathphys/digestion/liver/histo_gb.html

Diseases of the Biliary Tract

Intrahepatic

- Cholangitis, cholangioheptatitis, intrahepatic cholelithiasis, neoplasia

Extrahepatic

- Obstruction- pancreatitis, neoplasia, **mucocele**, cholangitis, cholelithiasis
- Blunt trauma- HBC, gunshot, stab, bite (usually CBD or cystic duct, rarely gallbladder)
- Iatrogenic- overexpression intra-op, post-op leakage biliary surgery

Gallbladder Mucocele

- Emergent disease of last 15-20 years
  - First report 1965
- Characterized by increased secretion of mucin-forming granules
  - Mucin granules form a gel
- Histopathology
  - Cystic mucosal hyperplasia +/- transmural necrosis
- Abnormally thick mucus → decreased gallbladder motility → EHBO → rupture → bile peritonitis
- 2-week post-operative mortality rate = 7-45%

"The Usual Suspects"

- **Shetland Sheepdog (ABCB4 gene)[13]**
- Border Terrier
- Cocker Spaniel
- Miniature Schnauzer
- Pomeranian
- Chihuahua

- Age: 9-10 years
- No true sex or neuter status predilection

Endocrine Diseases Linked to GBM Formation

- Hyperadrenocorticism (Cushing's)
- Hypothyroidism
- Hyperlipidemia
- +/- Diabetes mellitus
  - Controversial but unlikely
- Proteinuria (≥1.5)
- Pancreatitis

Genetic and Drug-Induced Etiologies

- Breed + specific drugs = more likely to form GBM
- Levothyroxine - 2.2x
- "Medications used to treat Cushing's Disease"- 3.6x
- Imidacloprid - 2.3x

Journal of Veterinary Internal Medicine ACVIM Open Access

J Vet Intern Med 2015;29:1464–1472

Association of Gallbladder Mucocele Histologic Diagnosis with Selected Drug Use in Dogs: A Matched Case-Control Study

J.L. Gookin, M.T. Correa, A. Peters, A. Malueg, K.G. Mathews, J. Cullen, and G. Seiler

Diagnosis: Clinical Signs & Biochemical Findings

CS often non-specific:

- **Vomiting - 69%**
- Lethargy - 44%
- Anorexia - 42%
- Abdominal pain - 19%
- Icterus - 16%
- PU/PD - 8%

Asymptomatic 29%

- Urinalysis
  - Proteinuria[10]
- CBC –unremarkable
  - Leukocytosis - 47%
  - +/- left shift
- Chemistry - increases in:
  - ALP – 98%
  - ALT – 87%
  - GGT – 85%
  - AST – 62%
  - T.Bil – 83%

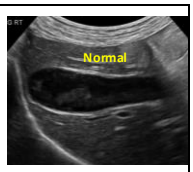
Proteinuria in dogs with gallbladder mucocele formation: A retrospective case control study

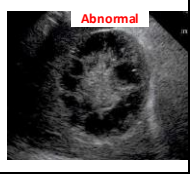
Correction(s) for this article

Crystal Lindaberry, Shelly Vaden, Kathleen M. Aicher, Gabriela Seiler, James Robertson, Rachel Cianciolo, Ching Yang, Jody L. Gookin

Diagnosis – Imaging

- Abdominal ultrasound – **gold standard**
  - Stellate "kiwi" appearance
  - Bile duct dilation, Major duodenal papilla
  - Repeat US - over days, or after CCK administration
  - Percutaneous US-guided cholecystography
  - "Mucocele type"
- Radiographs – limited utility
  - Choleliths usually incidental finding
  - Occasional mineralization in CBD/GB
  - Hepatomegaly





Diagnosis – Imaging

- US showed biliary rupture better than bilirubin serum increase
  - 85% accurate w/US vs. 40% accurate with bilirubin (blood)
  - W/rupture, evaluate blood vs abdominal bilirubin: ≥ 2 x higher in fluid

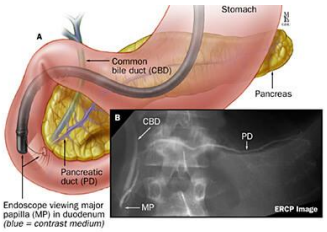
Original Investigation | Full Access

COMPARISON BETWEEN ULTRASONOGRAPHIC AND CLINICAL FINDINGS IN 43 DOGS WITH GALLBLADDER MUCOCELES

Jihye Choi, Ahyoung Kim, Seoyeon Keh, Juyeon Oh, Hyunwook Kim, Junghee Yoon

Diagnosis - Other

- Computed tomography
- Endoscopic Retrograde Cholangiopancreatography (ERC)



https://www.hopkinsmedicine.org/gastroenterology_hepatology/clinical_services/advanced_endoscopy/endoscopic_retrograde_cholangiopancreatography.html

Veterinary Clinics of North America: Small Animal Practice

Updates in Hepatobiliary Surgery: New Data on Portosystemic Shunts and Cholecystectomy in Dogs and Cats

Mandy L. Wallace DVM, MS, Diplomate, American College of Veterinary Surgeons (Small Animal)

If we are so good at diagnosing gallbladder mucoceles, why is the mortality rate so high?

Why such a high mortality rate?

EHBO → VERY severe pathophysiologic consequences

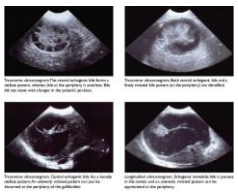
1. Hypotension
2. Decreased myocardial contractility
3. AKI/acute renal failure
4. Coagulopathy → DIC
5. Gastrointestinal hemorrhage
6. Sepsis +/- septic shock
7. Delayed wound healing
8. +/- liver failure
9. Biliary rupture → bile peritonitis

Bile Peritonitis

- Bile salts- cause of initial physiologic response
  - Inflammation
  - Tissue necrosis
  - Hemolysis
- Hyperosmolar- massive fluid shifts
  - Interstitium → peritoneum
- Aseptic vs septic
  - Aseptic = mild bile peritonitis
  - Septic = profound peritonitis, significantly worse prognosis and severity of clinical signs
  - Reported ~11-40% positive culture from bile

Poor Prognostic Indicators

- Hypotension
  - 20x more likely to die
- Hyperlactatemia
  - 1mmol/L increase=0.3X death risk
- Lower PCV in non-survivors
- Increased serum creatinine and phosphorus
- Mucocele type



GBM type	Description	Sx # (%)	Med # (%)	Med-Sx # (%)
1	Immobile echogenic bile	4 (11)	4 (13)	1 (12.5)
2	Incomplete stellate pattern	12 (32)	16 (52)	3 (38)
3	Typical stellate pattern	10 (26)	9 (29)	2 (25)
4	Kiwi-like pattern and stellate combination	4 (11)	2 (6)	1 (12.5)
5	Kiwi-like pattern with residual central echogenic bile	6 (16)	0 (0)	1 (12.5)
6	Kiwi-like pattern	0 (0)	0 (0)	0 (0)
Rupture	Concern for GB rupture in the ultrasound report	18 (47)	3 (10)	2 (25)

Medical Management

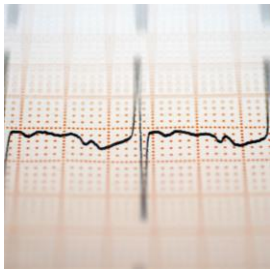
- Acceptable in *asymptomatic* patient
- Lack of standardized treatment protocol exists
- Choleretic +hepatoprotectant medications
  - Ursodiol
    - 10-15mg/kg PO/day
  - S-adenosylmethionine
    - 18 mg/kg – 20 mg/kg PO
- Low fat diet
- Regular monitoring with AUS, CBC/Chem every 2-4 weeks
- Can become emergency situation rapidly
  - *Owner education is absolutely vital!*

Do not let these get away from you!

Emergency Stabilization

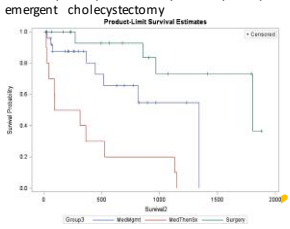
- Varying stages of disease and stability at presentation
  - Ambulatory → laterally recumbent, shock
- IV fluids- isotonic crystalloid bolus
- Coagulation parameters- if elevated:
  - Administer Vitamin K
  - Fresh frozen plasma 10ml/kg
- Anemia
  - pRBC or whole blood transfusion
- Microbial control
  - Rapid initiation, broad spectrum
    - Ampicillin/sulbactam + enrofloxacin

Surgical Intervention



Cholecystectomy

- Treatment of choice – *for any stage*
- Current trend → earlier surgical intervention
  - Parkansky, et al (2018) found a lower mortality rate of elective pre-emptive cholecystectomy compared with emergent cholecystectomy



Cholecystectomy

STANDARD ARTICLE

Journal of Veterinary Internal Medicine ACVIM

Long-term survival of dogs treated for gallbladder mucocele by cholecystectomy, medical management, or both

Max Parkanzky[1] | Janet Grimes[1] | Chad Schmiedt[1] | Scott Secrest[2] | Andrew Bugbee[1]

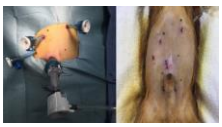
Outcome of elective cholecystectomy for the treatment of gallbladder disease in dogs

Gabina Yoon
Michelle J. Waschak
Kevin A. R. Kunkel
Patrick D. Gerard

OBJECTIVE
To determine mortality rates for dogs undergoing cholecystectomy and variables associated with failure to survive to hospital discharge.

DESIGN
Retrospective cohort study.

Laparoscopic Cholecystectomy



- Case selection is critical to survival
  - No biochemical or imaging evidence of gallbladder rupture or obstruction
- Potential complications
  - Bile spillage
  - Inadequate cystic duct ligation
- Small patients = difficult laparoscopic candidate
- Reduced pain and invasiveness
- Increased magnification of surgical field

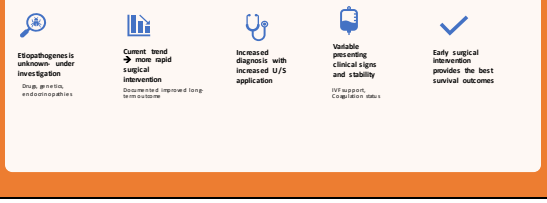
2018 Laparoscopic Cholecystectomy Update

Short-term outcome of laparoscopic cholecystectomy for benign gall bladder diseases in 76 dogs

Hiroo KANAI[1,6], Ken HAGIWARA[2,6]*, Aya NUKAYA[3,6], Motoki KONDO[4,6] and Toshihide ASO[5,6]

- Included patients with ruptured or suspected rupture of biliarytract - only 2 patients had confirmed rupture
- 3/76 converted to open laparotomy
- Median operative time 124 minutes (55-210min)

Summary



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Questions?