Lessons Learned from the K9 Liver

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Christian Veterinary Mission

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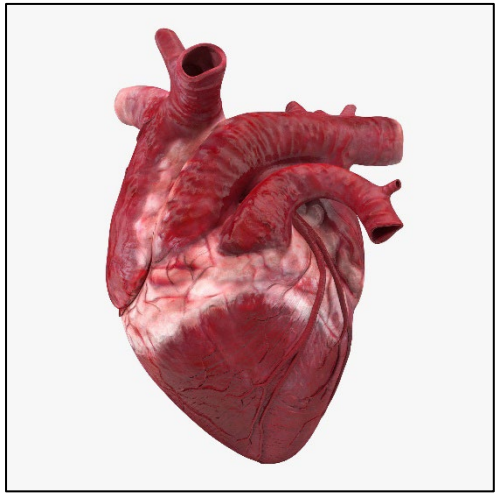
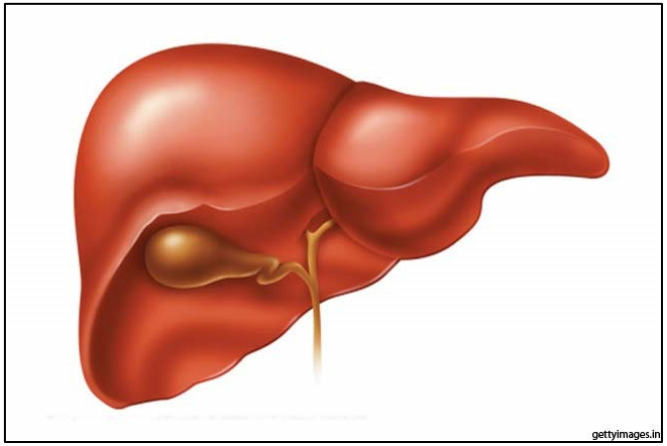
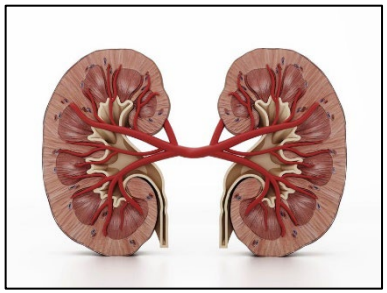
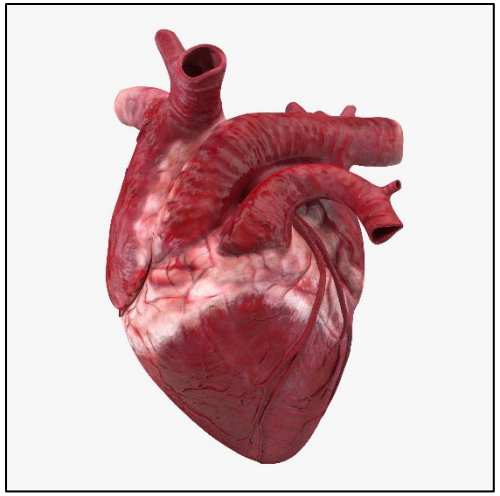
WD PARTICIPATION

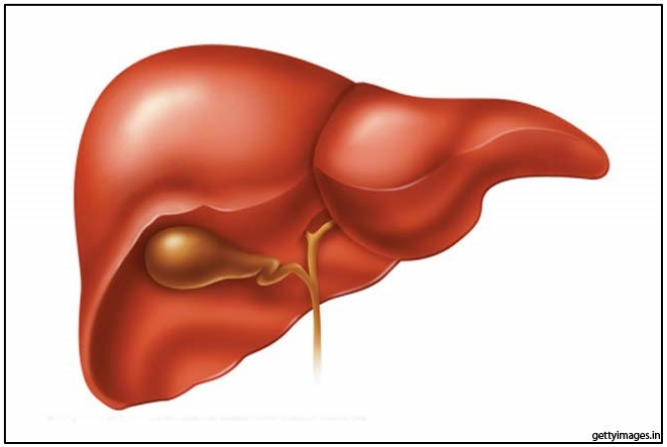


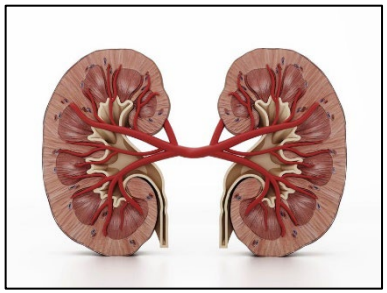

gettyimages.in





Nutrients (nutritious or otherwise)
Medications, Supplements, Toxins
Metabolites, Organisms

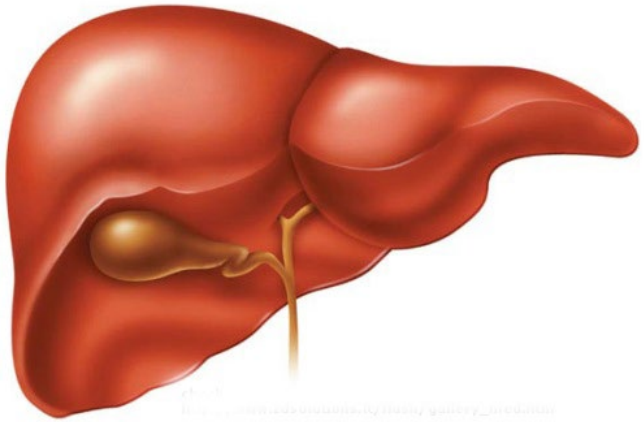




Damage

ALT

Histopathology



Function

Glucose

Albumin

Cholesterol

BUN

Bile Acids

Biliary

total bilirubin

PCV/TP

Imaging

Cytology & Culture

Reactive

ALP

Everything else

Sophie: 1 Year Old
Female Spayed Chihuahua

Intermittent lethargy
Dull mentation
Chronic diarrhea

Physical Examination

Small

Nervous

BIOCHEMICAL PROFILE

KEY: The Liver is Not Working Well

GLUCOSE	82		70 - 115 mG/dL
BUN	6	L	7 - 30 mG/dL
CREATININE	0.5	L	0.6 - 1.6 mG/dL
PHOSPHORUS	3.5		2.5 - 6.0 mG/dL
CALCIUM	9.1		9.0 - 11.5 mG/dL
MAGNESIUM	2.1		1.8 - 2.4 mG/dL
TOTAL PROTEIN	5.1		5.0 - 7.0 G/dl
ALBUMIN	2.9	L	3.0 - 4.3 G/dl
GLOBULIN	2.2		1.5 - 3.2 G/dl
A/G RATIO	1.3		0.9 - 2.4 RATIO
CHOLESTEROL	47	L	130 - 300 mG/dL
T-BILIRUBIN	0.2		0.0 - 0.2 mG/dL
ALP	190	H	15 - 140 IU/L
ALT	28		10 - 90 IU/L
AST	98	H	15 - 45 IU/L
CK	444	H	50 - 275 IU/L
GGT	0		0 - 9 IU/L

Young Dog
CNS (dull, lethargic)
Gastrointestinal (diarrhea)
Growth (small size)
Liver Not Working Well

Congenital Portosystemic Shunt

Congenital Portosystemic Shunt

Yellow Dog Design

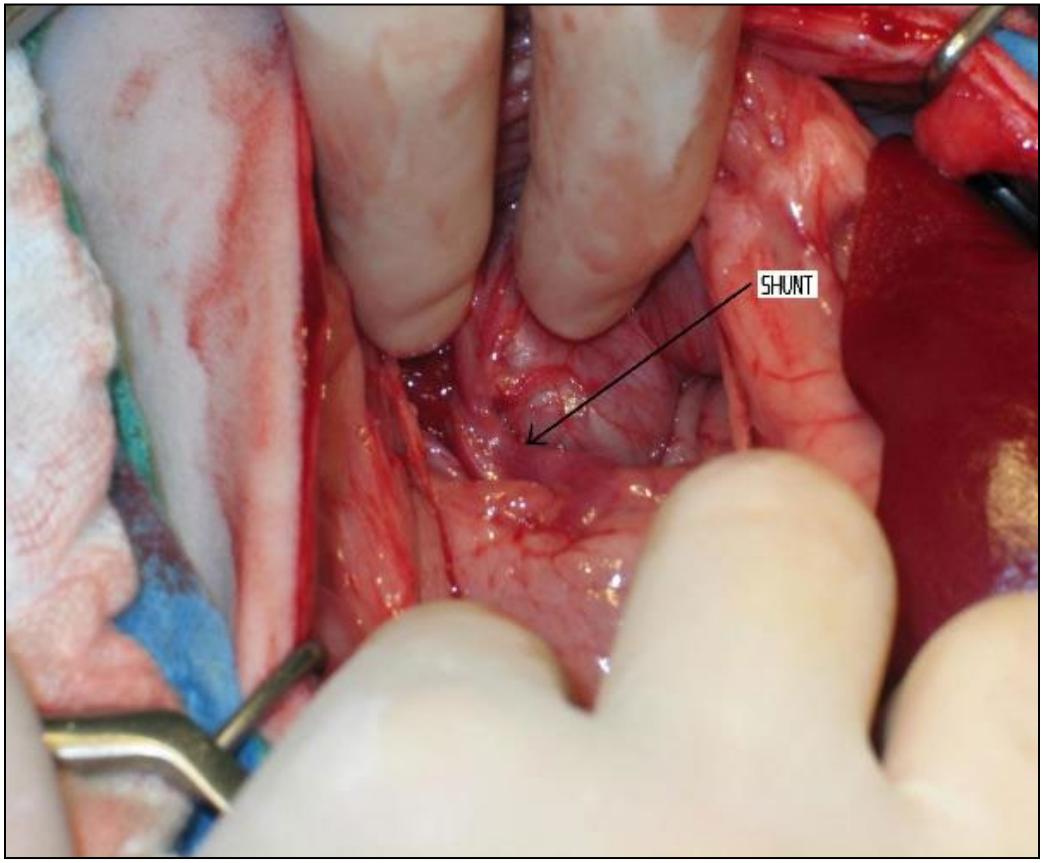
Clinical Signs: Wide Range and Variable

- CNS (Hepatic Encephalopathy)
- Urinary (Polyuria/Polydipsia, Stones)
- Growth (Poor doer)
- Gastrointestinal (Vomiting/Diarrhea)

BEN Sig: 1.5 year old FS Yorkie
PC: “Big belly” full of fluid, acting “funny”
Diarrhea

Young Dog
CNS (acting funny)
Gastrointestinal (diarrhea)
Growth (big belly, small dog)

Clinical Diagnosis – Must Be…!
Congenital Portosystemic Shunt



CPSS Chem Panel

KEY: They Rarely Develop Ascites

or Turn Yellow

GLUCOSE	82		70 - 115 mG/dL
BUN	6	L	7 - 30 mG/dL
CREATININE	0.5	L	0.6 - 1.6 mG/dL
PHOSPHORUS	3.5		2.5 - 6.0 mG/dL
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AST	98	H	15 - 45 IU/L
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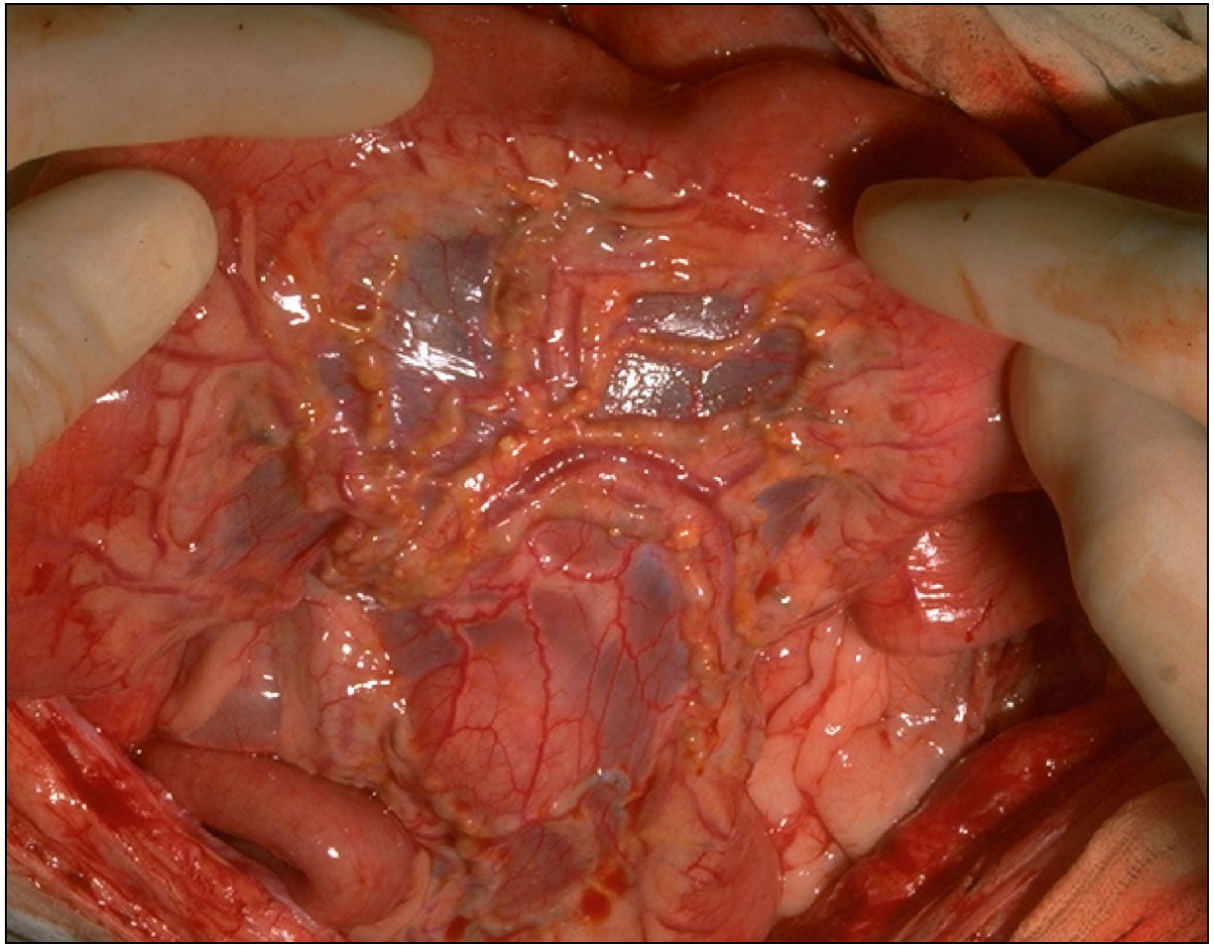
GGT	0		0 - 9 IU/L

What Protein-Losing Enteropathy are Young Yorkies Most Famous For?

A) Gastrointestinal Lymphoma
B) Celiac Disease
C) Antibiotic-Responsive Diarrhea
D) Lymphangiectasia

Intestinal Lymphangiectasia



CPSS Chem Panel

Liver Enzymes Do Not Equal Liver Function

GLUCOSE	82		70 - 115 mG/dL
BUN	6	L	7 - 30 mG/dL
CREATININE	0.5	L	0.6 - 1.6 mG/dL
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GGT	0		0 - 9 IU/L

Complete Blood Count (CBC)

KEY: Microcytosis

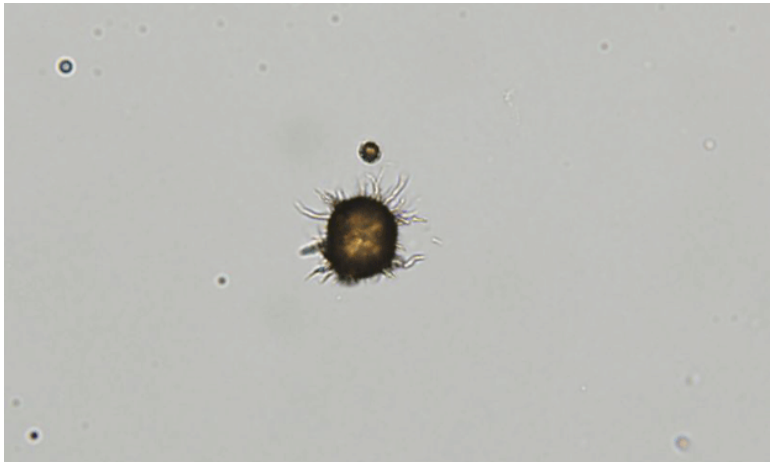
HCT	32		32 - 47 %
RBC	8.76		6.5 - 10.0 x10^6/ul
Cell Hgb	10.7		9.5 - 15.5 G/dl
MCV	37	L	40 - 52 fl
RDW	17.1		13.5 - 19 %
HGB	10.6		9.8 - 15.5 G/dl
MCHC	33		32 - 36 G/dl
CHCM	33		33 - 36 G/dl

Leukocytosis, normocytic, normochromic nonregenerative anemia

URINALYSIS

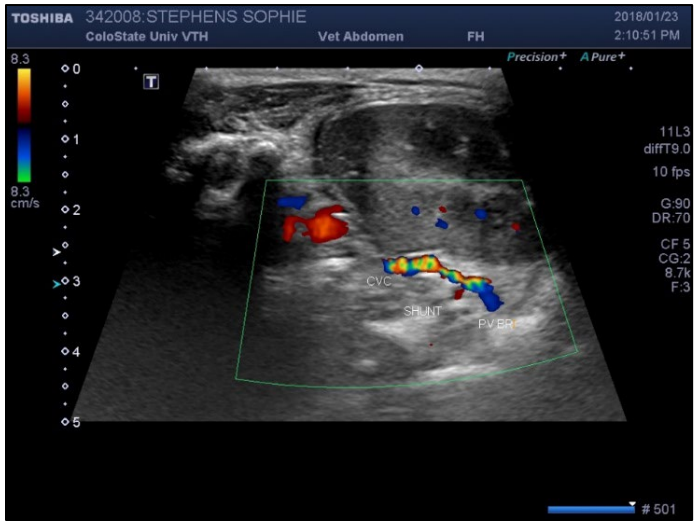
Low Specific Gravity (PU/PD)

Ammonium (Bi)urate crystalluria



Additional Diagnostics

- Bile Acids
  - KEY: Pre- and Post
  - KEY: Liver Function Test, *NOT* PSS Test
- Fasted Ammonium
  - Sensitive PSS Test
  - KEY: Handle Sample Correctly
- Abdominal Ultrasound
  - KEY: Doppler
  - KEY: The Bladder!



“Poofy” 1 yo MI Yorkie

- Presented for castration
- Undersized
- Post Prandial Bile Acids
  - Elevated
- Ultrasound – No Shunt
- Transcolonic Scintigraphy

  - Normal

The “Quiet” PSS

The “Quiet” PSS

Portal Vein Hypoplasia

formerly called Microvascular Dysplasia (MVD)

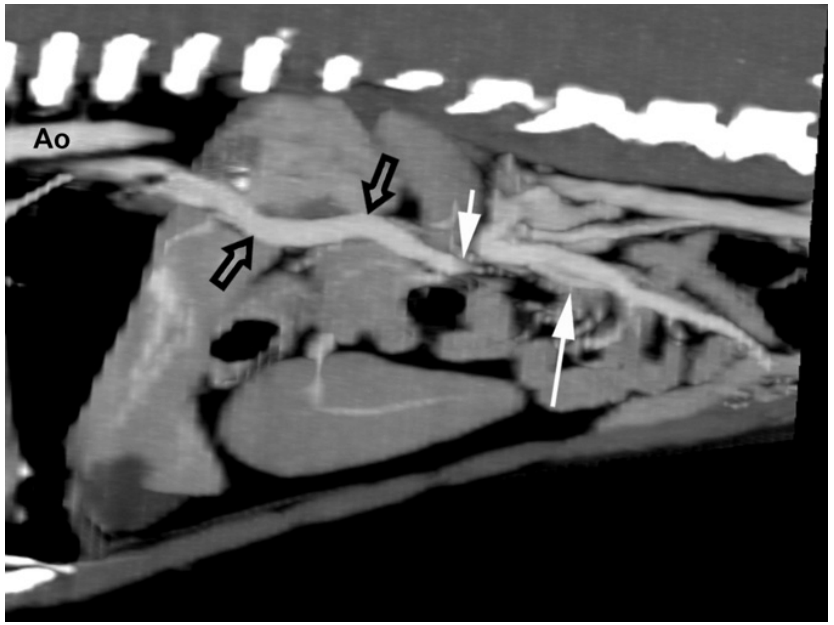
Looks like a Shunt, Smells like a Shunt

- Colonic Scintigraphy – Normal
- Histopathology - Shunt
- No Surgical Option

The Old “Quiet” PSS

Older Dogs

- Lesser Clinical Signs
- Different Anatomy: Porto-Azygos Shunt
- *This Is Not the same as An Acquired Shunt*
- Surgical vs. Medical?



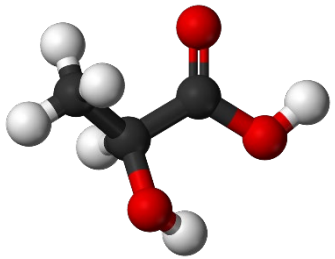

Rx

Emergent Treatment of Seizures

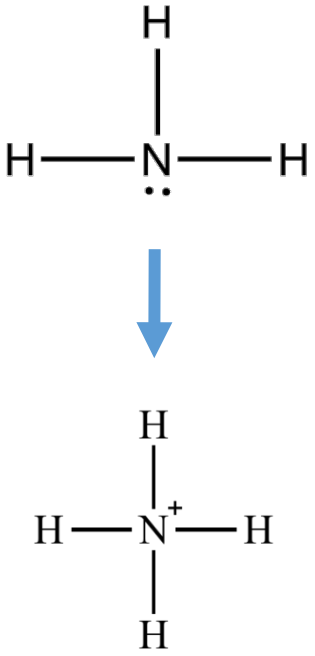
IV Fluids with Dextrose
Warm Water Enema with Lactulose
Diazepam
(Phenobarbitol or K^+ Bromide if necessary)
Levetiracetam to reduce post-op seizures
(20 mg/kg TID at least 24 hrs pre-op)

PSS Medical Treatment

- Lactulose
  - Acidify the colon, cathartic
  - Drives Ammonia to Ammonium (not absorbed)
  - 0.25-0.5 ml/kg, 3-4x/day, to effect

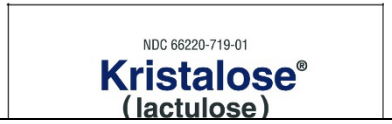


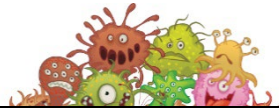
Lactic Acid



PSS Medical Treatment

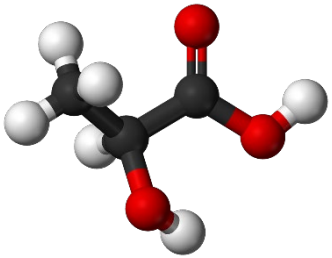
- Lactulose
  - Acidify the colon, cathartic
  - Reduces Ammonia production & absorption
  - ½ teaspoon/5 kg twice a day, to effect



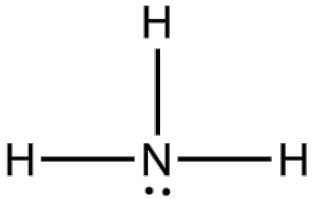


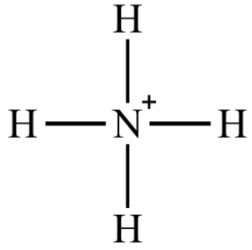
Good sources of insoluble fibre include:

- Wholegrain foods such wheat bra, brown rice and couscous.
- Root vegetables, such as carrots, parsnips and potatoes.
- Celery, cucumbers and courgettes.
- Fruit with edible seeds.
- Beans, pulses and lentils.
- Nuts and seeds.



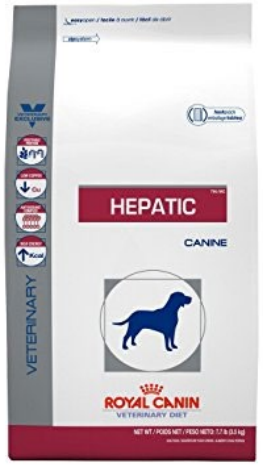
Lactic Acid



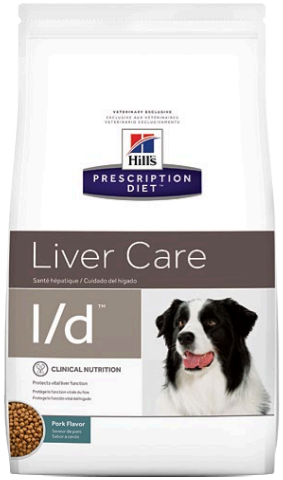


PSS Medical Treatment

- Diet
  - Protein Restriction IF Hepatic Encephalopathy
    - 11% Dry Matter basis
  - Hepatic Diets for Non-HE Liver dogs



14% DM
[Cu] 7 ppm

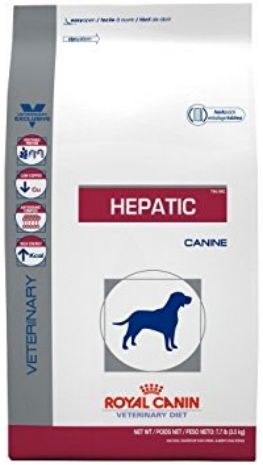


17.8% DM
[Cu] 4.6 ppm

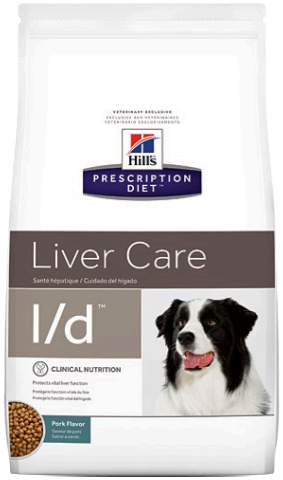
19% DM
[Cu] 4.9 ppm

PSS Medical Treatment

- Diet
  - Protein for a Growing Puppy (20-25% DM)
  - Add cottage cheese or vegetable-based protein



14% DM
[Cu] 7 ppm



17.8% DM
[Cu] 4.6 ppm

19% DM
[Cu] 4.9 ppm

PSS Medical Treatment

- Diet
  - Vitamin Supplementation
    - Water soluble: B1 (thiamine – cats!)
    - Fat soluble: Vitamin K (clotting) & Vitamin E (oxidative stress)
  - Fiber
    - SCFA = acidification = NH_3 to NH_4^+
  - Antioxidants

PSS Medical Treatment

- Microbiota
  - Lactic acid producing bacteria
  - Metabolism of fiber to SCFA
  - Decrease pH, Decrease [Ammonia]

Review > Front Cell Infect Microbiol. 2021 Feb 22;11:586427. doi: 10.3389/fcimb.2021.586427. eCollection 2021.

Novel Insights Into Pathogenesis and Therapeutic Strategies of Hepatic Encephalopathy, From the Gut Microbiota Perspective

Jiachen Liu [1], Yantao Xu [1], Bimei Jiang [2]

Review > Nutrition. 2020 May;73:110693. doi: 10.1016/j.nut.2019.110693. Epub 2019 Dec 6.

Manipulation of microbiota with probiotics as an alternative for treatment of hepatic encephalopathy

Renata Rivera-Flores [1], Segundo Morán-Villota [2], Luisa Cervantes-Barragán [3],

> Scand J Gastroenterol. 2021 May;56(5):560-569. doi: 10.1080/00365521.2021.1899277. Epub 2021 Apr 10.

Fecal microbiota transplantation in hepatic encephalopathy: a systematic review

Mathias Madsen [1], Nina Kimer [1 2], Flemming Bendtsen [1], Andreas Munk Petersen [1 3]

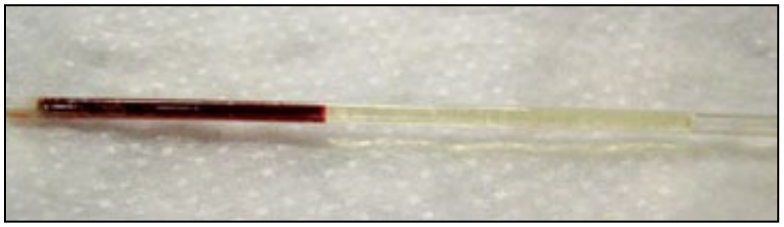
The Yellow Canine Patient
Hyperbilirubinemia

First Things First:

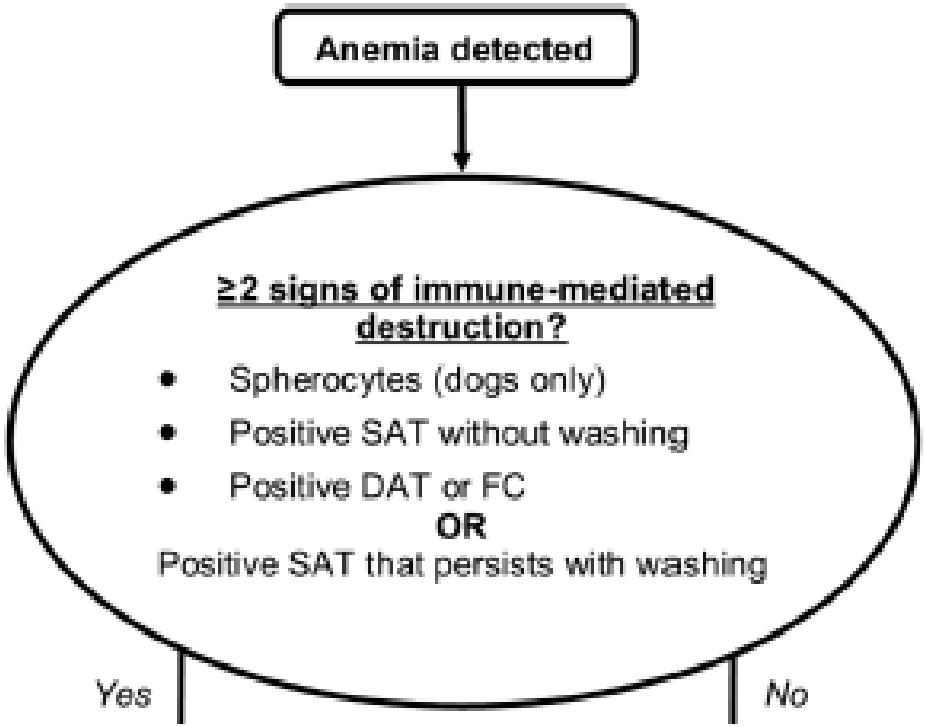
PRE-HEPATIC

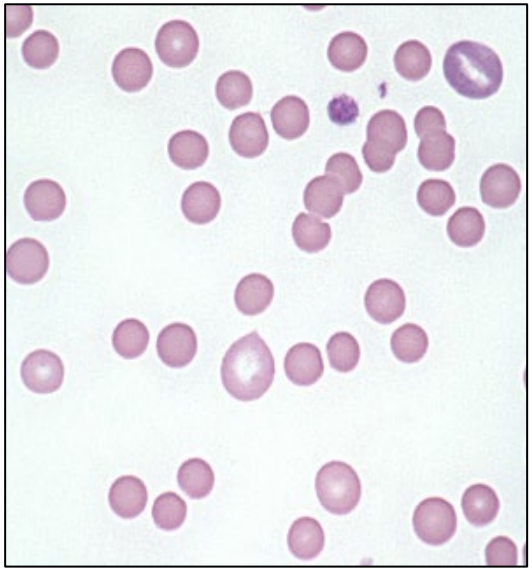
LOW PCV/NORMAL TP

e.g. Hemolysis (IMHA)

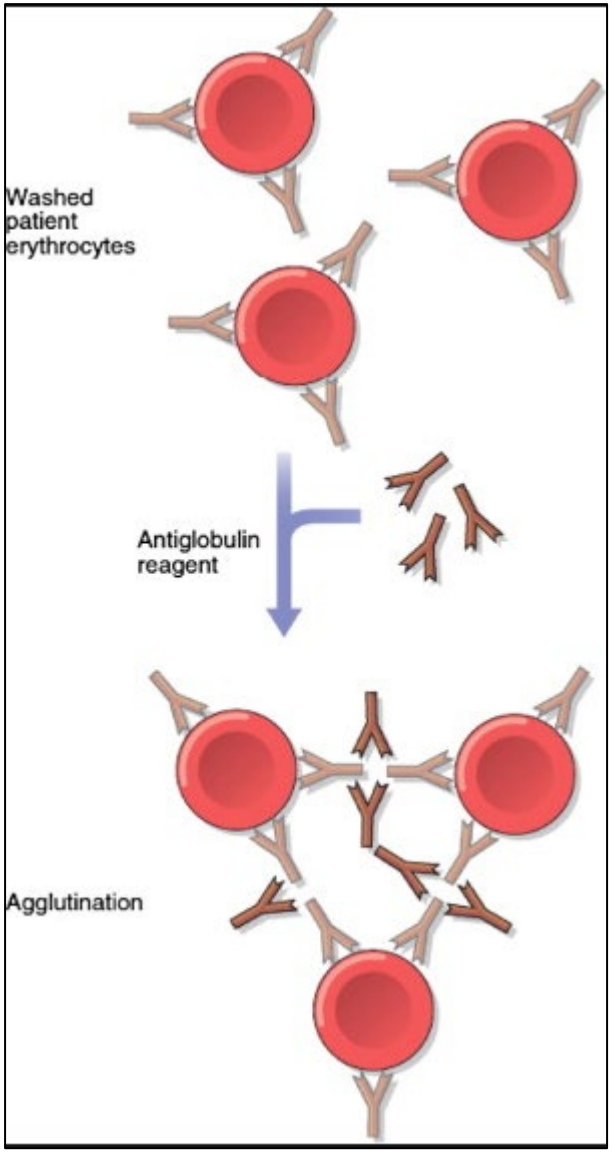


Packed cell volume/Total Protein


Anemia detected
≥2 signs of immune-mediated destruction?
• Spherocytes (dogs only)
• Positive SAT without washing
• Positive DAT or FC
OR
Positive SAT that persists with washing
Yes
No



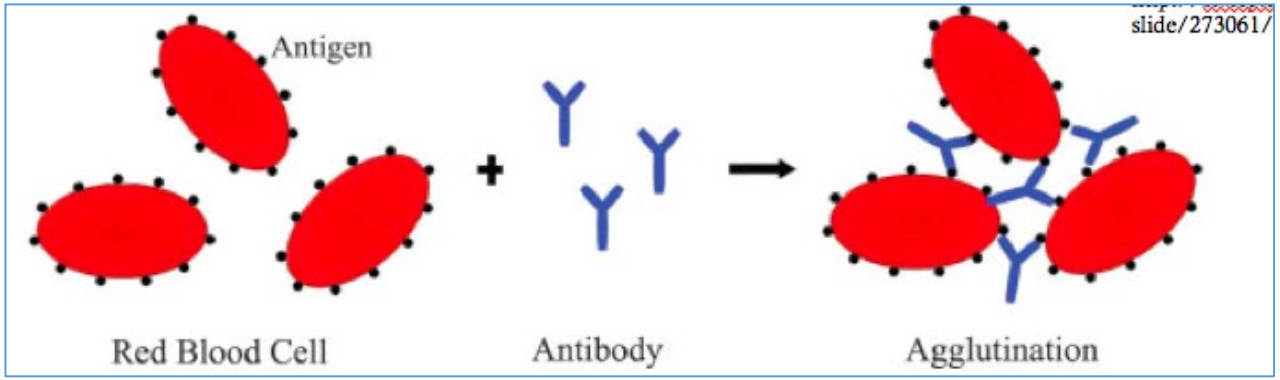
KLIMUD


Washed patient erythrocytes
Antiglobulin reagent
Agglutination

VCNA

Immune-Mediated Hemolytic Anemia (IMHA)

(Primary) (Idiopathic) “Nonassociative”: No Comorbidity
Cocker spaniels, Springer spaniels, Poodles

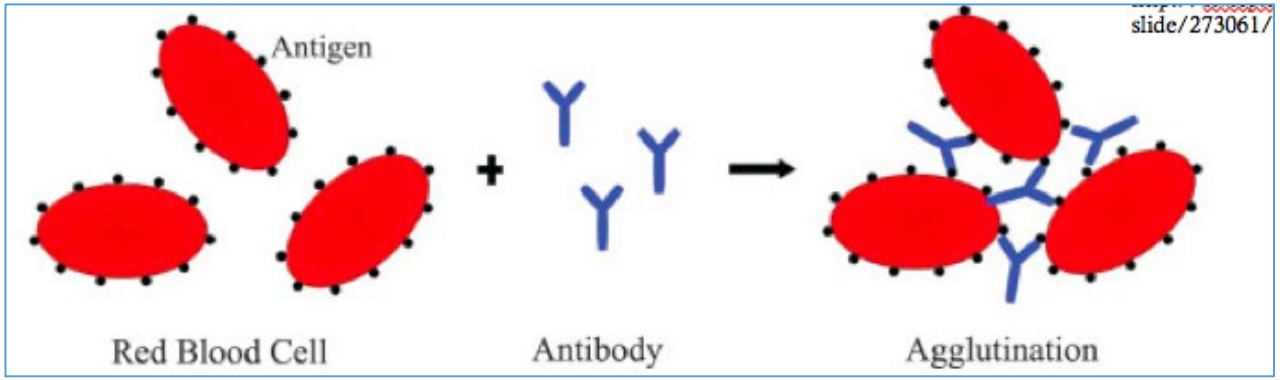


Immune-Mediated Hemolytic Anemia (IMHA)

(Primary) (Idiopathic)"Nonassociative": No Comorbidity
Cocker spaniels, Springer spaniels, Poodles

(Secondary) "Associative": Comorbidity Identified

Infection (e.g. K9 *Babesia*)
Cancer
Drugs (e.g. sulfur drugs)
Vaccines
Inflammation (e.g. bee sting, snake bite)



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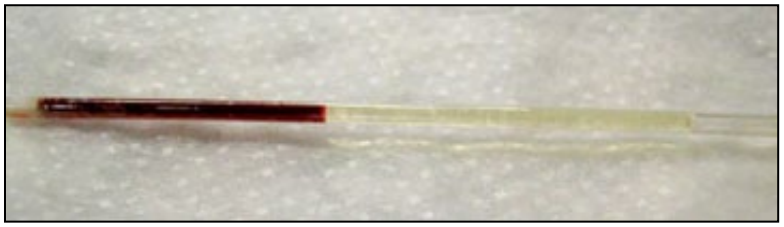
PRE-HEPATIC

LOW PCV/NORMAL TP

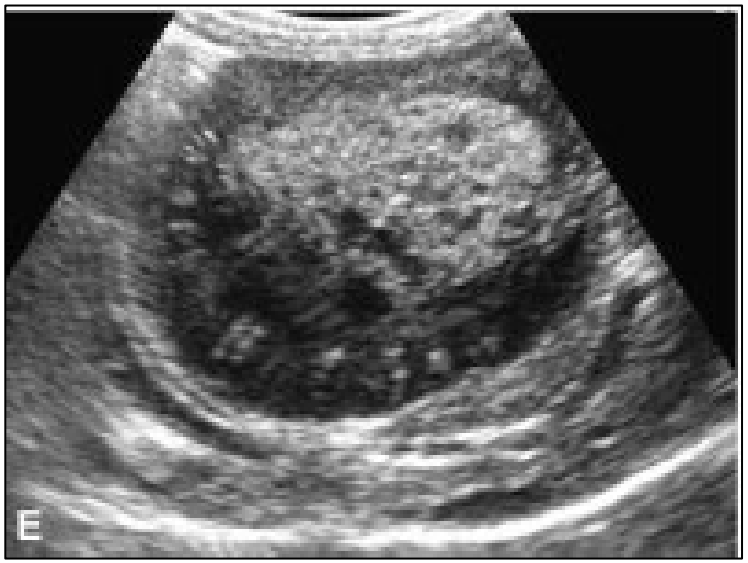
e.g. Hemolysis (IMHA)



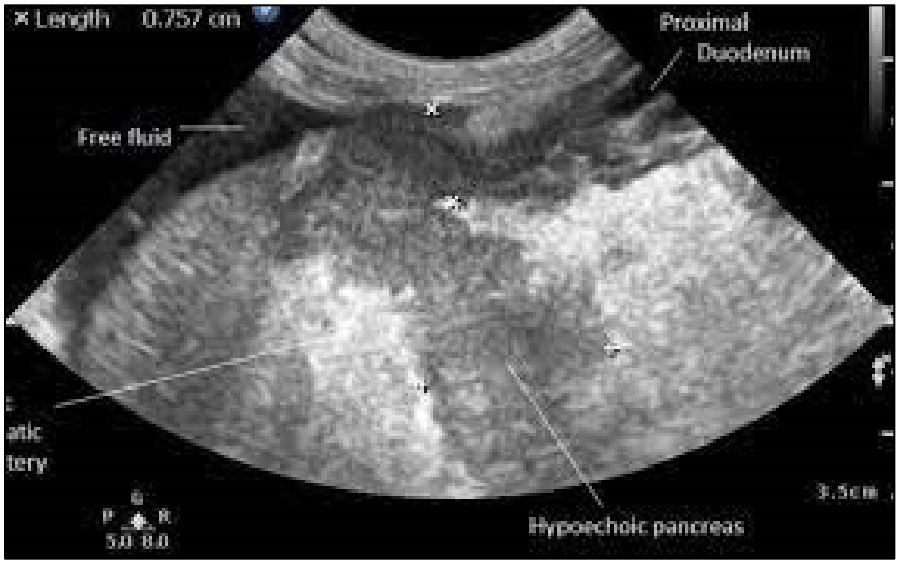
POST-HEPATIC

IMAGING (Ultrasound)

Gully Anim Hosp



Choi et al. 2014



BAR VETS

EHBO

ANATOMIC

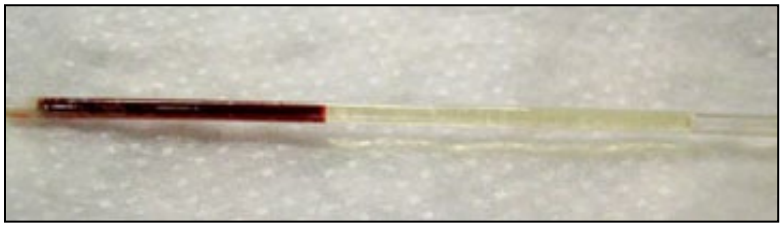
FUNCTIONAL

First Things First:
Packed cell volume/Total Protein

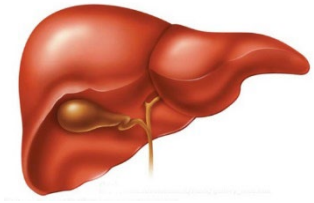
PRE-HEPATIC

LOW PCV/NORMAL TP

e.g. Hemolysis (IMHA)



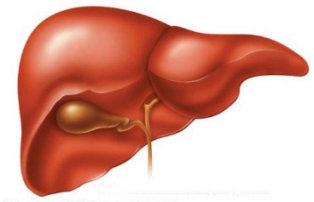
HEPATIC



POST-HEPATIC

IMAGING (Ultrasound)

Gully Anim Hosp



Liver Damage (Dogs)

HEPATIC

"Bella" 8 yo FS Labrador Retriever

PC: Anorexia, lethargy, vomiting, weight-loss, jaundice

Journal of Veterinary Internal Medicine
Open Access
ACVIM

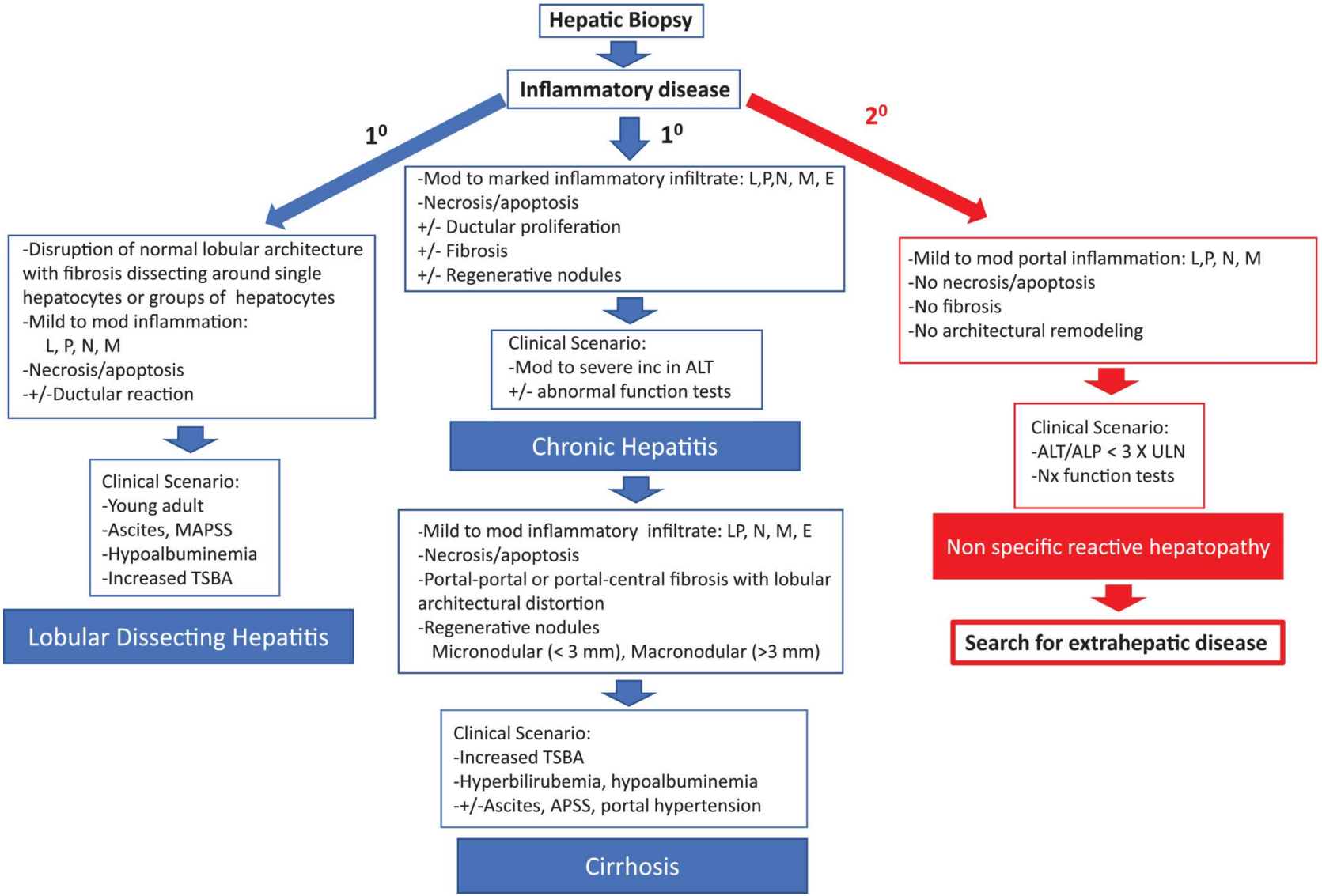
CONSENSUS STATEMENT | Open Access

ACVIM consensus statement on the diagnosis and treatment of chronic hepatitis in dogs

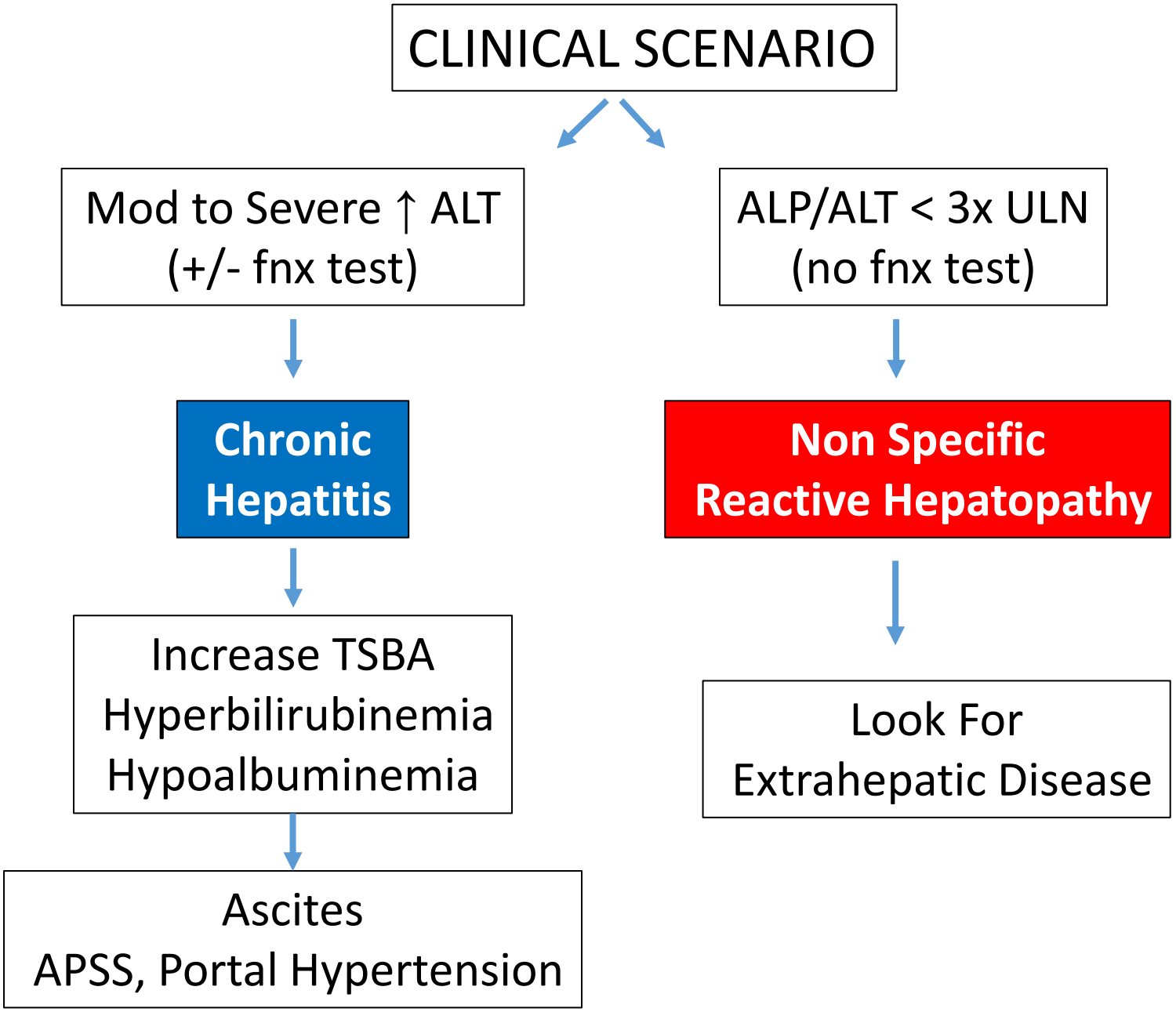
Cynthia R. L. Webster, Sharon A. Center, John M. Cullen, Dominique G. Penninck, Keith P. Richter, David C. Twedt, Penny J. Watson

A bunch of Brainiacs

ACVIM consensus statement on the diagnosis and treatment of chronic hepatitis in dogs



Journal of Veterinary Internal Medicine, Volume: 33, Issue: 3, Pages: 1173-1200, First published: 07 March 2019, DOI: (10.1111/jvim.15467)

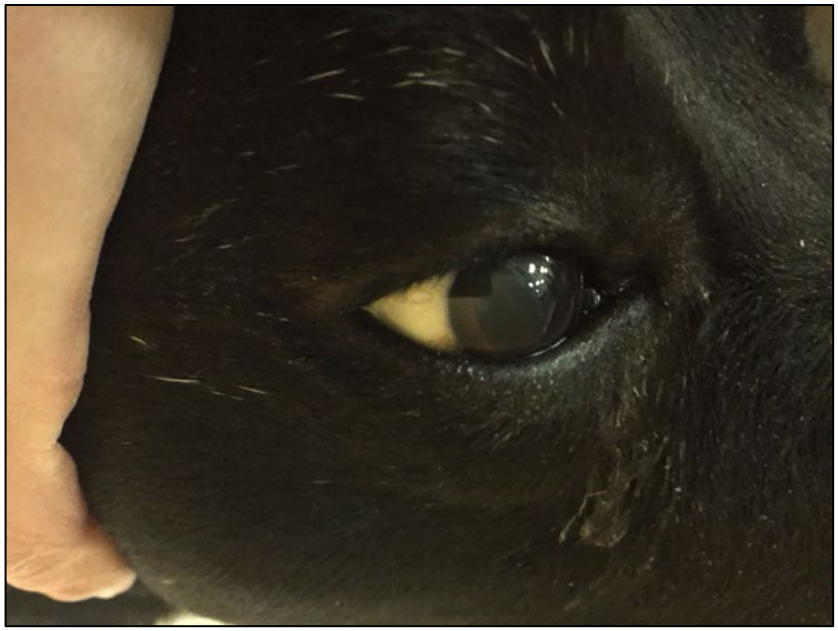

CLINICAL SCENARIO
Mod to Severe ↑ ALT
(+/- fnx test)
ALP/ALT < 3x ULN
(no fnx test)
Chronic Hepatitis
Non Specific Reactive Hepatopathy
Increase TSBA
Hyperbilirubinemia
Hypoalbuminemia
Look For
Extrahepatic Disease
Ascites
APSS, Portal Hypertension

First thing that jumps out at you...

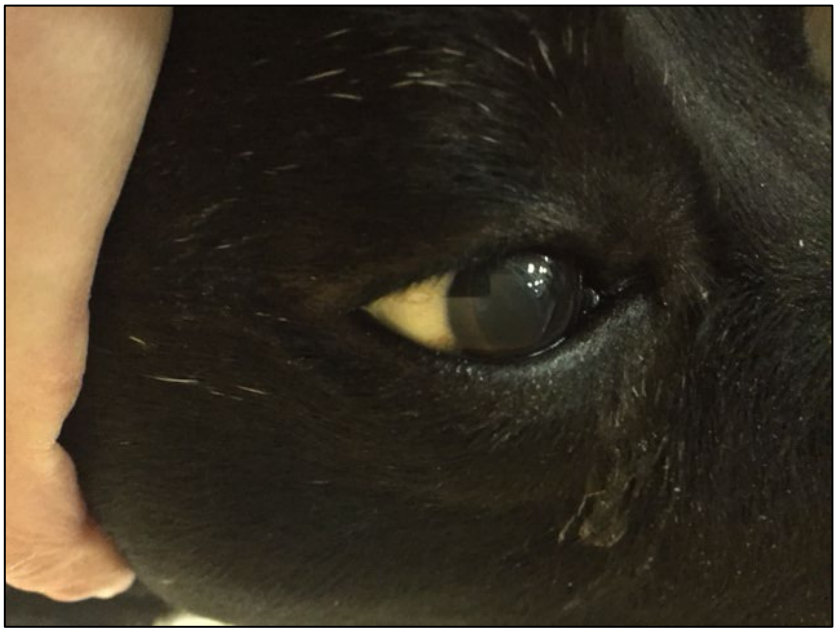
The Dog is Yellow

Next thing that jumps out at you...

The Dog is a Lab



Canine Hepatopathy
K9 Copper-associated Hepatitis



Vet Pathol 46:484–490 (2009)
DOI: 10.1354/vp.08-VP-0197-S-FL

Copper-Associated Hepatitis in Labrador Retrievers

R. Smedley, T. Mullaney, and W. Rumbeiha

Diagnostic Center for Population and Animal Health Michigan State University, Lansing, MI

K9 Copper-associated Hepatitis

Clinical Signs

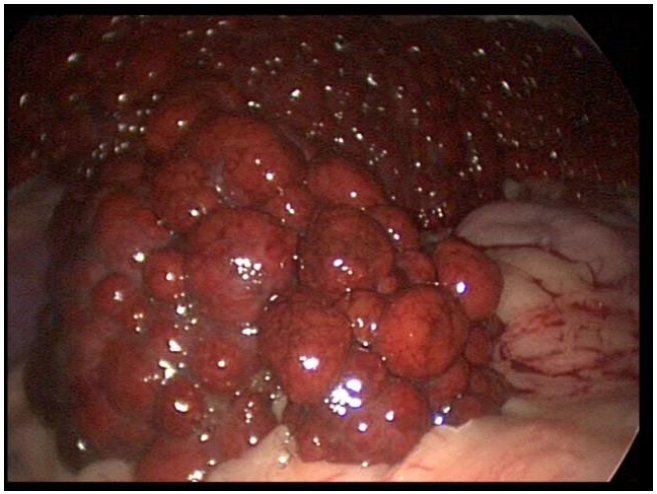
- Anorexia & Lethargy
- Vomiting
- Weight-loss
- Jaundice
- Hepatic encephalopathy
- Ascites
- PU/PD

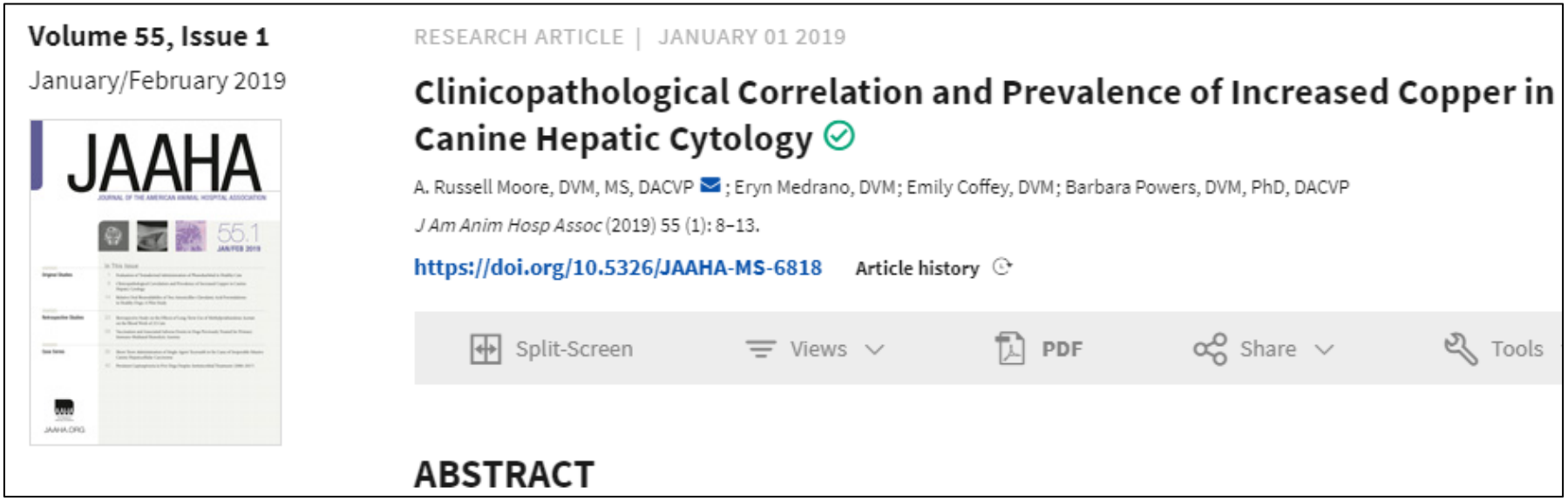
Laboratory Abnormalities

Non-Specific for [Cu] dz

- ALT (ALP) – Not Sensitive
- Bile Acids (IF NOT **YELLOW**)
- Total bilirubin
- Clotting times
- Decreased PCV
- {Fanconi's Syndrome}

LIVER BIOPSY with [Cu] quantification





Volume 55, Issue 1

January/February 2019

JAAHA

RESEARCH ARTICLE | JANUARY 01 2019

Clinicopathological Correlation and Prevalence of Increased Copper in Canine Hepatic Cytology

A. Russell Moore, DVM, MS, DACVP ; Eryn Medrano, DVM; Emily Coffey, DVM; Barbara Powers, DVM, PhD, DACVP

J Am Anim Hosp Assoc (2019) 55 (1): 8–13.

https://doi.org/10.5326/JAAHA-MS-6818 Article history

Split-Screen Views PDF Share Tools

ABSTRACT

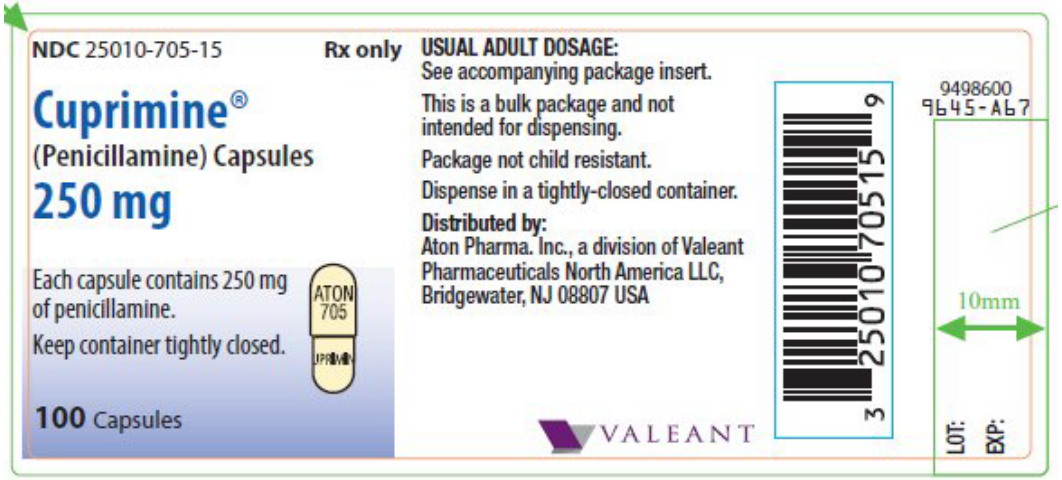
There was significant and modest correlation between cCu and hCu, interface hepatitis, portal inflammation, and fibrosis. Evidence of hepatocellular leakage may be indications for determination of cCu.

Treating K9
[Cu] - associated Hepatopathy

Avoid Copper in Diet, Treats, Supplements
Do not restrict protein unless HE

Chelate the Copper

- [Cu] > 600 µg/g - 1000 µg/g dry weight
  - Penicillamine on an empty stomach
  - 2-6 months



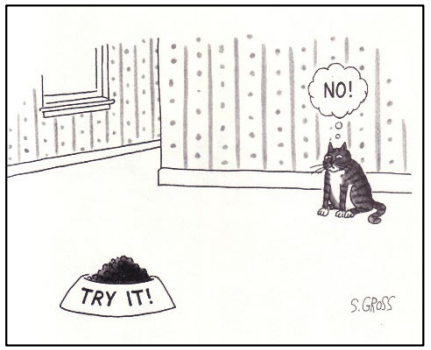
- Problem: Penicillamine on an empty stomach
  - Hyporexia, nausea, vomiting

How to Help

Stop the Vomiting

Decrease Nausea

Increase Appetite



“Rio”
9 year old MC Bali Dog

Chronic Weight Loss
Poor appetite
Elevated ALT

Treating K9 Hepatopathies
K9 (Immune) Chronic Hepatitis

1-2 mg/kg day
Taper
Steroid hepatopathy
Hard to monitor

5 mg/kg BID
Without steroids
Vomiting
Monitor Enzymes

Treating Any Liver Disease
"Drain the Swamp"
Support the Liver

Ursodiol

- Choleretic
- Hepatoprotective
- Biliary cirrhosis

Denamarin

- Antioxidant
- SAMe + Silybin

Case Report

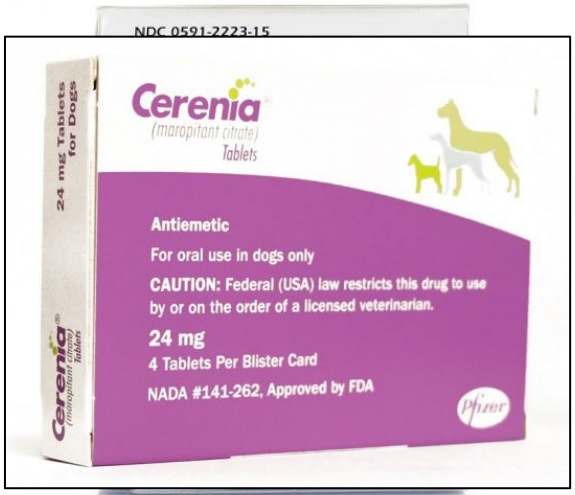
J Vet Intern Med 2014;28:666–671

Degenerative Liver Disease in Young Beagles with Hereditary Cobalamin Malabsorption Because of a Mutation in the Cubilin Gene

P.H. Kook, M. Drögemüller, T. Leeb, J. Howard, and M. Ruetten

Key words: Ascites; Hepatopathy; Neutropenia; Vitamin B12.

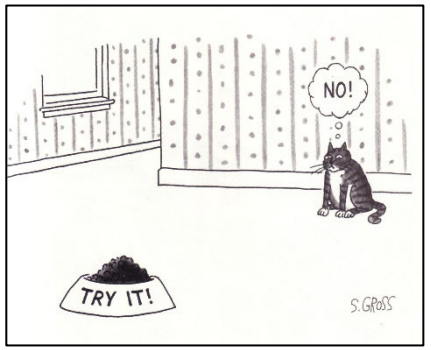
How to Help



Stop the Vomiting

Decrease Nausea

Increase Appetite



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Clinical Trial > J Vet Intern Med. 2011 Jul-Aug;25(4):838-45.
doi: 10.1111/j.1939-1676.2011.0743.x. Epub 2011 Jun 20.

Prospective randomized clinical trial assessing the efficacy of Denamarin for prevention of CCNU-induced hepatopathy in tumor-bearing dogs

K A Skorupski [1], G M Hammond, A M Irish, M S Kent, T A Guerrero, C O Rodriguez, D W Griffin

Affiliations + expand

Dogs with lymphoma, mast cell tumor, or histiocytic sarcoma that were prescribed CCNU with or without corticosteroids and with normal ALT activity were eligible for enrollment.

These results support the use of concurrent Denamarin to minimize increased liver enzyme activity in dogs receiving CCNU chemotherapy. Denamarin treatment also increases the likelihood of dogs completing a prescribed CCNU course.

DOI: 10.1111/jvim.16323

STANDARD ARTICLE

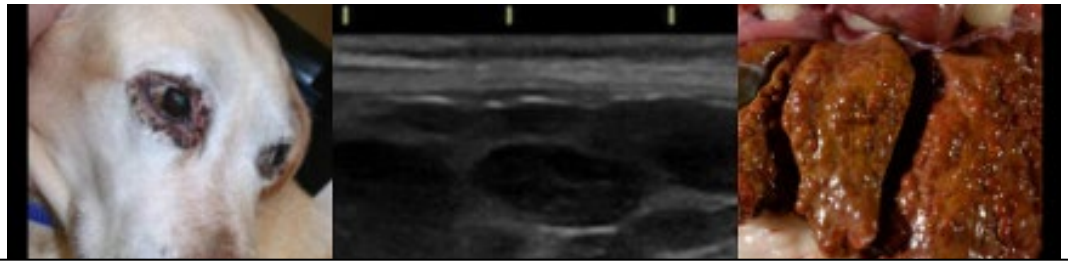
Journal of Veterinary Internal Medicine Open Access

ACVIM American College of Veterinary Internal Medicine

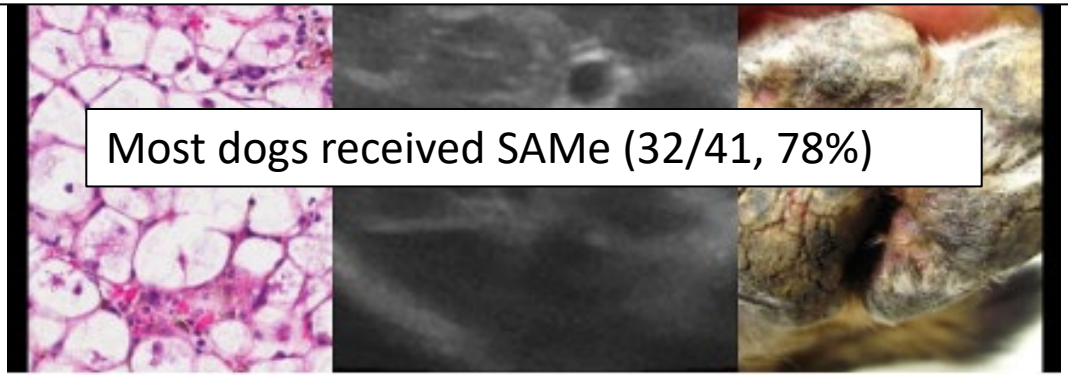
Treatment and outcomes of dogs with hepatocutaneous syndrome or hepatocutaneous-associated hepatopathy

John P. Loftus[1] | Adam J. Miller[1] | Sharon A. Center[1] | Jeanine Peters-Kennedy[1,2] | Michael Astor[1]

2021



Optimized management can resolve Superficial necrolytic dermatitis and Hepatocutaneous-associated Hepatopathy and confer long-term survival



Most dogs received SAMe (32/41, 78%)

J. Med. Toxicol. (2016) 12:201–205
DOI 10.1007/s13181-015-0531-7

TOXICOLOGY OBSERVATION

Acute Hepatic Failure in a Dog after Xylitol Ingestion

Renee D. Schmid [1] · Lynn R. Hovda [1]

Hypoglycemia, Acute Hepatic Failure< Coagulopathy

N-acetylcysteine (NAC) and S-adensoyl-L-methionine (SAMe) provided hepatic detoxification and support.

To date, this is the highest published xylitol dose survived by a dog

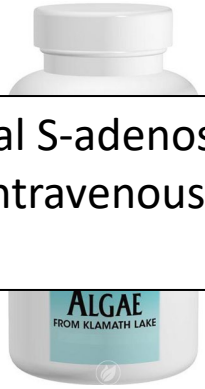
Bautista *et al. BMC Veterinary Research* (2015) 11:136
DOI 10.1186/s12917-015-0453-2

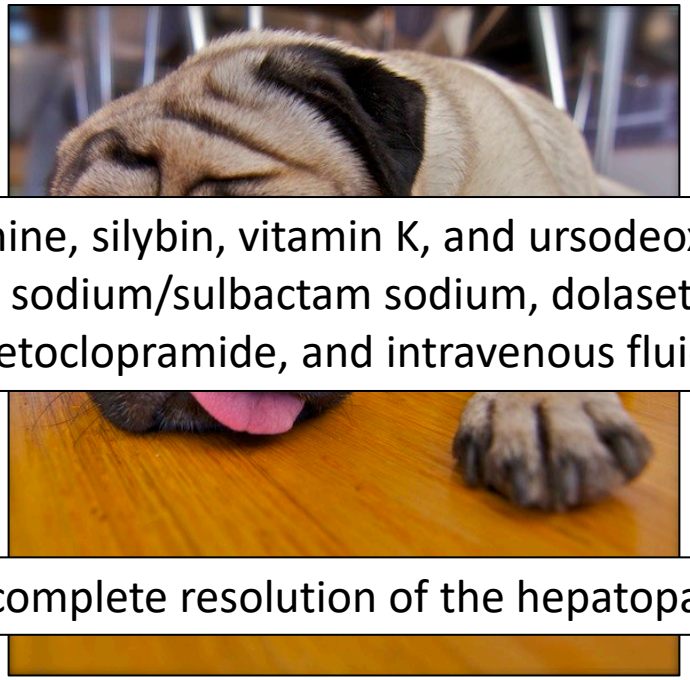
BMC Veterinary Research

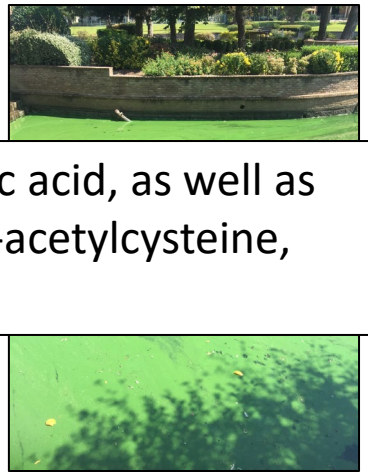
CASE REPORT Open Access

Hepatopathy following consumption of a commercially available blue-green algae dietary supplement in a dog

Adrienne C. Bautista[1†], Caroline E. Moore[2†], Yanping Lin[2†], Martha G. Cline[3†], Noemi Benitah[3†] and Birgit Puschner[1,2*†]







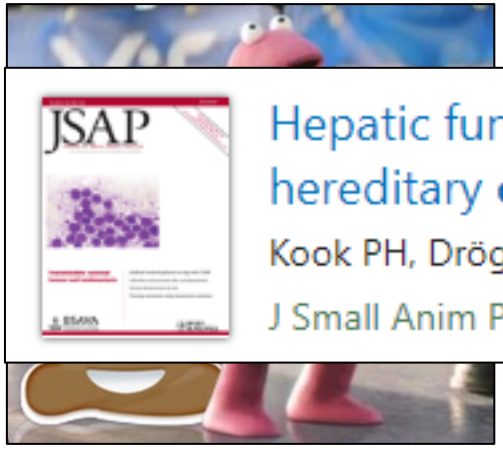
oral S-adenosylmethionine, silybin, vitamin K, and ursodeoxycholic acid, as well as intravenous ampicillin sodium/sulbactam sodium, dolasetron, N-acetylcysteine, metoclopramide, and intravenous fluids

a complete resolution of the hepatopathy

Degenerative **liver disease** in young Beagles with hereditary **cobalamin** malabsorption because of a mutation in the cubilin gene.

Kook PH, Drögemüller M, Leeb T, Howard J, Ruetten M.

J Vet Intern Med. 2014 Mar-Apr;28(2):666-71. doi: 10.1111/jvim.12295. Epub 2014 Jan 27.



Hepatic fungal infection in a young beagle with unrecognised hereditary **cobalamin** deficiency (Imerslund-Gräsbeck syndrome).

Kook PH, Drögemüller M, Leeb T, Hinden S, Ruetten M, Howard J.

J Small Anim Pract. 2015 Feb;56(2):138-41. doi: 10.1111/jsap.12251. Epub 2014 Aug 8.

Systemic Scedosporium prolificans infection in an 11-month-old Border collie with **cobalamin** deficiency secondary to selective **cobalamin** malabsorption (**canine** Imerslund-Gräsbeck syndrome).

Erles K, Mugford A, Barfield D, Leeb T, Kook PH.

J Small Anim Pract. 2018 Apr;59(4):253-256. doi: 10.1111/jsap.12678. Epub 2017 Apr 8.

THANK YOU!