Canine Protein Losing Enteropathy

Marc Myers, VMD

Residency Trained in Veterinary Internal Medicine

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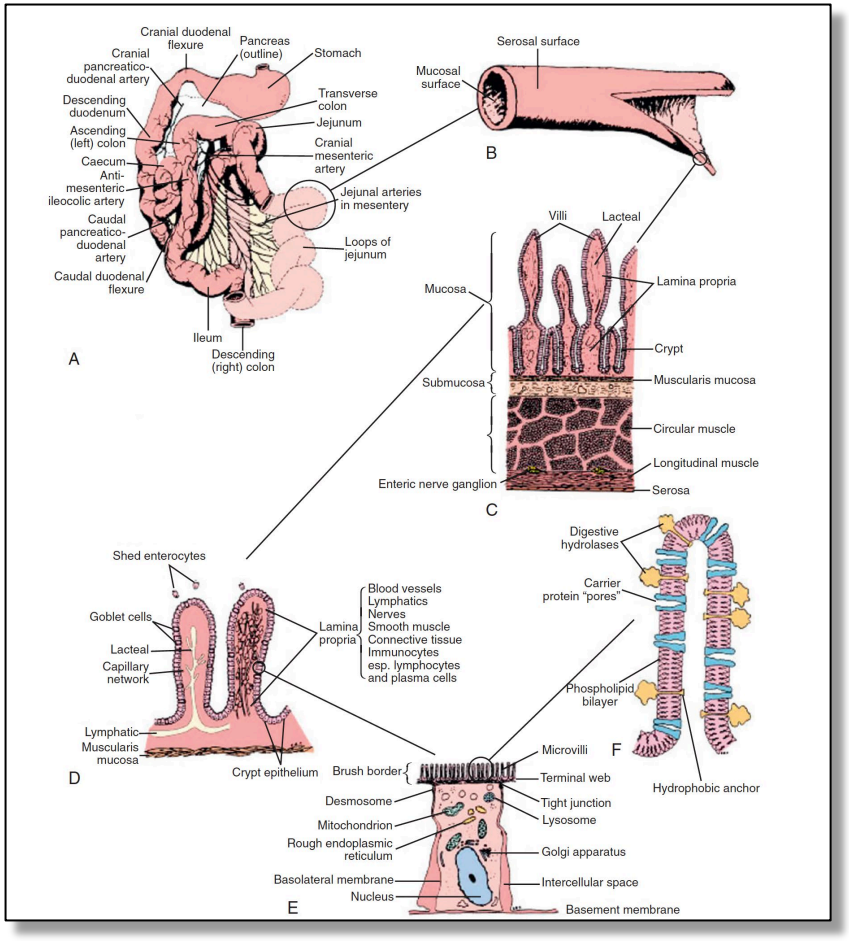
Leading Specialty Healthcare for Pets

Functional Anatomy of Small Intestine



Washbau & Day 2013

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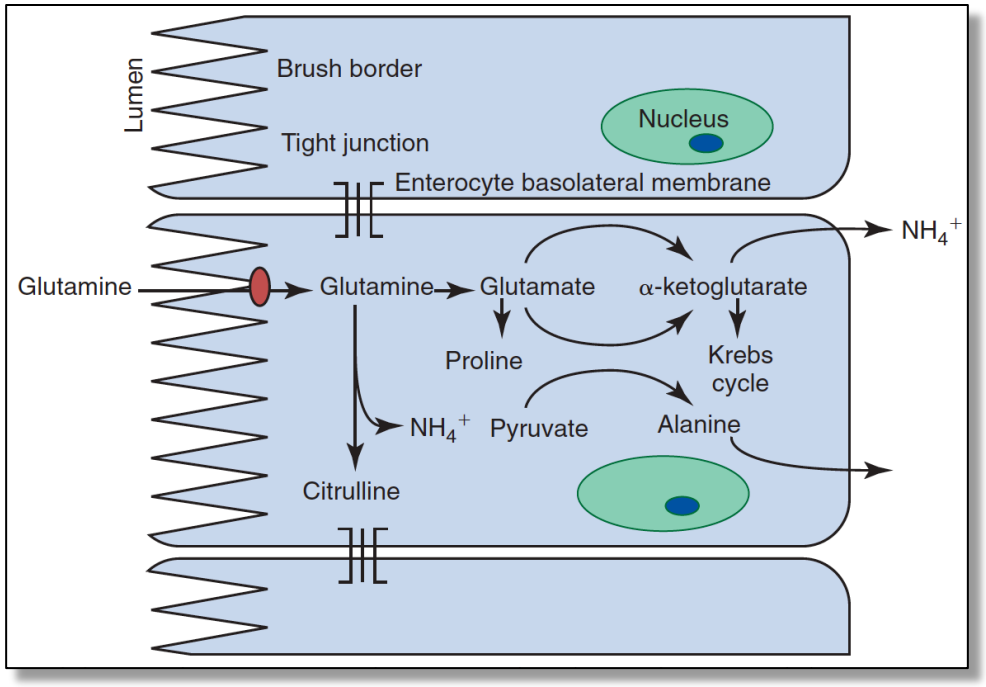
Feeding the Enterocyte

- Glutamine
- Hyperammonemia
- Tight Junctions



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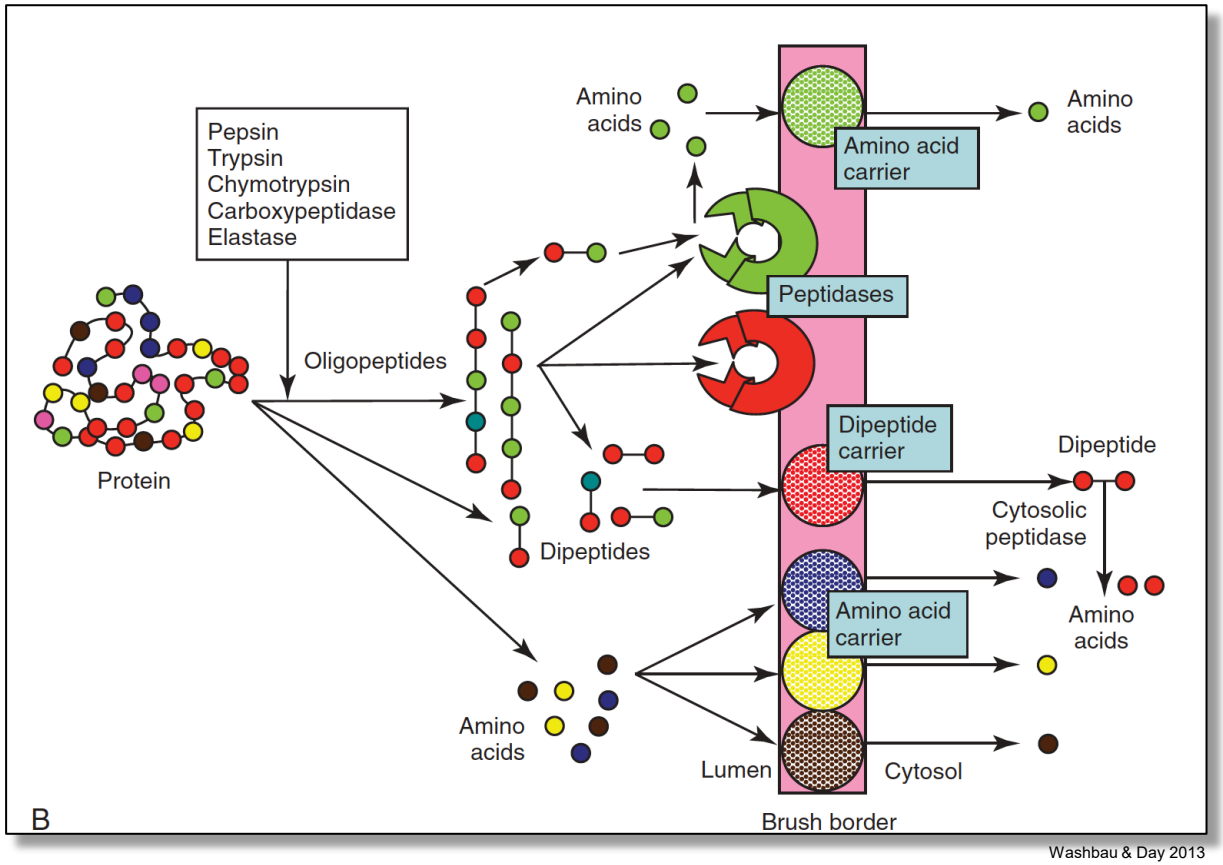
Protein Absorption

- Di-peptides: facilitated diffusion



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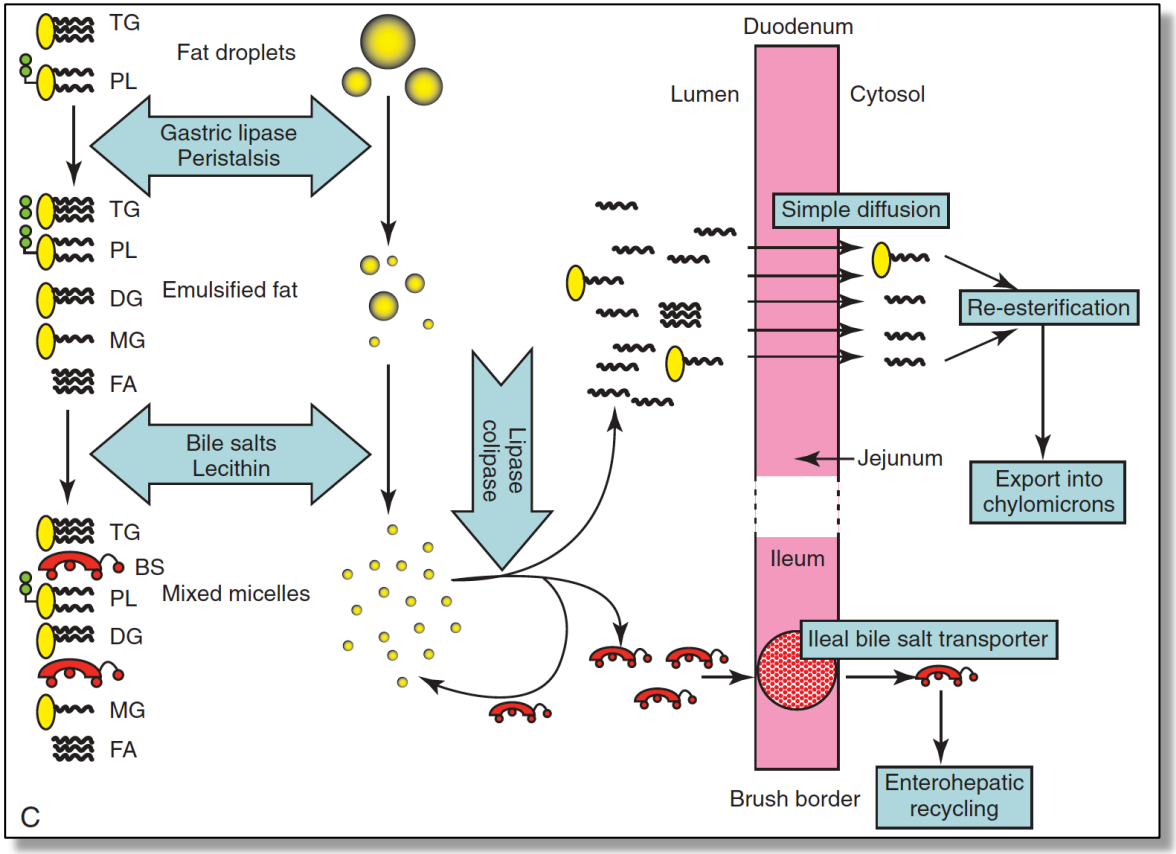
Fat Absorption

- Emulsified fats and the Mayonnaise War of 1756
- Exocytosis



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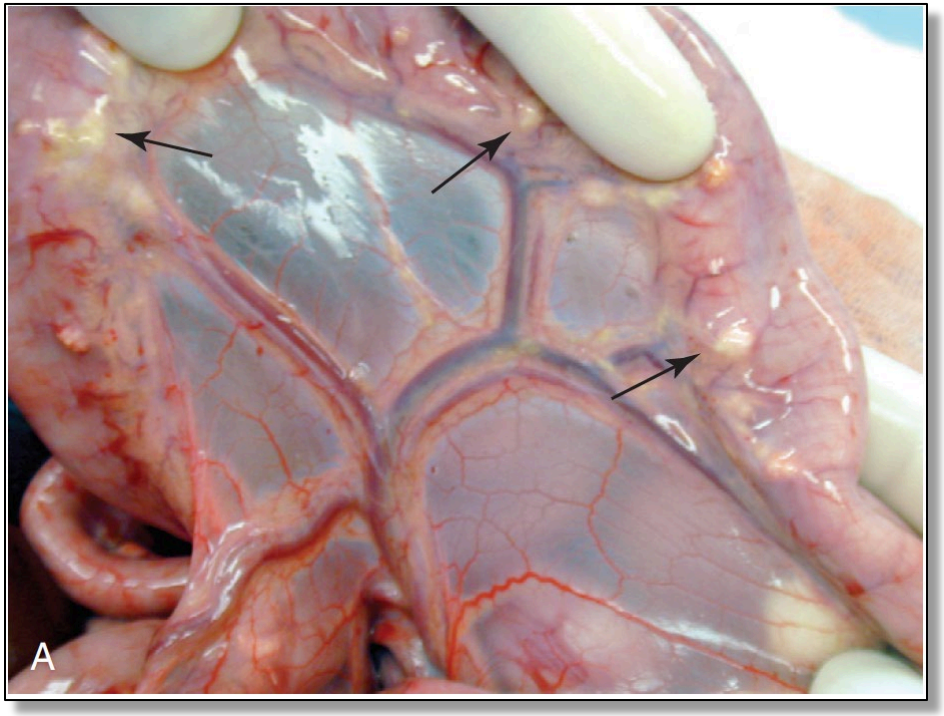
PLE Mechanisms

- Ruptured Lymphatics
- Mucosal Permeability
- Mucosal Erosions



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Lipogranulomas

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Clinical Presentation

- Ascites
- +/- hyporexia, weight loss, diarrhea, vomiting
- Presentation may be severe
  - Anorexia
  - Cachexia
  - Shock (hypovolemic)
  - Pitting edema

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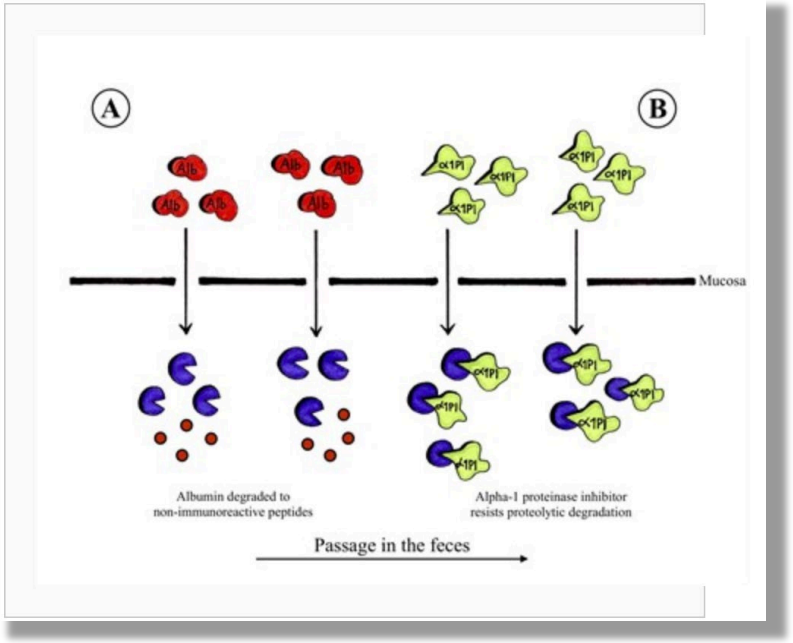
Diagnostic Workup

- CBC/Serum chemistry
  - +/- α1-PI
- UA and UP/C
- Fecal ova/parasites
- Fasting and post-prandial bile acids
- Ultrasound
- Biopsies
  - Endoscopic vs full thickness



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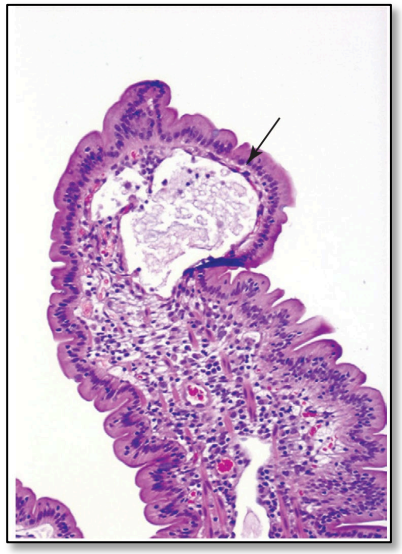
Lymphangiectasia

- Dilatation of small intestinal lacteals
- Primary or Secondary
- Panhypoproteinemia, Hypocholesterolemia, Lymphopenia
- 214/469 (58%) dogs with PLE had lymphangiectasia
  - Most secondary to LPE (Craven, JVIM 2019)
- Of 24 dogs with PLE almost all had evidence of lymphangiectasia
  - Immunophenotyping (Wennogle, JVIM 2019)
- Immunosuppression and diet



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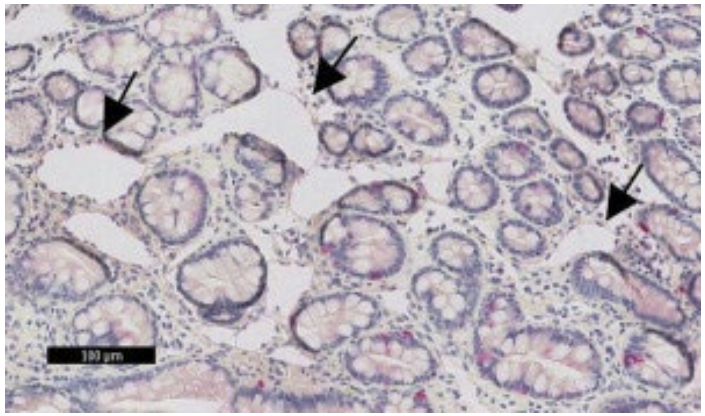

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Prognosis

- 50% overall survival
- Hypoalbuminemia, CCECAI score, BUN negative indicators
- Dogs with PLE caused by lymphangiectasia
  - 22.9% increased hazard of death for each unit increase in CCECAI score
  - CCECAI score >8 median survival time of only 109 days (Kathrani, JVIM 2019)

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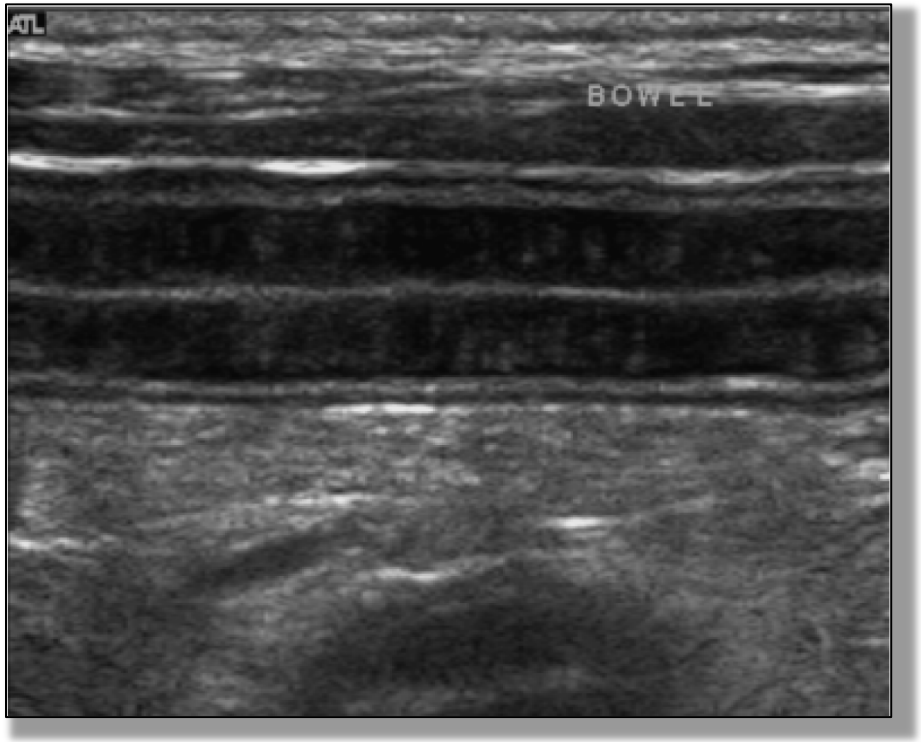
ULTRASONOGRAPHIC INTESTINAL HYPERECHOIC MUCOSAL STRIATIONS IN DOGS ARE ASSOCIATED WITH LACTEAL DILATION

JAMES SUTHERLAND-SMITH, DOMINIQUE G. PENNINCK, JOHN H. KEATING, CYNTHIA R. L. WEBSTER

- Vet Rad &Ultrasound 2007
- 23 dogs with striations and endoscopic or surgical biopsies
- 96% associated with histologic finding of lacteal dilation
- 78% associated with clinical finding of protein losing enteropathy



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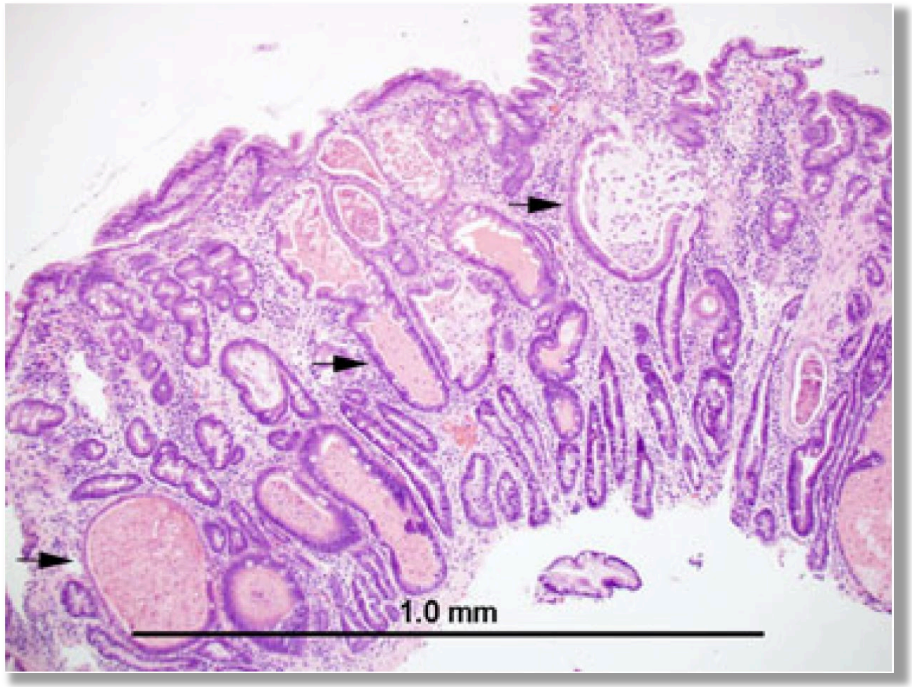
J Vet Intern Med 2014;28:331–337

Clinical Features, Intestinal Histopathology, and Outcome in Protein-Losing Enteropathy in Yorkshire Terrier Dogs

S.M. Simmerson, P.J. Armstrong, A. Wünschmann, C.R. Jessen, L.J. Crews, and R.J. Washabau

- 30 Yorkies with PLE
- All had lymphoplasmacytic inflammation
- 24/30 lacteal dilation
- 15/17 crypt dilation
- All immunosuppressed
- 7/23 did not respond to treatment
  - 13/23 resolution of clinical signs
  - 3/23 partial



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J Vet Intern Med 2014;28:809–817

The Clinical Efficacy of Dietary Fat Restriction in Treatment of Dogs with Intestinal Lymphangiectasia

H. Okanishi, R. Yoshioka, Y. Kagawa, and T. Watari

- 24 dogs w/ histologic evidence of IL – all breeds
- 10/24 dogs not responsive to steroid treatment
- 14/24 dogs relapsed when steroids weaned
- All started on fat restricted diet
- 19/24 responded favorably and prednisone was stopped (10/19) or reduced (0.25mg/kg EOD)

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Synopsis

PAPER

Dietary management of presumptive protein-losing enteropathy in Yorkshire terriers

A. J. Rudinsky*,[1], J. P. Howard*, M. A. Bishop[†], R. G. Sherding*, V. J. Parker* and C. Gilor*

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†Department of Small Animal Clinical Sciences, College of Veterinary Medicine and Biomedical Sciences, Texas A&M University, College Station, TX 77845, USA

[1]Corresponding author email: rudinsky.3@osu.edu

- 11 Yorkies with PLE managed by low-protein diet
- No immunosuppressives/anti-inflammatories
- Full resolution in 8 dogs, partial in 2, none in 1
- Responders mean albumin improved from 1.5 to 2.4 at 4 weeks, to 2.7 at 3 months
- Variable diets were given
- Not a controlled study, but suggests potential management strategy

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Discussion

PAPER

Dietary management of presumptive protein-losing enteropathy in Yorkshire terriers

A. J. Rudinsky*,[1], J. P. Howard*, M. A. Bishop[†], R. G. Sherding*, V. J. Parker* and C. Gilor*

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- Low fat diets decrease lacteal engorgement
- Novel/hydrolysed protein may decrease intestinal inflammation => improved lacteal flow
- Determining if the inflammation is primary disease process or secondary to lymphangiectasia important for determining best treatment modality.
  - Challenging because variable degrees of inflammation are noted in biopsies of Yorkshire terriers with PLE.

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Take home

- Standard of care with immunosuppression should be questioned
- Further study is merited to see if diet therapy alone is effective in a larger population and in other breeds

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Prospective Evaluation of Low Fat Diet Monotherapy in Dogs with Protein Losing Enteropathy

Marc Myers VMD, Stephen A. Martinez DVM, DACVIM, Jonathan T. Shiroma DVM, MS, DACVR, Adam T. Watson DVM, DACVR, Roger A. Hostutler DVM, MS, DACVIM

MedVet Medical and Cancer Centers for Pets
300 East Wilson Bridge Road
Worthington, OH, 43085, USA

- Unpublished MedVet IM research
- Is low fat/ultra-low fat diet an effective treatment for PLE in any breed?
  - Monotherapy
  - In conjunction w/immunotherapy
- Prospective
- Enrollment closed
- Inclusion criteria:
  - Clinical diagnosis of PLE based on Clinical signs, CBC, Chem, UA
  - Ultrasonographic or histopathologic evidence of dilated lacteals
  - No exposure to steroids in last 30 days

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Objectives

- Do dogs of any breed with PLE and ultrasonographic evidence of lymphangiectasia respond to treatment with a low-fat diet either as monotherapy or in conjunction with immunosuppression?
- Resolution of ultrasonographic evidence of lymphangiectasia in dogs who achieve remission?

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- 14 dogs met inclusion criteria
- Categorized on study completion
  - LOF: exclusive low fat diet (n=6)
  - LOP: low fat diet plus prednisone (n=5)
  - TXF: treatment failure (n=3)

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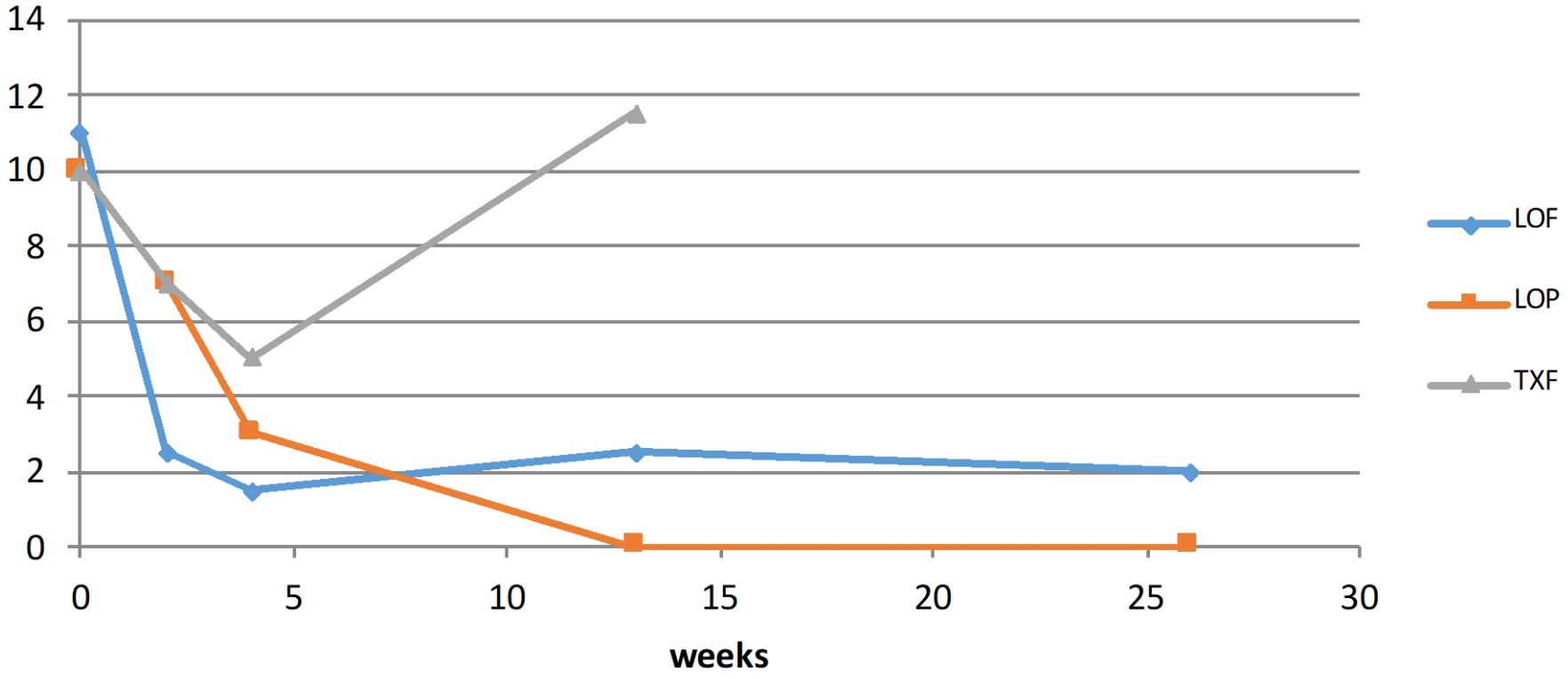
CCECAI



CCECAI Score is shown on the Y-axis. Significant improvements in CCECAI scores over time were seen for LOF and LOP dogs. TXF dogs who failed treatment appeared to initially improve before worsening.

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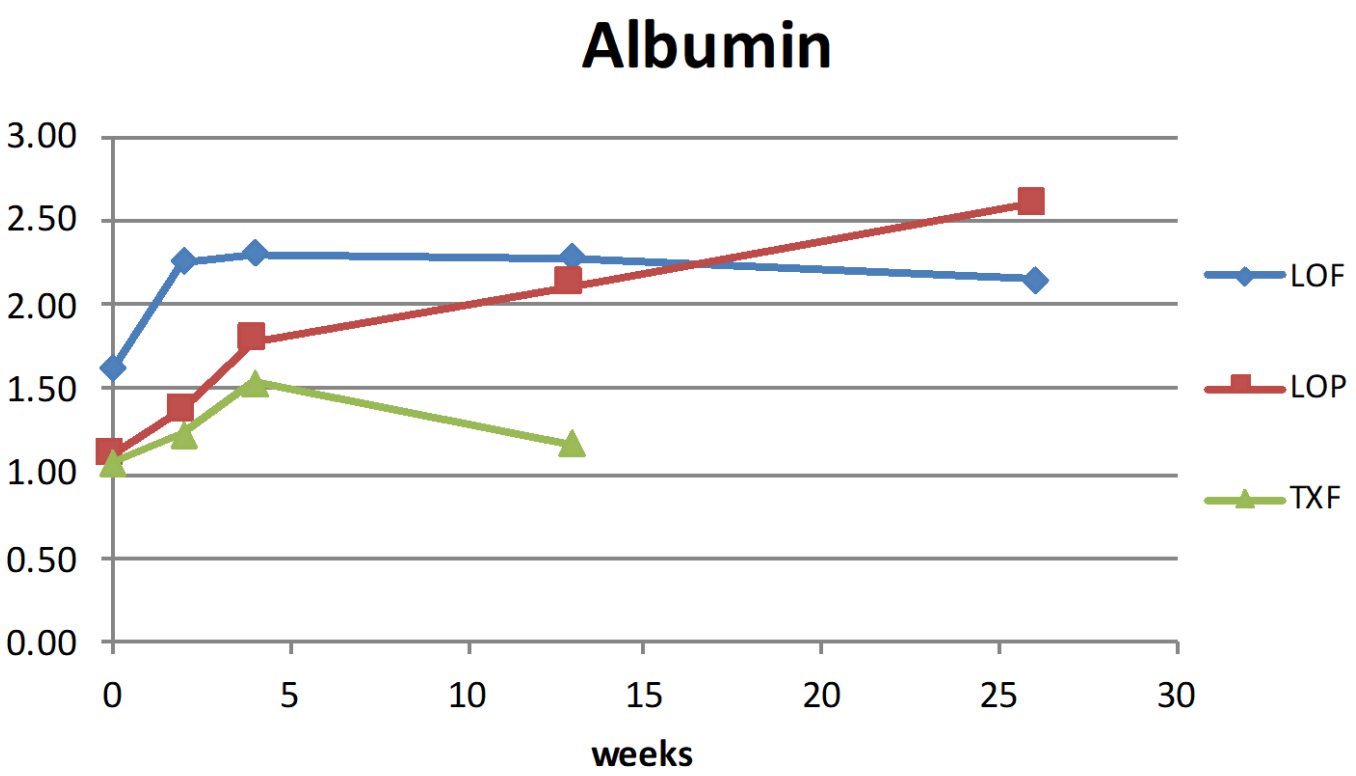

Serum albumin in g/dL is shown on the Y-axis. LOF and LOP dogs both had significantly improved median serum albumin levels over time, although LOF dogs dropped below the CCECAI cutoff for hypoalbuminemia (2.3mg/dL) at the 26 week recheck, to a median of 2.1 (1.6-2.7) mg/dL. There was no association between initial albumin and outcome.

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Case Study - Molly

- 5yo FS CKCSP
- Treated for pancreatitis September 2017
- Presented for ascites, weakness, weight gain
- Presenting bloodwork
  - panhypoproteinemia (Alb 1.5, Glob 2.4)
  - hypocholesterolemia (Chol 54)
- Recheck ~10 days later
  - Alb 1.7, Glob 3.6, Chol 138
- Did well until holidays then broke w/ diarrhea and ascites
  - Alb 1.3, Glob 1.8, Chol 77 on Jan 2nd
- No current medications

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Ultrasound Findings

- Generalized thickening ranging from mild to moderate (up to 0.54 cm)
- Multiple segments exhibit linear hyperechoic striations amongst the hyperechoic speckling.

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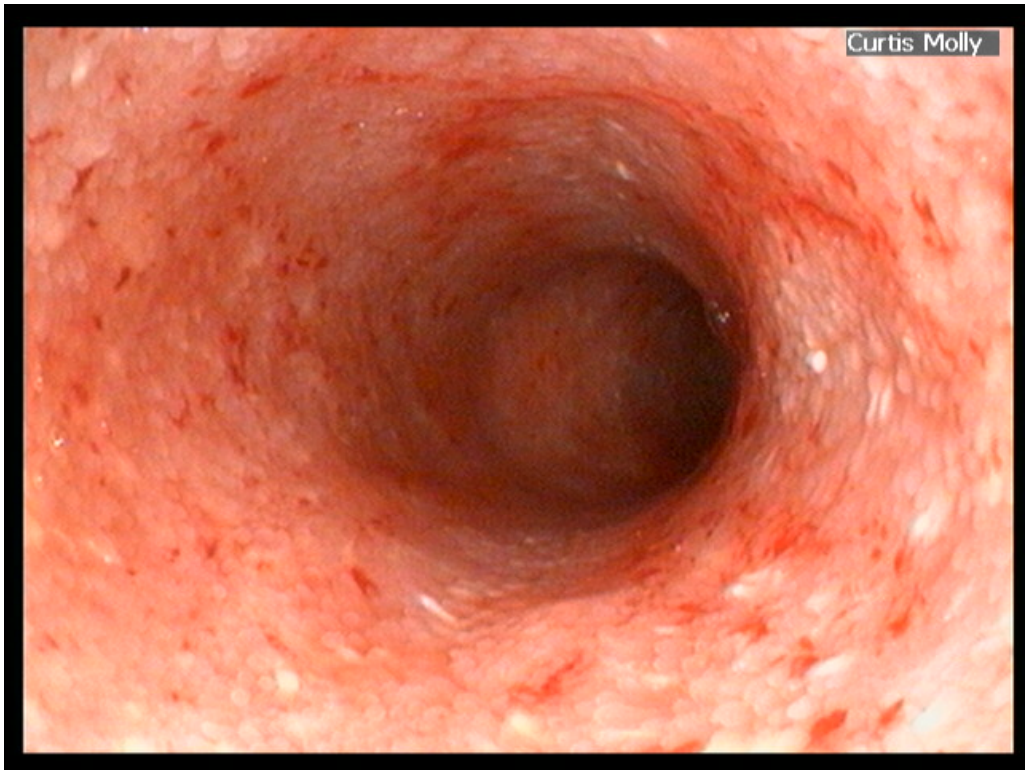
Endoscopy Findings



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Endoscopy Findings

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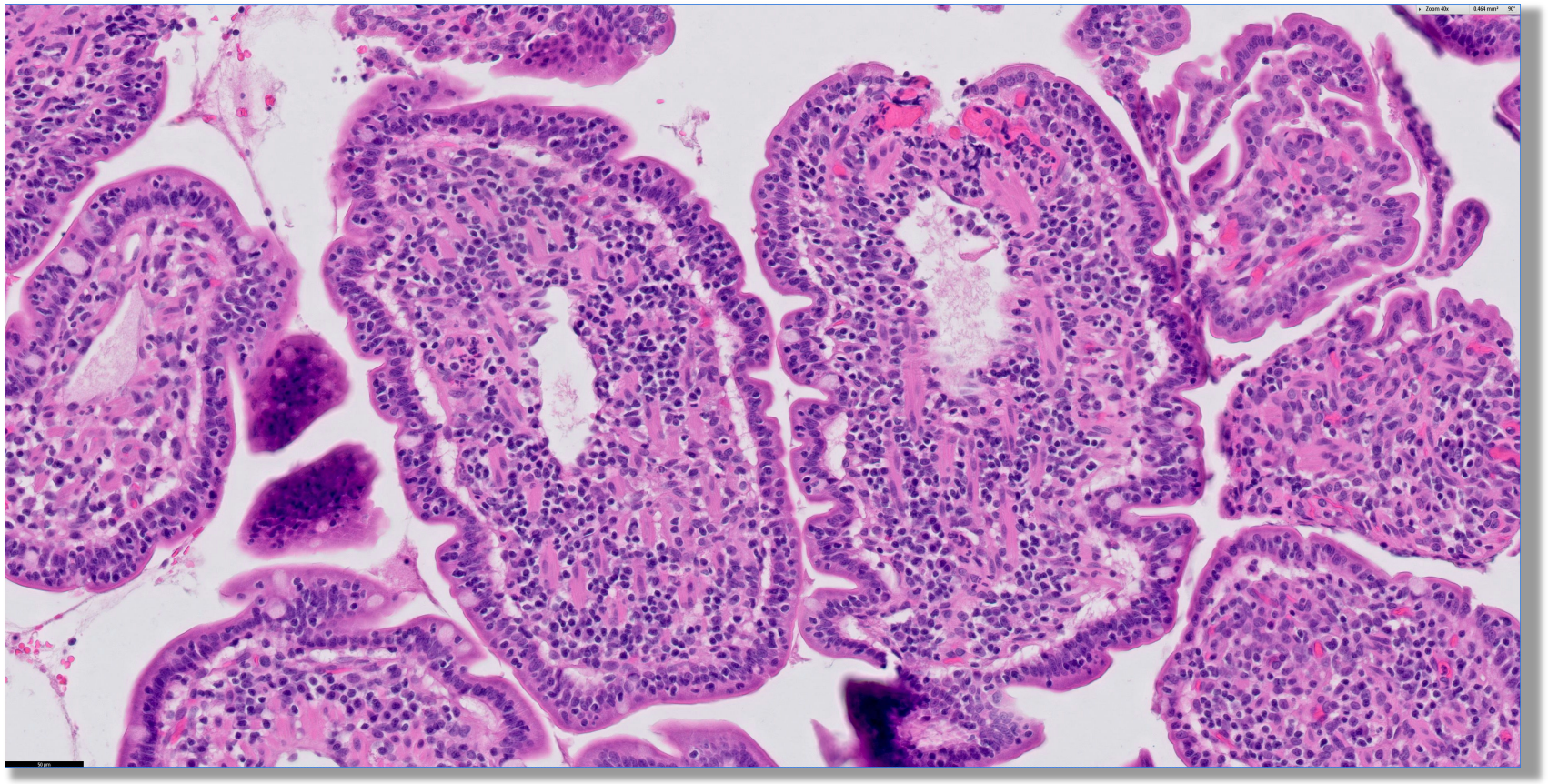
Biopsy Findings



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Pathology Comments

- It is uncertain whether this lymphocytic population represents a purely inflammatory (idiopathic inflammatory bowel disease, IBD) or neoplastic (EATL II) population
- IHC clonality assay recommended
- Prominent lacteal dilatation within the duodenum likely indicates lymphangiectasia

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Follow-up Diagnostics

- Molecular clonality testing at UC Davis: POLYCLONAL
- GI Panel

TLI B12 FOLATE - CANINE : FOLATE & VITAMIN B12 (COBALAMIN)

Test	Result	Reference Range	Low	Normal	High
COBALAMIN (B-12)	<150	284 - 836 ng/L	LOW		
FOLATE	9.4	4.8 - 19.0 ug/L			

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Tx Response

- Home on ULFD
- One week later presented to referral partner for bloody diarrhea
  - Ascites unresolved
- Started on Prednisone, continued on ULFD
- Immediate response seen
- 6 month recheck:
  - CCECAI: 0 from 10
  - Albumin: 2.8 from 1.2
  - Linear striations: resolved

IDEXX

MOLLY CURTIS

Chemistry

1/22/18 3:22 PM				1/10/18 10:41 AM	1/2/18 10:34 AM
Total Protein	4.3	5.2 - 8.2 g/dL	L	3.3	3.1
Albumin	2.0	2.3 - 4.0 g/dL	L	1.2	1.3
Globulin	2.3	2.5 - 4.5 g/dL	L	2.1	1.8
Cholesterol	55	110 - 320 mg/dL	L	75	77

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Case Study - Buoy

- 11yo MC PWD
- Presented to IM for
  - Weight loss
  - Soft stools
  - Urinary accidents
- PE
  - Thickened SI loops
  - Fluid wave
- Bloodwork
  - Panhypoproteinemia
  - Hypocholesterolemia
  - Low normal BUN
  - Normal liver values
  - Normal UA
  - Normal cortisol

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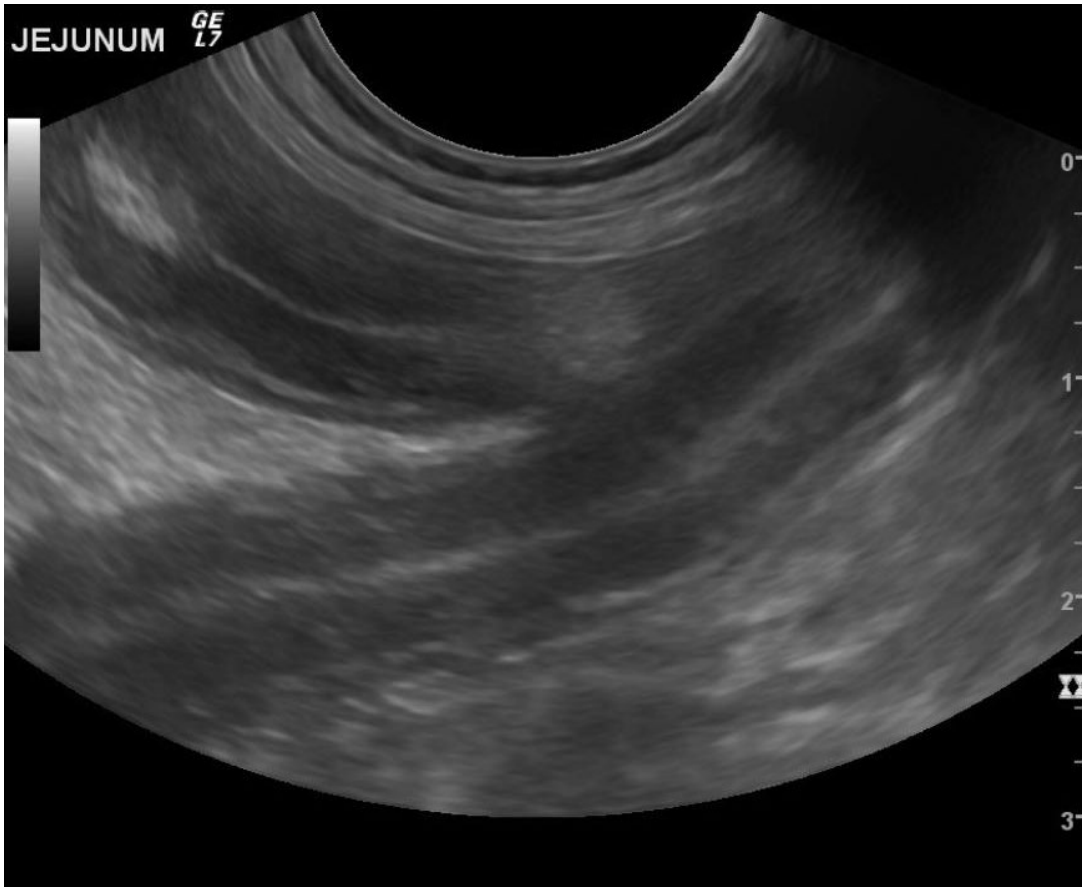
Ultrasound Findings

- Severe generalized thickening
- Hyperechoic mucosal wall speckling and linear hyperechoic striations
- Consistent with severe inflammatory bowel disease and primary or secondary lymphangiectasia.



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Tx Response

- Home on ULFD, no other GI meds
- Immediate response appreciated
- 6 month recheck:
  - CCECAI: 2 from 10
  - Albumin: 2.7 from 1.3
  - Linear striations: Resolved

2018 | **MAR 2** | **FEB 14** | **FEB 14** | **FEB 14**

	3/2/18 (Order Received) **3/2/18 12:00 PM** (Last Updated)	**IDEXX Reference Laboratories** Result Details	2/14/18
BUN	18	9 - 31 mg/dL	12
Total Protein	5.9	5.5 - 7.5 g/dL	**3.8**
Albumin	**2.3**	**2.7 - 3.9 g/dL**	e **1.3**
Globulin	3.6	2.4 - 4.0 g/dL	2.5
Cholesterol	143	131 - 345 mg/dL	**119**

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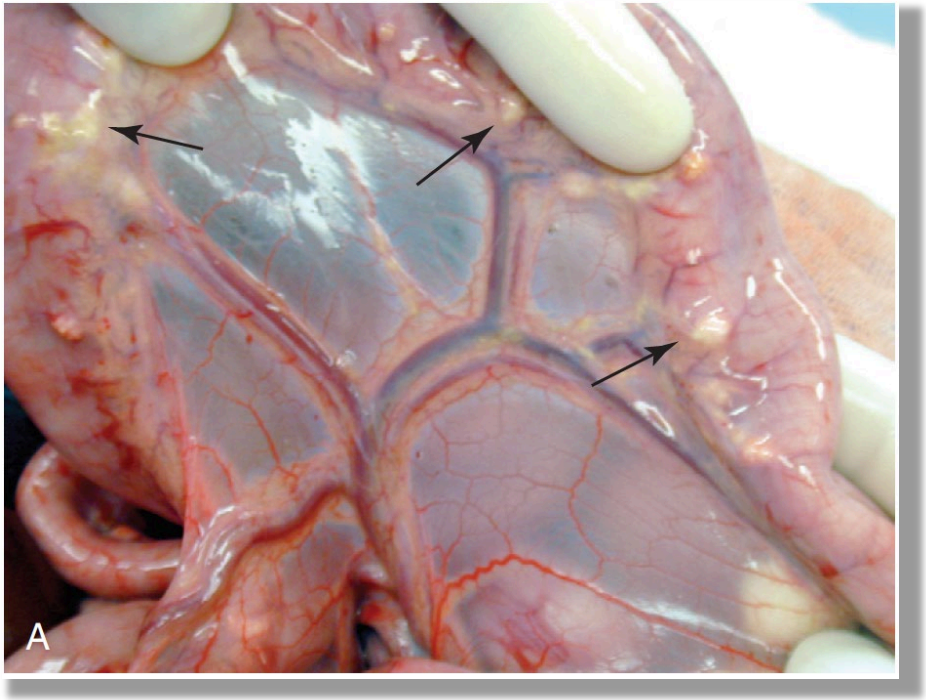
Summary and Take-Home Points

- Mechanisms of PLE:
  - Lymphatic Rupture
  - Mucosal Permeability
  - Mechanical
- Lymphangiectasia:
  - Primary vs Secondary
  - Low Fat Diet Therapy
    - Okanishi 2014
    - Rudinsky 2017
    - Myers 2020
- Prognosis: guarded
  - ~50% case fatality rate
  - Albumin, CCECAI, BUN, primary vs secondary lymphangiectasia, Vit D
- Individualized treatment plans indicated



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Addenda: Generalized Diet Recommendation

Home-cooked Ultra-low Fat Diet Options (adapted from Schench 2010)

1. Turkey and Pasta

Ingredient	Amount
Turkey, white meat, without skin, cooked	6 ounces
Pasta, enriched, cooked	3 cups
Canola oil	1 teaspoon
Salt substitute (potassium chloride)	½ teaspoon
Adult TUMS (Calcium Carbonate 500mg)	1 tablet
Salt, iodized (sodium chloride)	1 teaspoon
Multivitamin & mineral tablet, kids complete	1 tablet
Zinc, 100mg tablet	½ tablet

Prepared weight (approximately) = 610g
Total kcal as prepared = 976

Nutrient	DM%	% of KCal
Protein	32	31
Fat	6	14
Carbohydrate	55	54
Fiber	3.2	0

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Addenda: Individualized Dietary Recommendation

Home cooked diet for Chloe S**

The following is an option for a low-fat, high protein, novel protein home-cooked diet (please multiply based on amount of food needed)

1 cup steel cut oats *675kCal (can substitute white rice or millet)

1 cup white, red, or black quinoa *626kCal

1 medium sized sweet potato, any variety *115kCal

1.5 pounds tilapia filets *872kCal (can substitute ground venison, elk, or rabbit meat)

1 teaspoon sea salt
3 teaspoons Calcium Carbonate powder (NOW pharmaceuticals, or other manufacturer)
3 teaspoons Glutamine (Thorne Research, or other manufacturer) **
6 pumps of Salmon fish oil *180kCal (Alaska Naturals Wild Alaskan Salmon Oil Natural Dog Supplement available on Chewy.com)
3 heaping tablespoons Pure WHEY Protein powder *200kCal

2 daily multi-vitamins (Vetriscience Senior Multivitamin for Dogs, or other manufacturer)
Vitamin D3 400 IU every other day (available from Solgar Pharmaceuticals, or other manufacturer)

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Addenda: CCECAI

Attitude/activity
0 normal
1 slightly decreased
2 moderately decreased
3 severely decreased

Appetite
0 normal
1 slightly decreased
2 moderately decreased
3 severely decreased

Vomiting
0 normal
1 mild (1x/wk)
2 moderate (2–3x/wk)
3 severe (>3x/wk)

Stool consistency
0 normal
1 slightly soft feces
2 very soft feces
3 watery diarrhea

Stool frequency
0 normal
1 slightly increased (2–3x/d) or fecal blood, mucus or both
2 moderately increased (4–5x/d)
3 severely increased (>5x/d)

Weight loss
0 none
1 mild (<5%)
2 moderate (5–10%)
3 severe (>10%)

Albumin levels
0 albumin >20g/L
1 albumin 15–19.9 g/L
2 albumin 12–14.9 g/L
3 albumin <12 g/L

Ascites and peripheral edema
0 none
1 mild ascites or peripheral edema
2 moderate amount of ascites/peripheral edema
3 severe ascites/pleural effusion and peripheral edema

Pruritus
0 no pruritus
1 occasional episodes of itching
2 regular episodes of itching, but stops when dog is asleep
3 dog regularly wakes up because of itching

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Poll Question 1:

What is the name of the central channel in the villus tip through which lymph is transported?

a) Central lymph channel
b) Lymphatic vessel
c) Lymphoblastic vessel
d) Lacteal

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Poll Question 2:

What ultrasound finding is most commonly associated with lymphangiectasia?

a) Linear striations, hyperechoic
b) Mucosal speckling, hyperechoic
c) Loss of wall layering of small intestine
d) Jejunal plication

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Poll Question 3:

What is the gold standard for a diagnosis of PLE?

a) Bloodwork plus ultrasound
b) Biopsy of the duodenum
c) Segmental intestinal biopsy
d) Bile acids assay

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Poll Question 4:

What's the prognosis for a dog with minimal symptoms that is newly diagnosed with PLE?

a) Poor
b) Guarded
c) Fair
d) Good

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Poll Question 5:

What breed of dog has been associated with resolution of PLE via dietary therapy alone?

a) Yorkshire Terrier
b) Miniature Schnauzer
c) Portuguese Water Dog
d) English Bulldog

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Questions?

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