PURINA® PRO PLAN® SYMPOSIUM 2025

Integrative Approach to Gastrointestinal Health

Protein - Losing Enteropathy in Canines - Where Are We in 2025?

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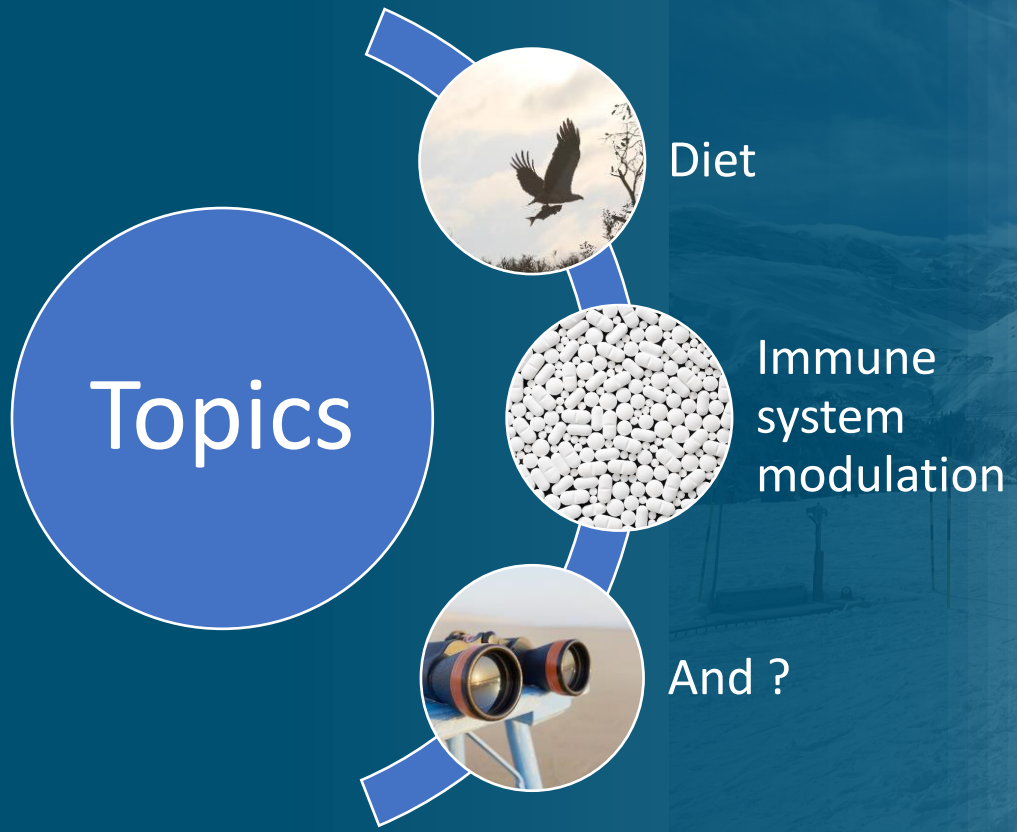
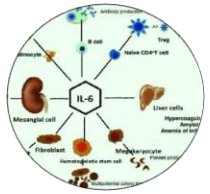
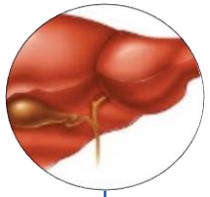


www.ed.ac.uk/vet

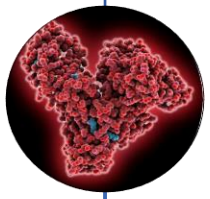
Causes of hypoalbuminaemia



Inflammation



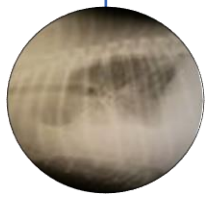
Liver



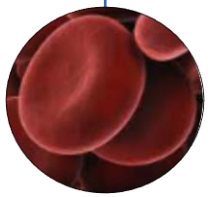
Albumin

Dilution

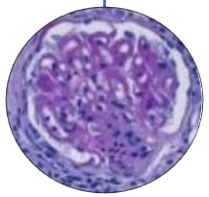
Skin loss



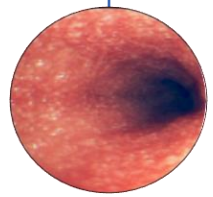
3rd space



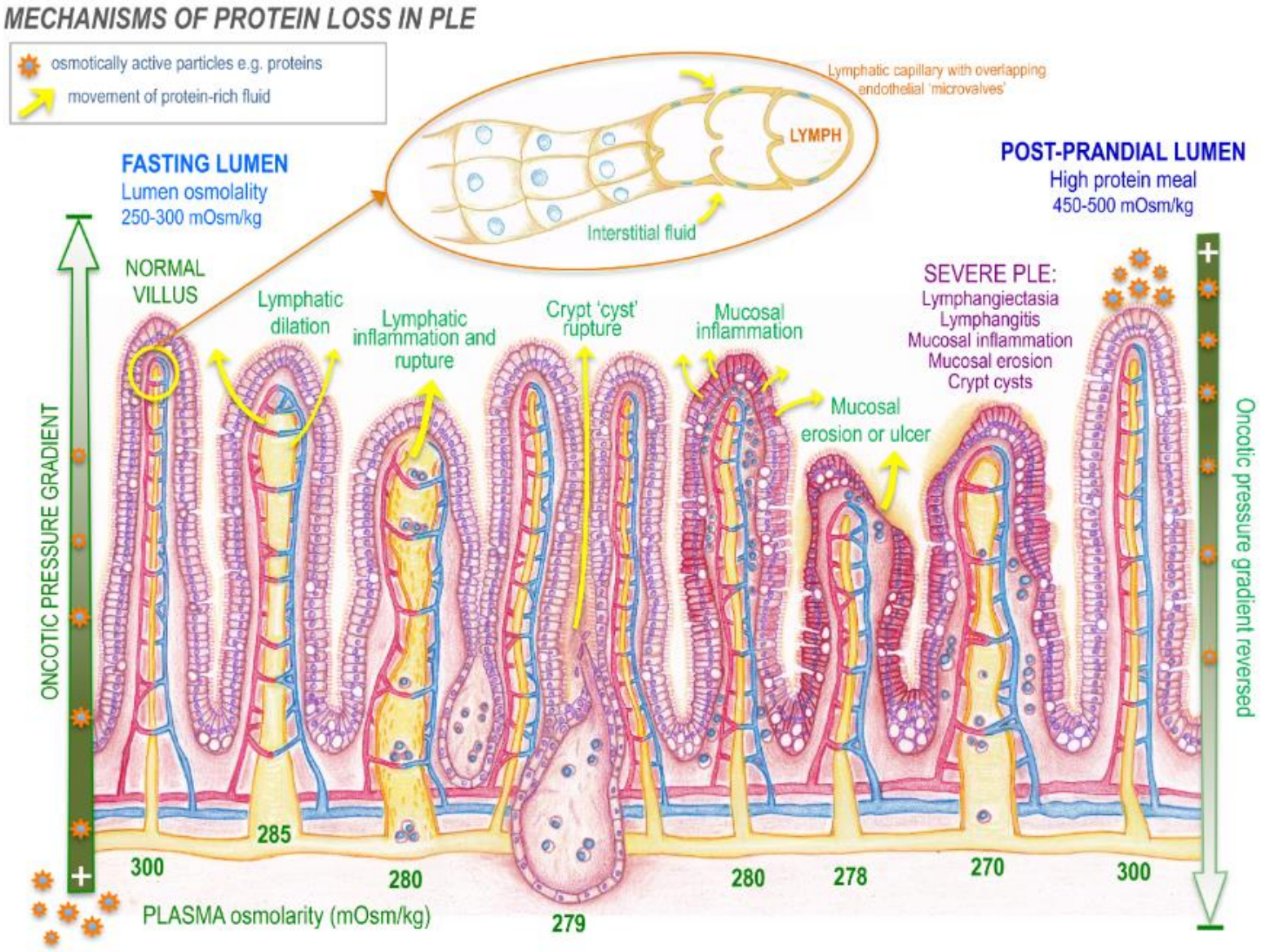
Blood loss

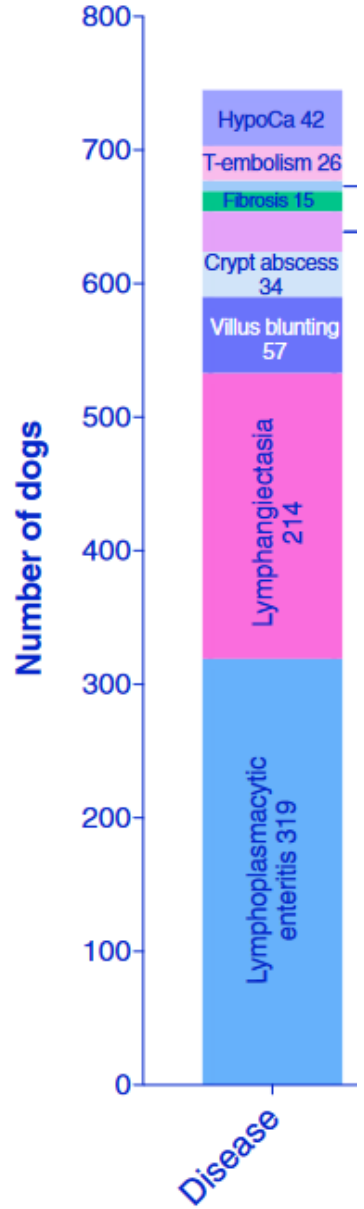


PLN



PLE





Craven 2019 – DOI: 10.1111/jvim.15406

1-4 120

Time bomb !?!?!?

You have diagnosed this dog with PLE secondary to CIE. What treatment(s) do you consider to start with?

- Low fat diet
- Hydrolysed diet
- Home-cooked diet
- Prednisolone
- Other immuno-modulator
- Antibiotic
- Anti-thrombotic
- Anti-emetic
- Appetite-stimulant

Scan & Answer

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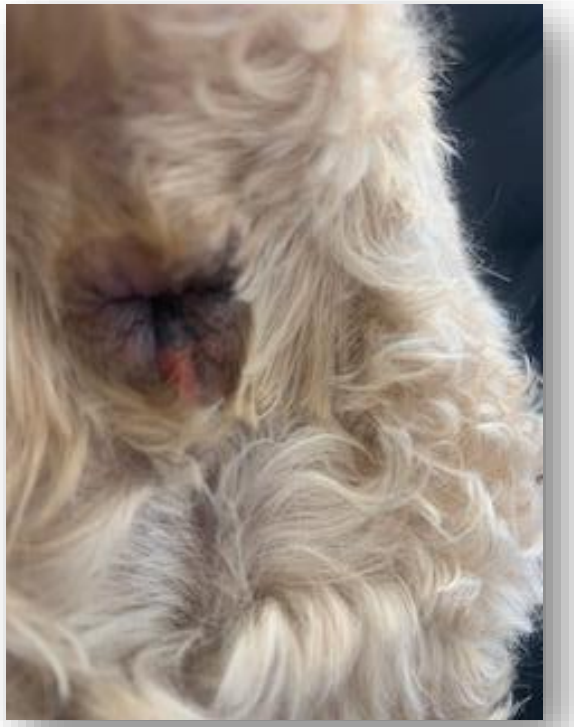
Bob, 5.5y old, MN Cavoodle – Day 0

- **Abdominal distension**
  - Soft stools, but formed. Previous history “sensible” gut. One episode of vomiting
  - Gained 1kg

- **Work up**
  - Laboratory work
  - Ultrasound (ascites)
  - Fluid analysis: transudate

- **Treatment**
  - Fenbendazole 50mg/kg PO q24h for 5 days
  - Hydrolysed diet



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Bob, 5.5y old, MN Cavoodle

- Laboratory work
  - Urinalysis: USG 1.053, protein neg.

- "Discussion with O re pros/cons of referral for advanced imaging + endoscopic biopsies vs starting pred on assumptive diagnosis of chronic enteropathy (bearing in mind will impact further diagnostics if doesn't respond). O feels best option to continue medical management here."

Parameter	Reference	Day 0
Albumin [g/L]	23.0 – 40.0	**14**
Globulin [g/L]	25.0 – 45.0	**24**
Bilirubin [µmol/L]	≤ 5.1	1.1
Bile acids pre [µmol/L]	0.1 – 5.0	1.0
Bile acids post [µmol/L]	0.1 – 10.0	3.0
TLI [µg/L]	6.1 – 35.0	**38.3**
Vitamin B12 TLI [ng/L]	≥ 275	249
Cortisol (basal) [nmol/L]	25.0 – 125.0	84.7

Bob, 5.5y old, MN Cavoodle

- **Treatment**
  - Appetite: Maropitant and Mirtazapine
  - CIE (suspected)
    - Prednisolone 2mg/kg PO q24h
    - Vitamin B12 supplementation

- **Plan – Recheck in 7 days**
  - Consider second-line immunosuppressant
  - Clopidogrel

Parameter	Reference	Day 0	Day 10	Day 23
Albumin [g/L]	23.0 – 40.0	14	**14**	**16**
Globulin [g/L]	25.0 – 45.0	24	**21**	**24**
Weight		10.3	**9.5**	**9.2**
Overall			☺	☹

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What is your experience with treating dogs diagnosed with PLE with diet alone

- It works in ≥ 50% of cases
- It works in < 50% of cases
- I don’t use food alone

Scan & Answer

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Diet – The evidence

- **The clinical efficacy of dietary fat restriction in treatment of dogs with intestinal lymphangiectasia**
  - H. Okanishi, et al – JVIM 2014, DOI: 10.1111/jvim.12327
- **Dietary management of presumptive protein-losing enteropathy in Yorkshire terriers**
  - A. J. Rudinsky et al – JSAP 2017, DOI: 10.1111/jsap.12625
- **Clinical charecteristics of dogs with food-responsive protein-losing enteropathy**
  - N. Nagata et al – JVIM 2020, DOI: 10.1111/jvim.15720
- **Prospective evaluation of low-fat diet monotherapy in dogs with presumptive protein-losing enteropathy**
  - M. Myers et al – JAAHA DOI 10.5326/JAAHA-MS-7248

Fat restriction in lymphangiectasia (histology)

Non-responders (n=10)

Steroid-dependent (n=24)

Ultra-low fat diet

Responders n=19 (79%)

Non-responders n=5

JVIM, 2014 – DOI: 10.1111/jvim.12327

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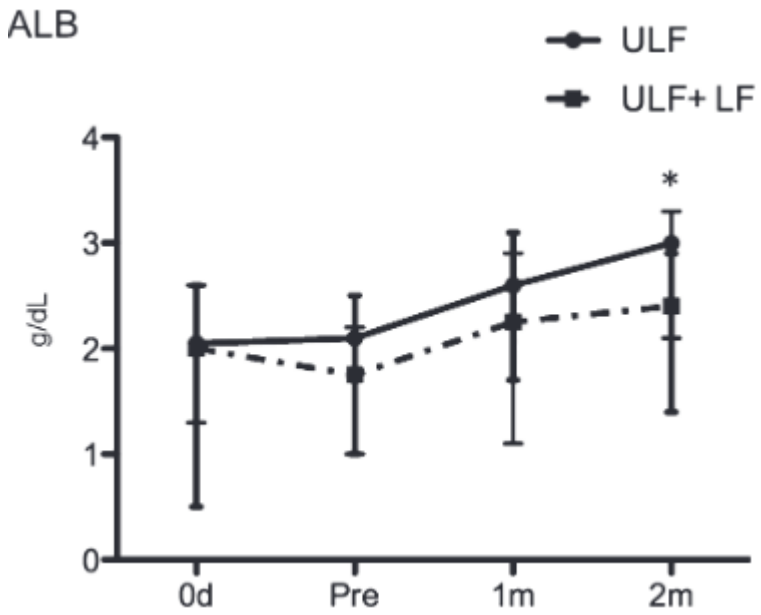
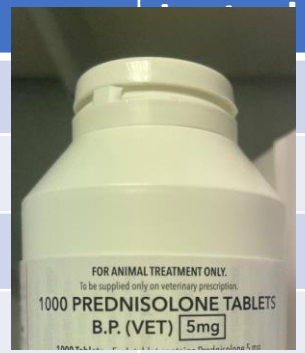
Fat restriction in lymphangiectasia (histology)



- Ultra-low fat (ULF) diet: 1 part chicken : 2 parts white potatoes, boiled.
- ULF group: fed ULF exclusively
- ULF + LF: 1 part ULF and 1 part commercial low fat diet

24 dogs	dilatio	P inflammation
Score 0	0	6
Score 1	16	12
Score 2	6	5
Score 3	2	1



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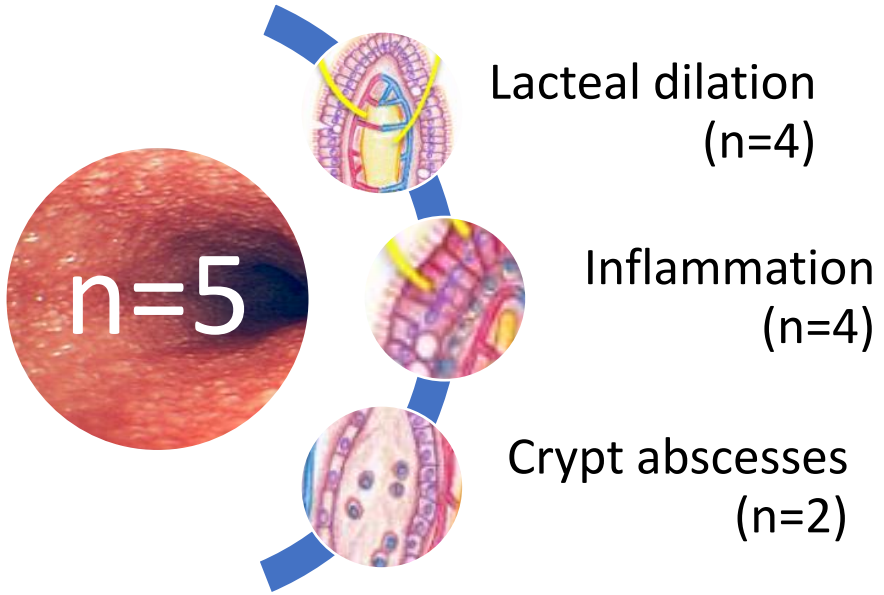
Effect of diet in Yorkshire with presumptive PLE

11 dogs	Low-fat	Home-cooked	Hydrolysed	Time to response
Responders	4	3	1	1 – 4 weeks
Partial responder	1	1		1 – 4 weeks
None-responders		1		



Craven – 2018

A. J. Rudinsky et al – JSAP 2017, DOI: 10.1111/jsap.12625

Diet

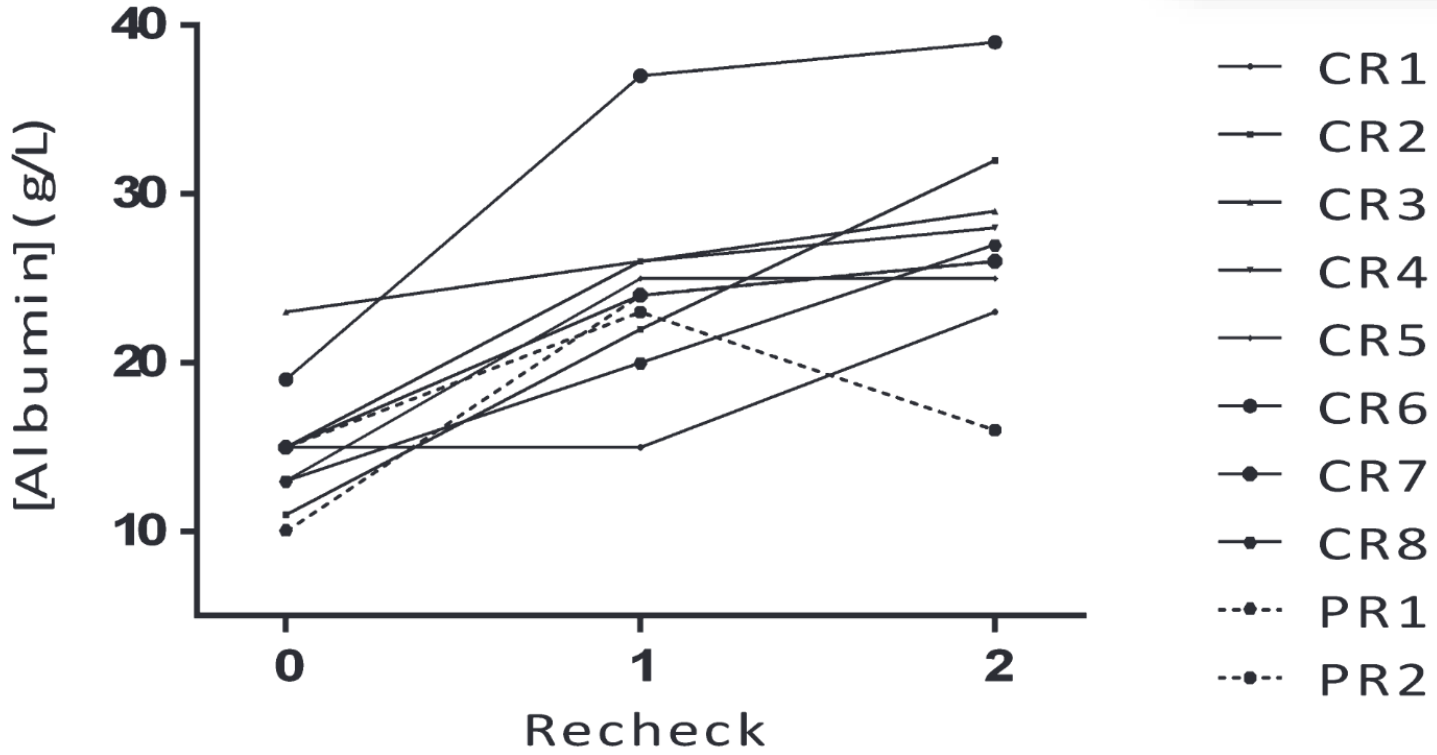


FIG 2. Change in serum albumin from baseline, recheck one (1 to 3 weeks), and recheck two (3 to 4 months). The non-responder was censored from this data due to euthanasia at 2 weeks. (CR – complete responder, PR – partial responder)

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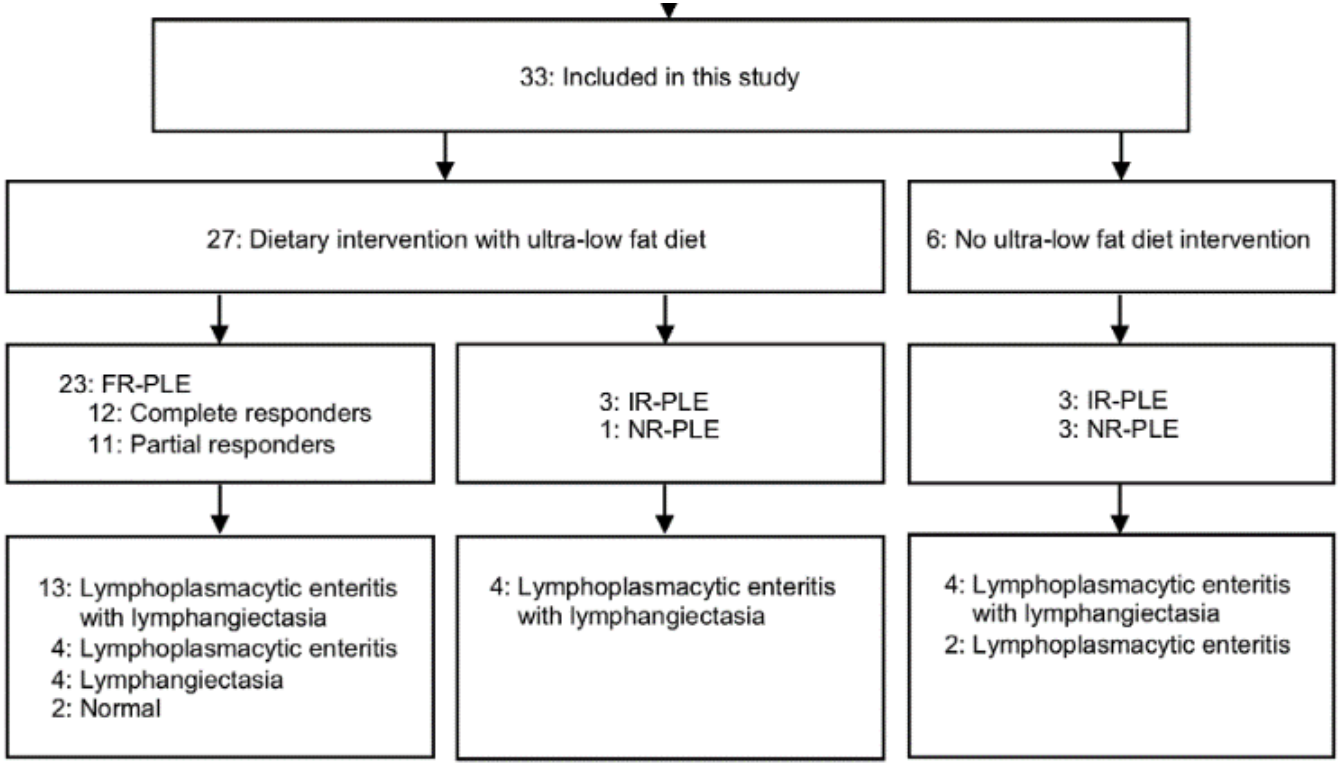
Clinical characteristics of dogs with FRE-PLE

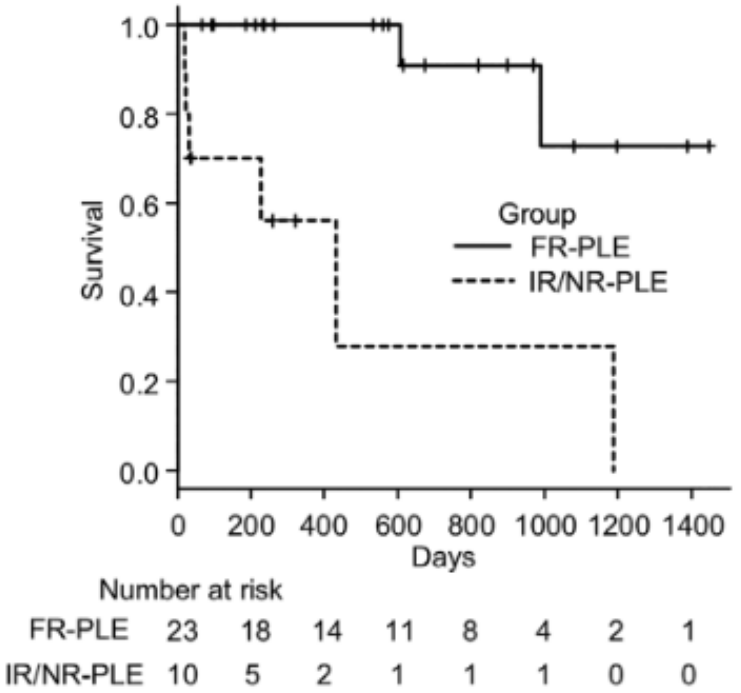
57 PLE dogs with endoscopy	
Concurrent diseases	8
No follow up	8
LCL	4
SCL	4
DOGS INCLUDED	**33**



N. Nagata et al – JVIM 2020, DOI: 10.1111/jvim.15720

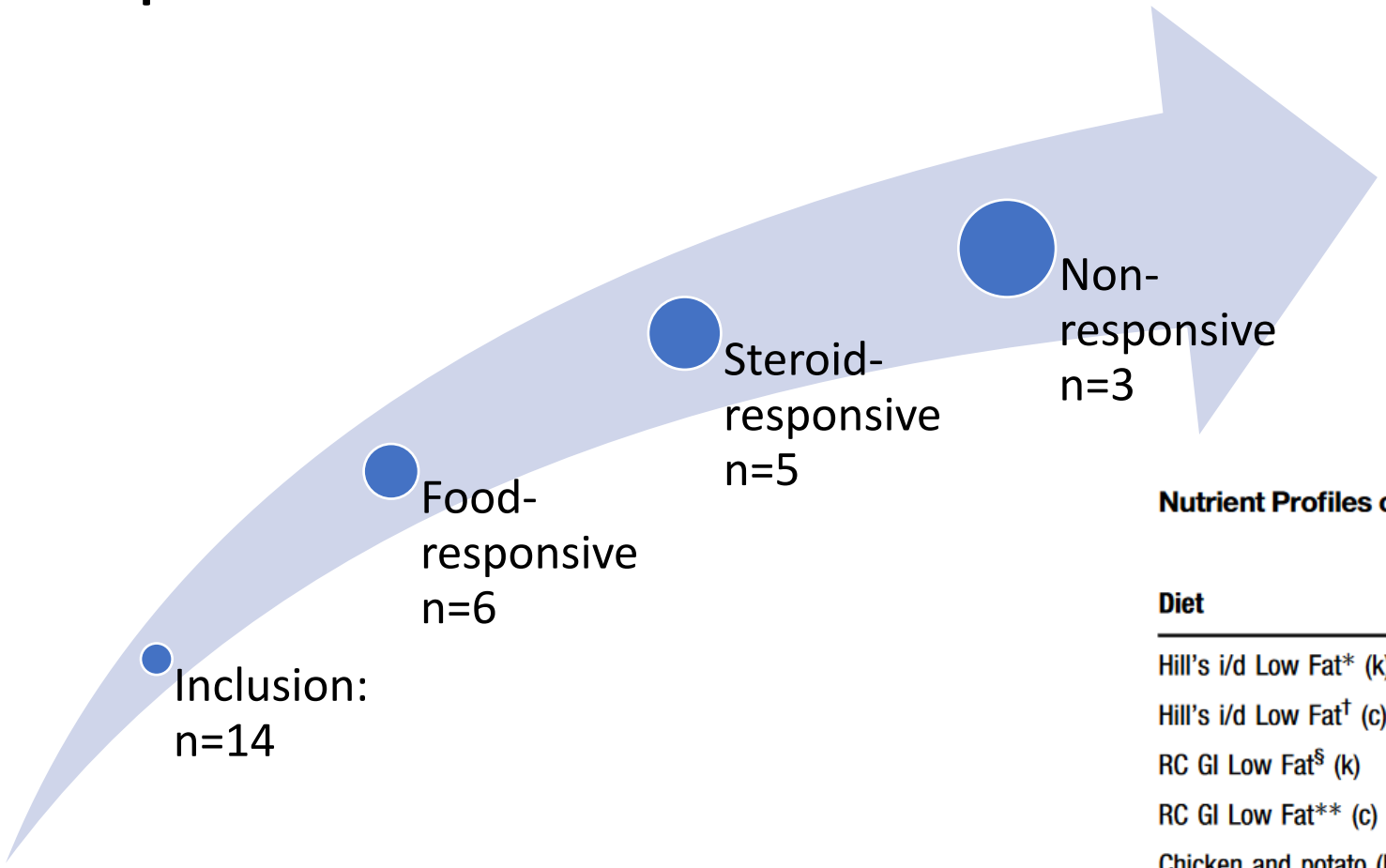
Clinical characteristics of dogs with FRE-PLE

FRE vs IRE/NRE	Cut-off	AUC (95% CI)	Sensitivity	Specificity
Age [years]	9.1	0.843 (0.698–0.989)	0.826	0.800
CIBDAI	5	0.928 (0.836–1.000)	0.913	0.778
CCECAI	8	0.935 (0.845–1.000)	0.826	0.889



N. Nagata et al – JVIM 2020, DOI: 10.1111/jvim.15720

Prospective evaluation of low-fat-diet



Nutrient Profiles of Dietary Options

Diet	Protein g/1000 kcal	Fat g/1000 kcal	Dietary Fiber g/1000 kcal
Hill's i/d Low Fat* (k)	71.0	20.0	17.0
Hill's i/d Low Fat† (c)	69.0	23.0	19.0
RC GI Low Fat§ (k)	63.3	18.7	25.1
RC GI Low Fat** (c)	79.8	18.1	28.2
Chicken and potato (hc)	84.9	13.6	11.7
Turkey and pasta (hc)	76.9	14.4	7.5

M. Myers et al – JAAHA DOI 10.5326/JAAHA-MS-7248

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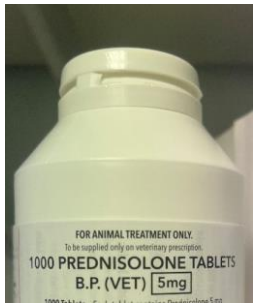
Diet – Where are we?

- Fat-restriction can be effective in dogs with lymphangiectasia
  - Primary vs secondary?
- What about the inflammatory component?
  - Hydrolysed diet?
  - Low-fat diet?
  - Home-cooked diet?
  - Hydrolysed low-fat diet?



- Food-responsive or not?
  - Age, severity of clinical signs

"Patients with PLE may benefit from both dietary fat restriction as well as a novel or hydrolysed protein source, although it is **often difficult to distinguish which dietary characteristic will provide the best clinical outcome"**

Dietary management of chronic enteropathy in dogs

M. K. Tolbert, M. Murphy, L. Gaylord and A. Witzel-Rollins

Which dog ?

When to recheck ?

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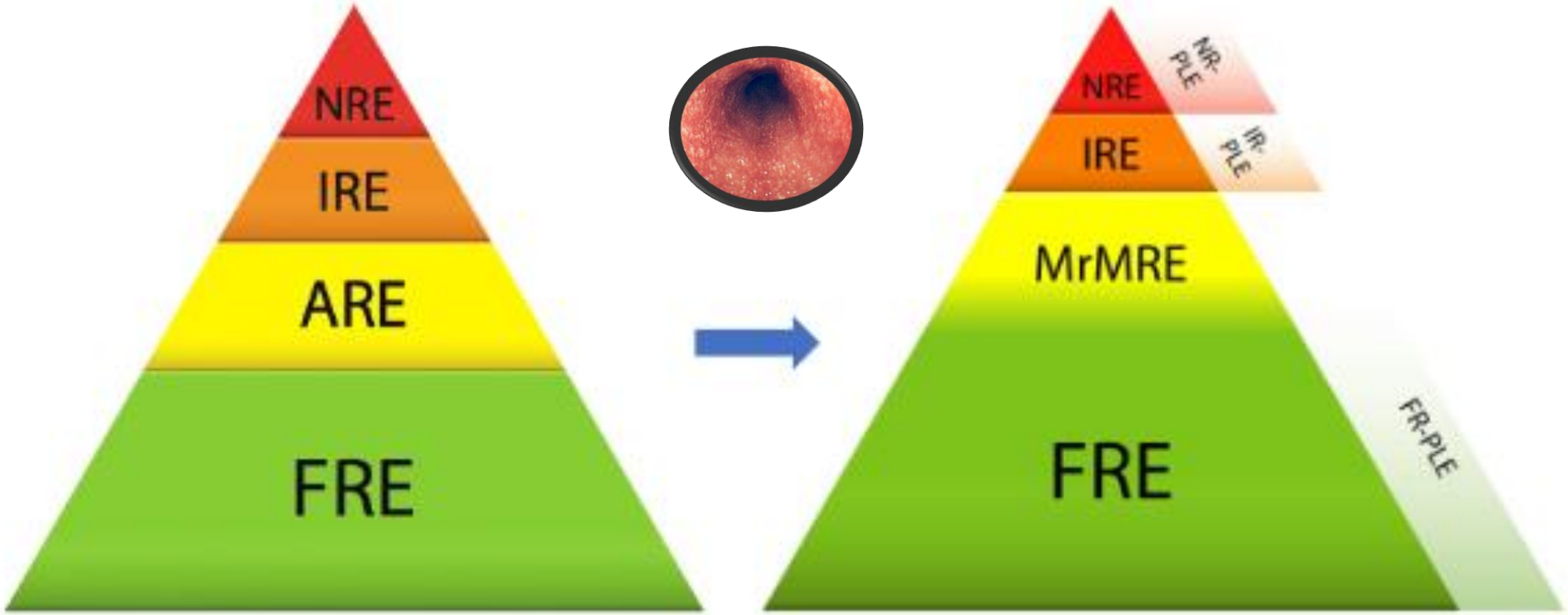
4. Proposition of a Refined Classification of CIEs in Dogs

A proposal for an updated classification of canine CIEs is depicted in Figure 2.



Dupouy-Manescau 2024 – doi.org/10.3390/ani14050681

Bob, 5.5y old, MN Cavoodle – Ultrasound

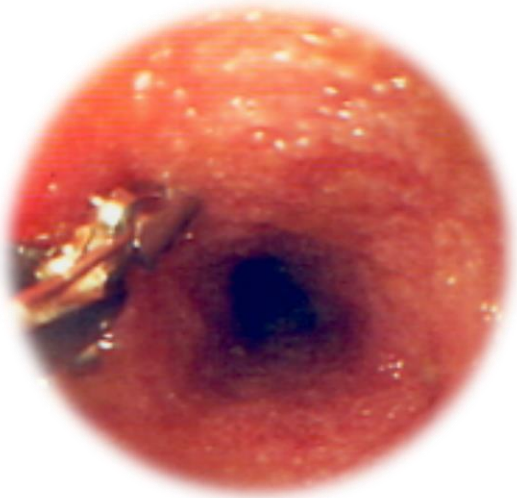
Bob, 5.5y old, MN Cavoodle – Ultrasound

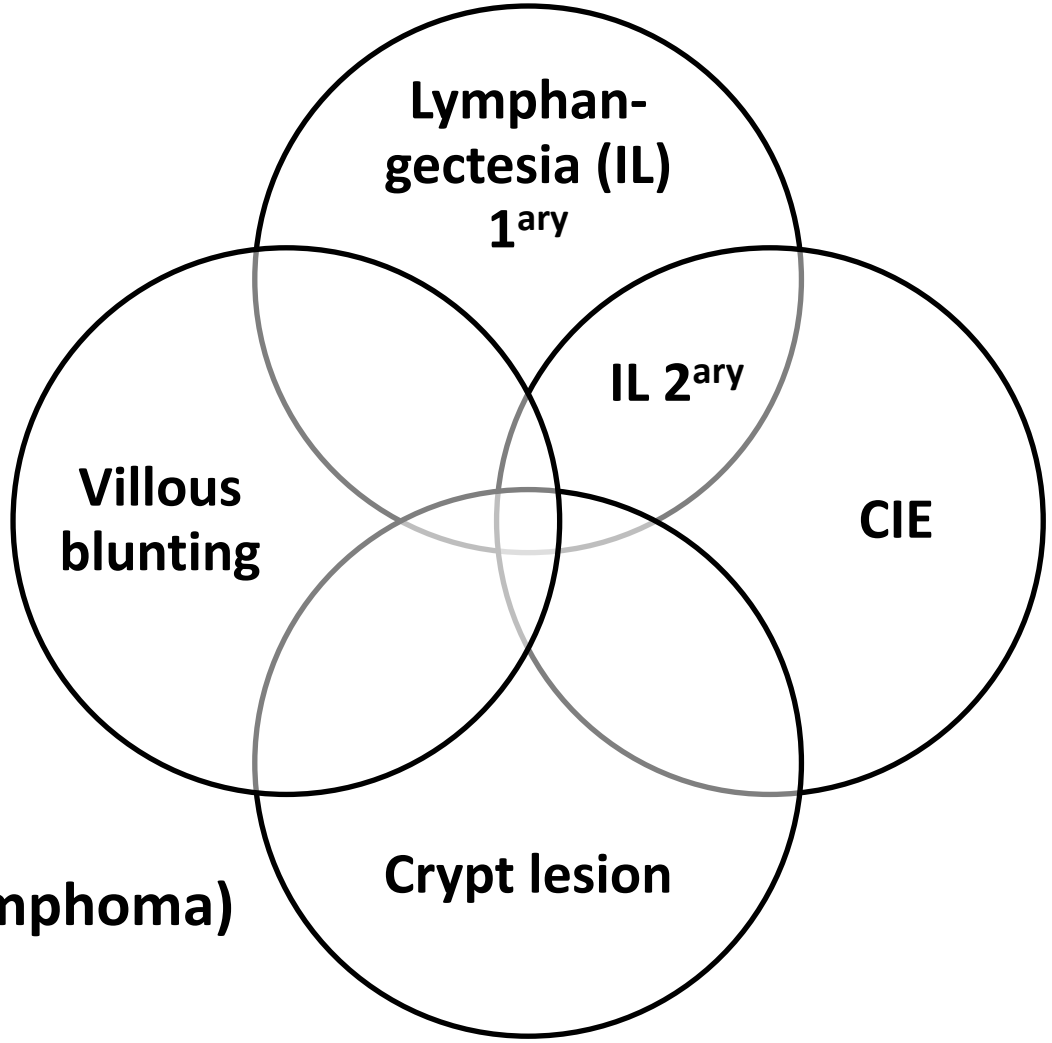
Would you consider taking biopsies in Ben's case?

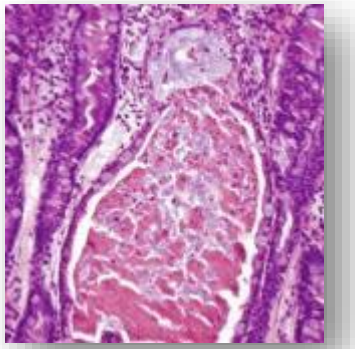
- World cloud

Scan & Answer

PLE – Consider biopsies early!





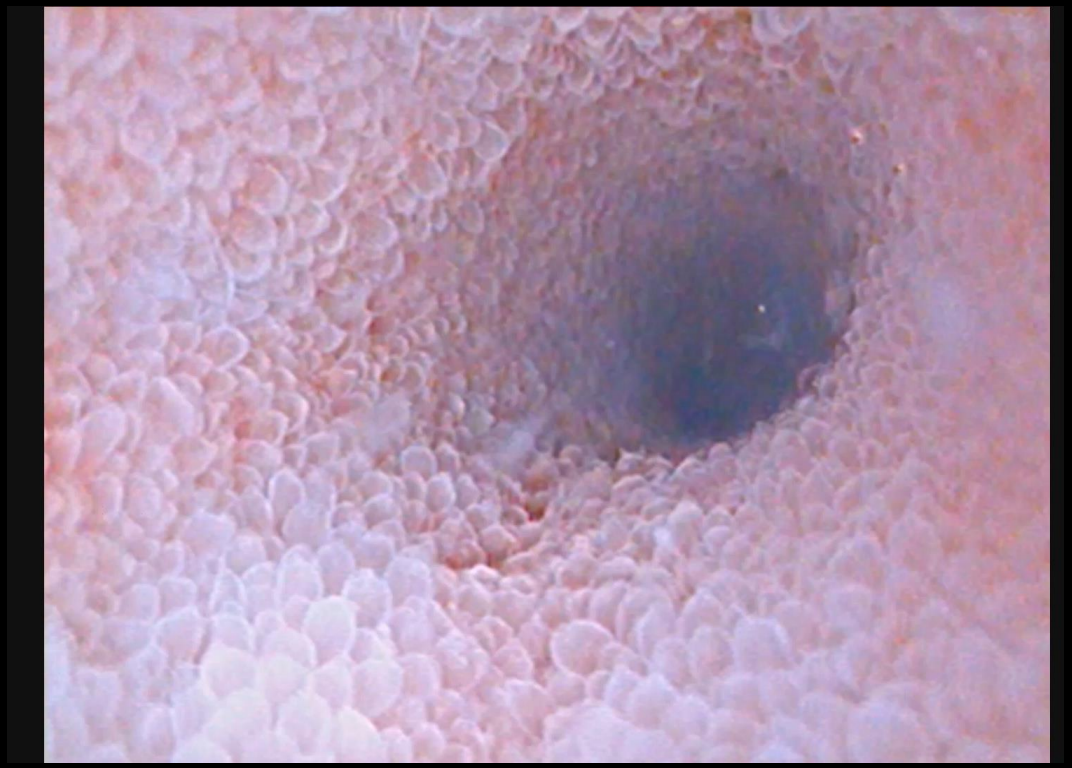


Dr. F. Gaschen ©

Rule out

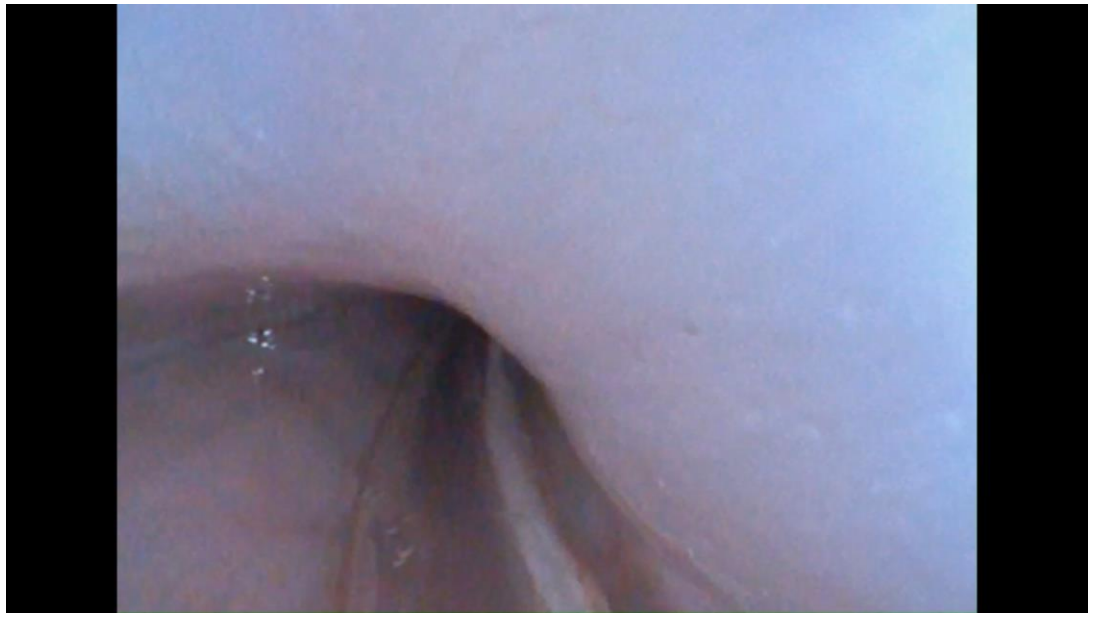
- **Neoplastic diseases (lymphoma)**
- **Ulcerative diseases**

Bob, 5.5y old, MN Cavoodle – Ultrasound



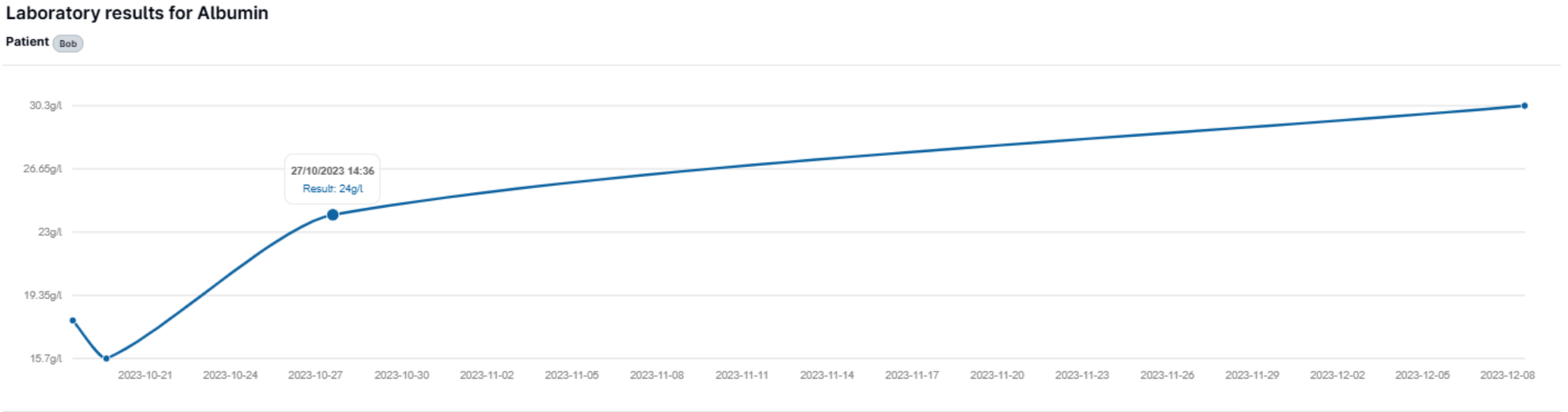
1. Mild, multifocal, chronic active, lymphoplasmacytic gastritis with mild laminal proprial oedema and haemorrhage – Stomach
2. Moderate, multifocal to coalescing, chronic, lymphoplasmacytic duodenitis with moderate crypt distention, mild lacteal dilation and mild laminal proprial oedema – Duodenum
3. Mild, multifocal to coalescing, chronic active, lymphoplasmacytic to eosinophilic ileitis with moderate lacteal dilation, mild mucosal fibrosis, mild laminal proprial oedema and minimal crypt dilation – Ileum
4. Mild, multifocal, laminal proprial oedema - Colon

Bob, 5.5y old, MN Cavoodle



- **Diet**
  - Ultra-low fat (home-cooked)
- **Inflammation**
  - Prednisolone: Reduced to 1mg/kg PO q24h
  - Chlorambucil: 5mg/m^2
- **Thromboembolism**
  - Clopidogrel: 2mg/kg PO q24h
  - Rivaroxaban: 1mg/kg PO q24h
- **Maropitant and vitamin B12**

Bob, 5.5y old, MN Cavoodle



Albumin within 2 months

Treatment after a year:
Low fat diet (commercial)… that's it!

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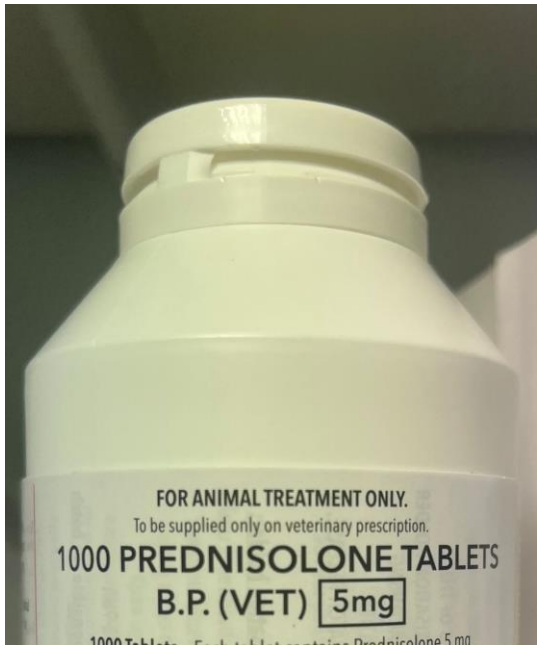
You have diagnosed a 40kg dog with chronic enteropathy that has not responded to serial treatment trials. You decide to start treatment with prednisolone. What dose of prednisolone are you considering?

1. 25mg (20mg/m^2)
2. 40mg (1mg/kg)
3. 50mg (40mg/m^2)
4. 80mg (2mg/kg)



Scan & Answer

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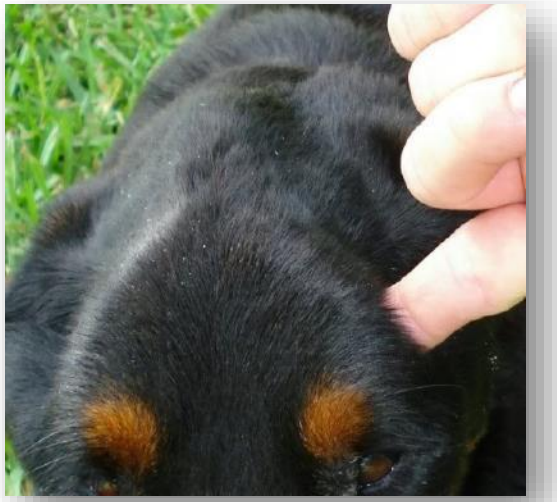
Prednisolone – Side effects?



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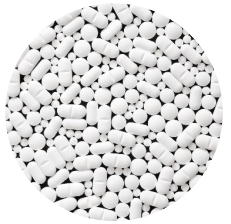
Other side effects of prednisolone

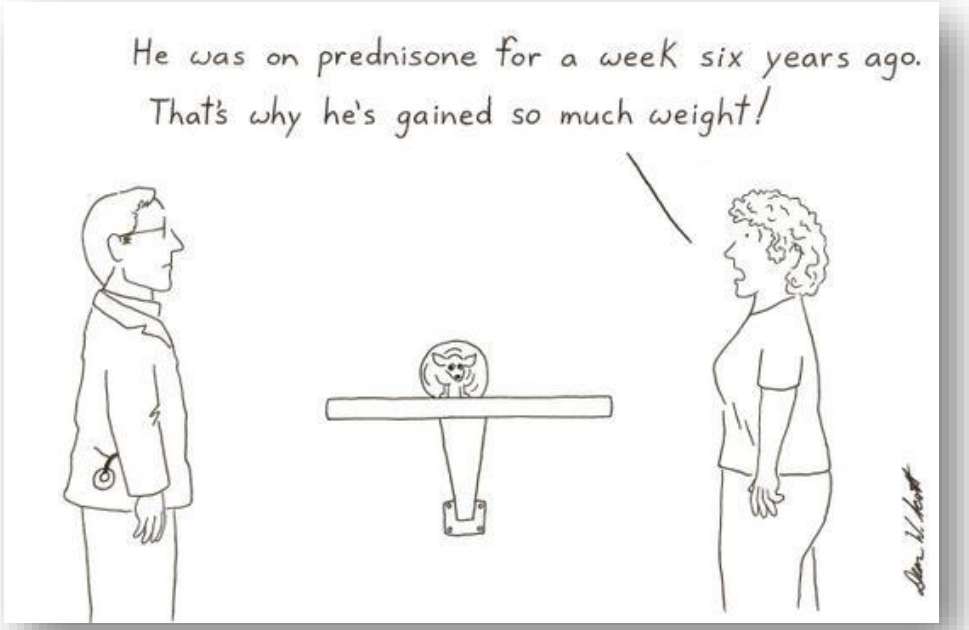


Other side effects

- Thromboembolism
- Infection
- Diabetes
- Delayed healing
- GI bleeding

Why do we use steroids?

- Cheap
- Rapid onset of action
- Does the job!



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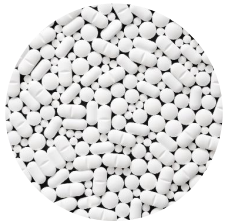
Prednisolone dosage



Small (Beagle, 10kg) vs large (mixed-breed, 29kg)

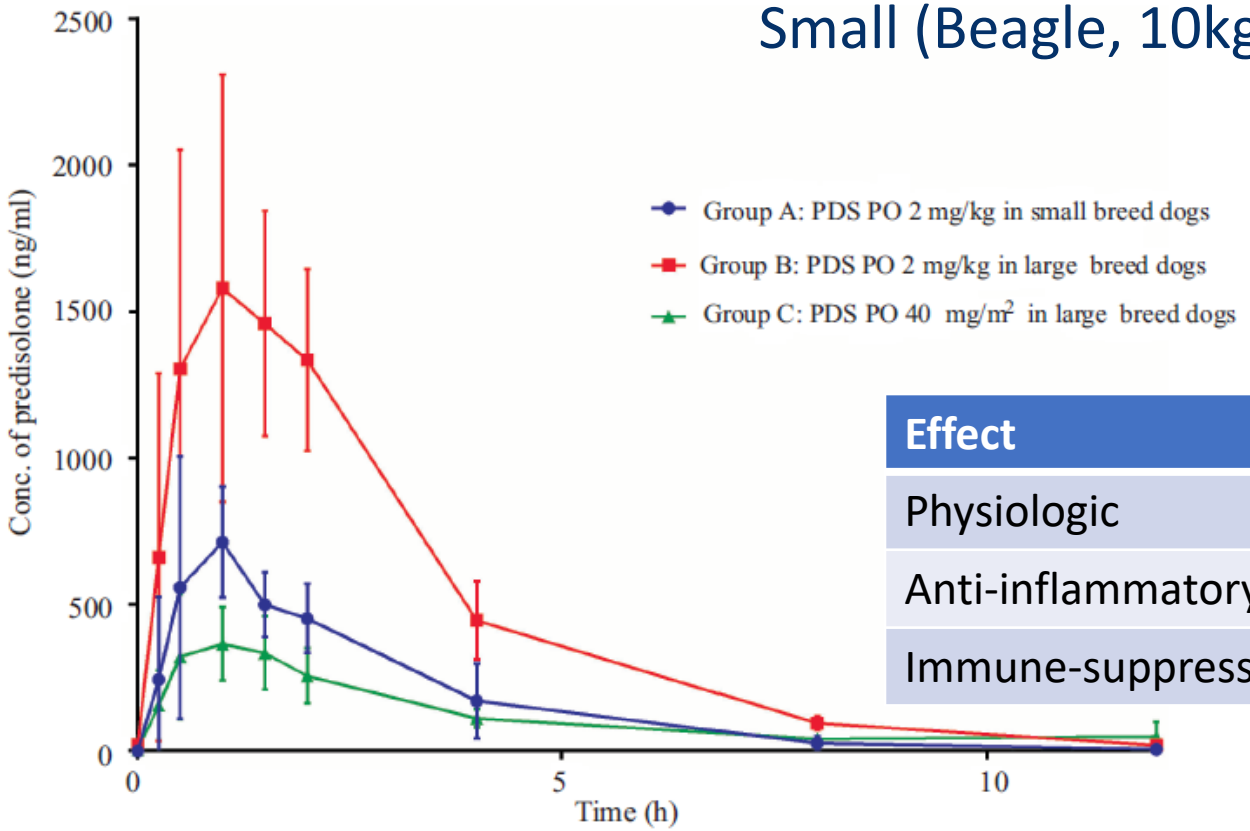


Fig. 1. Plasma concentration-time profiles of prednisolone following oral administration to small-breed dogs (Group A) and large-breed dogs (Group B and Group C).

Effect	≤ 25kg	> 25kg
Physiologic	< 0.5 mg/kg	< < 0.5 mg/kg
Anti-inflammatory	0.5 – 1 mg/kg	20 mg/m^2 ?
Immune-suppressive	1 – 2 mg/kg	40 mg/m^2

Nam 2017 – DOI 10.1515/pjvs-2017-0076

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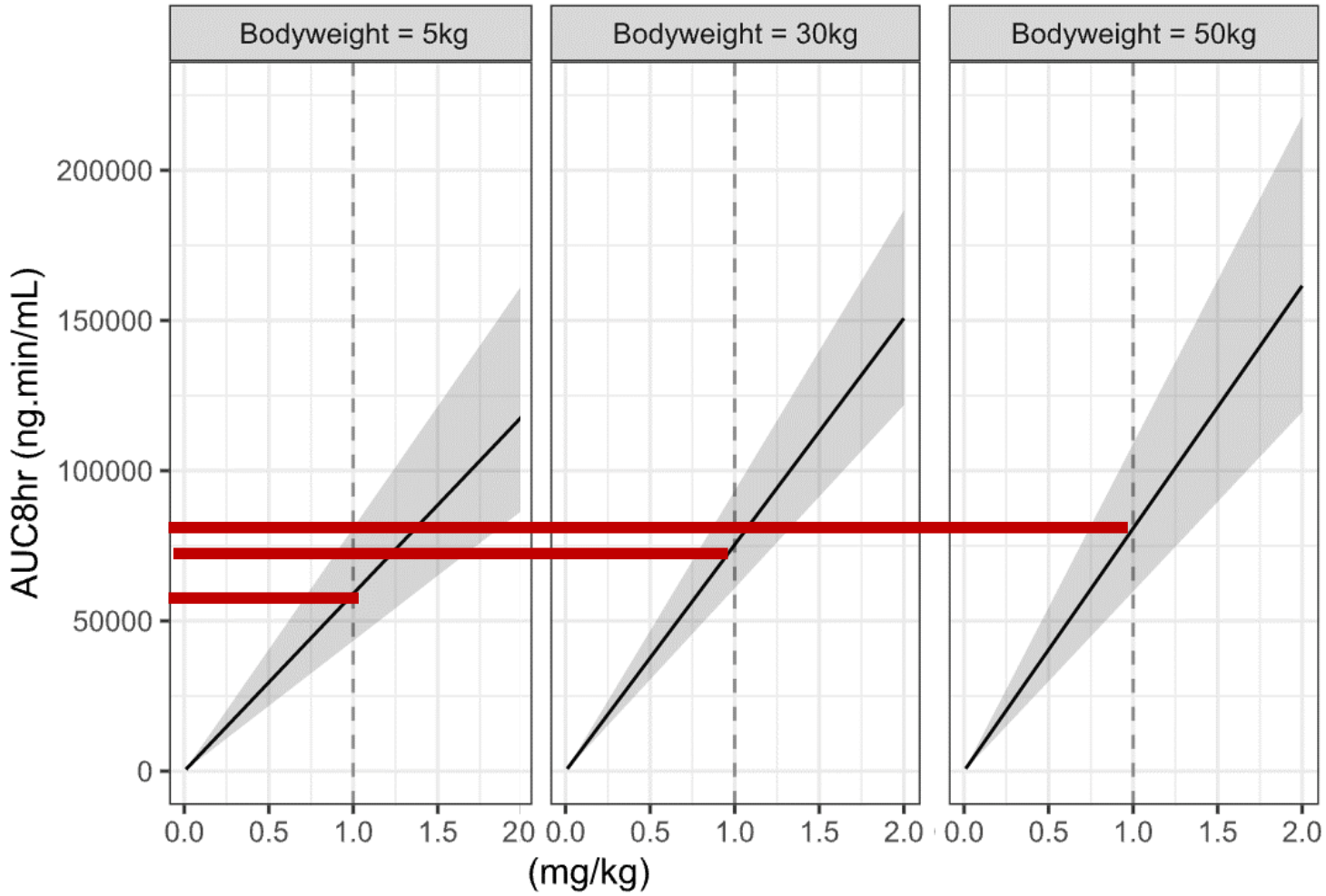
Prednisolone dosage



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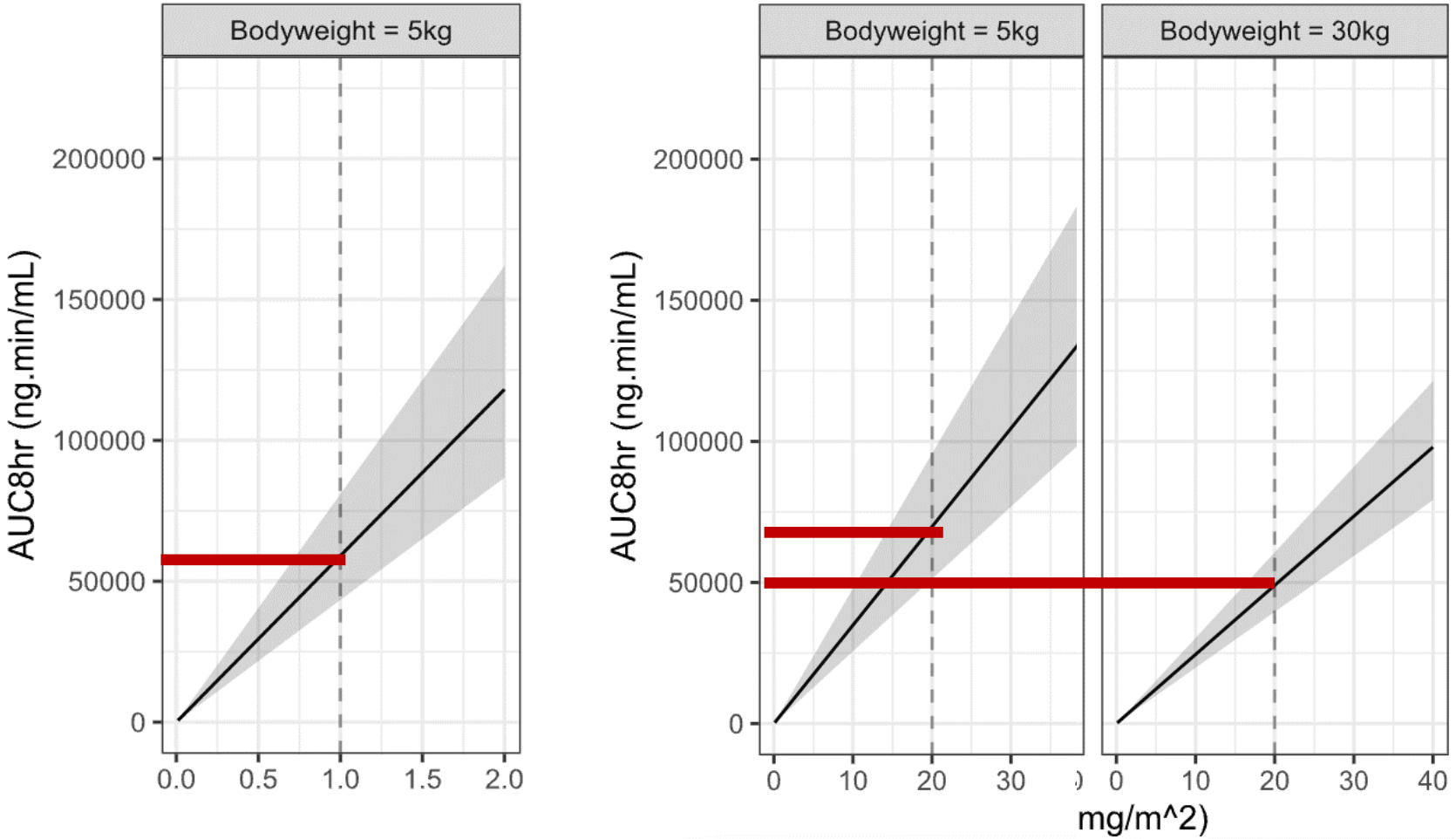
Prednisolone dosage



CIE/PLE → anti-inflammatory

- **≤ 25kg** 0.5 – 1mg/kg
- **> 25kg** ~ 20mg/m²

HOW LONG DO YOU TREAT?!?

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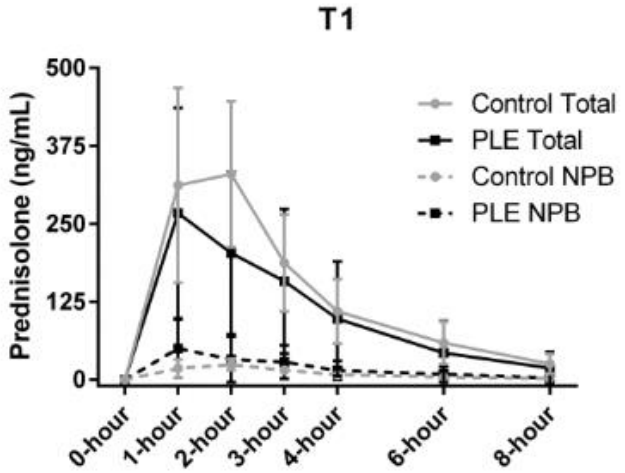
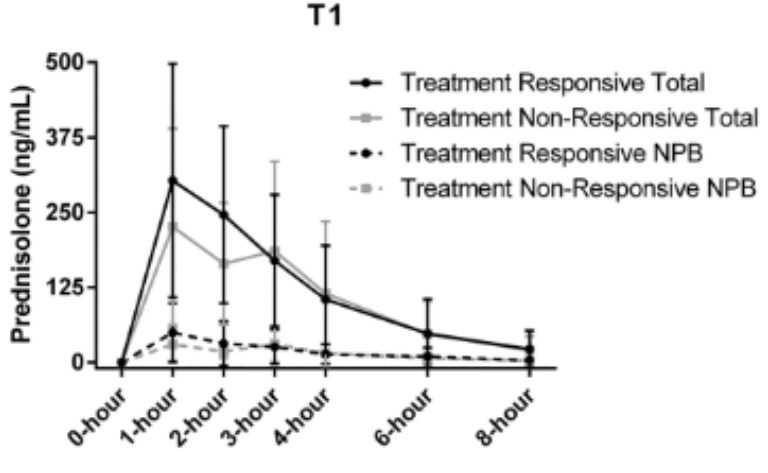
My patient does not respond to prednisolone, time for dexamethasone?

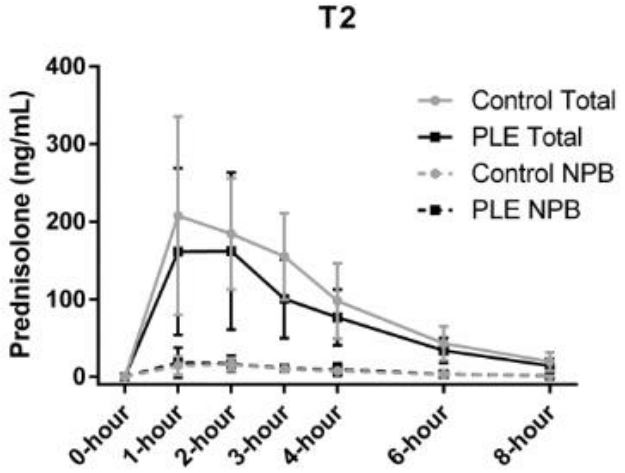
Prednisolone pharmacokinetics in dogs with protein-losing enteropathy

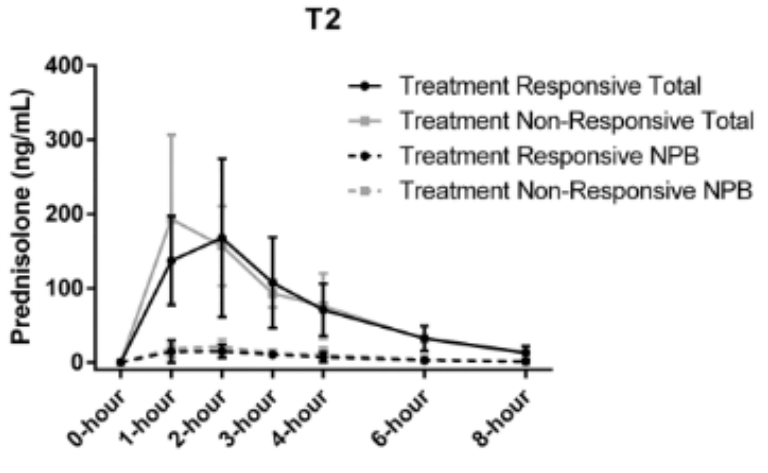
Sara A. Jablonski[1] | Jessica L. Strohmeyer[1] | John P. Buchweitz[2] | Andreas F. Lehner[3] | Daniel K. Langlois[1]

- Absorption unlikely to be an issue
- Non-responders not due to reduced prednisolone absorption









JVIM, 2024 – DOI: 10.1111/jvim.17277

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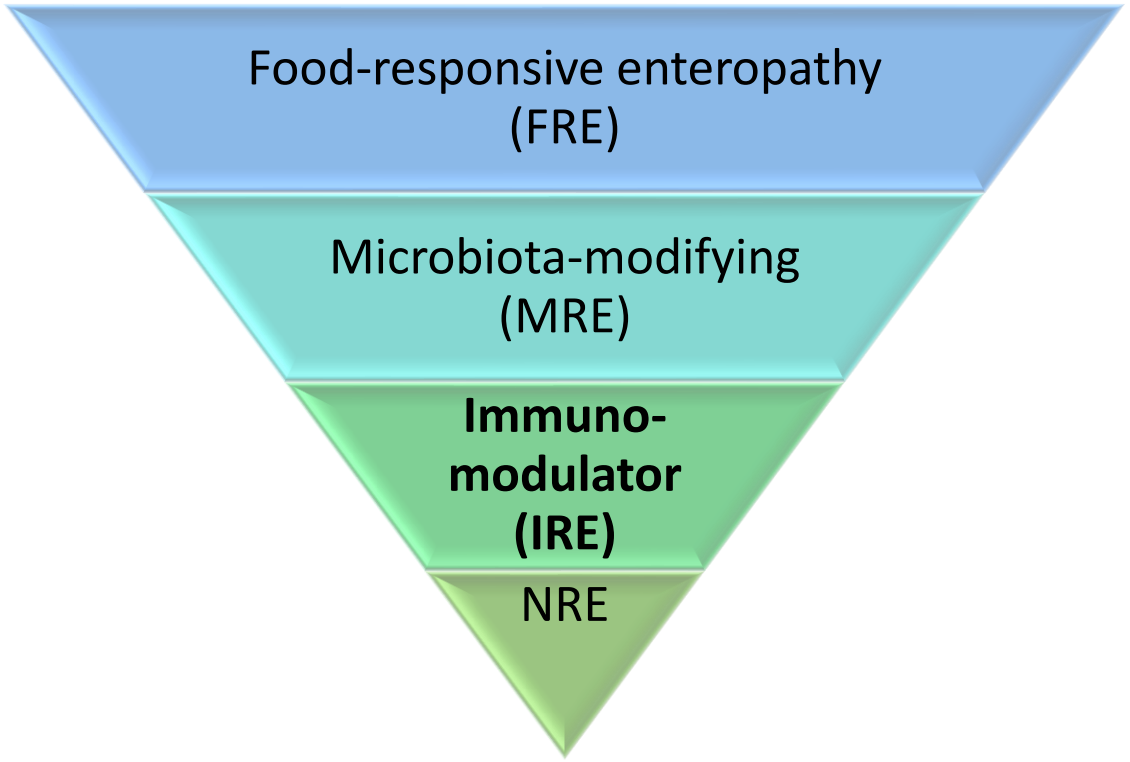
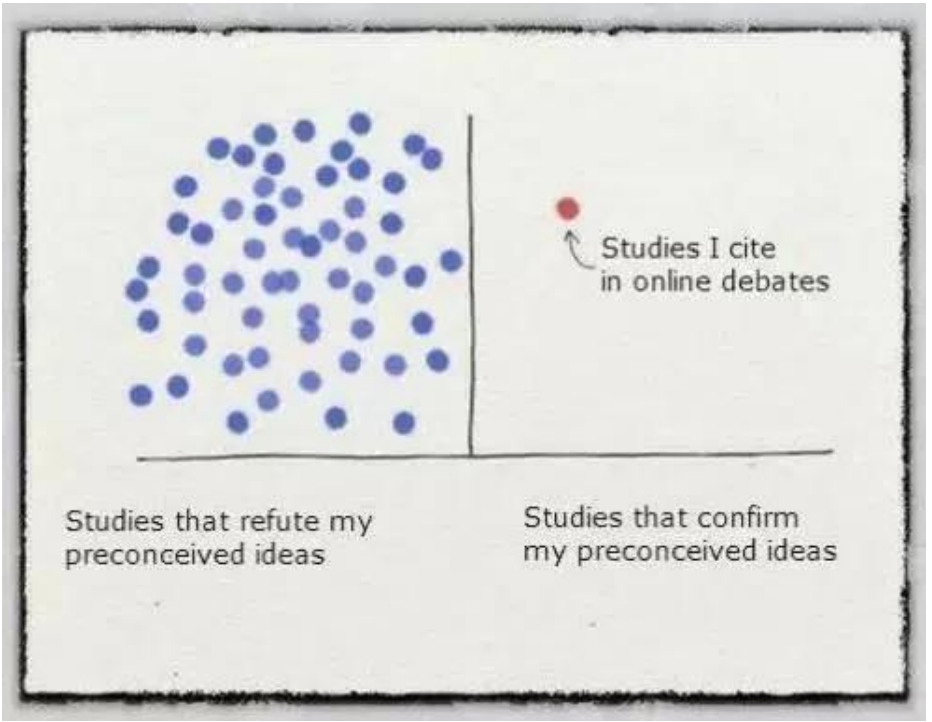
What immunomodulation to consider ?





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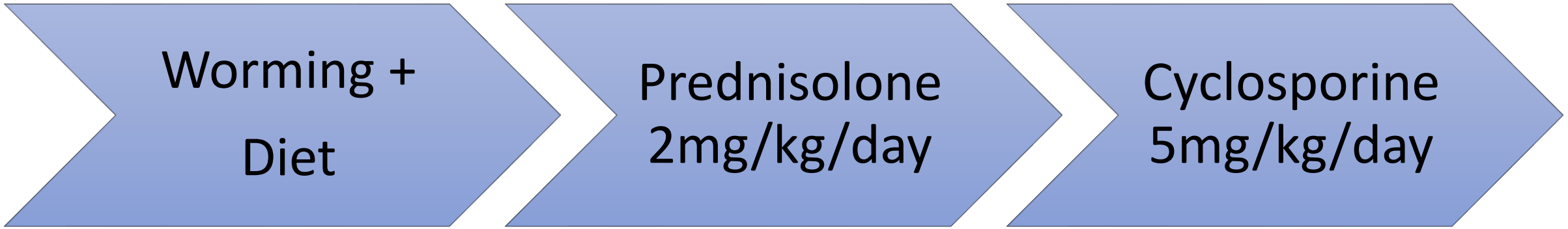
Chronic Enteropathies in Dogs: Evaluation of Risk Factors for Negative Outcome

K. Allenspach, B. Wieland, A. Gröne, and F. Gaschen

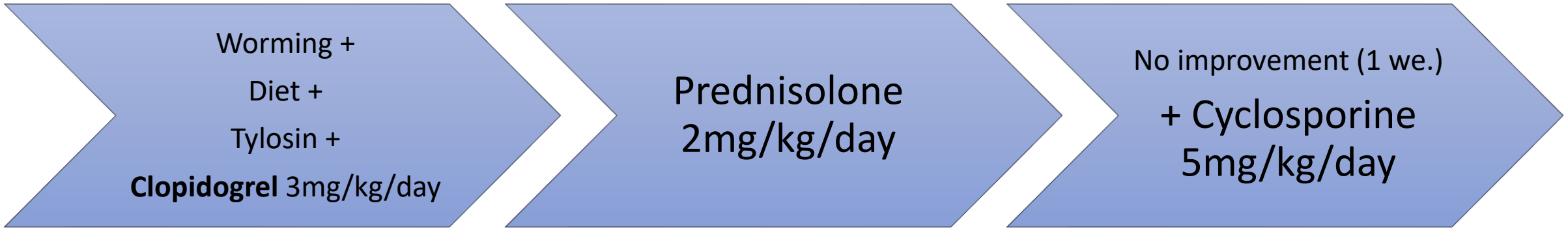


PLE dogs	n=10	n=10	n=10
Response	n=0	n=0	n=7

JVIM, 2007 – DOI: 10.1892/0891-6640(2007)21[700:ceideo]2.0.co;2

Diagnostic features, treatment, and outcome of dogs with inflammatory protein-losing enteropathy

Silke Salavati Schmitz[1] | Adam Gow[1] | Nick Bommer[1] | Linda Morrison[2] | Richard Mellanby[1]



PLE dogs	n=31	n=17	n=14
Survival		85d [13-463]	166d [8-390]

JVIM, 2019 – DOI: 10.1111/jvim.15571

Second-line immuno-modulator?

Comparison of a chlorambucil-prednisolone combination with an azathioprine-prednisolone combination for treatment of chronic enteropathy with concurrent protein-losing enteropathy in dogs: 27 cases (2007–2010)

Julien R. S. Dandrieux, Dr med vet, DACVIM; Peter-John M. Noble, BVM&S, PhD; Timothy J. Scase, BVM&S, PhD, DACVP; Peter J. Cripps, BVSc, PhD; Alexander J. German, BVSc, PhD

n=13
Worming +
Diet and

Prednisolone
2mg/kg/d [1.3-3.8]
Azathioprine
1.6mg/kg/d [0.8 – 2.3]

6-month survival
2 out of 13 dogs

n=14
Worming +
Diet and

Prednisolone
1.7mg/kg/d [1.0-2.3]
Chlorambucil
4.4mg/m^2/d [2.1-5.8]

6-month survival
12 out of 14 dogs

doi: 10.2460/javma.242.12.1705

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Considerations, when there is no response… ?

- **Re-assess diet (nutritionist)**
- **Re-assess diagnosis (imaging/biopsies)**
- **Octreotide?**

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Prospective evaluation of a change in dietary therapy in dogs with steroid-resistant protein-losing enteropathy

S. A. Wennogle[1], J. Stockman and C. B. Webb

Response	Diet prior	Diet study	Remission	Death
CR1	Hydrolysed	Low fat	30 months	
CR2	Hydrolysed	Low fat	28 months	
CR3	Hydrolysed	Hydrolysed	12 months	
CR4	Hydrolysed	Home-cooked	12 months	15 months (relapse)
CR5	Hydrolysed	Home-cooked	12 months	
CR6	Low fat	Home-cooked	48 months	
CR7	Hydrolysed	Home-cooked	12 months	
CR8	Low fat	Home-cooked	12 months	
PR1	Hydrolysed	Low fat	3 months	6 months
NR1	Hydrolysed	Low fat		1 month

- Fat-restriction (7/9)
- Limited ingredients?
- Compliance?
- Right diet?

- Improvement in 15 to 30 days
- n=3 off steroids, others <0.5mg/kg/day

JSAP 2021 - DOI: 10.1111/jsap.13334

Re-assess diet

Article

A Preliminary Study of Modulen IBD Liquid Diet in Hospitalized Dogs with Protein-Losing Enteropathy

Aarti Kathrani * and Gina Parkes

European College of Veterinary and Comparative Nutrition

American College of Veterinary Nutrition

Animals 2022, 12, 1594. https://doi.org/10.3390/ani12121594

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Low-grade gastrointestinal lymphoma in dogs?

- **Prognostic factors in dogs with PLE**
  - Nakashima, et al – TVJ 2015
  - http://dx.doi.org/10.1016/j.tvjl.2015.05.001
- **Low-grade gastrointestinal lymphoma in dogs: 20 cases (2010 to 2016)**
  - J. Lane, et al – JSAP 2017
  - DOI: 10.1111/jsap.12769
- **Clinical characteristics and outcome in dogs with small cell T-cell intestinal lymphoma**
  - Couto, et al – VCO 2017
  - DOI: 10.1111/vco.12384

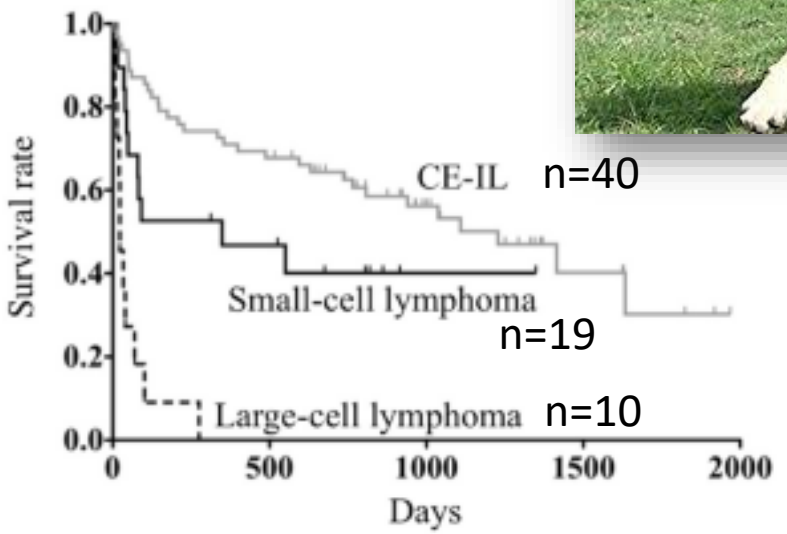

Fig. 2. Kaplan–Meier survival curves showing survival for the three histologic categories. There were significant differences in survival time between dogs diagnosed with chronic enteritis or intestinal lymphangiectasia (CE-IL) and large-cell lymphoma ($P < 0.0001$), between CE-IL and small-cell lymphoma ($P = 0.039$), and between small-cell lymphoma and large-cell lymphoma ($P = 0.0005$).

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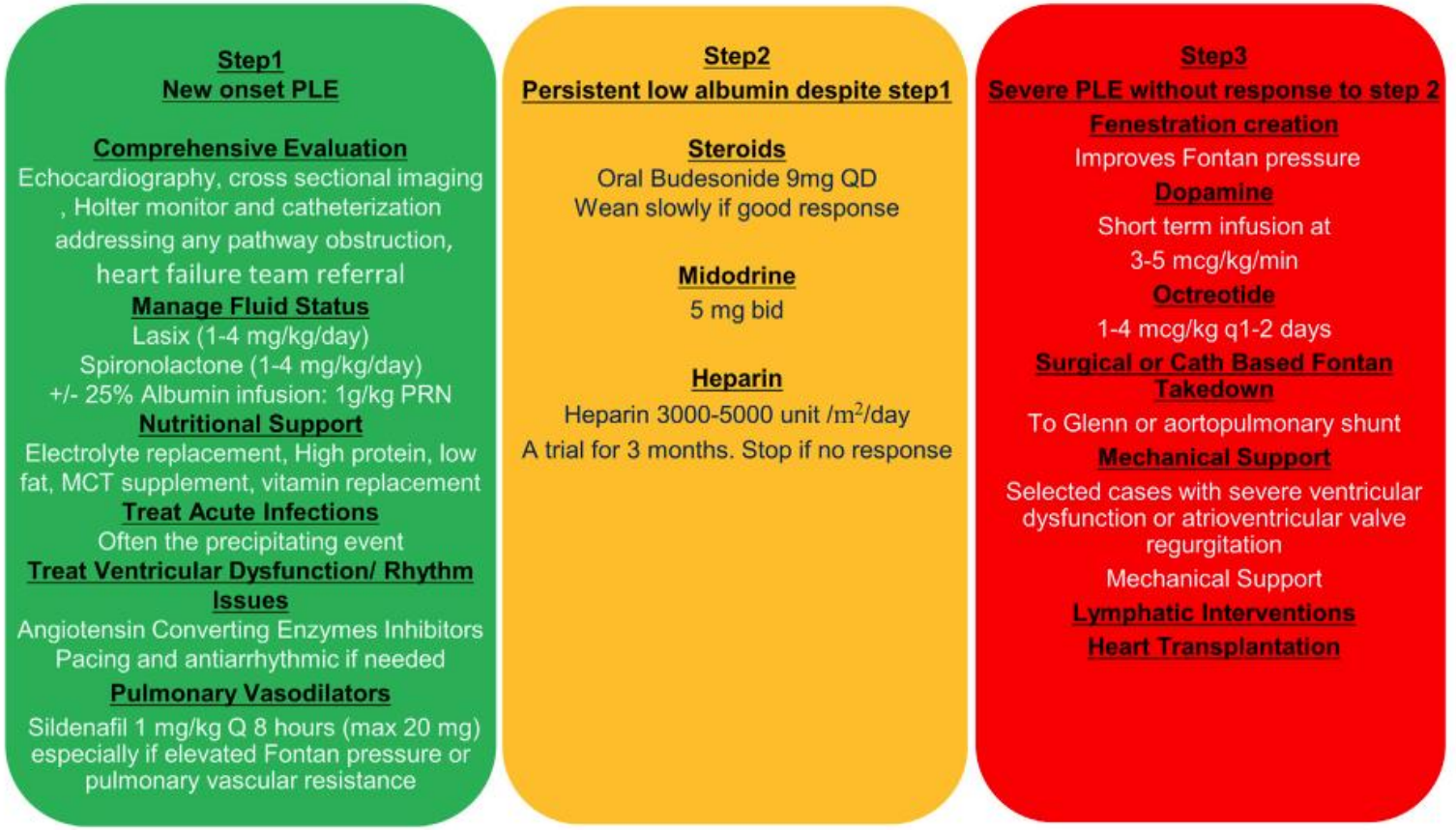
Use of octreotide

- **Somatostatin analogue**
  - Decrease gall bladder contractility
  - Reduce intestinal blood flow
  - Reduce lymphatic flow
  - Inhibit TG absorption

- **One descriptive study**
  - Improvement in 6 out of 12 dogs
    - All dogs on a low/ultra-low fat diet
    - Octreotide dose of 30 μg/kg SQ daily (30-60μg/kg)
  - AE in 3 out of 18 dogs: Pain (n=1) and diarrhoea within 30' of injection (n=2)



Alsaeid 2022 - https://doi.org/10.1016/j.ijcchd.2022.100338

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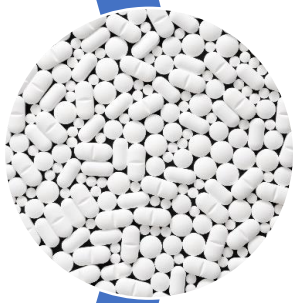
Jablonski 2023, JVIM – DOI: 10.1111/jvim.16966

Conclusion

- Central role
- Which diet?
- How many trials?



- When?
- Weight…
- Anti-inflammatory…

- Diet?
- Home-cooked?
- Diagnosis?
- LGIL?

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Thank you!