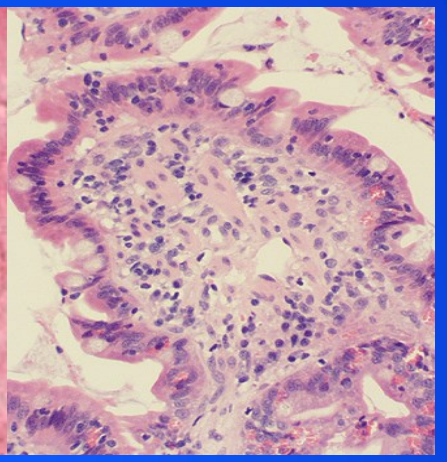
Managing Chronic Enteropathies / IBD in Dogs





K.W. Simpson

Professor of Medicine

BVM&S, PhD, DipACVIM, DipECVIM

Discosure:

Grant support:

Canine IBD / Chronic Enteropathy:

- Morris Animal Foundation
- AKC -CHF
- Nestle-Purina
- Farmina Petfoods

Scientific Advisory Board

- Nestle-Purina
- Farmina Petfoods

ITHACA

MYTHAC
A

IBD traditionally defined by histopathology

Cellular Infiltrate

Architecture

Lymphocytes/ plasma cells

Eosinophils

Neutrophils

Macrophages

Villus atrophy or fusion

Crypt hyperplasia

Crypt cysts / abscesses

Lymphangiectasia

Chronic Enteropathy is defined by response to treatment

Cbl	Diet	Antibiotic	Immuno-suppression	Non-responsive

There are many approaches……

Chronic Enteropathies / IBD — Achieving a Diagnosis

- Signalment, History, Physical Exam
- Clinical Pathology
- Imaging
- Intestinal function testing, biomarkers
- Intestinal biopsy
- Therapeutic trials

Chronic Enteropathies /IBD

- Achieving a Diagnosis
  - Signalment, Hx., PE
  - Clin path testing
    - Detect infectious / parasitic-fecal
    - Detect non-GI dz.
      - CBC, profile, UA
      - ±TLI, fT_4, ACTH stim, bile acids
    - Characterize GI disease
      - Hypoalbuminemia? Hypocalcemia? Hypocholesterolemia?
  - Imaging
    - Detect non-GI dz. — Liver, spleen, pancreas, lymph nodes
    - Characterize GI disease — Masses, thickening, FB, intussusception, loss of layering, hyperechoic striations
  - Intestinal function testing, biomarkers
    - Cobalamin and folate, α-1-PI, CRP, ASCA, ANCA
  - Intestinal biopsy
  - Diagnosis by Treatment trial
    - Anti-parasitic, Diet, Antibiotics

Hall of Fame

- Gluten Sensitive Enteropathy

- Antibiotic Responsive Enteropathy
- ? IgA deficiency

- Immuno-proliferative Small Intestinal Disease

- Protein Losing Enteropathy, Lymphangiectasia
- Atrophic Gastritis, Gastric carcinoma

- Protein Losing Enteropathy, Lymphangiectasia, Crypt Lesions

- Protein Losing Enteropathy, Lymphangiectasia, and Nephropathy

- Cobalamin Deficiency

Laboratory Evaluation CBC

- Anemia
- Microcytosis / macrocytosis
- Nucleated red cells, basophilic stippling
- Leukocytosis / leukopenia
- Eosinophilia
- Lymphocytosis / penia

Laboratory Evaluation

- **Hypoalbuminemia**
- *Albumin <2mg/dl poorer prognosis, OR 11.4
- ↑ liver enzymes
- Hypocholesterolemia
- Hyperkalemia / hyponatremia

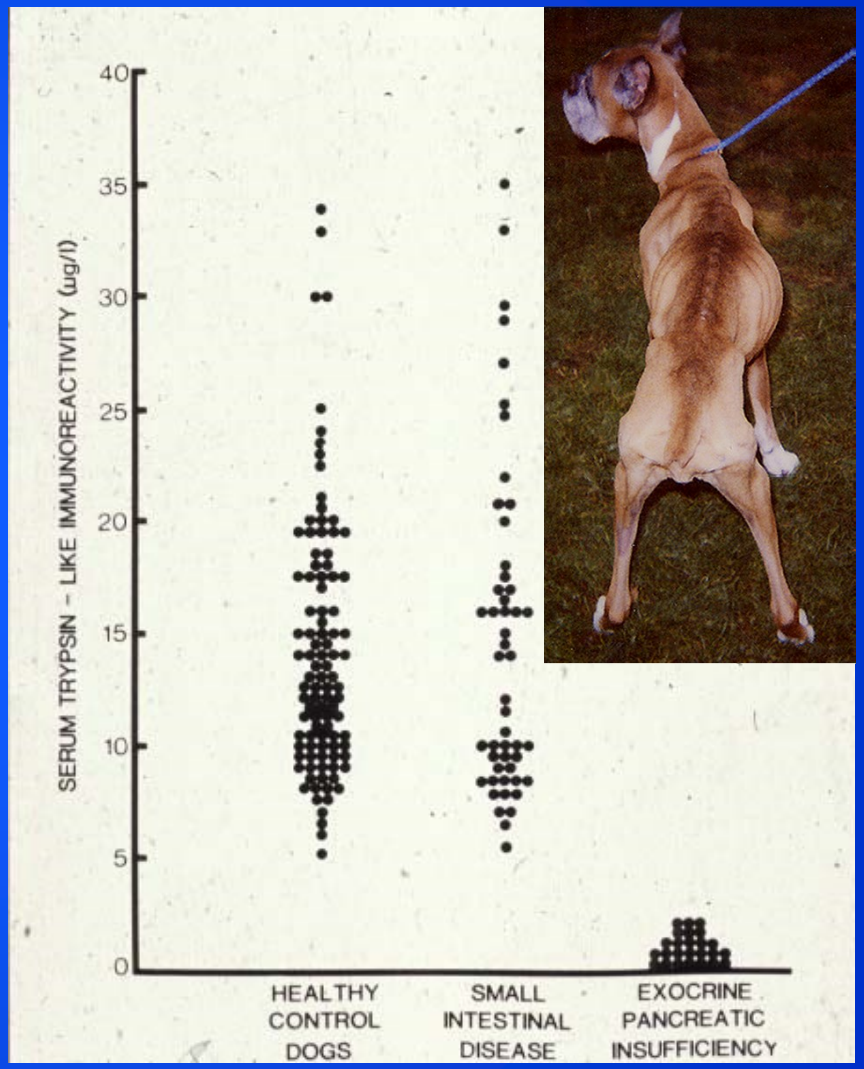
Profile

Protein losing enteropathies	
Infectious	Parvo, Salm., Histo.
Endoparasites	Giardia, Ancylost.
Lymphangiectasia	
Neoplasia	Lymphosarcoma
IBD	LPE, eos., granulom.
HGE	
G.I. haem.	Neoplasia, ulcers
Structural	Intussusception

*JSAP 2004, 45,336-343, Craven et al 80 dogs retrospective
*JVIM 2007,21,703-708, Allenspach et al 70 dogs prospective

EPI - Diagnosis

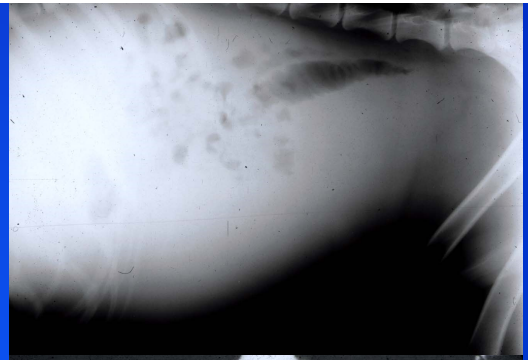
- Normal CBC and UA
  - mildly elevated ALT
  - Low cholesterol
  - Low cobalamin, high folate
- Absence of hypoproteinemia despite massive diarrhea and weight loss
- LOW TLI

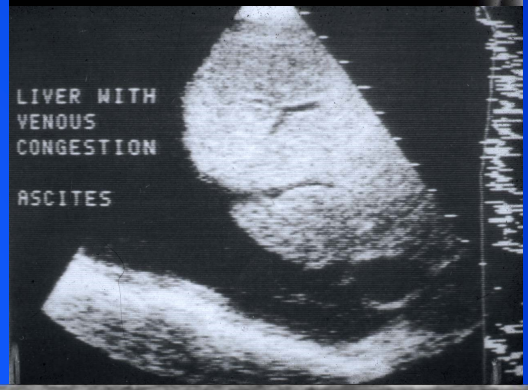


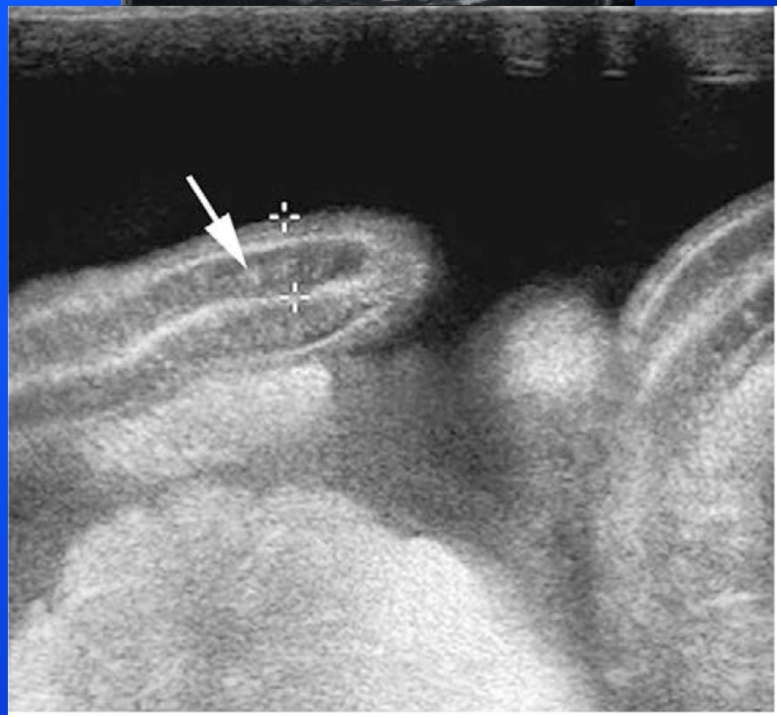
Diagnostic Imaging

- Radiographs usually low yield
- Ultrasonography
  - Parenchymal changes in G.I.T. and other organs
  - Ascites
  - *Hyperechoic striations
  - Lymphadenopathy
  - Radioluscent foreign bodies
  - Helps target biopsy procedure

*Vet Radiol Ultrasound 2008,49, 56-64



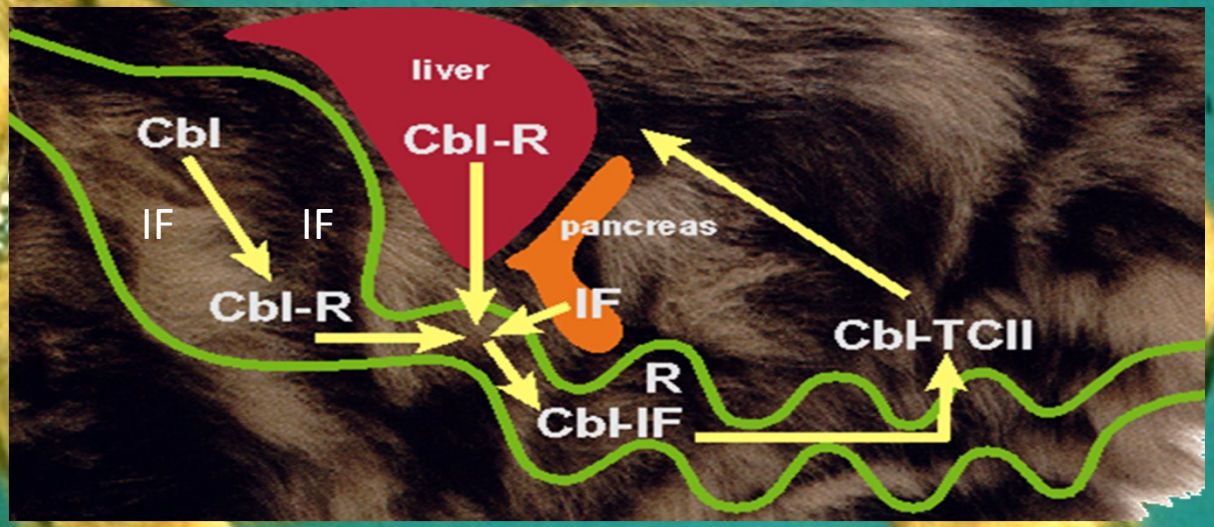




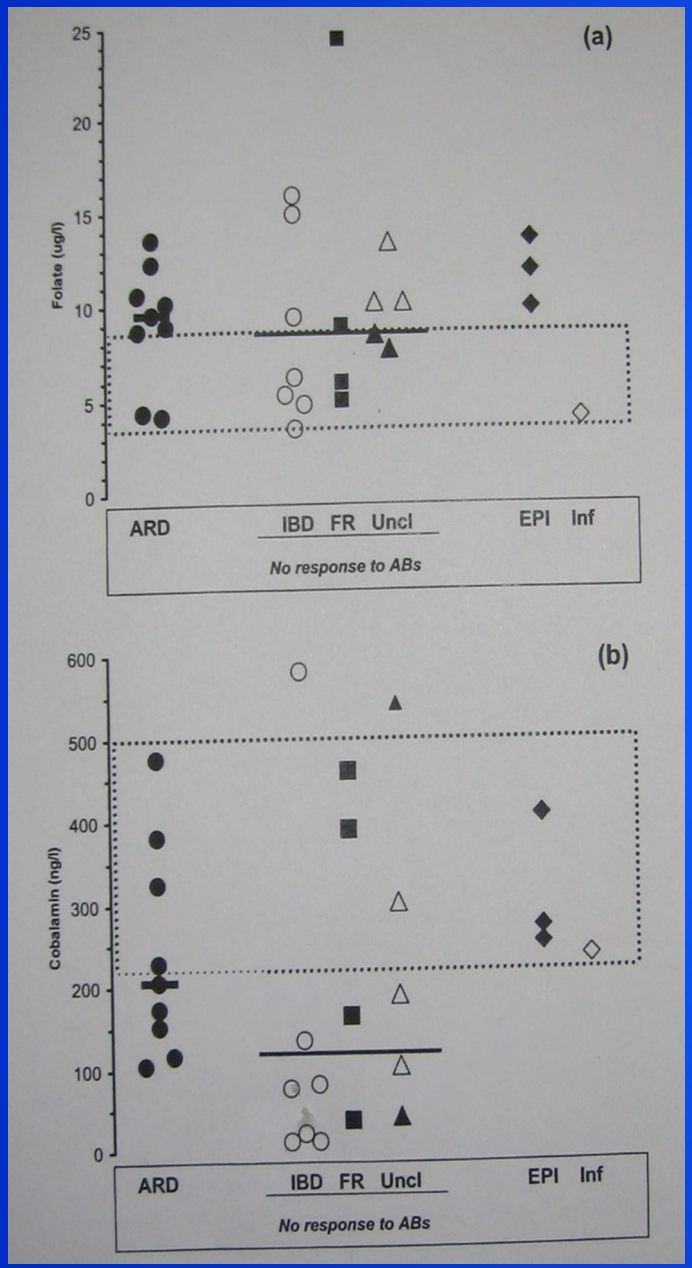
Chronic Enteropathies

- Gastrointestinal function
  - Cobalamin (B_{12}) and folate
  - GI protein loss (fecal alpha-1-PI)
  - Breath hydrogen
  - Permeability testing
  - Unconjugated bile acids
  - Motility testing

Cobalamin absorption



Hypocobalaminemia in Dogs



Giant Schnauzers, Collies, Shar peis

J Vet Intern Med 2003;17:33–43

Comparison of Direct and Indirect Tests for Small Intestinal Bacterial Overgrowth and Antibiotic-Responsive Diarrhea in Dogs

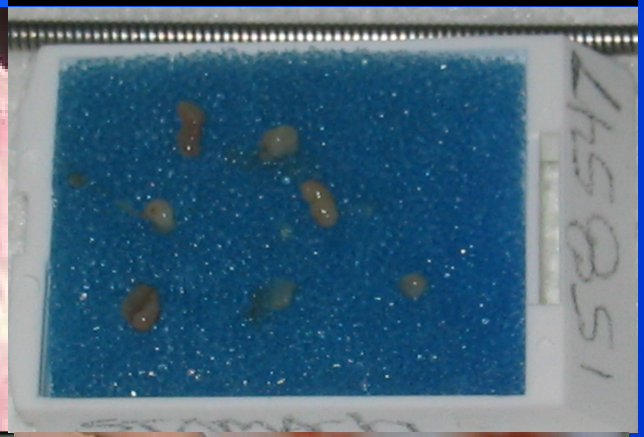
A.J. German, M.J. Day, C.G. Ruaux, J.M. Steiner, D.A. Williams, and E.J. Hall

- Increased folate (19/29)
- Decreased cobalamin (16/29) (13/70)
- Combination 9/29
- Cbl and folate not different in ARD vs IBD, FR, Uncl
- Cobalamin <200ng/l poorer prognosis (13/70:7/13 euth,OR 9.5)

JVIM 2007,21,703-708

Intestinal Biopsy

- Endoscopy ?
- Surgery ?



Endoscopy score >3, OR 10.5 for negative outcome

JVIM 2007,21,703-708

EVALUATION OF HISTOPATHOLOGY

Interobserver variation among histopathologic evaluations of intestinal tissues from dogs and cats.

"Substantial interobserver variation was detected. Clinicians must be cautious about correlating clinical signs and histopathologic descriptions of intestinal biopsy specimens."

Willard MD, et al. J Am Vet Med Assoc. 2002 Apr 15;220(8)

Histopathological Standards for the Diagnosis of Gastrointestinal Inflammation in Endoscopic Biopsy Samples from the Dog and Cat: A Report from the World Small Animal Veterinary Association Gastrointestinal Standardization Group

M. J. Day, T. Bilzer, J. Mansell, B. Wilcock, E. J. Hall, A. Jergens, T. Minami, M. Willard and R. Washabau.

J.Comp Path 2008 138, S1-S43

WSAVA
Global Veterinary Development

STANDARD FORM FOR ASSESSMENT OF COLONIC MUCOSA

Pathologist_____ Case number_____

Number of pieces of colonic tissue on slide_____

Tissue present

☐ Inadequate ☐ Too superficial ☐ Adequate depth

Number of colonic tissues abnormal_____

MORPHOLOGICAL FEATURES

	Normal	Mild	Moderate	Marked
Surface epithelial injury	☐	☐	☐	☐
Crypt hyperplasia	☐	☐	☐	☐
Crypt dilation/distortion	☐	☐	☐	☐
Fibrosis/atrophy	☐	☐	☐	☐

INFLAMMATION

Lamina propria lymphocytes and plasma cells	☐	☐	☐	☐
Lamina propria eosinophils	☐	☐	☐	☐
Lamina propria neutrophils	☐	☐	☐	☐
Lamina propria macrophages	☐	☐	☐	☐

FINAL DIAGNOSIS

- ☐ Normal colon
- ☐ Lymphoplasmacytic inflammatory
- ☐ Eosinophilic inflammatory
- ☐ Neutrophilic inflammatory
- ☐ Histiocytic/granulomatous inflammatory
- ☐ Mucosal atrophy/fibrosis (non-inflammatory)
- ☐ Other

OTHER COMMENTS

Effect of Tissue Processing on Assessment of Endoscopic Intestinal Biopsies in Dogs and Cats

M.D.Willard and WSAVA group. J Vet Intern Med 2010;24:84–89

Animals: 62 dogs and 25 cats.

Methods: Histopathology examined by 4 pathologists using pictorial templates.

Table 1. Agreement between 4 pathologists assessed by the k statistic.

Variable	Lesion Score (2-point scale)	(4-point scale)
Crypt lesions	0.300	0.250
Lacteal dilation	0.160	0.228
Lymphocytes/plasma cells	0.187	0.145
Neutrophils	0.240	0.128
Eosinophils	0.036	0.119
Villus epithelial injury	0.156	0.080
Intraepithelial lymphocytes	0.259	0.062
Villus stunting	0.167	0.049
Fibrosis	0.013	0.030

A k statistic >0.6 is considered good agreement.

Lacteal dilation was significantly associated (P 5 .019- .04) with hypoalbuminemia by 3 / 4 Crypt lesions (P=0.043) and villus stunting (P=..005) with hypoalbuminemia by 1 pathologist.

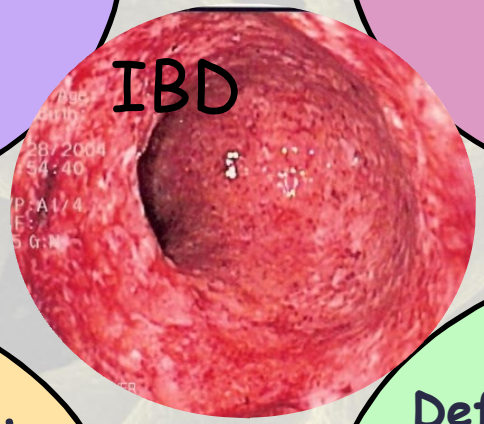
Theories of IBD pathogenesis:

Luminal microbes:

- Specific pathogen
  e.g. Mycobacteria, H. hepaticus
- 'Dysbiosis'

Mucosal barrier:

- Altered mucus layer
- Permeability changes
- Cellular starvation
- Impaired epithelial repair



Host genetic defects:

- Impaired bacterial sensing
- Defective bacterial killing,
- Defunct cell signalling
- Reduced autophagy
- Mucosal barrier defects

Defective immunoregulation

- Abnormal Ag processing
- Loss of tolerance
- Defective apoptosis
- Aggressive T cell responses

Canine IBD

- **Breed predispositions**
  - "Lymphocytic Plasmacytic"
    - Basenji, Sharpei, GSD, Soft Coat Wheaten
  - Granulomatous colitis:
    - Boxer
  - Lymphangiectasia:
    - Lundehund, Yokshire Terrier,
    - SC Wheaten
- **Associated disorders**
  - Protein losing nephropathy
    - SC Wheaten







Disease Susceptibility

Gluten Sensitive Enteropathy autosomal recessive

Antibiotic Responsive Enteropathy

? IgA deficiency TLR5 SNPG22A

Immuno-proliferative Small Intestinal Disease

Protein Losing Enteropathy, Lymphangiectasia

Atrophic Gastritis, Gastric carcinoma

Protein Losing Enteropathy, Lymphangiectasia, Crypt Lesions

Protein Losing Enteropathy, Nephropathy

Chromosome 1 , nephrin and filtrin

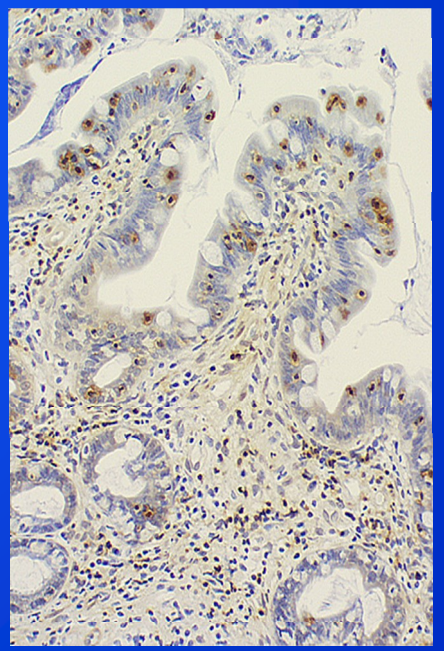
Cobalamin Deficiency Chromosome 13, 4SNPs

26,440,813-28,178,693

Granulomatous Colitis (HUC) SLAM/CD48 locus

Lymphocytic-Plasmacytic Enteritis

- Most common form of IBD in dogs
- Variable signs, site and severity of inflammation
  - Diarrhea, wt loss, vomit
- Physical examination
  - ± poor body condition
  - ± ascites, peripheral edema, pleural effusion if
  - ± thickened bowel loops or lymphadenopathy
- What is LPE?
  - No change in $CD3^+$ T cells in FRD or SRD dogs before or after successful treatment
  - No difference in healthy cats and cats with clinical signs
  - No difference in FR vs. ST vs. PLE (ascites)
  - ± correlation with CIBDAI

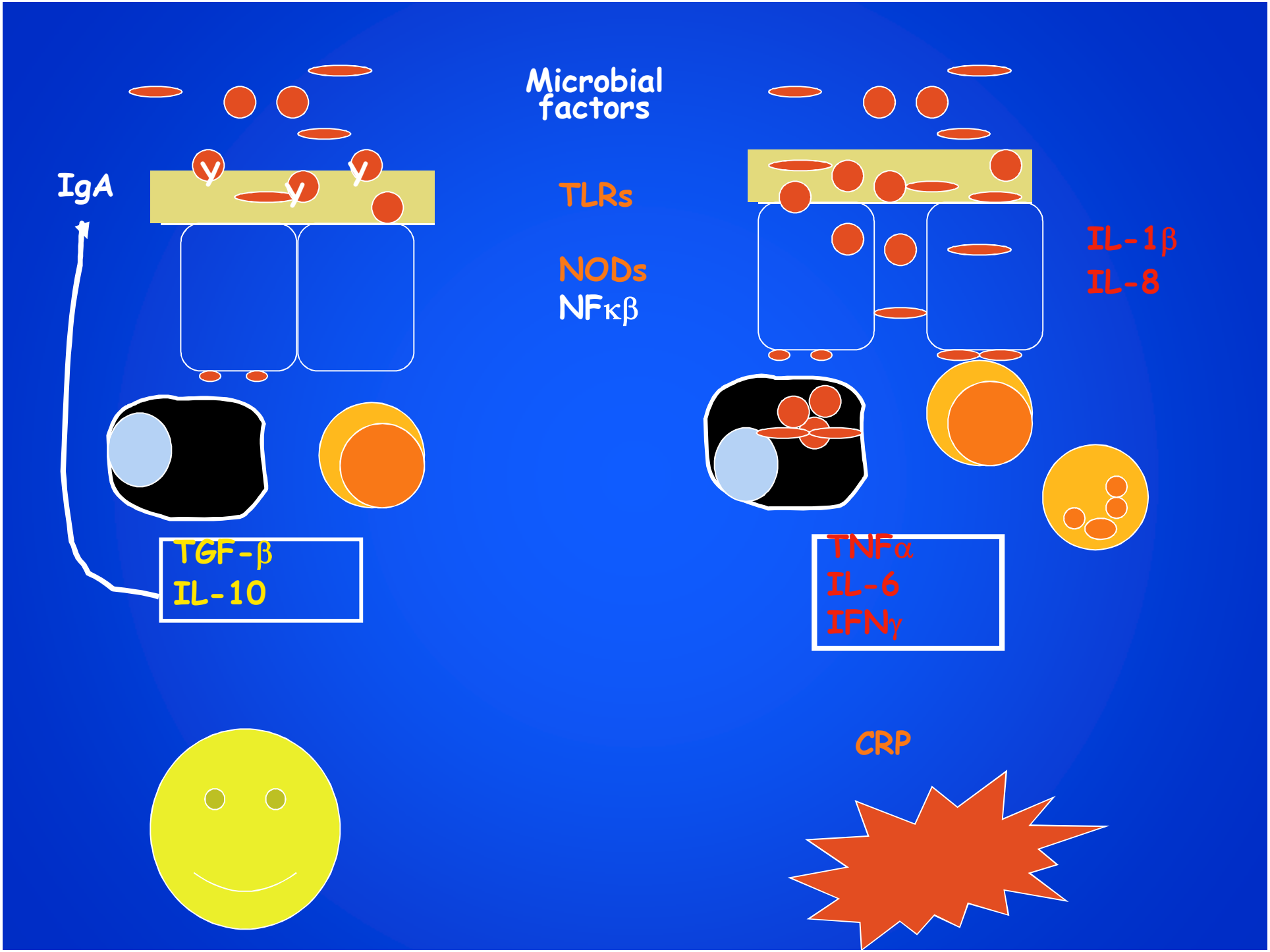


Are we evaluating the wrong features?

JVIM 2008,22,1079-1083

Treatment by Therapeutic Trial

Disease severity	Mild albumin >2g/dl endo,histo N-mild	Moderate albumin >2g/dl endo,histo Mod	Moderate-Severe albumin <2g/dl endo,histo,Mod-Sev
Diet	+	+	+
Antibiotics	+	+	+
Steroids	+	+	+
	?		
Other immuno	+	+	+


Microbial factors
IgA
TLRs
NODs
NFκβ
IL-1β
IL-8
TGF-β
IL-10
TNFα
IL-6
IFNγ
CRP

What diet would you recommend ?

1. Canine maintenance
2. Highly digestible, fat restricted, GI profile
3. Novel protein source
4. Hydrolyzed protein
5. Home cooked

Dietary modification

- Global modification
- Optimise assimilation
  - Highly digestible fat restricted diet
  - Easily digested fats? e.g. MCT
  - Fiber (large bowel)
- "Antigenic modification"
  - Novel protein source
  - Protein hydrolysate
- Immunomodulation
  - Altered fat composition (Omega 3:6, Fish oil)
  - Probiotics / prebiotics

Does dietary modification work?

- 13 dogs with lymphocytic, plasmacytic colitis
- Clinical signs resolved in all 13 dogs (2-28mo follow-up) after they were fed boiled white rice and low-fat cottage cheese diet
- In 11 dogs, 2 commercial diets not previously fed to these dogs were successfully substituted for the initial test diet, without causing recurrence of signs (5/7 D/D, 6/6 Max Stress).
- Only 2 / 11 dogs subsequently tolerated a switch to diets fed at the time of onset of signs of colitis.

JVIM 1988,2,133-7 Nelson et al.

Does dietary modification work?

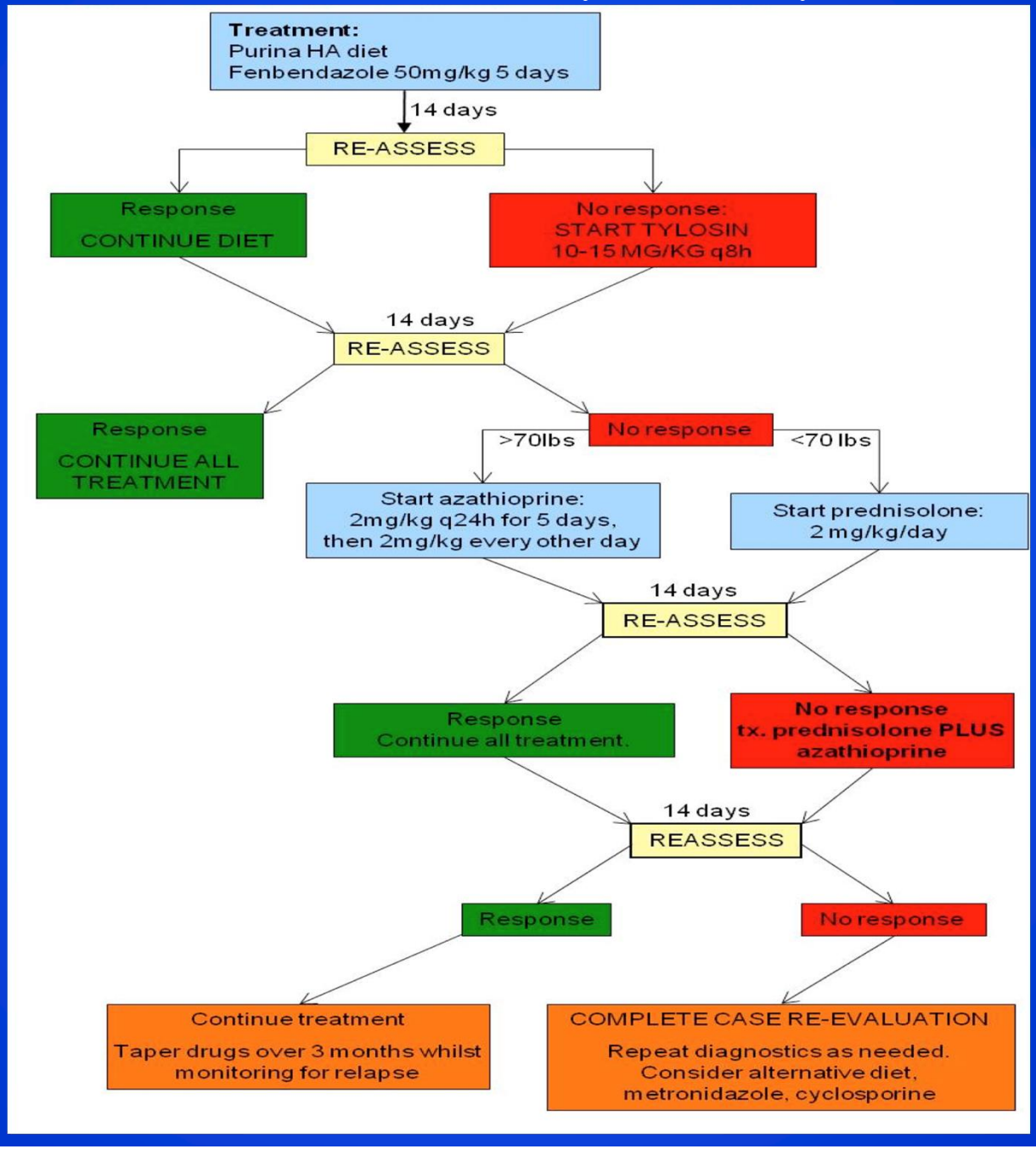
- Response to LA salmon and rice (10d)
  - 39/70 (56%) responsive
  - Diet responsive tend to be younger and have LI involvement and less severe dz. and endoscopic activity
  - Prognosis
    - 38/39 OK after 3 yrs

JVIM 2007 21,703-708

Dietary trial using a commercial hypoallergenic diet containing hydrolyzed protein for dogs with inflammatory bowel disease. Marks SL, Laflamme DP, McAloose D. Vet Ther. 2002 Summer;3(2):109-18.

- 6 dogs with inflammatory bowel disease (IBD) received HA
- Five of the six dogs refractory to previous diets, and four dogs failed to respond to previous medical therapy.
- Dietary therapy : clinical improvement in four of 6 dogs
- Concurrent medical therapy needed in two dogs, one had EPI
- Five dogs showed mild to moderate histologic improvement in duodenal biopsies after therapy.

LP enteritis normal albumin



Does dietary modification work?

- Response to sequential TX: Normal albumin

Study #	Breed	vomit y n	diarr si1 li 2	wt loss	blood stool	skin	other	albumin	ultrasound
A37	Xpug	1	0	0	0	0	anorexia	3	l adrenal
A08	Labrador	1	2	1	1	0	inapp	3.5	jej LN
A09	Malamute	1	0	0	0	0		3.6	wnl
A38	GSD	1	0	0	0	skin and GI flare		3.1	wnl
A29	Boxer	1	1	0	0	pustular derm ch	inapp	3.6	wnl
A05	Irish Setter	0	2	1	1			3.2	wnl
A16	Pomeranian	1	1	1	1	open lesions	inapp	3.3	focal duod inc
A11	WHWT	1	1	0	1	0		3.7	wnl
A27	X breed	1	1 and 2	1	0	0		3.8	wnl
A42	Chinook	1	2	0	0	0	occ inapp	3.8	wnl
A15	Bichon	1	0	0	0	contact derm		3.9	wnl
A13	X breed	1	1	0	1	atopy		3.9	wnl
A30	Y.Terrier	1	0	0	0	0	int inapp	3.9	wnl
A32	GSD	0	2	0	0	very flaky and dry		3.9	wnl
A04	St. Bernard	0	1	1	1	0		4	wnl
A33	Pomeranian	1	0	0	0	0	excess swallo lick	4.1	hyper speckles
A20	Am. Bulldog	1	0	0	0	0		4.5	wnl
A21	Labrador	1	0	0	0	0	gagging	3.7	wnl
A39	Gt. Dane	1	1 and 2	1	0	non seasonal pruritus licks feet, pustules		3.3	focal stom wall
A01	Boxer	1	1	0	0	staph, follicle, pinnal vasculitis		3.7	wnl
A12	Bulldog	1	1	0	1	atopy		3.1	wnl
A36	Schnauzer	1	1	0	0	0	weakness	3.4	stria, speckles
A31	Bassett	1	0	0	0	0		3.5	wnl
A14	X breed	0	1	0	0	0	oaning lip smacki	4	hepatopathy

Morris Animal Foundation
Nestle-Purina

Does dietary modification work?

- Response to sequential TX: Normal albumin

Study #	Breed	vomit y n	diarrsi1li2	wt loss	blood stool	other	albumin	ultrasound	Response
A37	Xpug	1	0	0	0	anorexia	3	ladrenal	FR
A08	Labrador	1	2	1	1	inapp	3.5	jejLN	FR
A09	Malamute	1	0	0	0		3.6	wnl	FR
A38	GSD	1	0	0	0		3.1	wnl	FR
A29	Boxer	1	1	0	0	inapp	3.6	wnl	FR
A05	Irish Setter	0	2	1	1		3.2	wnl	FR
A16	Pomeranian	1	1	1	1	inapp	3.3	focal duod inc	FR
A11	WHWT	1	1	0	1		3.7	wnl	FR
A27	X breed	1	1and2	1	0		3.8	wnl	FR
A42	Chinook	1	2	0	0	occ inapp	3.8	wnl	FR
A15	Bichon	1	0	0	0		3.9	wnl	FR
A13	X breed	1	1	0	1		3.9	wnl	FR
A30	Y.Terrier	1	0	0	0	int inapp	3.9	wnl	FR
A32	GSD	0	2	0	0		3.9	wnl	FR
A04	St. Bernard	0	1	1	1		4	wnl	FR
A33	Pomeranian	1	0	0	0	excess swallo lick	4.1	hyperspeckles	FR
A20	Am.Bulldog	1	0	0	0		4.5	wnl	FR
A21	Labrador	1	0	0	0	gagging	3.7	wnl	FR 5mo
A39	Gt. Dane	1	1and2	1	and vomit		3.3	fo cal sto m wall	FA
A01	Boxer	1	1	0	0		3.7	wnl	FA
A12	Bulldog	1	1	0	1,melena		3.1	wnl	SR
A36	Schnauzer	1	1	0	0	weakness	3.4	stria, speckles	SR
A31	Bassett	1	0	0	0		3.5	wnl	SR
A14	X breed	0	1	0	0	moaning lip smacking	4	hepatopathy	UR

Morris Animal Foundation
Nestle-Purina

A randomized, open-label, positively-controlled field trial of a hydrolyzed protein diet in dogs with chronic small bowel enteropathy. Mandigers PJ, Biourge V, van den Ingh TS, Ankringa N, German AJ. J Vet Intern Med. 2010 Nov-Dec;24(6):1350-7

- Twenty-six dogs (18 test diet, 8 control diet) with chronic small intestinal disease.

METHODS: Randomized, open-label, positively controlled trial.

- Assigned to the test diet or control diet on a 2:1 basis (test:control).
- re-evaluated 3 times (at approximately 3, 6-12 months, and 3 years).

RESULTS: No significant differences in baseline characteristics (eg, signalment, body weight, and duration of clinical signs), and histopathologic severity between test and control diet groups.

- CIBDAI was higher in the test diet group (P=.013).
- Most dogs had responded by first evaluation, with no difference between groups (P=.87) at 3 months.

Nutritional management of chronic enteropathies in dogs and cats

Adam J. Rudinsky, John C. Rowe, Valerie J. Parker *JAVMA* , 2018, Vol. 253, No. 5, Pages 570-578

Table 2— Summation of studies conducted to evaluate nutritional management of dogs and cats with chronic enteropathies.

Dietary strategy	Species	Indication	Evidence level†	Reference
Hydrolyzed diet	Canine	Chronic enteropathy	4	34,bb
	Canine	Chronic enteropathy	2	35
	Canine	Chronic enteropathy	3	36
	Canine	Chronic enteropathy	3	37
	Feline	Chronic enteropathy	4	38
Limited-ingredient diet	Canine	Chronic enteropathy	2	39
	Canine	Chronic enteropathy	2	40
	Canine	Chronic enteropathy	2	41
	Canine	Chronic enteropathy	2	37
	Feline	Chronic enteropathy	2	42
	Feline	Colitis	4	43
Fiber modification	Canine	Colitis	4	44
	Canine	Colitis	4	45
	Feline	Colitis	3	46
Highly digestible diet	Canine	Chronic enteropathy	2	35
	Canine	Colitis	4	47
	Feline	Chronic enteropathy	2	48
	Feline	Chronic enteropathy	2	56
Fat restriction	Canine	PLE	4	28
	Canine	PLE	3	29
	Canine	PLE	4 or 5	49–52,cc

†Evidence-based medicine levels are as follows: 1, high-quality randomized trial; 2, lesser-quality randomized trial or prospective comparative study; 3, case-control study or retrospective comparative study; 4, case series; and 5, expert opinion.

"Dietary modification can induce clinical remission in quite a lot of dogs with chronic enteropathy"

Why does dietary modification work?

Is it food allergy?

- 31/39 responding to LA Salmon did NOT relapse on re-challenge with original diet
- Those that relapsed were NOT sensitive to beef, lamb, chicken or milk JVIM 2007 21,703-708
- Similar response rates on 2 different hydrolysates, a completely different diet!

J Vet Intern Med 2013;27:862–874

A Comprehensive Pathological Survey of Duodenal Biopsies from Dogs with Diet-Responsive Chronic Enteropathy

D. Walker, A. Knuchel-Takano, A. McCutchan, Y-M. Chang, C. Downes, S. Miller, K. Stevens, K. Verheyen, A.D. Phillips, S. Miah, M. Turmaine, A. Hibbert, J.M. Steiner, J.S. Suchodolski, K. Mohan, J. Eastwood, K. Allenspach, K. Smith, and O.A. Garden

Background: The detailed pathological phenotype of diet-responsive chronic enteropathy (CE) and its modulation with dietary therapy remain poorly characterized.

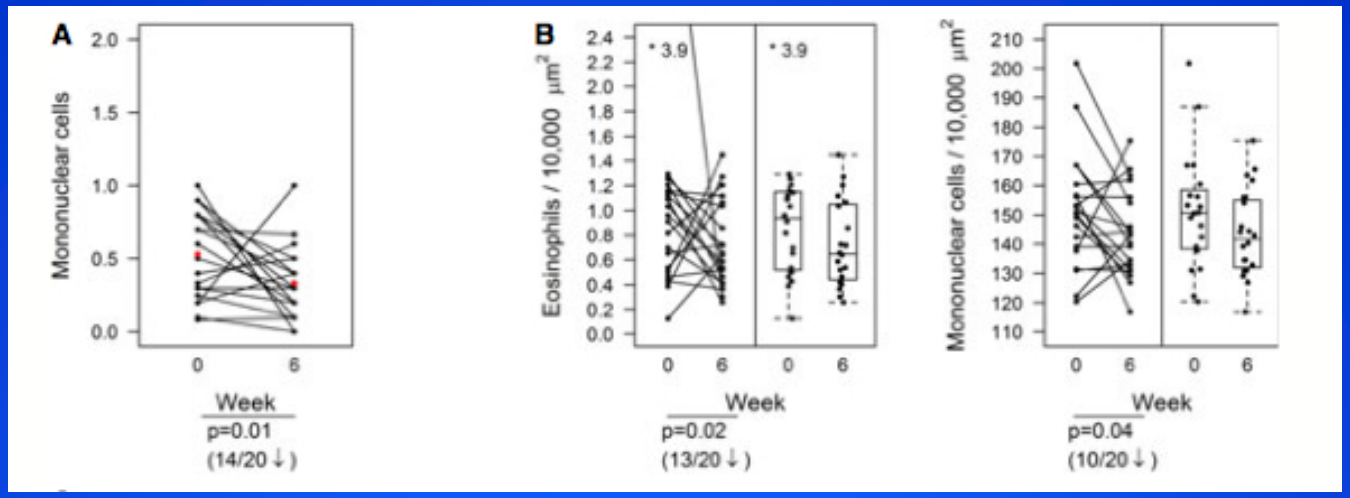
Hypothesis/Objectives: Key mucosal lesions of diet-responsive CE resolve with dietary therapy.

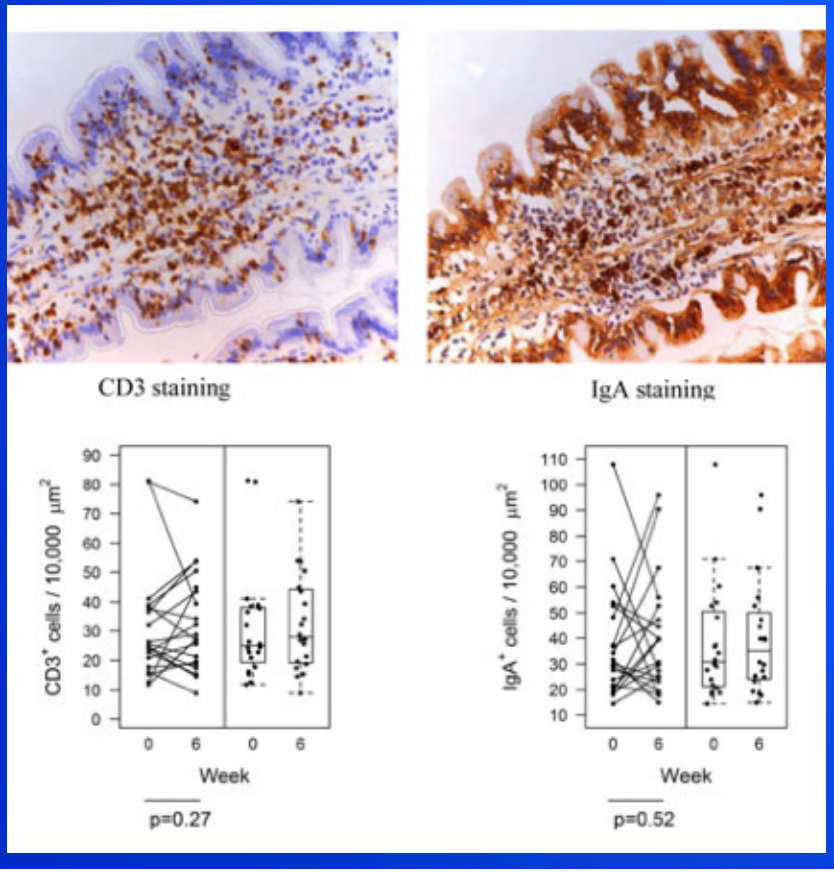
Methods: This was a prospective observational study of 20 dogs with diet-responsive CE. Endoscopic duodenal biopsies collected before and 6 weeks after the start of a dietary trial were assessed by means of qualitative and quantitative histopathological, immunohistochemical, and ultrastructural criteria. Control duodenal biopsies were obtained from 10 healthy Beagle dogs on 1 occasion.

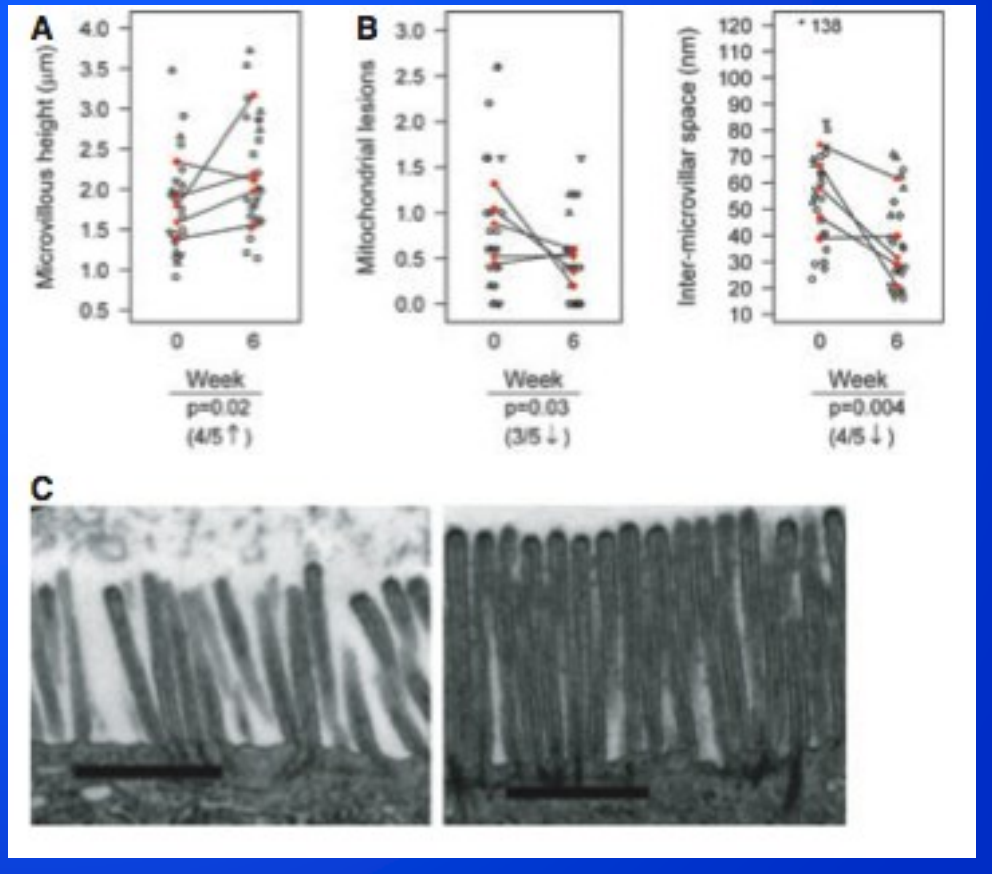
Results: Compared with control dogs, the CE dogs had higher villus stunting scores and higher overall WSAVA scores, a lower villus height-to-width ratio, and higher lamina propria density of eosinophils. The CE dogs also had ultrastructural lesions of the mitochondria and brush border. In common with other studies in which the disease and control populations are not matched for breed, age, sex, and environment, these comparisons should be interpreted with caution. Comparing biopsies collected at presentation and 6 weeks after starting the dietary trial, mean lamina propria mononuclear cell score and lamina propria densities of eosinophils and mononuclear cells decreased. Dietary therapy also improved ultrastructural lesions of the mitochondria and brush border, eliciting a decrease in intermicrovillar space and an increase in microvillus height.

Conclusions and Clinical Importance: In dogs with diet-responsive CE, the remission of clinical signs with dietary therapy is associated with subtle decreases in lamina propria density of eosinophils and mononuclear cells, and resolution of ultrastructural lesions of the enterocyte.

Key words: Eosinophil; Inflammatory bowel disease; Microscopy; Permeability; Ultrastructure; WSAVA standards.


A
Mononuclear cells
Week
p=0.01
(14/20 ↓)
B
Eosinophils / 10,000 µm²
* 3.9
* 3.9
Week
p=0.02
(13/20 ↓)
Mononuclear cells / 10,000 µm²
Week
p=0.04
(10/20 ↓)


CD3 staining
IgA staining
CD3⁺ cells / 10,000 µm²
Week
p=0.27
IgA⁺ cells / 10,000 µm²
Week
p=0.52


A
Microvillous height (µm)
Week
p=0.02
(4/5 ↑)
B
Mitochondrial lesions
Week
p=0.03
(3/5 ↓)
Inter-microvillar space (nm)
* 138
Week
p=0.004
(4/5 ↓)
C

Placebo Controlled Trial of Hydrolyzed Fish Diets in Dogs With Chronic Enteropathy

Kenneth Simpson, Meredith Miller, John Loftus, Mark Rishniw,
Carol Frederick and Joseph Wakshlag

PLACEBO CONTROLLED TRIAL OF HYDROLYZED FISH DIETS IN DOGS WITH CHRONIC ENTEROPATHY

KENNETH SIMPSON, MEREDITH MILLER, JOHN LOFTUS, MARK RISHNIW, CAROL FREDERICK AND JOSEPH WAKSHLAG

Background:

- Dietary modification can induce clinical remission in dogs with chronic enteropathy:

  What is the basis of these responses?

- Palatability impacts dietary therapy in dogs with protein losing enteropathy (PLE).

Objectives:

To compare the ability of **isocaloric diets** protein (19.2% DM), fat (15.3% DM) and carbohydrate (55.2% DM),

(as fed g/100kcals minimum: protein 4.62, fat 3.71, carbohydrate 13.23) composed of:

(A) hydrolyzed fish, rice starch and fish oil: HF

(B) HF plus **prebiotics** (inulin 0.6%, FOS 0.4%, MOS 0.4%), **turmeric** (33mg/kg) and **high cobalamin** (10mg/kg): **HF+**

(C) highly digestible **non-hydrolyzed mixed protein / fat / CHO** diet: dehydrated chicken and fish, chicken fat and fish oil, corn, rice, beet pulp: **Placebo**

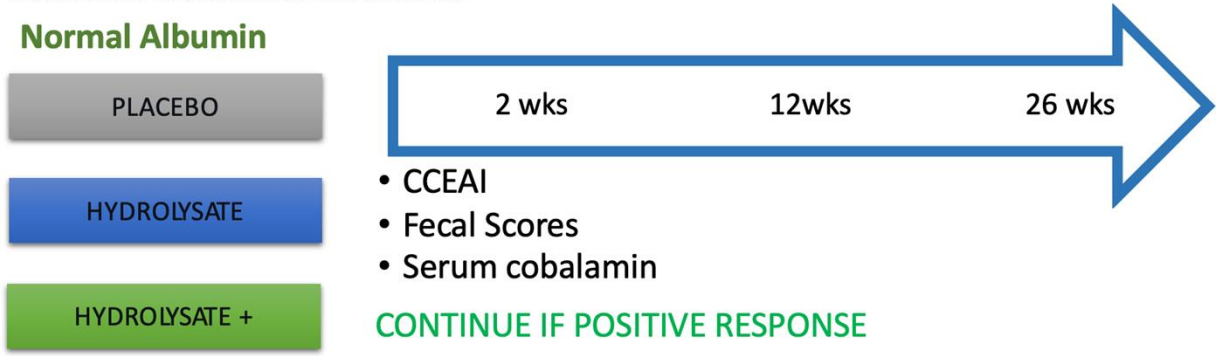
- To resolve clinical signs and maintain serum B_{12} in dogs with CE.
- To evaluate palatability and weight gain in dogs with PLE.

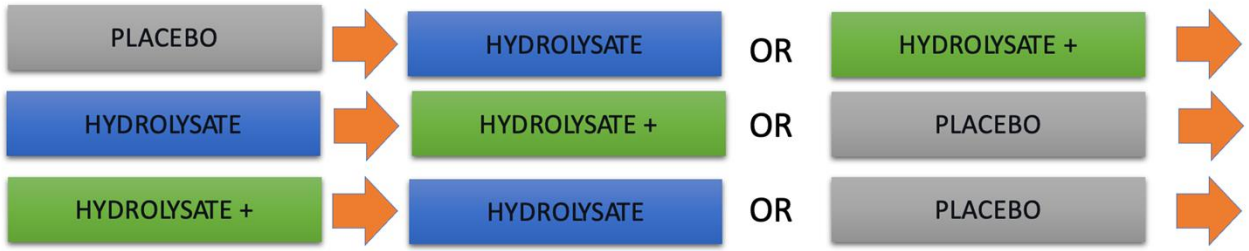
PLACEBO CONTROLLED TRIAL OF HYDROLYZED FISH DIETS IN DOGS WITH CHRONIC ENTEROPATHY

***Methods*:**

- Randomized, blinded, placebo-controlled
- Each diet fed for 2wks, with responders continuing for 12wks. Non-responders cross over to another diet for 12wks.
- Concurrent medications not allowed.

Normal Albumin





OUTCOME

Normal Albumin

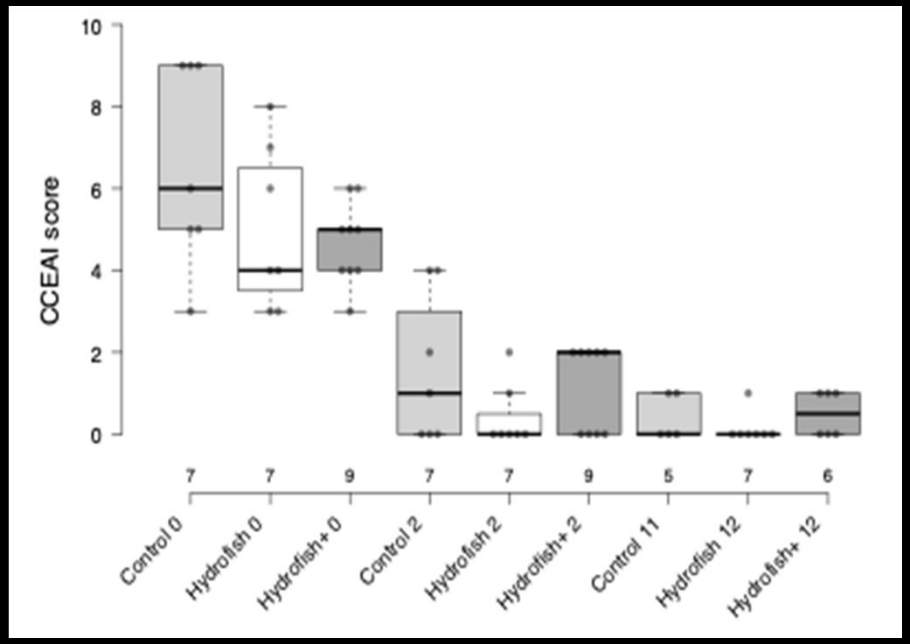
Non-PLE n = 23

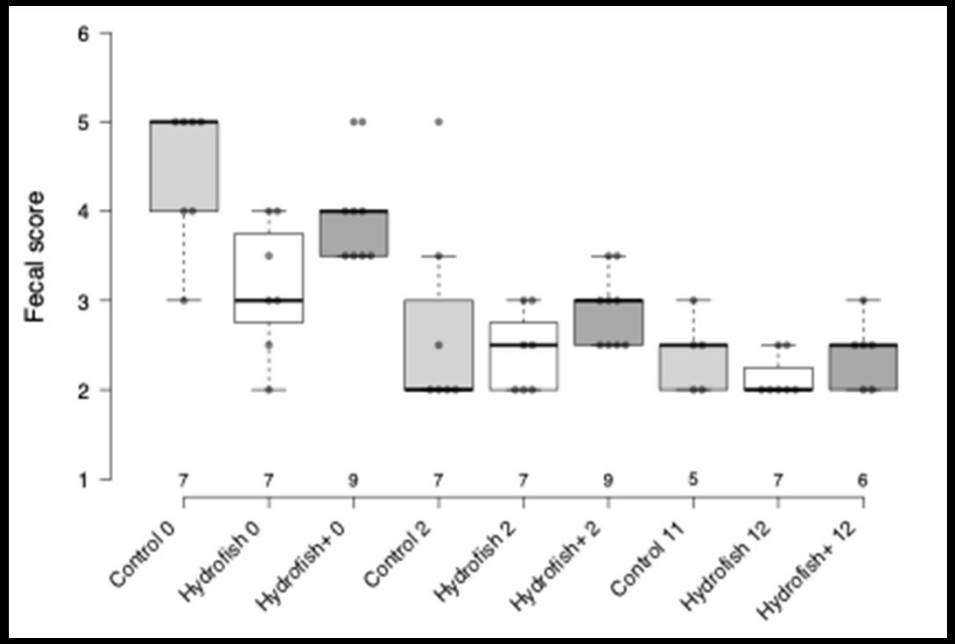
Diet	HF n = 7	HF⁺ n = 9	Placebo n = 7
Response			
Initial	7/7	6/9	6/7
cross-over		3	1
Final	10/10	7/10	6/7
Sustained	7/7	7/7	4/4

3/23 with histopathology :

1 marked, diffuse, eos, LP (**Placebo**); 1 mild to moderate eos LP (**Placebo**) ; 1 mild diffuse LP eos (**HF⁺**).

Clinical Response





a = P<0.05 vs baseline
b = P<0.05 vs 6wks

Non-GI

BEFORE

AFTER

IMAGINE THE POSSIBILITIES!

100%

BEFORE

AFTER

SERUM COBALAMIN

		Number	Cobalamin	
			Baseline	12wks
	Placebo	6	565 (149-1176)	688 (554-1001)
non-PLE	HydroFISH	7	275 (183-1001)	473 (251-1373)
	HydroFISH^{+}	10	621 (237-969)	853 (669-1908)
	HydroFISH	3	543 (272-1008)	737 (580-1414)
PLE				
	HydroFISH^{+}	1	149 (149-149)	1512 (1512-1512)

Summary and Conclusions

- Changing diet, independent of antigen restriction or supplementation, was associated with long-term clinical remission in dogs with chronic enteropathy.
- Further study is required to determine the basis of this clinical response.
- It is important to consider possibilities other than hypersensitivity to intact proteins and cereals.