What's New in Canine and Feline Chronic Enteropathies

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Presentation overview

- Canine dysbiosis index (DI)
- Bile acids in GI health and disease
  - Role for *Clostridium hiranonis* (CH) in BA synthesis
- Frequencies/outcomes for chronic diarrhea in dogs
- Differentiation of LPE vs. LSA in cats
  - Disease (histology) distribution in "healthy cats"
- Fecal microbiota transplant - EBO
- Canine autoantibodies for dx of IBD - biomarkers

#1 Canine dysbiosis index (DI)

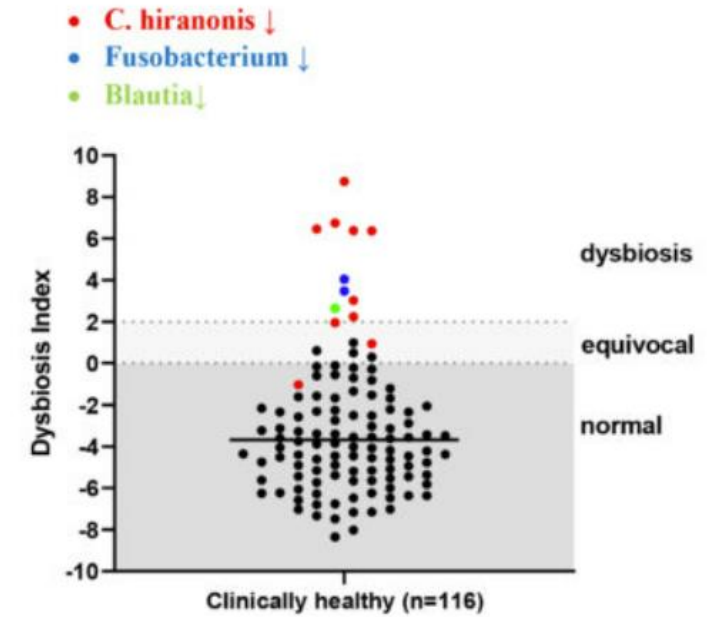
What is it and how do we use it?

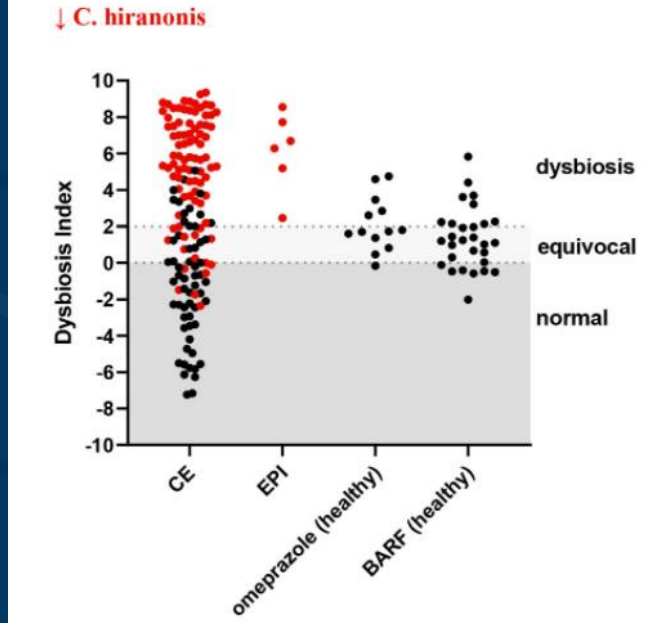
- Gut microbiome is important contributor to health and disease; bacterial products = metabolome (SCFAs)
- An abnormal microbiome is defined as dysbiosis
  - Dysbiosis is common in dogs (and cats) with GI disease
- Microbiota assessment is best performed using molecular techniques targeting bacterial genes
  - 16S rRNA sequencing studies are $$ and time consuming
- The dysbiosis index is a qPCR assay that quantifies the abundances of 7 bacterial groups and total bacteria in dogs and summarizes them in one single number*

**AlShawaqfeh, FEMS Microbiol Ecol 2017*

Table 1. Reference intervals

	Normal abundance	Change observed in dysbiosis
Faecalibacterium	3.4 – 8.0	decreased
Turicibacter	4.6 – 8.1	decreased
Streptococcus	1.9 – 8.0	increased
E. coli	0.9 – 8.0	increased
Blautia	9.5 – 11.0	decreased
Fusobacterium	7.0 – 10.3	decreased
C. hiranonis	5.1 – 7.1	decreased
Dysbiosis Index	< 0 normal 0-2 equivocal > 2 dysbiosis	



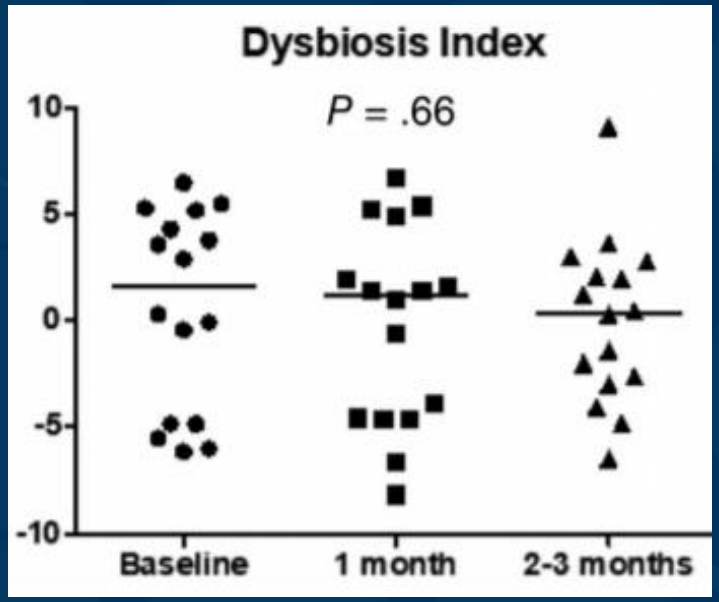


Data from TAMU GI lab and ~30 clinical studies

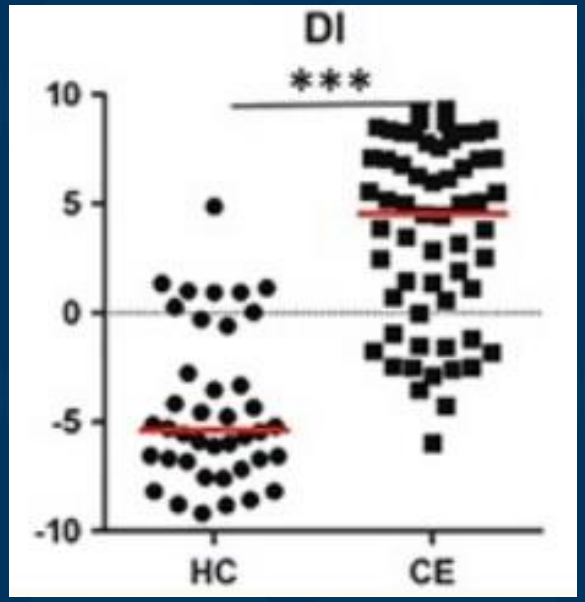
Key points: relevance of the DI

- DI allows veterinarians to assess whether a dog has changes in the fecal microbiota composition
  - < 0 normal microbiota
  - 0-2 equivocal
  - > 2 dysbiosis
- Easy to perform → ship feces to lab (keep cool)
- *Based on Clostridium hiranonis abundance*, the DI may predict a lack of conversion of primary to secondary bile acids, since the lack of secondary BA is a major contributor to an abnormal microbiota

DI is now commonly reported in publications



DI in response to steroid-responsive chronic enteropathy (IBD)
Guard et al, JVIM 2019

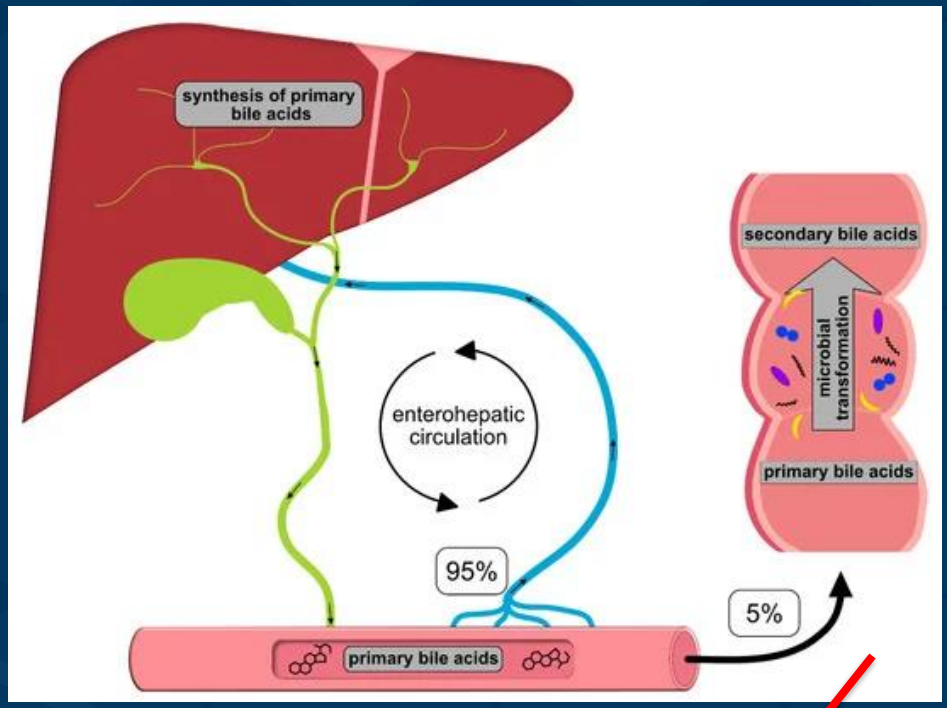


DI used in evaluation of SCFAs and dysbiois in dogs with CE
Minamoto et al, JVIM 2019

Decreased SCFAs were accompanied by significant changes in the fecal microbiota (dysbiosis)

#2 Role of bile acids in GI health and disease

- BAs and the gut microbiota, *Clostridium hiranonis* (CH), are important
- Maintain host health and promote a normal microbiota
- Primary BAs - made in liver
- Secondary BAs - derived in colon primarily by CH
- Secondary BAs are important signaling molecules and have anti-inflammatory properties
- Secondary BAs are depleted in dogs with acute and chronic enteropathies

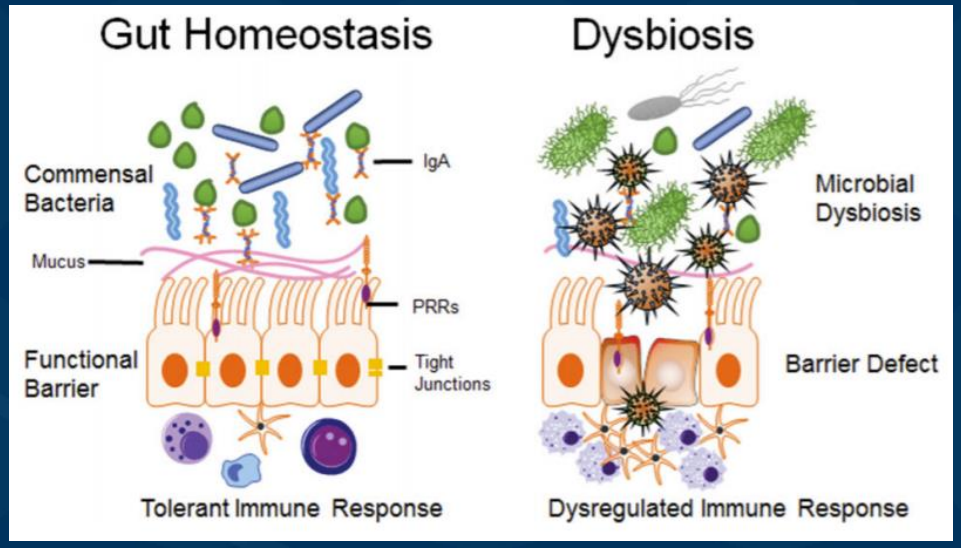


Abnormal BA profiles impact canine enteropathies and diabetes mellitus

Diet-induced remission of canine CE alters microbiota and ↑ secondary BAs

Bile acids↔dysbiosis↔gut inflammation

Relevance to clinicians: What is the role of BAs in canine CIE?



Wang, Toxicologic Pathology 2017

- Gut dysbiosis is well documented with canine chronic enteropathy → IBD, FRE
- With dysbiosis, disturbances in BA metabolism can occur and promote intestinal inflammation
- Mounting evidence supports a role for BA dysmetabolism in human chronic GI diseases, including IBD, IBS, and CRC
- Data supporting a role for BAs with canine CE have only recently been investigated

Longitudinal assessment of microbial dysbiosis, fecal unconjugated bile acid concentrations, and disease activity in dogs with steroid-responsive chronic inflammatory enteropathy

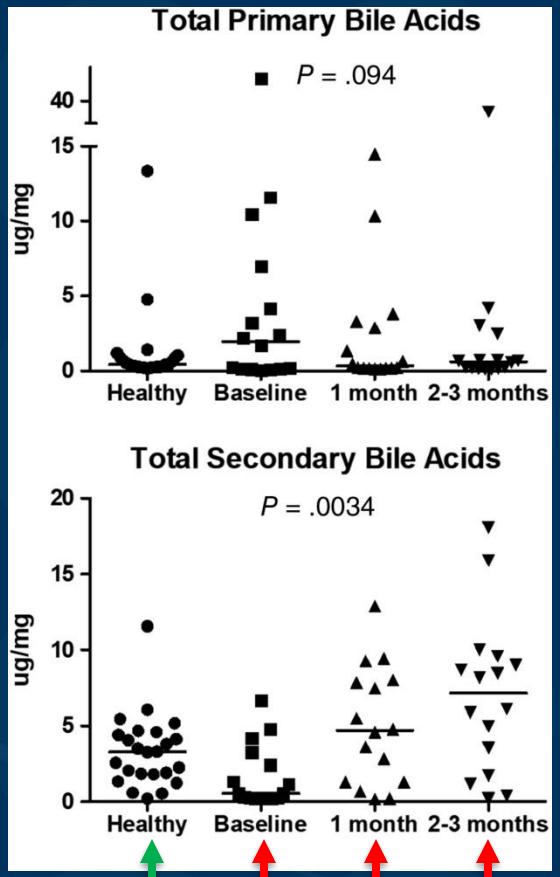
Blake C. Guard, Julia B. Honneffer, Albert E. Jergens, Michelle M. Jonika, Linda Toresson, Yuri A. Lawrence, Craig B. Webb, Steve Hill, Jonathan A. Lidbury, Joerg M. Steiner, Jan S. Suchodolski

JVIM 2019

- Aim: to assess microbial dysbiosis, fUBAs, and disease activity in dogs with steroid-responsive CE (IBD)
- Design: retrospective study derived from clinical trial
- Animals: 24 healthy controls, 23 dogs with IBD
- Methods: fUBAs were measured and associated with changes in the fecal microbiota and disease activity. Response to steroids was assessed over 2-3 months
  - fUBAs analyzed by GC/MS
  - Fecal microbiota analyzed by qPCR → dysbiosis Index
  - Clinical disease activity scored by CIBDAI

Bile acids and steroid-responsive CIBD

- No differences in primary BAs between controls/IBD
- Decreased secondary BAs IBD dogs at diagnosis
- Secondary BAs increased with therapy
- Clinical severity (CIBDAI) decreased with therapy
- Abundance of *C. hiranonis*, a BA converting bacterium, was associated with ↑ secondary BAs



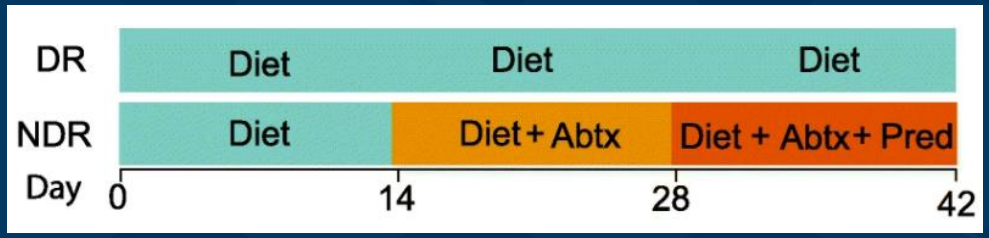
BA dysmetabolism linked to ↓ C. hiranonis and ↑ clinical disease activity. Steroid therapy is associated with improved secondary BA profiles.

Diet-induced remission in chronic enteropathy is associated with altered microbial community structure and synthesis of secondary bile acids

Shuai Wang, Rene Martins, Megan C. Sullivan, Elliot S. Friedman, Ana M. Misic, Ayah El-Fahmawi, Elaine Cristina Pereira De Martinis, Kevin O'Brien, Ying Chen, Charles Bradley, Grace Zhang, Alexander S. F. Berry, Christopher A. Hunter, Robert N. Baldassano, Mark P. Rondeau & Daniel P. Beiting

Wang, Microbiome 2019

- Aim: spontaneous canine CE - examine relationship between diet, remission, microbiome, and metabolome
- Design: prospective clinical trial of dogs with CE
- Animals: 29 dogs; 20 dogs = DR; 9 dogs = NR



- Methods: Dogs fed hydrolyzed diet +/- drugs over 42 d
- Outcomes: DA, microbiome, metabolome (BAs)

Key points: diet-induced remission of canine CE

- DR was accompanied by improved microbial community
  - ↓ abundance of pathobionts *E. coli* and *C. perfringens*
- 16S rRNA sequencing identified the BA producer *C. hiranonis* (CH) was elevated after dietary therapy
- Further analysis identified CH as the likely source of fecal secondary BAs (LCA, DOCA)
- In mice administered CH, levels of secondary BA (DCA) were preserved and DSS colitis severity was ↓
- Diet improves microbial structure, ↑ expansion of BA-converting CH, and ↑production of secondary BAs

#3

Standard Article
J Vet Intern Med 2017;31:1043–1055

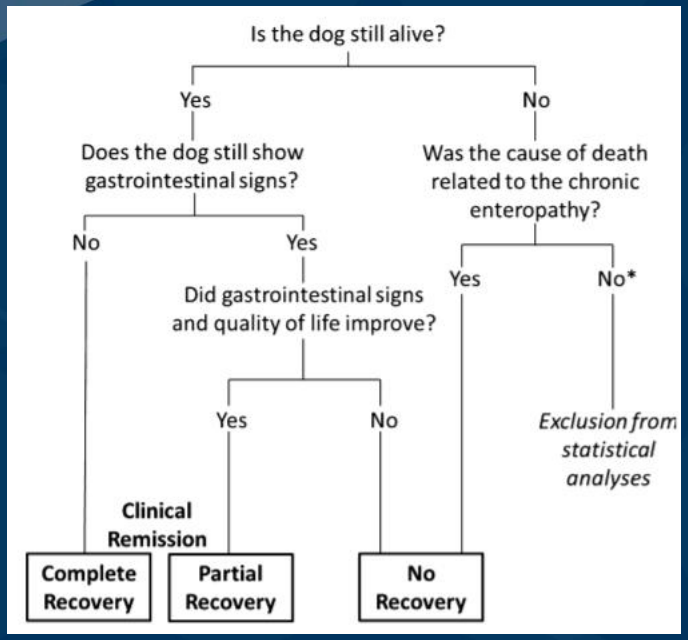
Chronic Diarrhea in Dogs – Retrospective Study in 136 Cases

M. Volkmann, J.M. Steiner, G.T. Fosgate, J. Zentek, S. Hartmann, and B. Kohn

- Background: chronic diarrhea (CD) is common and information on frequency of types/outcome is lacking
- Aim: to evaluate underlying causes and predictors of LT outcome (1 year) in dogs with CD
- Animals: 136 client-owned dogs with CD (>3 weeks)
- Design: Retrospective study evaluating primary vs. secondary causes for GI disease
  - Complete recovery (CR)
  - Partial recovery (PR)
  - No recovery (NR)

Client questionnaire up to one-year post diagnosis

Chronic diarrhea (inflammatory) in dogs

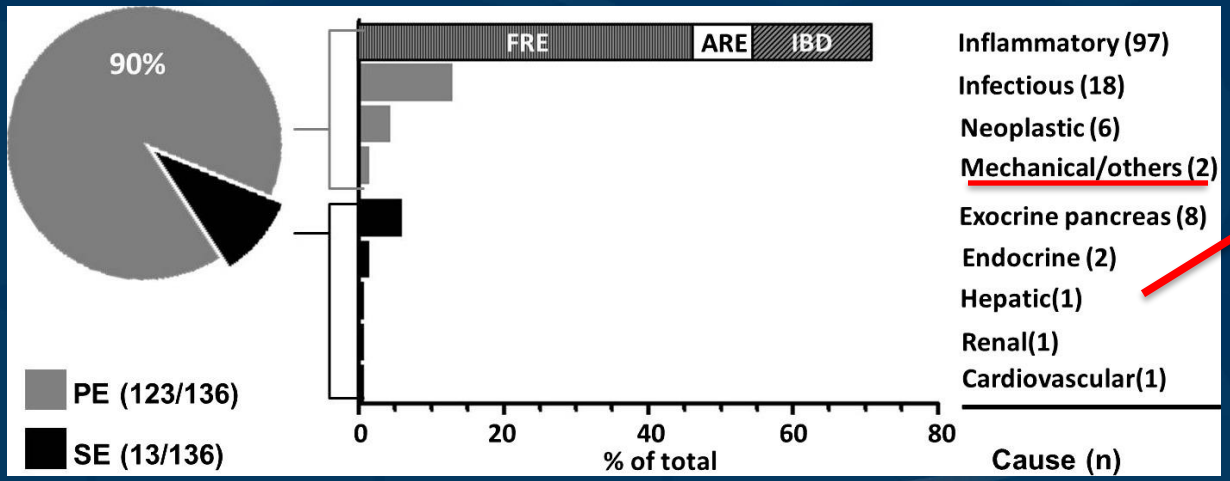


Distribution of causes for chronic diarrhea in dogs with PE:

ARE = 11/123 → 9%

FRE = 64/123 → 52%

SRE = 22/123 → 18%

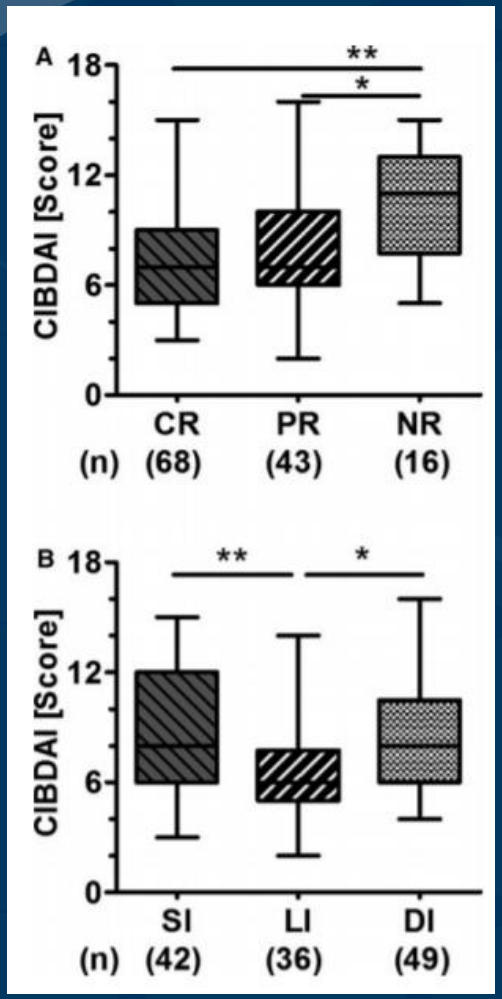


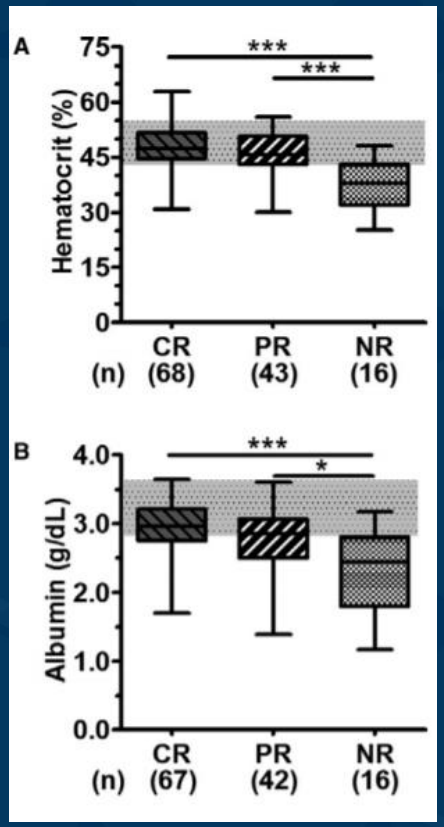
Causes for SE are uncommon (10%) of dogs

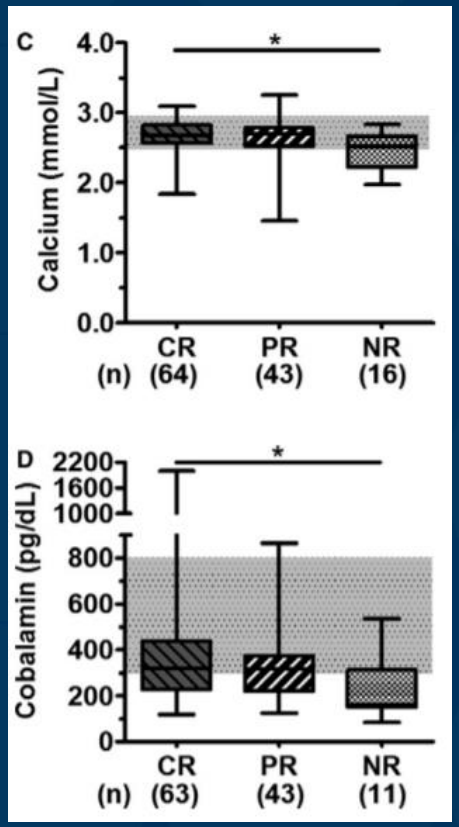
Key points for chronic diarrhea (1)

- Inflammatory enteropathies are most common cause for canine chronic diarrhea
  - FRE was most common in this cohort (66% of dogs)
  - 38% of FRE dogs had pruritus (AJ does not see this)
- IBD is also common, but not most common here
  - Most common cause for CE in dogs at ISU
- Intestinal neoplasia (LSA) was relatively uncommon
  - Advanced diagnostics (IHC, flow cytometry, PARR) - N.P.
- Parasitic infections - 2nd most common of PE → 11%
  - *Giardia* spp. infection; bacterial/viral pathogens were rare

Key points (2) - outcome measures







Key study outcome measures:

Clinical severity

Hematocrit

Serum albumin

Cobalamin concentration

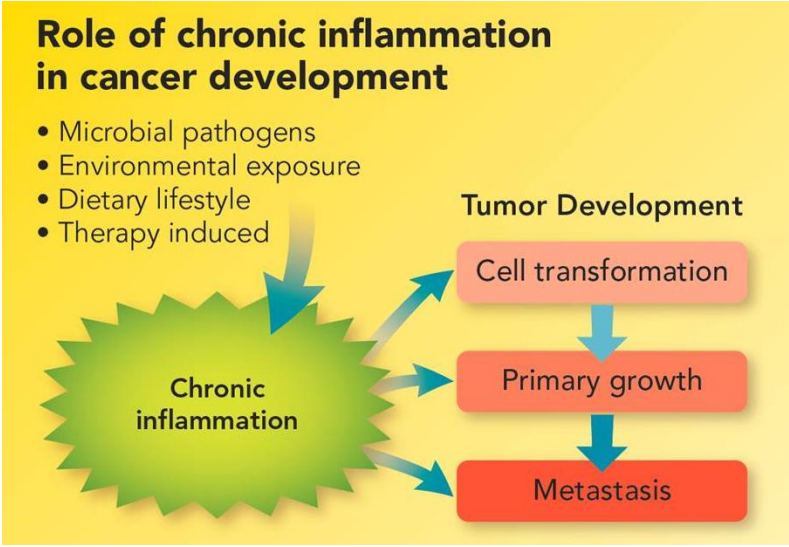
#4 Differentiating IBD vs. LSA in cats?

Overlapping clinical, laboratory, imaging and histologic findings

- History of chronic GI signs (SI diarrhea), weight loss, or anorexia/hyporexia
- PE: weight loss (↓ BCS) anemia, thickened intestinal loops, ↑mesenteric lymph nodes, ± hepatomegaly
- Anemia, hypoalbuminemia, ↑ liver enzymes, low cobalamin (ileum); screen for FeLV/FIV
- Abdominal ultrasound - ↑ mesenteric lymph nodes, ↑ intestinal wall thickness (muscularis), loss of layers
- Routine histology (H&E stain) may not be definitive

Indirect evidence suggests association with chronic inflammation

- Link suggested between feline IBD and GI lymphoma[1,5-7]
  - Other studies have not supported this theory[8]
- Gastric *Helicobacter* infection associated with feline gastric MALT lymphoma[9]
  - Recognized syndrome in humans
- Additional investigation needed
  - See *new evidence* for role of microbiota in feline GI cancer

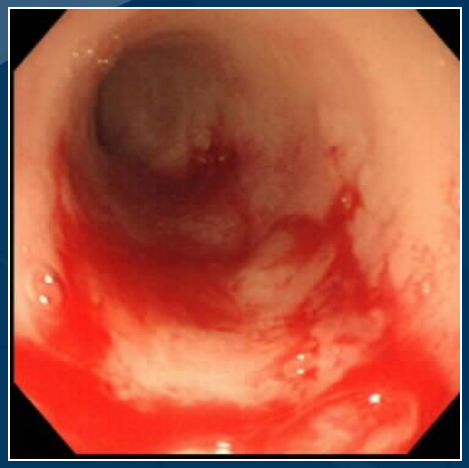


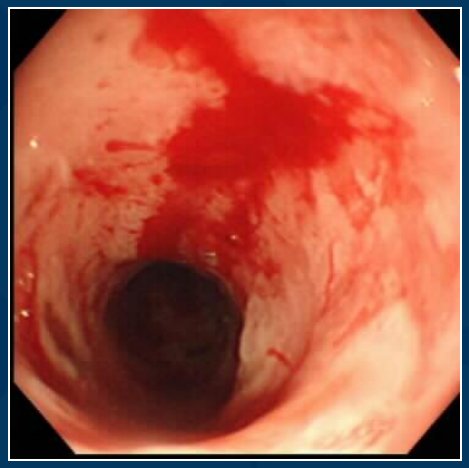
http://4.bp.blogspot.com/-Hx62iQsPbr0/UiSuQgqaKtI/AAAAAAAAAuA/Nh8we6oBkAY/s1600/136_Tumor+cell+development+diagram.jpg

Chad M. Johannes, DVM, DACVIM (SAIM, Oncology)

[1]Louwerens M, London CA, Pedersen NC, et al. J Vet Intern Med 2005;19:329-335. [5]Carreas JK, Goldschmidt M, Lamb M, et al. J Vet Intern Med 2003;17:326-331. [6]Ragaini L, Aste G, Cavicchioli L, et al. Vet Res Commun 2003;27(Suppl I):791-793. [7]Tams TR: Inflammatory bowel disease. WB Saunders 1991, pp. 409-414. [8]Hart JF, Shaker E, Patnaik AK, et al. J Am Anim Hosp Assoc 1994;30:505-514. [9]Bridgeford ED, Marini RP, Feng Y, et al. Vet Immunol Immunopathol 2008;1123:106-113.

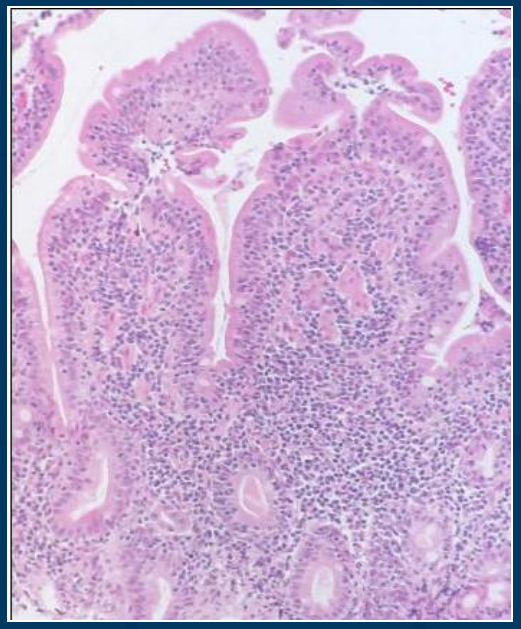
Do microbial imbalances contribute to FIBD?

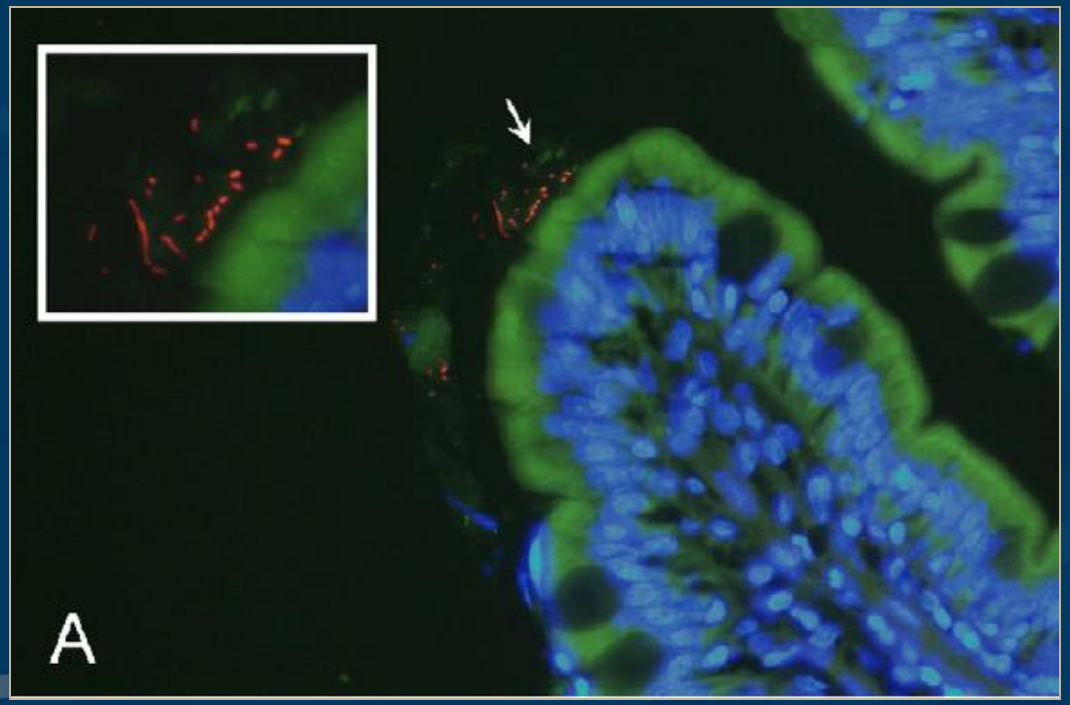




RESULTS

FISH confirms mucosal bacteria
Increased Enterobacteriaceae
Increased cytokine mRNA
Association with clinical signs
Association with histology





Janeczko, Vet Microbiol 2008

Identification of Mucosa-Invading and Intravascular Bacteria in Feline Small Intestinal Lymphoma

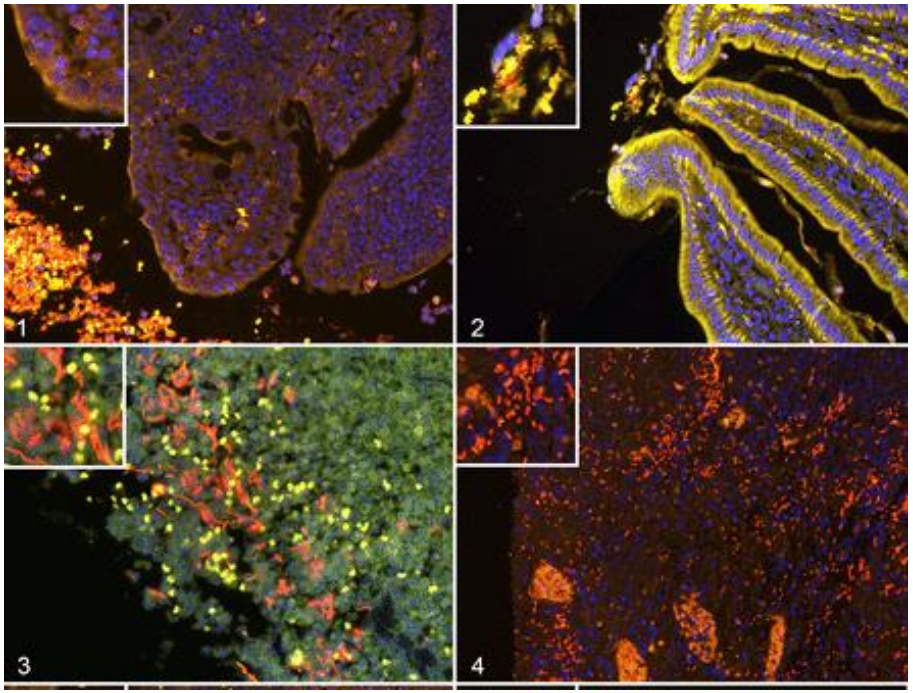
S. N. Hoehne[1,2], S. P. McDonough[3], M. Rishniw[1], and K. W. Simpson[1]

Table 1. Spatial Distribution of Bacteria in Small Intestinal Samples of Cats.

	Luminal, n_{pos} (%)	Mucus, n_{pos} (%)	Adherent, n_{pos} (%)	Invasive, n_{pos} (%)	Vascular, n_{pos} (%)	Serosal, n_{pos} (%)
NMC	8 (44)	4 (22)	4 (22)	0 (0)	0 (0)	1 (8)
LPE	12 (60)	2 (10)	5 (25)	1 (5)	0 (0)	1 (6)
SCL	27 (82)**	12 (39)	13 (42)	6 (18)	0 (0)	2 (11)
LCL	17 (100)***,##	5 (56)##	5 (56)	14 (82)***,####,○○○	5 (29)*,##,○○	8 (57)**,####,○○

Fisher's exact test vs NMC: $^{*}P \leq .05$, $^{**}P \leq .01$, $^{***}P \leq .001$; vs LPE: $^{\#}P \leq .05$, $^{\#\#}P \leq .01$, $^{\#\#\#}P \leq .001$; vs SCL: $_{\circ}P \leq .05$, $_{\circ\circ}P \leq .01$, $_{\circ\circ\circ}P \leq .001$. Luminal: in the luminal cellular debris; Mucus: in the villus-associated mucus; Adherent: adherent to the villous enterocytes; Invasive: in the lamina propria; Vascular: in mucosal blood vessels; Serosal: adherent to the serosal surface. LCL, large cell lymphoma; LPE, lymphoplasmacytic enteritis; NMC, normal to minimal change; SCL, small cell lymphoma.

SCL
bacteria in
adherent mucus



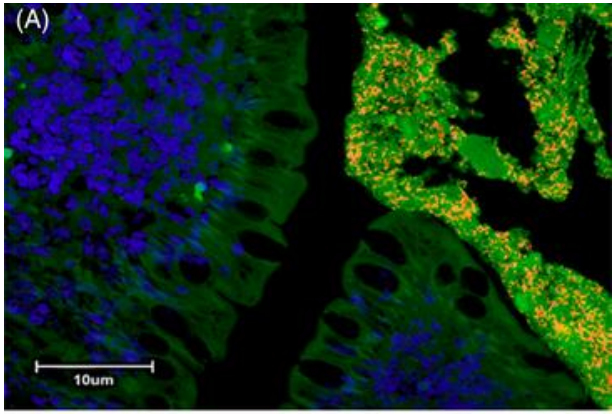
Normal
Few bacteria

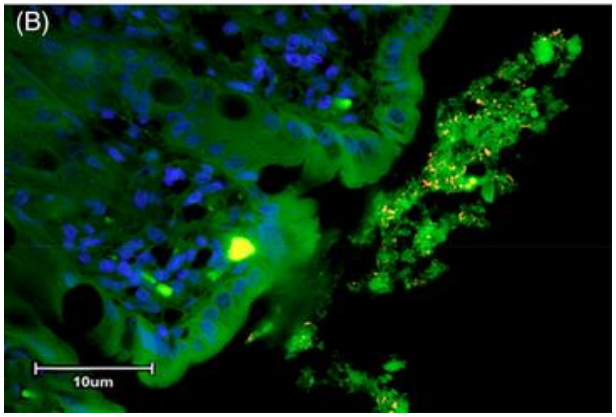
SCL
bacteria in ulcerated
mucosa

SCL
Invading bacteria

Relationship of the mucosal microbiota to gastrointestinal inflammation and small cell intestinal lymphoma in cats

K. Garraway, C. Johannes, A. Bryan, J. Peauroi, G. Rossi, M. Zhang, C. Wang, K. Allenspach, A. Jergens

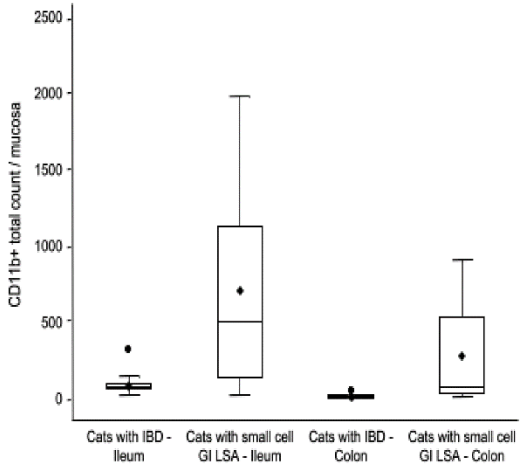


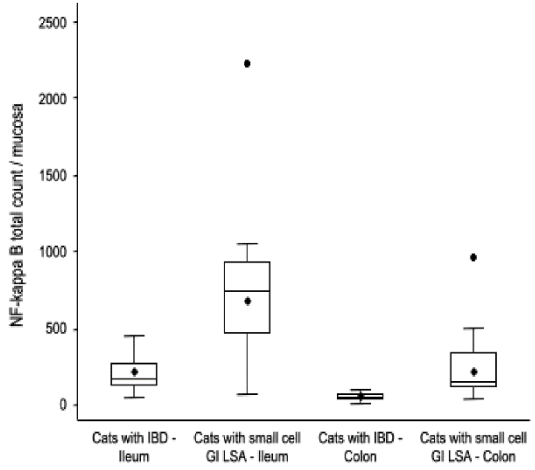


Fusobacterium spp. and LSA NF-κB and CD11b+ macros

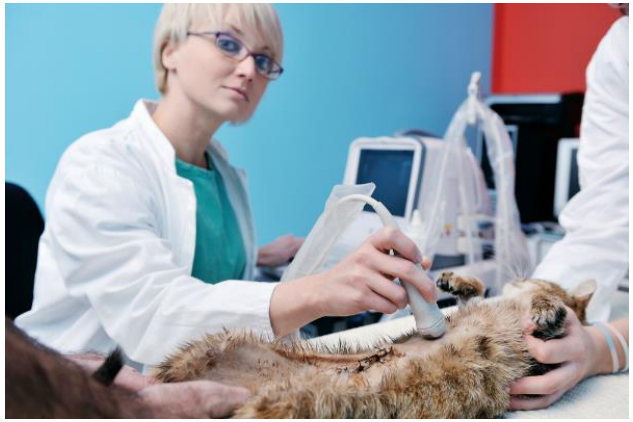
Table 3. Spatial distribution of colonic mucosal bacteria based on FISH.

Probe	Group	FM	AM	A	I
Eub338	IBD	0	42	2	0
	Lymphoma	0	52	0	0
Erec482	IBD	0	10	0	0
	Lymphoma	0	16	0	0
Ebac1790	IBD	0	2	0	0
	Lymphoma	0	7	0	0
BacPrev1080	IBD	0	18	1	0
	Lymphoma	0	28	0	0
Hel717	IBD	0	0	0	0
	Lymphoma	0	0	0	0
Fecali896	IBD	0	10	0	0
	Lymphoma	0	12	0	0
Fusobac TA	IBD	0	7	0	0
	Lymphoma	0	28	0	0





Diagnostic approach when GI LSA vs. IBD suspected



- Minimum data base
  - CBC with differential; FeLV / FIV
  - Serum biochemistry profile
  - Urinalysis
- Abdominal radiographs/US
- Fine-needle aspirate of masses/nodes
- Biopsy procurement
  - Exploratory laparotomy vs. GI endoscopy
- H&E, immunophenotyping, PARR
- AJ uses sequential approach to IBD/LSA diagnosis
- Are current diagnostic strategies adequate?

[3]Vail DM in Small Animal Clinical Oncology (5th Edition), Elsevier Saunders, 2013, pp. 645-646.
Image: http://www.catster.com/wp-content/uploads/2015/06/600px-cat-getting-ultrasound.jpg

C. Johannes, 2016

Results of histopathology, immunohistochemistry, and molecular clonality testing of small intestinal biopsy specimens from clinically healthy client-owned cats

Sina Marsilio[1] | Mark R. Ackermann[2,1] | Jonathan A. Lidbury[1] | Jan S. Suchodolski[1] | Jörg M. Steiner[1]

JVIM 2019

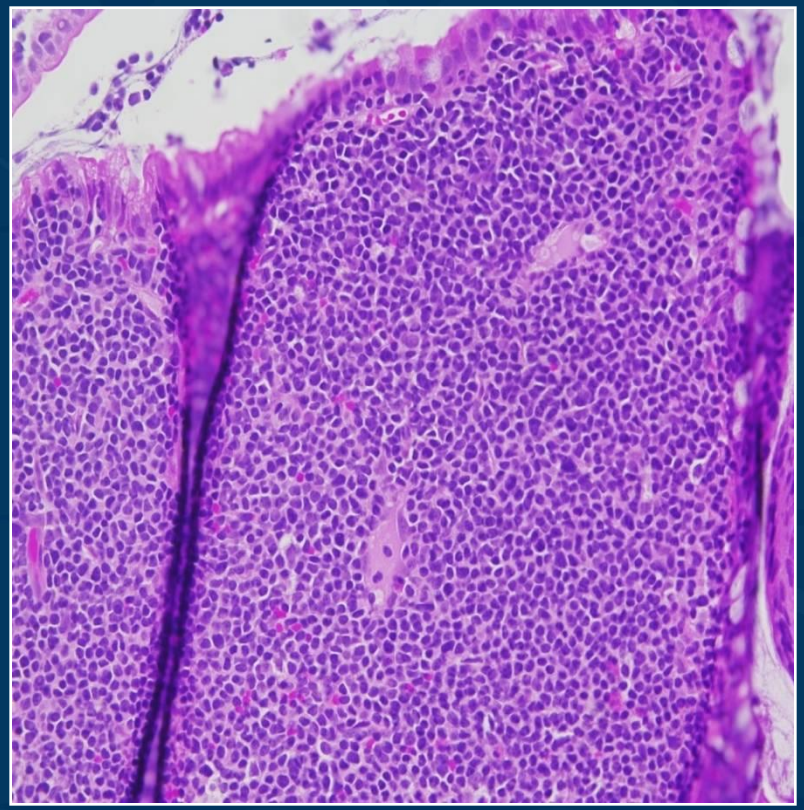
- Background: Histopathology, IHC, and PARR are testing metrics for CIE in cats. Normal values for these metrics may not be accurate based on earlier criteria.
- Aim: Using upper GI endoscopy (duodenoscopy), describe these indices in healthy client-owned cats
- Animals: 20 healthy client-owned cats ≥ 3 years old
- Methods: tissues collected (n=6) from stomach and duodenum of each cat
  - Histology reviewed by a single pathologist (MA)
  - Routine H&E, IHC (T-, B-, NK cells), clonality tests (FFPE)

Results

- None of the healthy cats exhibited GI signs initially
- H&E, IHC and clonality tests integrated to arrive at a final histologic diagnosis
  - SCL, n=12
  - Lymphocytic enteritis (n=6)
  - Pseudoclonality (n=1)
- 3 cats developed GI signs, 2 euthanized at 295 and 654 days; other 17 cats remained healthy
- Conclusions: Intestinal biopsies of healthy cats may have abnormal findings on histology, IHC and PARR. Current guidelines for defining healthy vs. CE may need further modification

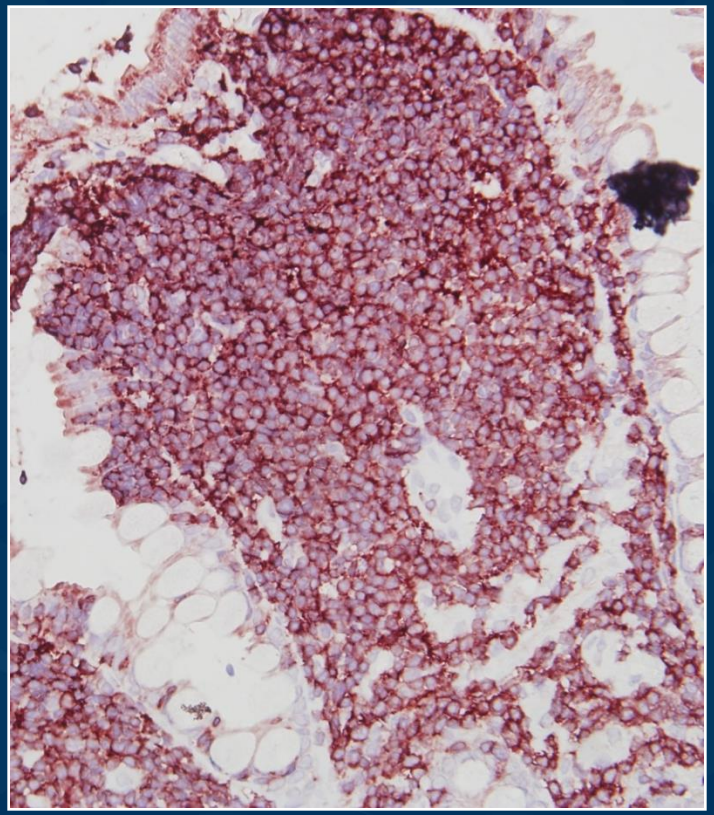
Histopathologic findings - ileum

H&E and special stains of ISU case



Ileum - H&E stain

Note diffuse infiltrate of lymphocytes and absence of plasma cells

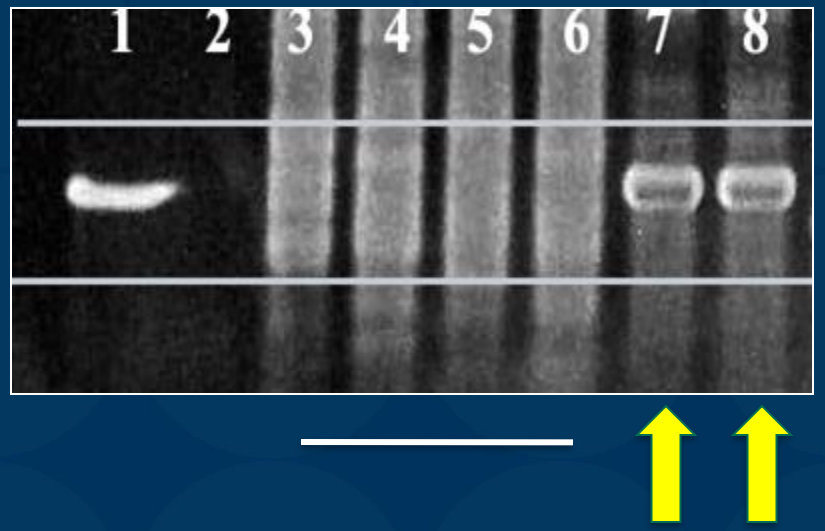


Duodenum – Immunophentyping

Note application of T cell (CD3+) antibody - >90% T lymphocytes

Severe feline IBD vs. LSA?

- Similar GI signs
- Baseline diagnostics
  - Laboratory results
  - Imaging findings
- *GI mucosal biopsies*
  - Exfoliative cytology
  - H&E stain
  - Immunophenotyping
  - Clonality testing



Courtesy of Dr. Kenneth Simpson
Cornell University

Sequential histopathologic testing is recommended
IF LAPAROTOMY → MULTI-ORGAN BIOPSIES RECOMMENDED

#5 Fecal microbiota transplant (FMT)

Is it useful?

- "infusion of a fecal suspension from a healthy individual into the GI tract of an individual with colonic disease". First used in 1958.
- Idea: reintroduce a complete, stable, and functional microbiota aimed at correcting dysbiosis (CDI)
- Alternative to manipulating the gut microbiota
  - Probiotics → variable and modest effects
- Useful for spectrum of human diseases (GI, non-GI)
  - Constipation, IBS, IBD, HE, CRC, autism, MS

Practical guidelines for FMT

Parameter	Consideration
Donor selection	Breed – GI disease susceptible? Vaccination history Diagnostic screening for infectious agents Recent history of antibiotic use
Recipient preparation	Role of diet? Perform bowel lavage? Perform antibiotic trial prior to FMT?
Donor sample storage	Fresh vs. frozen feces
Type of diluent	Saline vs. water vs. milk
Volume of stool required	~ 60 grams feces in 250-300 ml diluent
Route of administration	Nasogastric/enteric vs. enema vs. colonoscopy

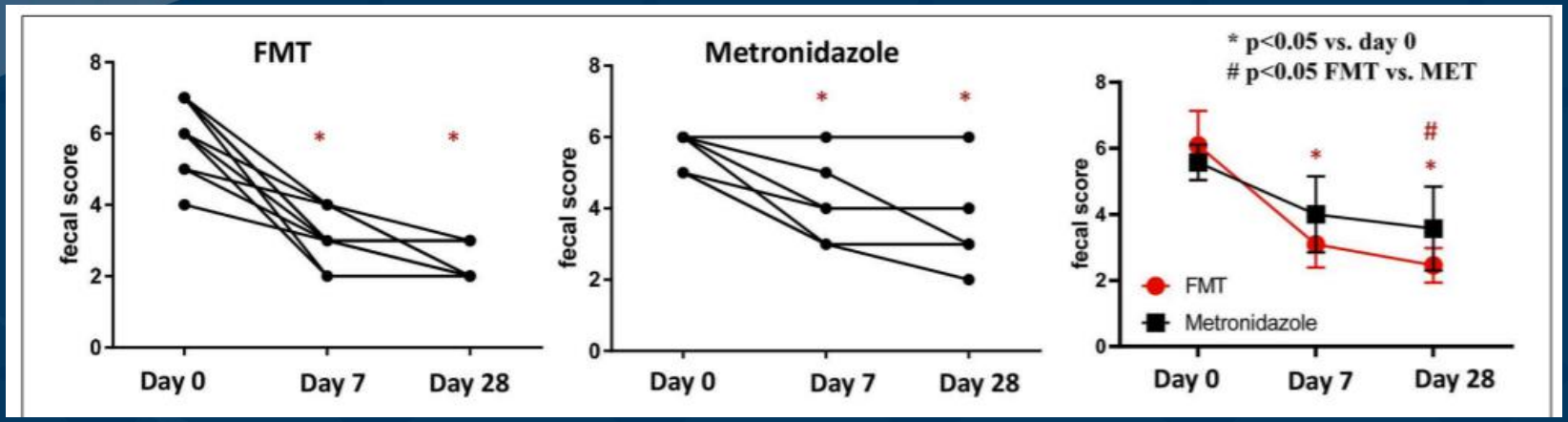
Guidelines are currently under review and have yet to be designed for dogs, cats, or humans

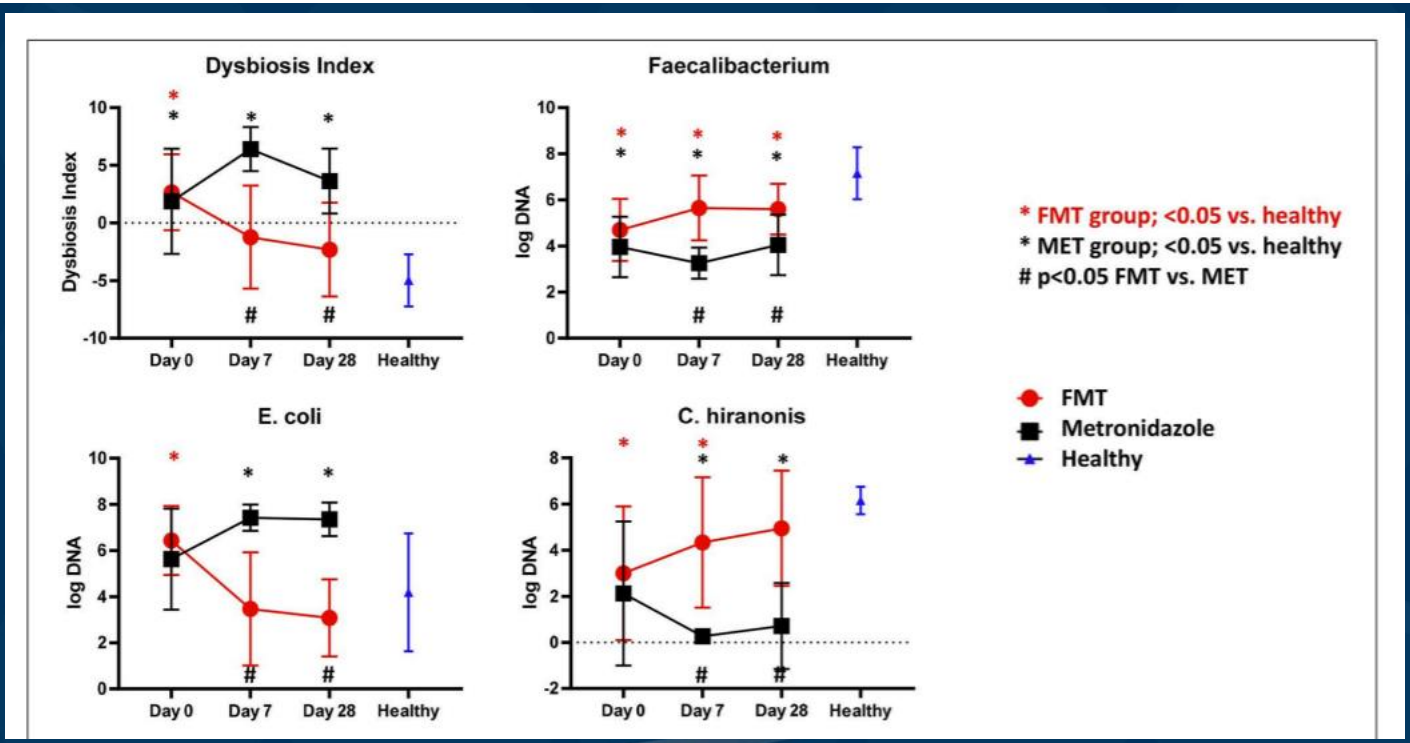
Clinical trials using FMT

Efforts to restore eubosis have had limited investigation

- RCT - puppies with parvoviral diarrhea that received FMT + std therapy vs. std therapy improved faster
- Oral FMT failed to improve acute diarrhea in research puppies
- Adult dogs with acute diarrhea show differences in the microbiome and metabolome with FMT vs. MTZ
- One small study with AHDS showed that a single FMT did not improve GI signs and dysbiosis
- Studies in dogs with CE (2 reports, n=17) show that severity of clinical disease improved in most dogs
- Limitations: small sample size, different delivery routes, lack of controls, failure of rigorous molecular testing for bacteria

FMT vs. MTZ for acute diarrhea in dogs





FMT
N=11

MTZ
N=7

**Chaitman, Front Vet Sci 2020*

Suggested protocol for FMT*

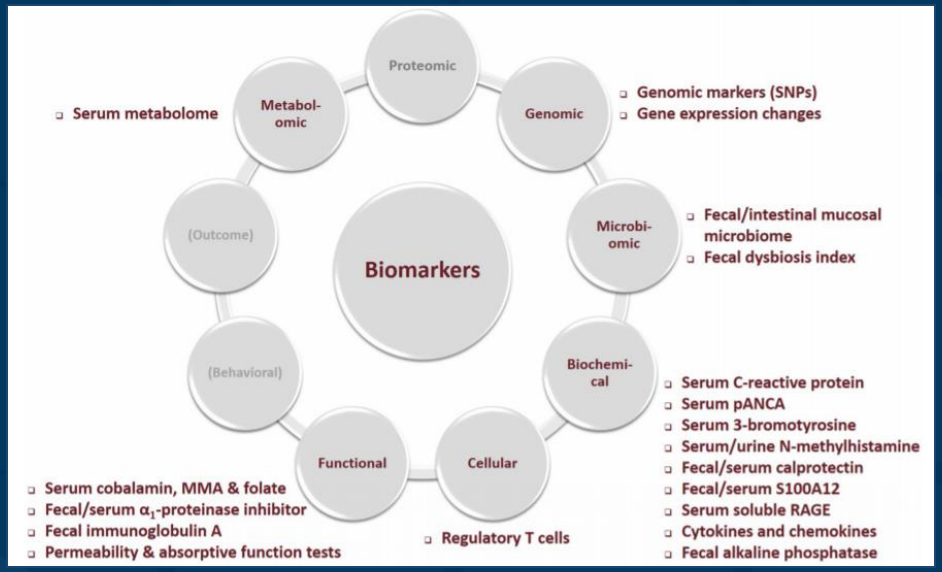
- Donor should be healthy - no history of GI disease and recent antibiotic use. Screen for parasites and enteropathogens.
- Assess for *C. hiranonis* via DI, if possible
- Stool can be fresh or stored at 4 C for one week in plastic bags. For longer storage, mix stool with glycerol before freezing.
- FMT as enema - donor feces (5 grams per kg of recipient BW) is blended in 60 ml of 0.9% NaCl. The stool is then infused into the colon via a 60 ml syringe attached to a 12- or 14-inch French red rubber catheter. The recipient does not need to be sedated. Restrict activity for 4-6 hours after FMT to prevent BM.

**Chaitman, Front Vet Sci 2020*

#6 Biomarkers of GI inflammation (CIE)

What works best?

- Biomarkers potentially may:
  - Aid in diagnostic evaluation
  - Aid in patient monitoring
  - Assess treatment response and disease progression
- There are well-recognized biomarkers currently used:
  - Serum cobalamin (D)
  - Serum albumin (D)
  - Serum hsCRP (D)
  - Fecal dysbiosis index (D)
  - Cats - cobalamin



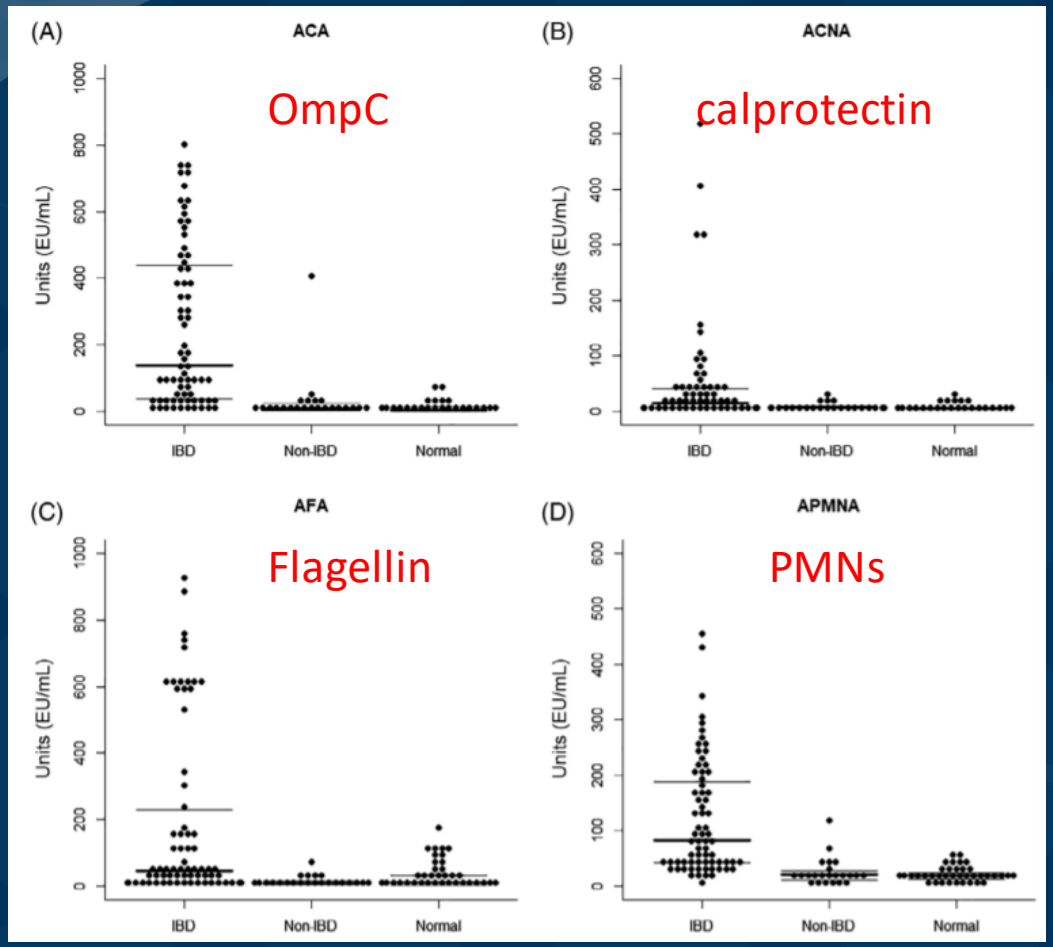
Evaluation of novel serological markers and autoantibodies in dogs with inflammatory bowel disease

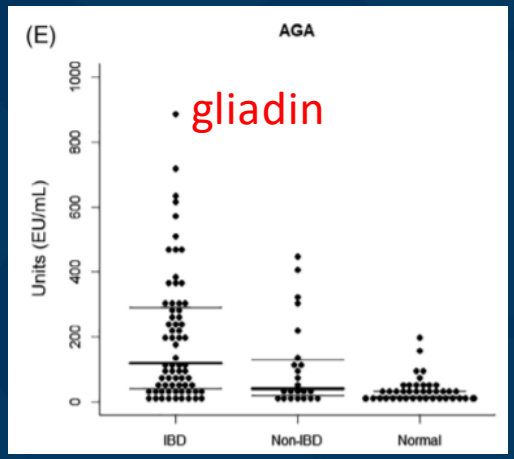
Juan J. Estruch[1] | Derren Barken[2] | Nicole Bennett[3,4,5] | Donald K. Krawiec[3,4,5] | Gregory K. Ogilvie[3,4,5] | Barbara E. Powers[6] | Benjamin J. Polansky[3,4,5] | Michael T. Sueda[3,4,5]

Estruch, JVIM 2019

- Background: Use of biomarkers to diagnose HIBD is well established; new approaches are needed for diagnosis of IBD in dogs?
- Aim: Develop novel serologic markers to distinguish between cohorts with GI disease vs. HC
- Animals: 70 dogs with IBD; 23 dogs with acute GI disease; 58 normal dogs
- Methods: Prospective controlled study; ELISA developed to detect IgA antibodies against:
  - PMNs, calprotectin, gliadins, *E. coli* OmpC, flagellin

Results





	ACA	ACNA	AFA	APMNA	AGA
IBD versus normal	0.915	0.774	0.766	0.924	0.843
IBD versus non-IBD	0.847	0.698	0.789	0.883	0.650

All AUC values, $P < .001$ for IBD

**IgA directed against OmpC was highest

Critical assessment of results

Numerous study limitations

- Dogs with primary vs. secondary CE were not clearly differentiated
  - Pancreatitis (n=10), hypoadrenocorticism (n=9), EPI (n=2)
  - These can be easily diagnosed; no need for novel biomarkers
- IBD dogs need to be differentiated from other forms of CE
  - A group of non-IBD chronic enteropathy dogs was not included
  - Examples could include chronic giardiasis, histoplasmosis, GC (boxers)
  - Biomarkers in IBD dogs would need to show no overlap with above
- No mention of diagnostic imaging findings in non-IBD dogs
- Only 24% of 157 CE/IBD dogs had histologic IBD
- No mention of results of empiric therapies - deworming, diets

View these results cautiously – other biomarkers are useful

Presentation key points

- DI - a simple tool for detection of dysbiosis in dogs
- BA dysmetabolism in common in dogs with CIE
  - Dogs with CIE have ↓ secondary BAs and dysbiosis
  - *C. hiranonis* is an important BA converting bacterium
- Hematocrit, albumin, cobalamin and disease severity best predict LT outcome in dogs with chronic diarrhea
- Intestinal biopsies of healthy cats may have abnormal findings - H&E, IHC, clonality testing for IBD vs. LSA
- FMT is evolving in dogs; technique needs standardization
- IgA antibodies may distinguish CIBD from other CEs

Questions?

Differentiation of lymphocytic-plasmacytic enteropathy and small cell lymphoma in cats using histology-guided mass spectrometry *JVIM 2019*

Sina Marsilio[1,2] | Shelley J. Newman[3] | James Scot Estep[4] | Paula R. Giaretta[5] | Jonathan A. Lidbury[2] | Emma Warry[6] | Andi Flory[7] | Paul S. Morley[8] | Katy Smoot[9] | Erin H. Seeley[9] | Matthew J. Powell[9] | Jan S. Suchodolski[2] | Jörg M. Steiner[2]

- Differentiation of LPE vs. SCL investigated in 17 cats with LPE and 22 cats with SCL
  - Panel (5-7 specialists) investigated GI signs, clinical findings, H&E, IHC, and clonality in cohorts
  - Consensus opinion made diagnosis of LPE or SCL
- Results of HGMS were compared to expert opinion; HGMS was shown to be superior to opinion
- Limitations of study: biopsy collection (ileum?); some samples removed (no consensus); HGMS on duodenal LP only; clinical practicality of assay

Clinical signs typically non-specific for small cell, low-grade cases[3]

Clinical Sign / Finding	Occurence (% of cases)
Weight loss	83-100
Vomiting and/or diarrhea	73-88
Abnormal abdominal palpation	70
→ Intestinal wall thickening	50
→ Palpable mass	33
Inappetence	66
Icterus	7

Signs usually present for several months (median = 6)

[3]Vail DM in Small Animal Clinical Oncology (5th Edition), Elsevier Saunders, 2013, pp. 643-644.

Preliminary clinical and microbiome assessment of stool transplantation in the dog and cat[1]

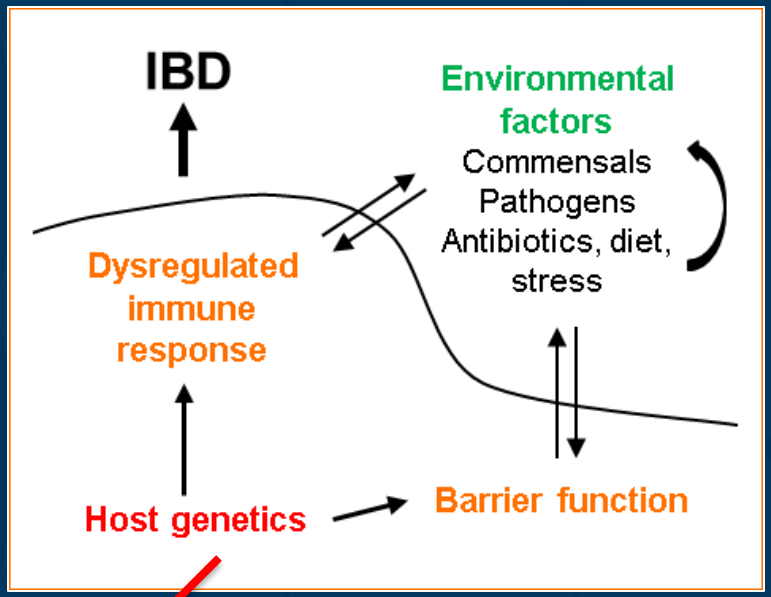
- Case 1 → 6 yr DSH with 16 months diarrhea
  - Unremarkable biopsies, poorly responsive to therapy
  - Fresh feces from healthy donors via enema
- Case 2 → 3 yr dog with eosinophilic IBD
  - 2 years duration and poorly controlled with std tx.
- HTS of 16S rRNA genes
  - Rapid improvement (24 hours) in stool + GI signs
  - Bacterial sequences like donors by day 2
- Consider FMT as therapy when other therapies fail

[1]*Weese, ACVIM proceedings, 2013*

Canine CIE and biomarkers

IBD, FRE, and ARE

- CIE - group of GI disorders having chronic GI signs, histologic inflammation, and exclusion of other underlying GI/ non-GI causes
- Pathogenesis is linked to host genetic-microbiota-immune interactions
- Diagnosis is retrospective based on response to therapy +/- gut biopsy
  - *FRE*
  - *ARE*
  - *SRE (IBD)*



GI signs
Histopathologic lesions
Immune responses
Dysbiosis

Initial diagnostic approach to chronic diarrhea

Integrate signalment, history, and PE	→	Breeds at risk, environment, diet GI signs, localizing findings
Detection of parasites	→	Nematodes, protozoa (Giardia)
Clinicopathologic testing Detect non-GI disease	→	CBC, biochemistry, U/A, ACTH, T_4, FeLV/FIV, bile acids
Detect GI disease (+/- multi-organ)		Low albumin, hypocholesterolemia, leukopenia, low folate/cobalamin
Advanced diagnostics Detect GI disease	→	DI of liver, pancreas, lymph nodes, masses, effusions
Detect non-GI disease		Ultrasound of liver, pancreas, lnn, bw layering/organization, foci

Empiric therapies for chronic enteropathy

Sequential therapy strategy

- Parasites - fenbendazole; treat for Giardia
- Food-responsive enteropathy
  - *Cats* → 7 day trial; elimination diet → no challenge
  - *Dogs* → 14 day trial; elimination diet → no challenge
- *Antibiotic-responsive enteropathy??*
  - Metronidazole ++
  - Tylosin +
  - Oxytetracycline
- Fermentable fiber (psyllium) for colitis
- Cobalamin supplementation; Pre- and probiotics