



TEXAS A&M UNIVERSITY
Gastrointestinal
Laboratory



TEXAS A&M
UNIVERSITY

The therapeutic effect of diet and fiber in acute and chronic diarrhea

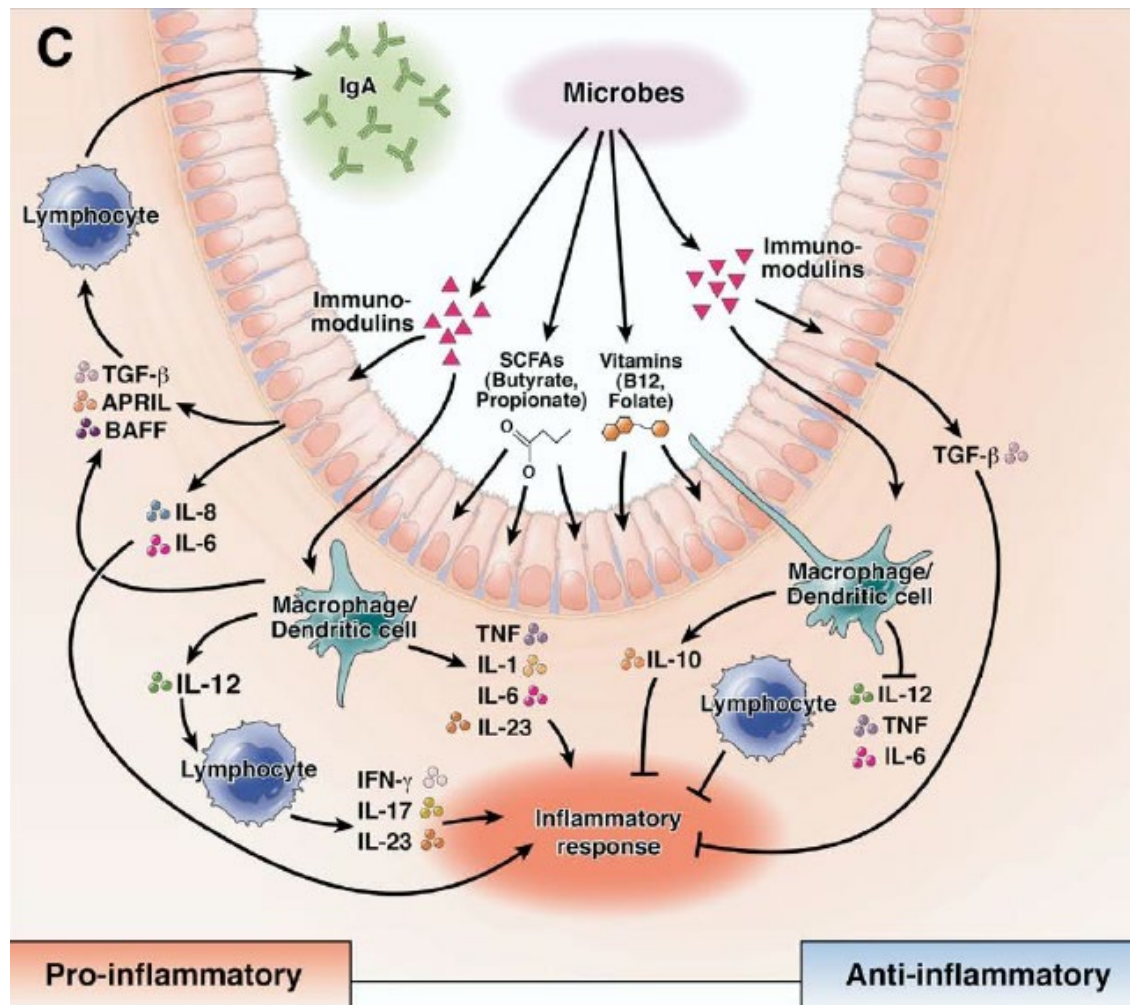
Jan S. Suchodolski, DrMedVet, PhD, DACVM, AGAF

Professor & Associate Director Research

Head of Microbiome Sciences, Gastrointestinal Laboratory

Department of Small Animal Clinical Sciences

Texas A&M University, College Station, TX, USA



TOBIE

- 5 year old Dachshund
- chronic diarrhea > 2 year duration
 - mixed origin
 - soft/watery, occasionally tenesmus
 - diarrhea sometimes 2-3x per day
- fed commercial kibble diet

HISTORY

- history of parvovirus as puppy
- several unsuccessful treatment attempts over last year
 - short-term improvement on home-made diet (duck)
 - deworming (fenbendazole)
- intermittently on metronidazole
 - 15 mg/kg PO q12 hours
 - partial improvement when on, relapses when stopped
 - last dose 2 months ago

PHYSICAL/LABORATORY RESULTS

- physical exam unremarkable
- BCS 4/9
- CBC, serum chemistry profile, basal cortisol (2.3 $\mu\text{g}/\text{dL}$)
 - no abnormalities

GI PANEL

Test		Unit	Reference interval
cPLI	133	μg/L	< 200 μg/dl
cTLI	20	μg/L	5.7 – 45.2
Cobalamin	301	ng/L	251 - 908
Folate	21.4	ng/L	7.7 – 24.4

Cobalamin low normal – may indicate malabsorption associated with chronic enteropathy

FECAL EXAMINATION

- Fecal flotation for parasites
- Previous PCR enteropathogen panel – **positive** for *Clostridium difficile*
- Fecal Dysbiosis Index

Test	Result	Reference interval
Dysbiosis Index	4.2 = dysbiosis	<0
<i>Clostridium hiranonis</i>	0.1 = decreased	5.1 – 7.1

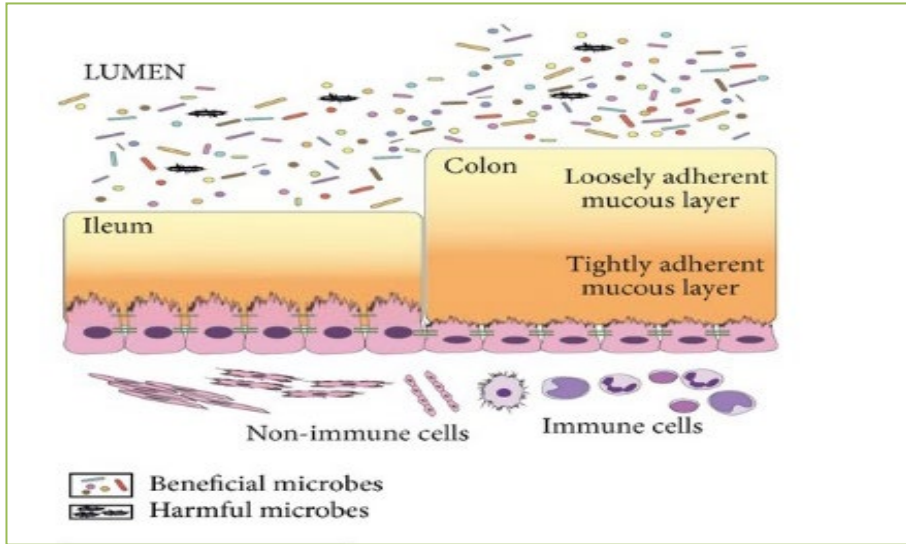
“TOBY” PROBLEM LIST

- chronic diarrhea, responsive to metronidazole, but frequent relapse
- low normal cobalamin
 - possible chronic inflammatory enteropathy
- increased dysbiosis index together with decreased *Clostridium hiranonis*
 - indicates fecal dysbiosis
- positive for *C. difficile*

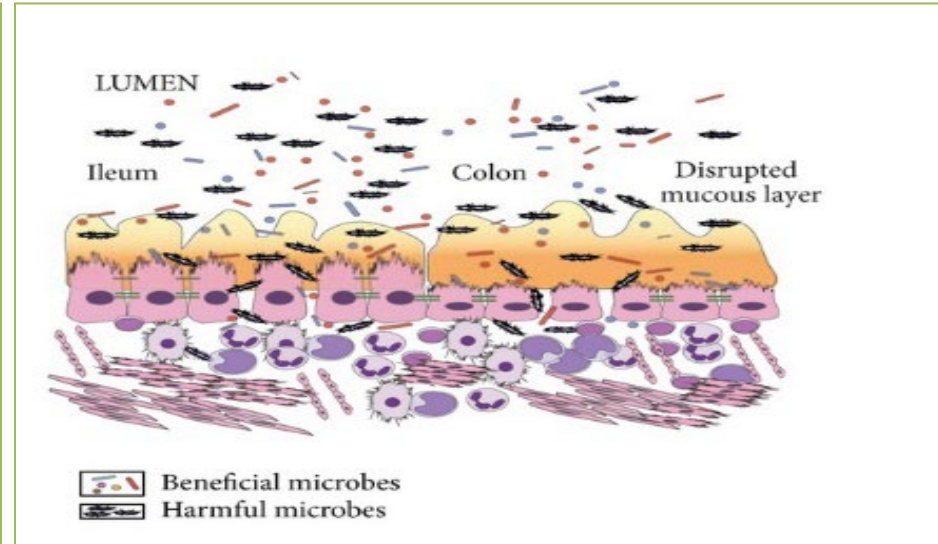
WHAT SHOULD WE TREAT?

- a) continue metronidazole (to eliminate *C. difficile*)
- b) change to another antibiotic (eg, tylosin)
- c) dietary change to novel or hydrolyzed protein diet
- d) probiotics to balance microbiota dysbiosis
- e) fecal microbiota transplant (FMT) to improve dysbiosis

Microbiota in GI health and disease

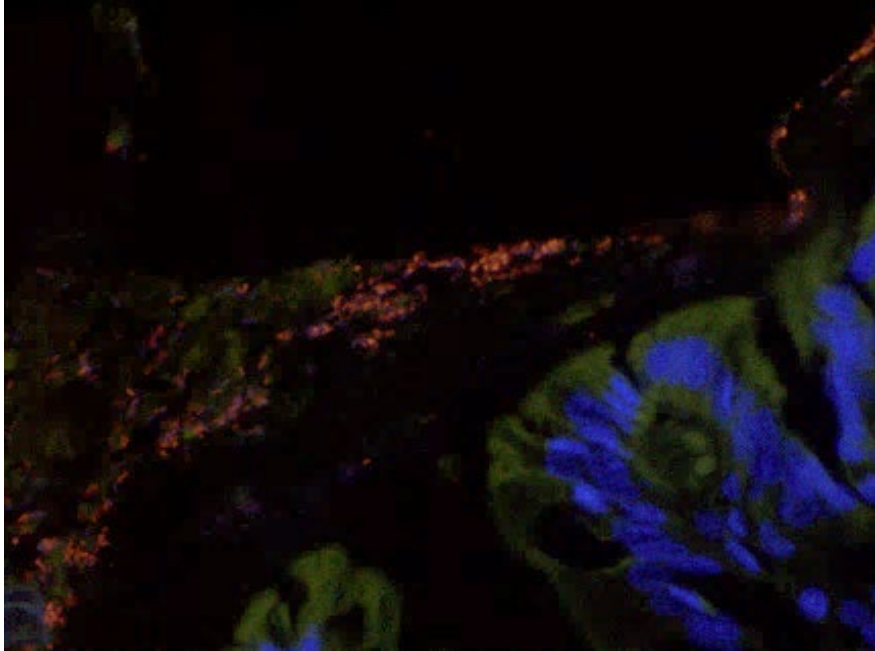


*Intestinal microbiota
in health*

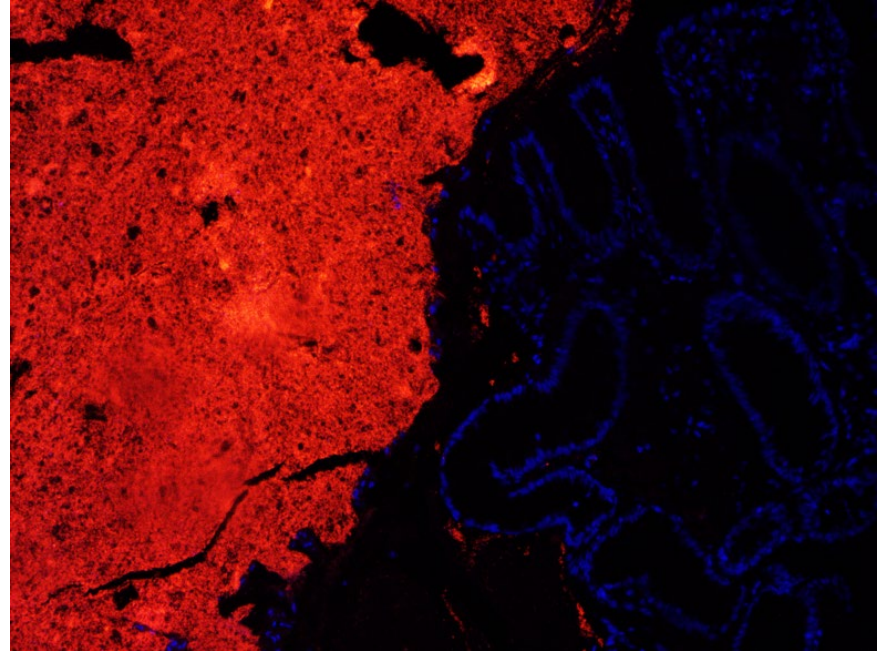


*Intestinal microbiota
in chronic enteropathy*

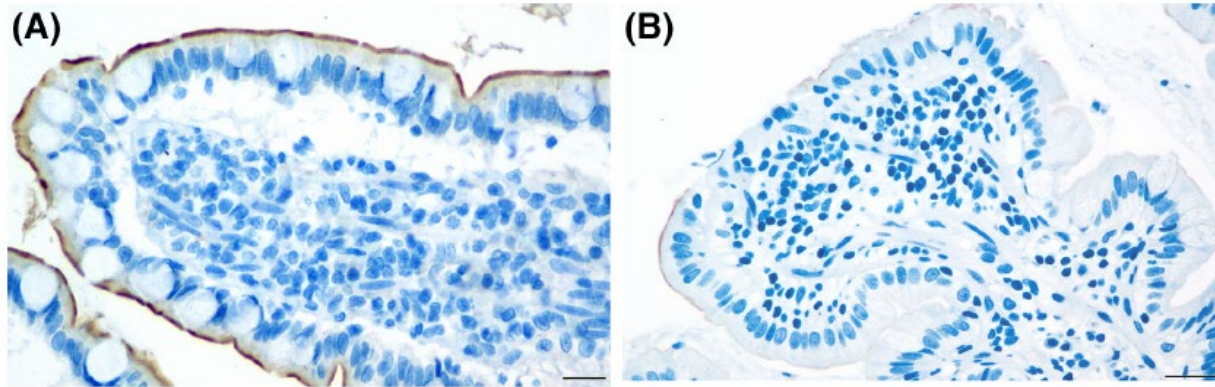
Healthy dog



Dog with antibiotic responsive enteropathy

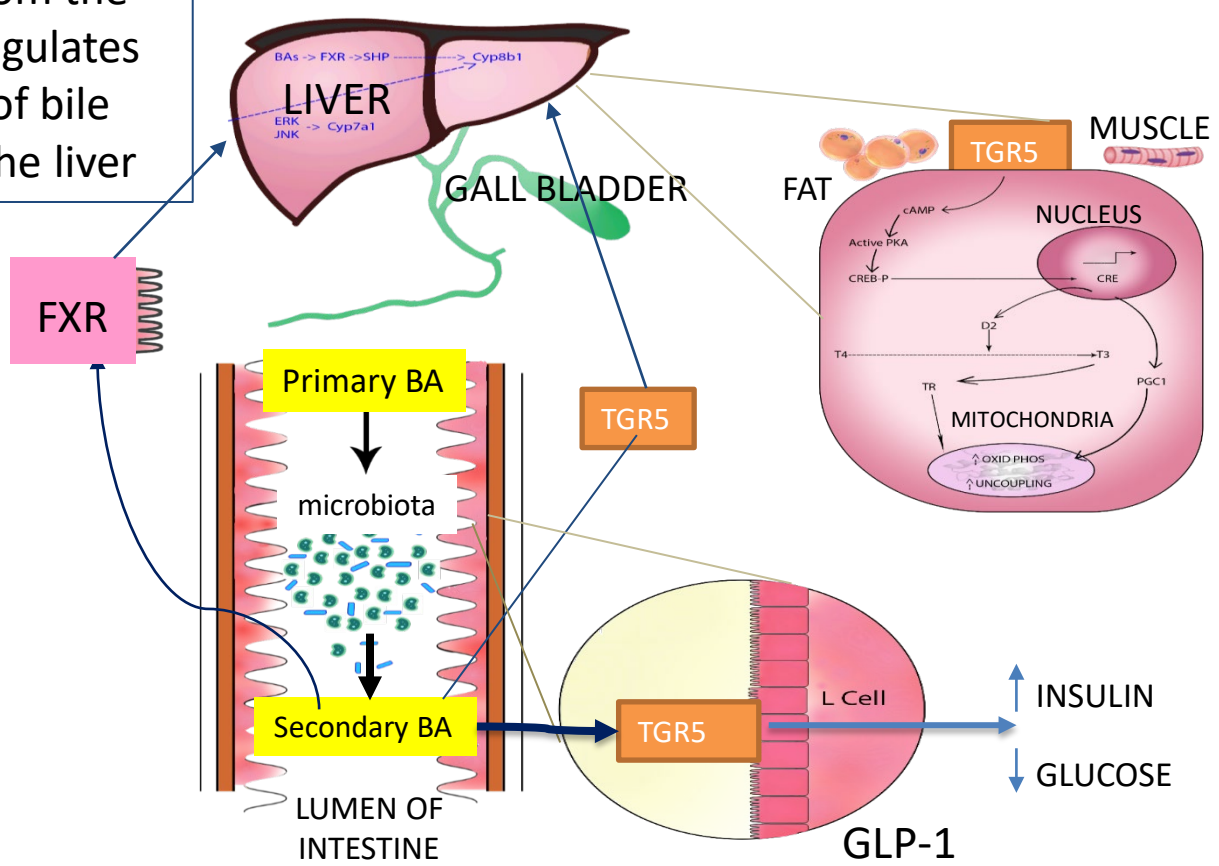


MALABSORPTION IN DOGS WITH CE



Bile acid transporter (ASBT) protein in healthy dog (A) and dog with CE(B)

Feedback from the intestines regulates production of bile acids from the liver



Secondary bile acids inhibit TNF- α , IL-1 β and IL-6 through activation of TGR5

secondary BA inhibit germination of *C. difficile* spores

primary BA promote germination

abnormal metabolite ratios lead to
activation of virulence factors

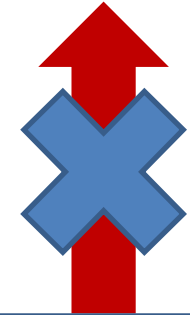
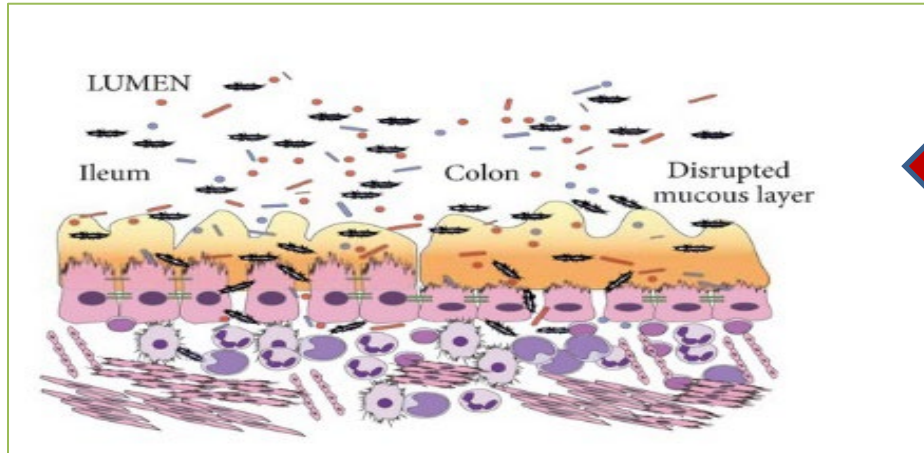
abnormal bile acid conversion
leads to overgrowth with

Salmonella, E. coli

C. difficile, C. perfringens, E. coli

Dysbiosis

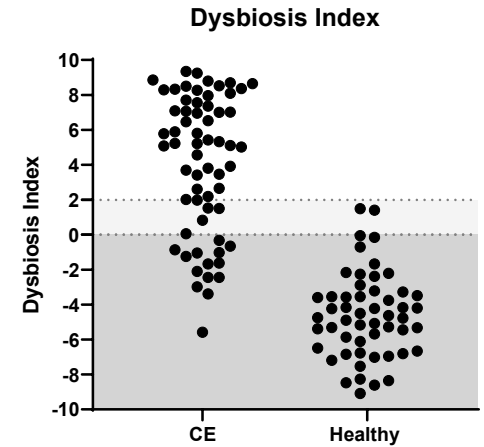
inflammation, maldigestion, malabsorption



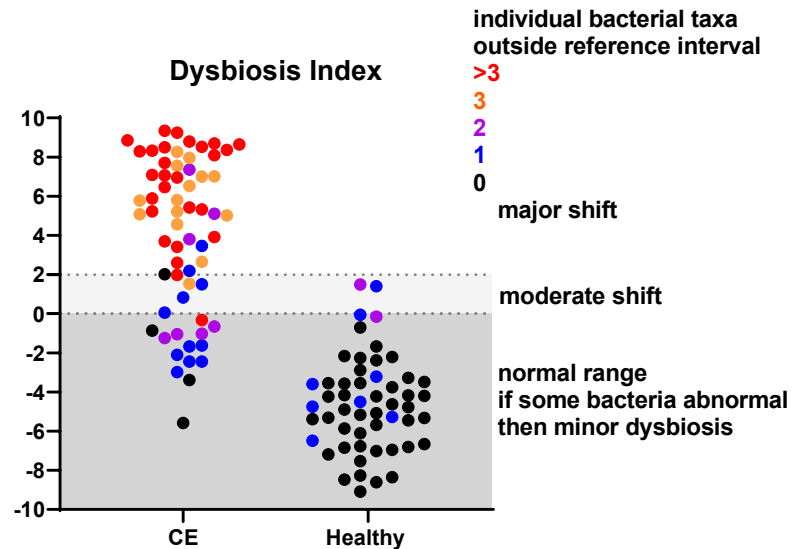
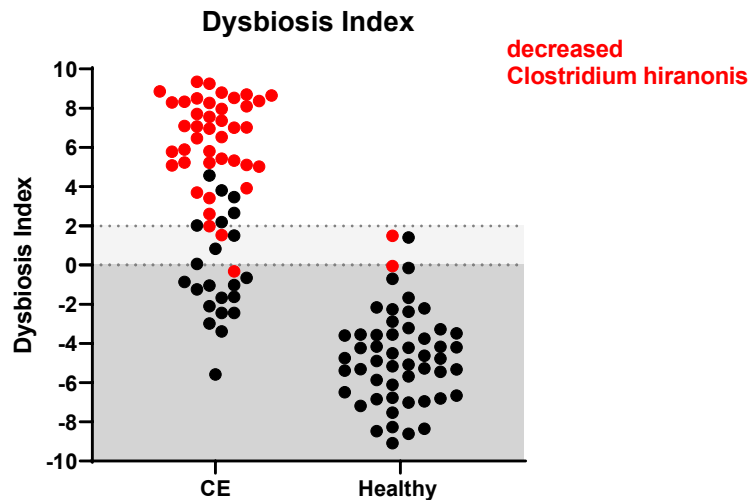
**need to identify
and treat
underlying
disorder**

A dysbiosis index to assess microbial changes in fecal samples of dogs with chronic inflammatory enteropathy

MK AlShawaqfeh^{1,2}, B Wajid^{1,3}, Y Minamoto¹, M Markel¹, JA Lidbury¹, JM Steiner¹, E Serpedin² and JS Suchodolski^{1,*}



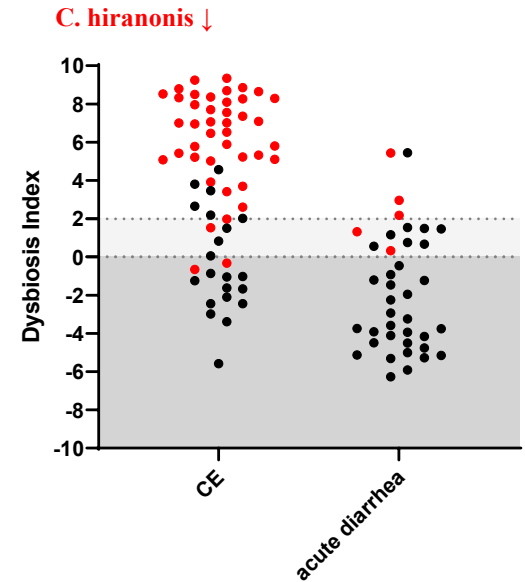
	Change in dysbiosis	Properties
beneficial		
Faecalibacterium	↓	anti-inflammatory
Turicibacter	↓	short-chain fatty acids
Blautia	↓	short-chain fatty acids
Fusobacterium	↓	short-chain fatty acids
Clostridium hiranonis	↓	bile acid converter
harmful		
Streptococcus	↑	overgrowth in maldigestion
E. coli	↑	pro-inflammatory



Dysbiosis Index	Sensitivity	CI (95%)	Specificity	CI (95%)
2	0.63	0.53-0.72	1	0.96-1.00
0	0.74	0.65-0.82	0.95	0.89-0.98
-1	0.82	0.73-0.88	0.91	0.84-0.96
-2	0.86	0.78-0.92	0.83	0.74-0.90

Dysbiosis patterns vary across GI disease

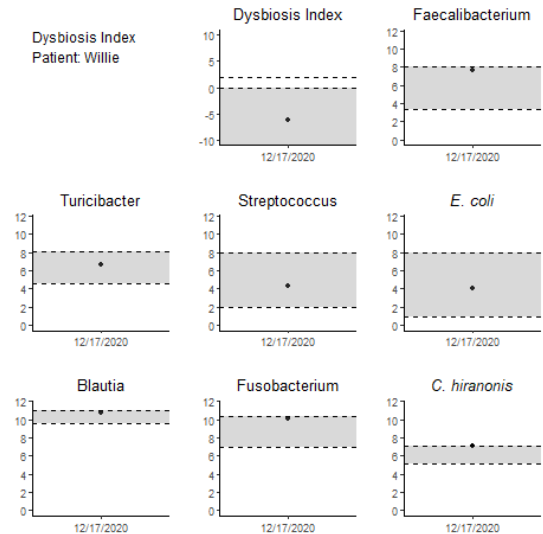
- dogs with chronic diarrhea
 - food-responsive
 - antibiotic-responsive
 - idiopathic IBD
 - exocrine pancreatic insufficiency (EPI)
- acute diarrhea
 - rarely increased DI and decreased *C. hiranonis*



- antibiotic-induced dysbiosis: should be off antibiotics for 2-4 weeks
- omeprazole-induced dysbiosis: should be off omeprazole for 10-14 days

Blue – 10 month old Golden Retriever

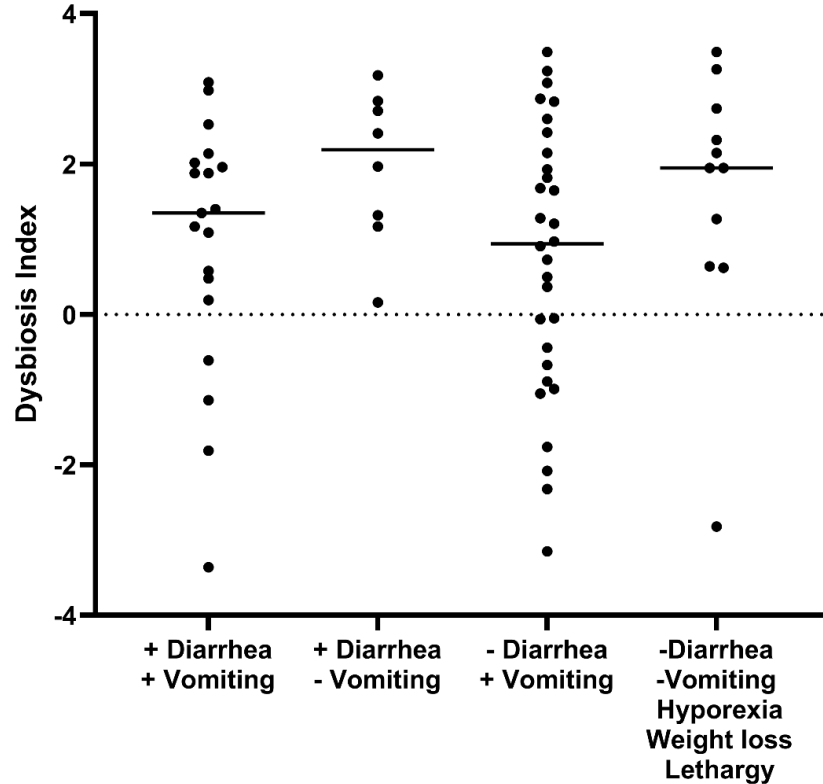
- every 6-8 weeks episodes of watery diarrhea
- received metronidazole at 4 months of age
- testing because of repeated episodes of diarrhea
 - fecal parasites negative
 - enteropathogen panel - increase in *C. perfringens* toxin A
 - fecal dysbiosis index – all bacteria normal



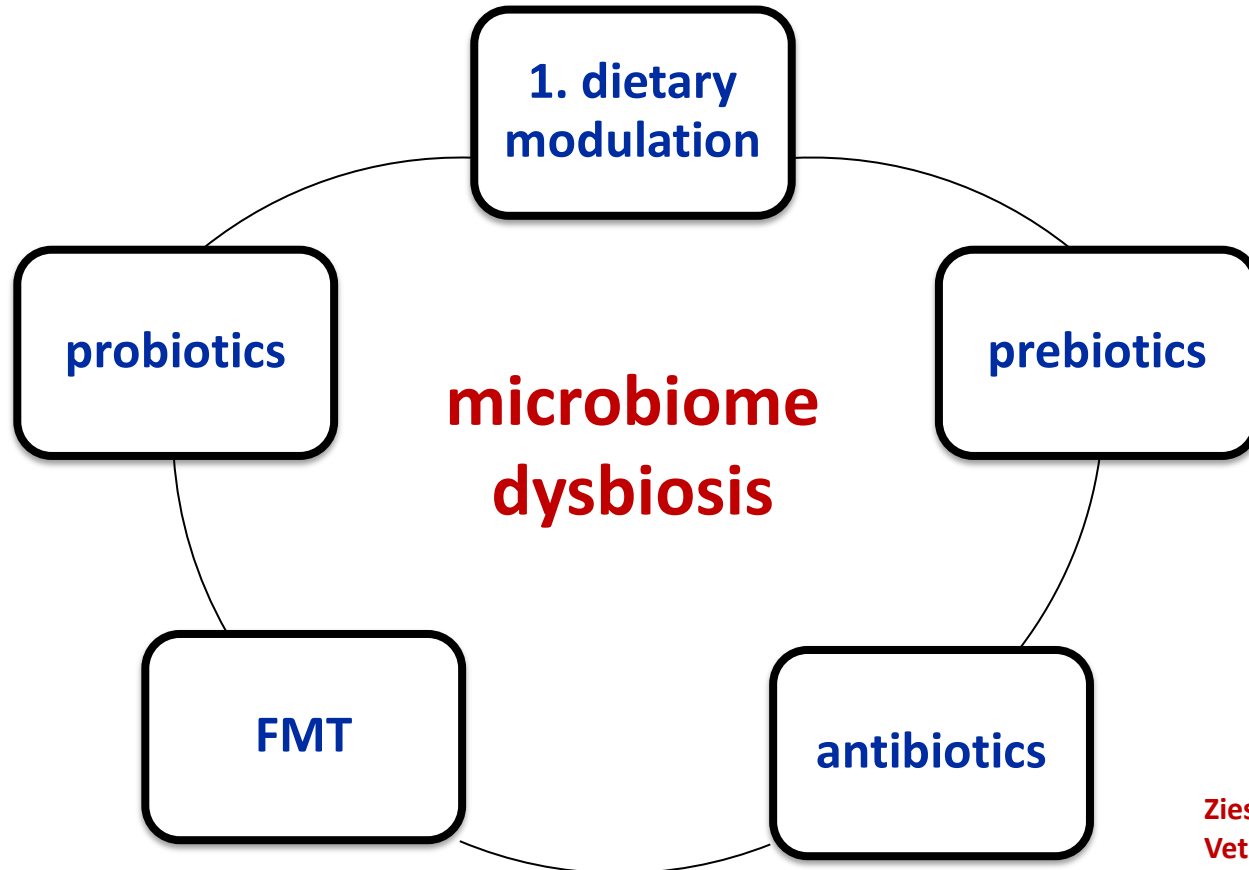
Result - Clinicopathological findings of cats with CE

Variables	number (%)	total number evaluated
increased dysbiosis index (>0)	52 (76%)	68
decreased serum cobalamin (<290 ng/L)	21 (34%)	61
increased serum folate (>21.6 µg/L)	15 (28%)	53
increased fPLI (>3.5 µg/L)	14 (28%)	50
increased fTLI (>82 µg/L)	10 (21%)	47
decreased serum folate (<9.7 µg/L)	6 (11%)	53
decreased serum albumin (<2.5 g/dL)	2 (4%)	53

Increased Dysbiosis Index in cats with CE and non-specific clinical signs



Different treatments address different mechanisms



Type of treatment

Likely mechanism

Potential disadvantage

Dietary change

- improved digestibility leads to less dietary substrate available for bacterial growth
- hypoallergenic – reduces inflammation and secondary dysbiosis

- none when no food sensitivity

Type of treatment

Likely mechanism

Potential disadvantage

Dietary change

- improved digestibility leads to less dietary substrate available for bacterial growth

- none when no food sensitivity

Probiotics

- can improve barrier function
 - immunomodulatory

- minor effect on total microbiota

Type of treatment

Likely mechanism

Potential disadvantage

Dietary change

- improved digestibility leads to less dietary substrate available for bacterial growth

- none when no food sensitivity

Probiotics

- can improve barrier function
 - immunomodulatory

- minor effect on total microbiota
- unclear which patient would benefit from which strain

Prebiotics/fibers

- increase in beneficial bacteria
- bind bacterial metabolites

- can initially cause flatulence
- individual patient response

Type of treatment

Likely mechanism

Potential disadvantage

Antibiotics

- reduction in total and mucosa-adherent bacteria
 - less toxic bacterial metabolites
- negative changes in microbiota
 - when stopped re-growth of bacteria
 - antimicrobial resistance

Type of treatment

Likely mechanism

Potential disadvantage

Antibiotics

- reduction in total and mucosa-adherent bacteria
- less toxic bacterial metabolites

- negative changes in microbiota
- when stopped re-growth of bacteria
- antimicrobial resistance

Fecal microbiota transplantation (FMT)

- alters luminal microbiota and metabolites
- reduction of enteropathogens

- minor effect on mucosa-adherent bacteria
- recurrence of dysbiosis when intestinal inflammation still present

CHRONIC ENTEROPATHY

- umbrella term that encompasses different chronic GI disorders, with etiology unknown
- food-responsive enteropathy (FRE) is most common, 50-70% of patients respond to
 - novel or hydrolyzed protein or fiber-enriched diet
- antibiotic-responsive enteropathy (ARE)
 - 11-15% - tylosin or metronidazole
- steroid-responsive enteropathy (SRE)
 - 20-25% require immunosuppression

Dandrieux J et al, Australian Vet J 2019
Allenspach K et al, Vet Rec 2016
Volkman M et al, J Vet Intern Med 2017

FOOD-RESPONSIVE ENTEROPATHY (FRE)

- **diet trials represent important FIRST step**
- hydrolyzed or novel protein diets
 - strict owner compliance important – no treats etc
 - improvement noticed in 10-14 days

FOOD-RESPONSIVE ENTEROPATHY (FRE)

- commercial hydrolysed protein diet
 - proteins <10 kDa do not elicit an immune response
- Toby responded to hydrolyzed protein diet within 2 weeks

COBALAMIN (VITAMIN B12)

- important for various metabolic pathways
- many animals with CE are deficient in B12
- studies have shown that low cobalamin is associated with poorer outcome
- therefore, cobalamin supplementation is needed
 - start supplementing when cobalamin is already in low normal range

COBALAMIN (VITAMIN B12)

- oral (PO) daily cobalamin supplementation
 - cyanocobalamin 1 mg/tablet
 - dogs < 10 kg: ¼ tablet/day
 - dogs 10-20 kg: ½ tablet/day
 - dogs ≥ 20 kg: 1 tablet/day
 - cats: ¼ tablet/day
- parenteral (PE)
 - cats: 250 µg
 - dogs <10 kg : 250 µg; 10-20kg: 500 µg; >20kg: 1000 µg
 - cobalamin injection/week during 6 weeks and a final injection 4 weeks later



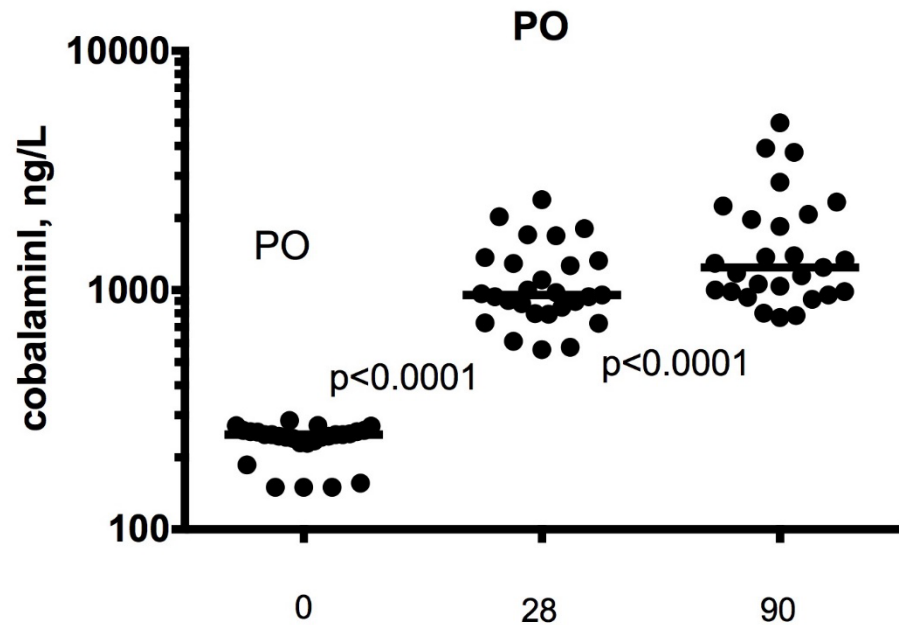
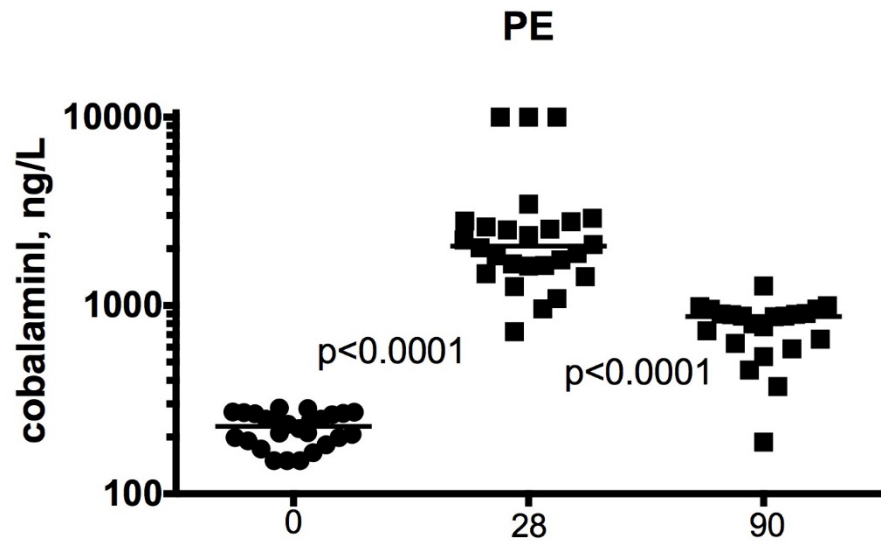


Fig 3. Serum cobalamin concentrations at baseline, after 28 days and 90 days in the parenteral group (left; n=26 at inclusion and 28 days, 22 after 90 days) and oral group (right, n=27). Log₁₀ scale, long horizontal line represents median.

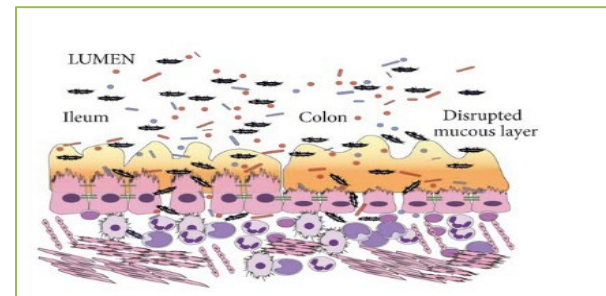
COBALAMIN (VITAMIN B12)

- most animals need indefinite treatment (serum concentrations will fall without supplementation in most patients)
- folate/ folic acid: daily oral 200 µg for cats and smaller dogs (<20 kg BW) and 400 µg for larger dogs (20 kg BW)
- risk of toxicity is very low as both vitamins are water-soluble

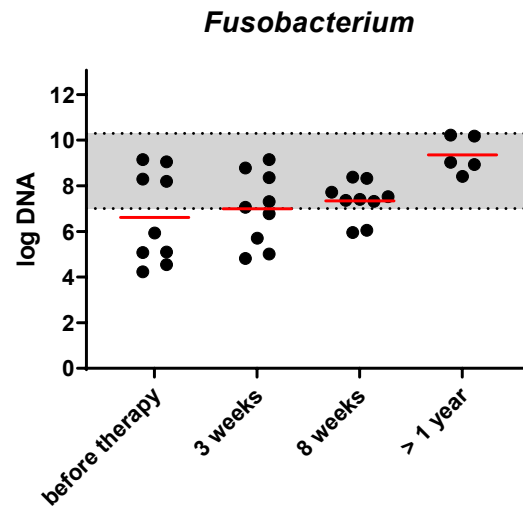
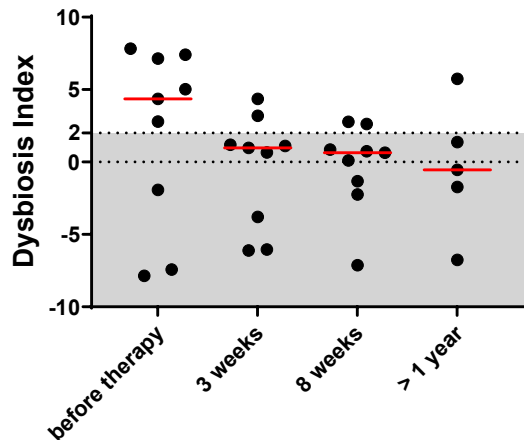
Article

Long-Term Recovery of the Fecal Microbiome and Metabolome of Dogs with Steroid-Responsive Enteropathy

Rachel Pilla ^{1,*}, Blake C Guard ¹, Amanda B Blake ¹, Mark Ackermann ², Craig Webb ³, Steve Hill ^{4,5}, Jonathan A Lidbury ¹, Jörg M Steiner ¹, Albert E. Jergens ⁶ and Jan S Suchodolski ¹



**it takes LONG time for GI tract to recover –
dysbiosis still present after clinical signs improve**



PREBIOTICS

- fiber is fermented by microbiota into different products
 - short-chain fatty acids (especially butyrate)
 - beneficial effects of colonocytes
- fibers induce anti-inflammatory cytokines, and regulatory T cells that can ameliorate an inflammatory response

PSYLLIUM

- Plantago psyllium
- Odorless and almost tasteless
- Husks contain mucilage
- Rich in soluble fiber but not in fermentable fibers
- Water binding capacity > 10 times its weight



PSYLLIUM

- Adds bulk
 - supports colon passage / defecation
- Constipation / obstipation
- Diarrhea, fecal thickening
- Increases viscosity, slows gastric emptying
- Mucilage might reduce inflammatory irritations

PSYLLIUM - DOSAGE

- approx. 0.5 - 1 g/kg BW
- **Increase slowly** at beginning
- Distribute daily dosage evenly across meals
- Stir with 10 – 20-fold amount of water
- Leave to swell
- Milled husks up to 5 min, unmilled up to 15 min
- Provide enough drinking water
- Note: feces might be „in chains“ the first days
- Flatulence might occur

CELLULOSE

- Insoluble nonfermentable „bulk“ fiber
 - high water binding capacity
- Tasteless and odorless
- Very (!) high acceptance by dogs and cats
- No nutritional value

CELLULOSE

- Main indications
 - improves stool consistency
- Fecal cosmetics" (e.g. colitis, IBD, stress diarrhea)
- Symptomatic effect due to water retention
- Immediate response

CELLULOSE - DOSAGE

- Dosage: 0.5 - 1 g / kg BW / day
- Dosage according to the desired effect
- Individual tolerance
- **Increase dose slowly**
- Quick overdosing can lead to softer feces
- Divide into daily portions
- Mix in wet food or stir with water
- Use cellulose with minimum fiber length of 200µm

OPEN ACCESS





Veterinary Clinics of North America: Small Animal
Practice

Volume 51, Issue 1, January 2021, Pages 155-169



Impact of Changes in Gastrointestinal Microbiota in Canine and Feline Digestive Diseases

Anna-Lena Ziese Dr med vet ^a, Jan S. Suchodolski Dr med vet, PhD ^b  

jsuchodolski@cvm.tamu.edu

<https://tx.ag/DysbiosisGI>