LONDON VET SHOW

CREATING CLARITY

Prescription poop: The microbiome, dysbiosis and FMT

Fabio Procoli

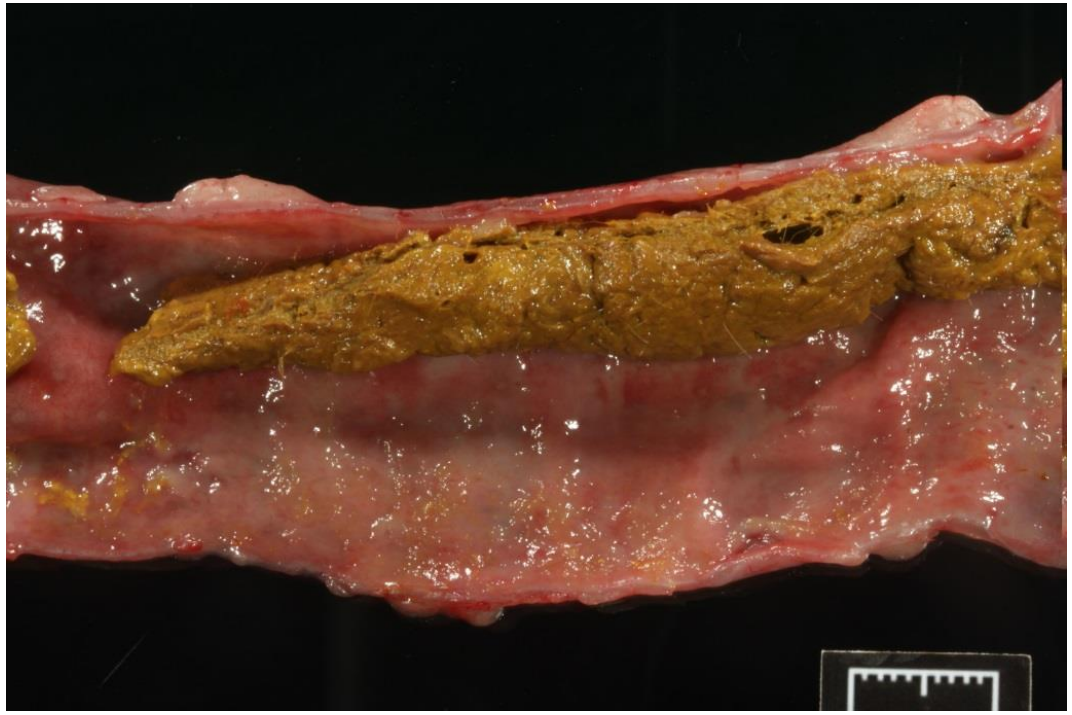
DVM, MVetMed, DACVIM, DECVIM-CA, MRCVS

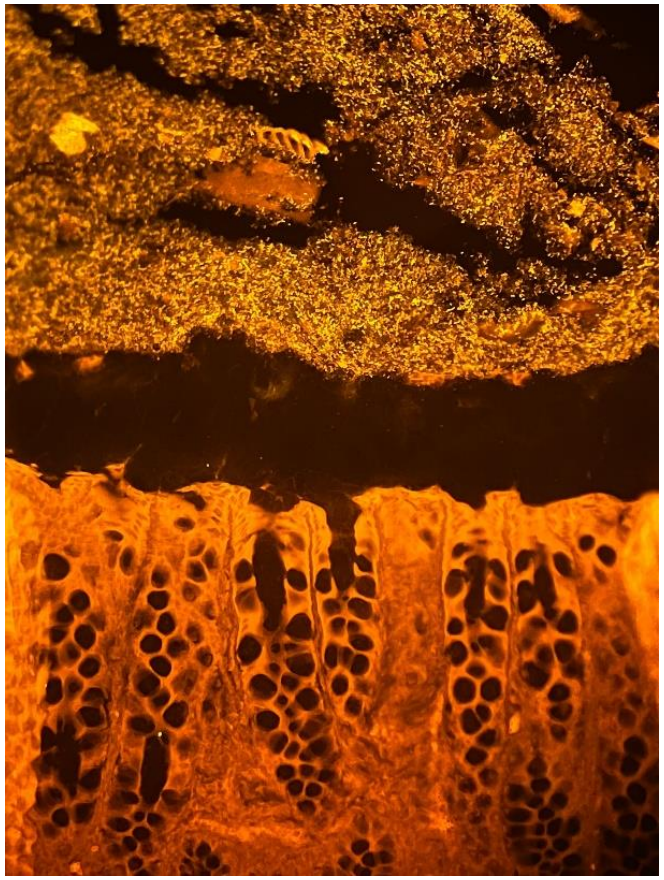
AniCura
OSPEDALE VETERINARIO
I PORTONI ROSSI

IDEXX

Intestinal microbiota

Courtesy of Jan Suchodolski GI LAB Texas A&M





Highly diverse and balanced ecosystem

Bacteria most represented with100 x 10^{12} microorganisms from >1000 species

Metabolic function

Beneficial metabolites

Short chain fatty acids (SCFA) – from dietary NFE/fiber

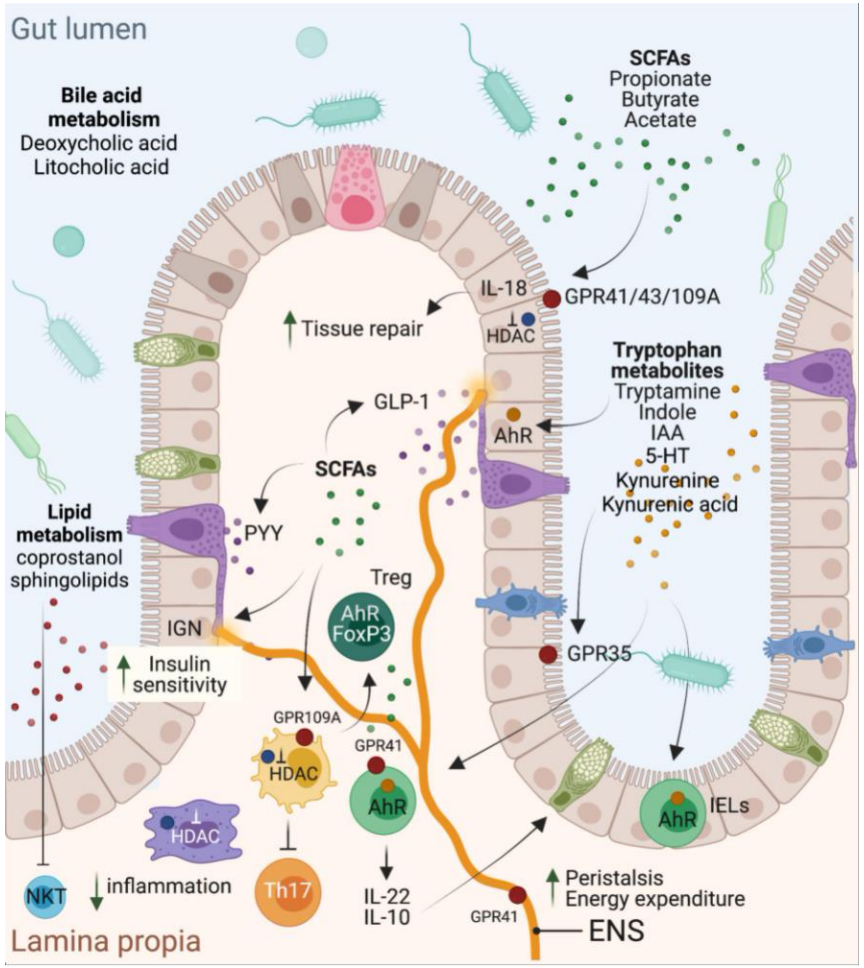
Faecalibacterium prausnitzii & others

Tryptophan + lipid metabolites (indole, kynurenine and kynurenic acid, sphingolipids)

Many bacterial species

Secondary bile acids (SBA) – from primary bile acids

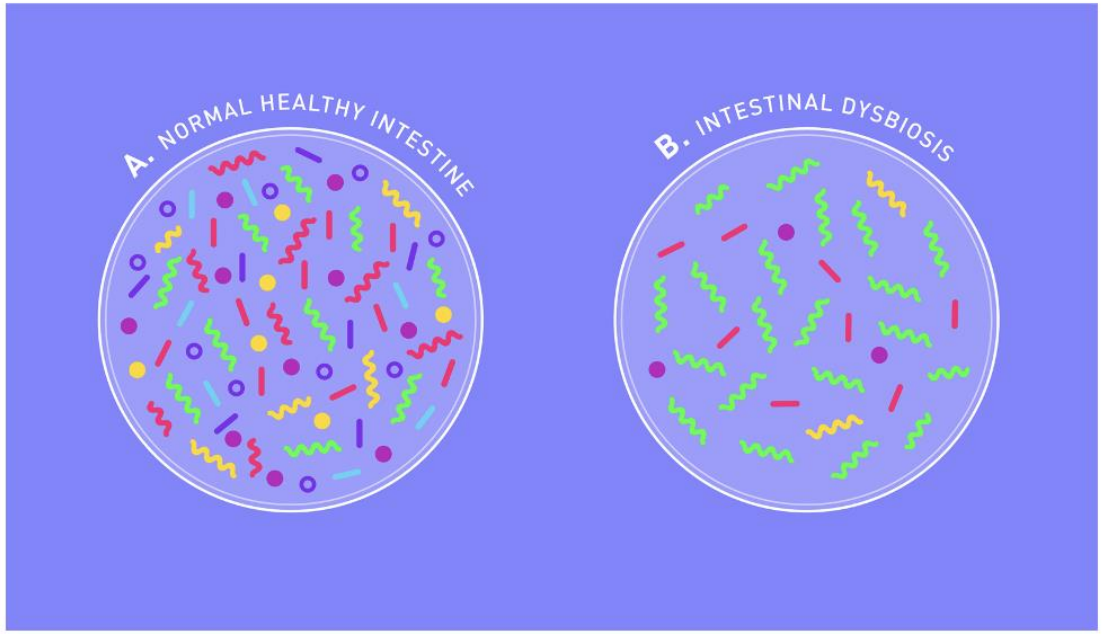
Clostridium (Peptacetobacter) hiranonis (dogs & cats)



Tudela H, Claus SP, Saleh M. Front Cell Dev Biol. 2021;9:719072

Intestinal dysbiosis

Changes in composition and/or function of the intestinal microbiota



DeGruttola AK, et al. Inflamm Bowel Dis. 2016 May;22(5):1137-50

Disruptors of GI homeostasis

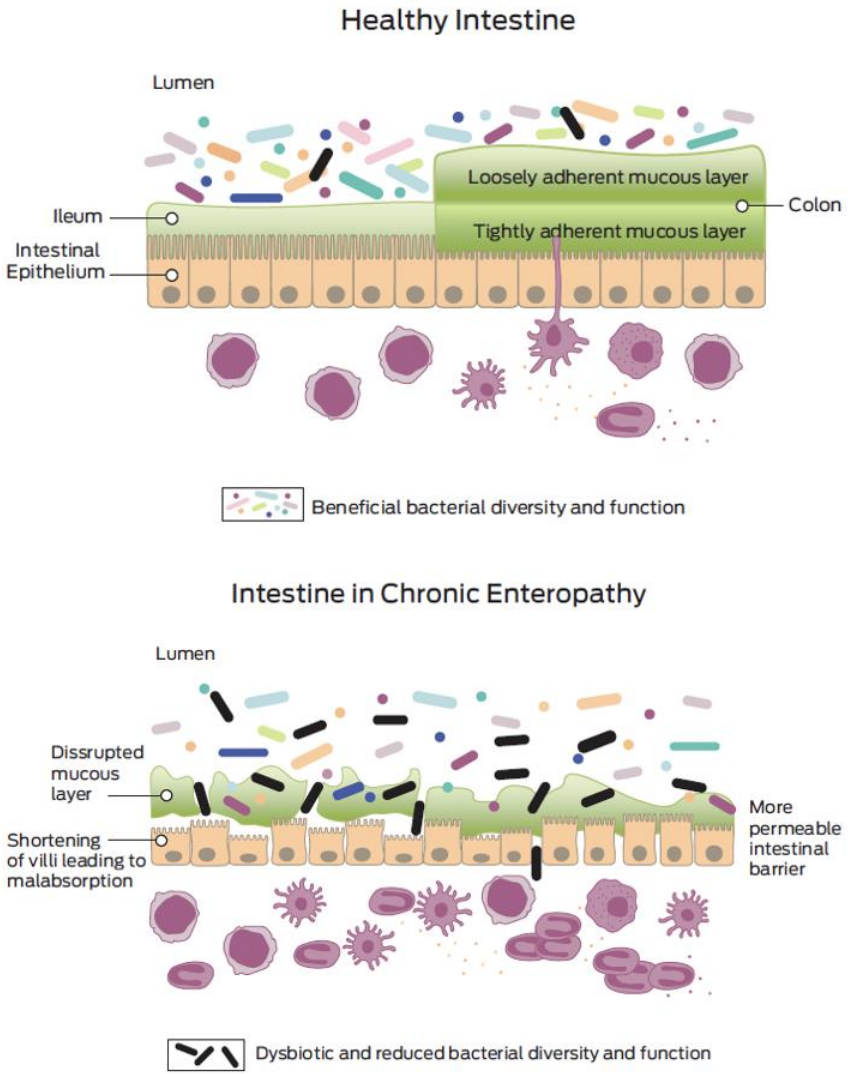
Poor quality and/or imbalanced diet*

Enteropathogens (CPV, FPV, FeCV)*

Antimicrobials*, NSAIDs, PPIs

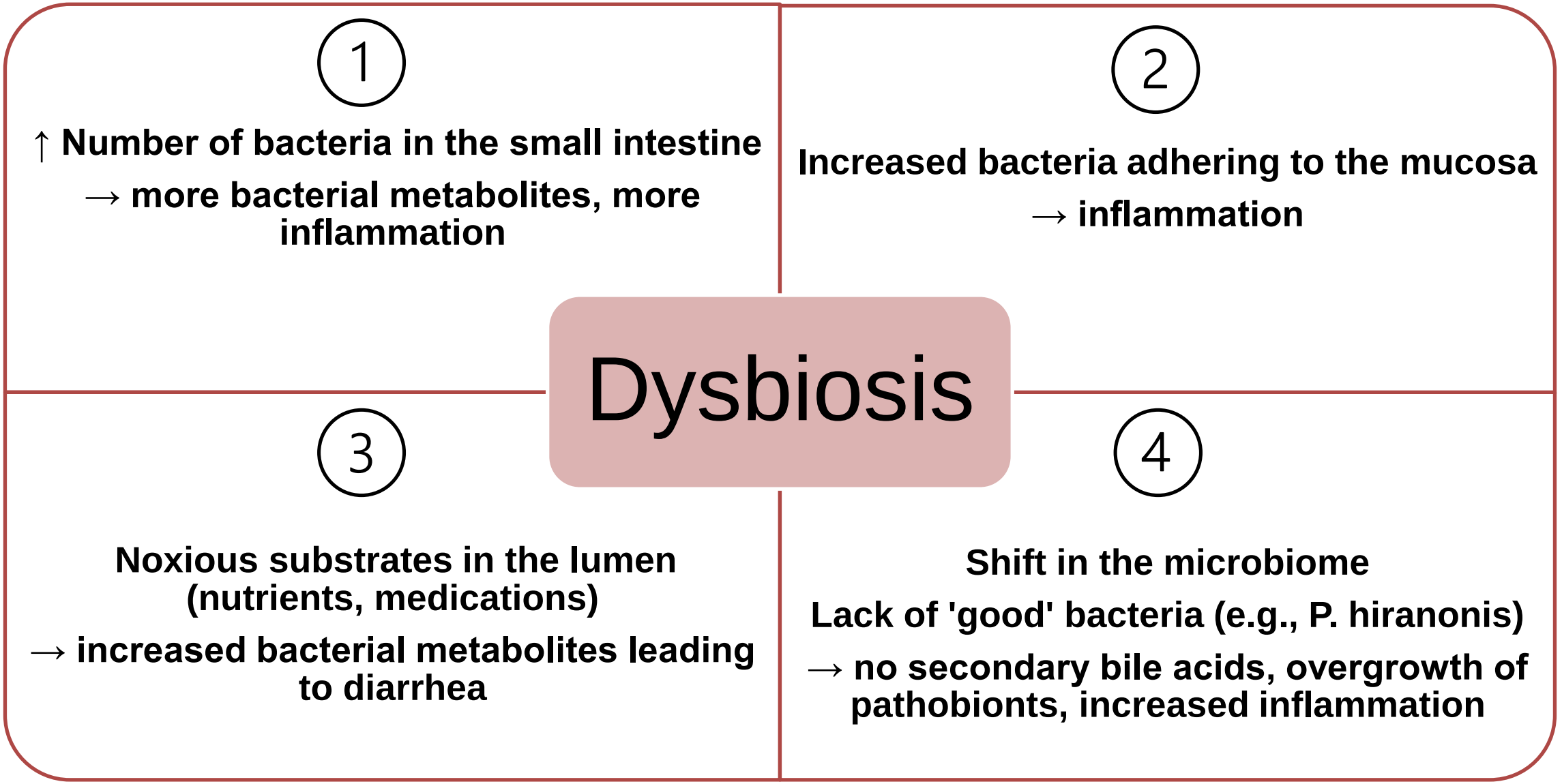
Inflammation

especially early in life*

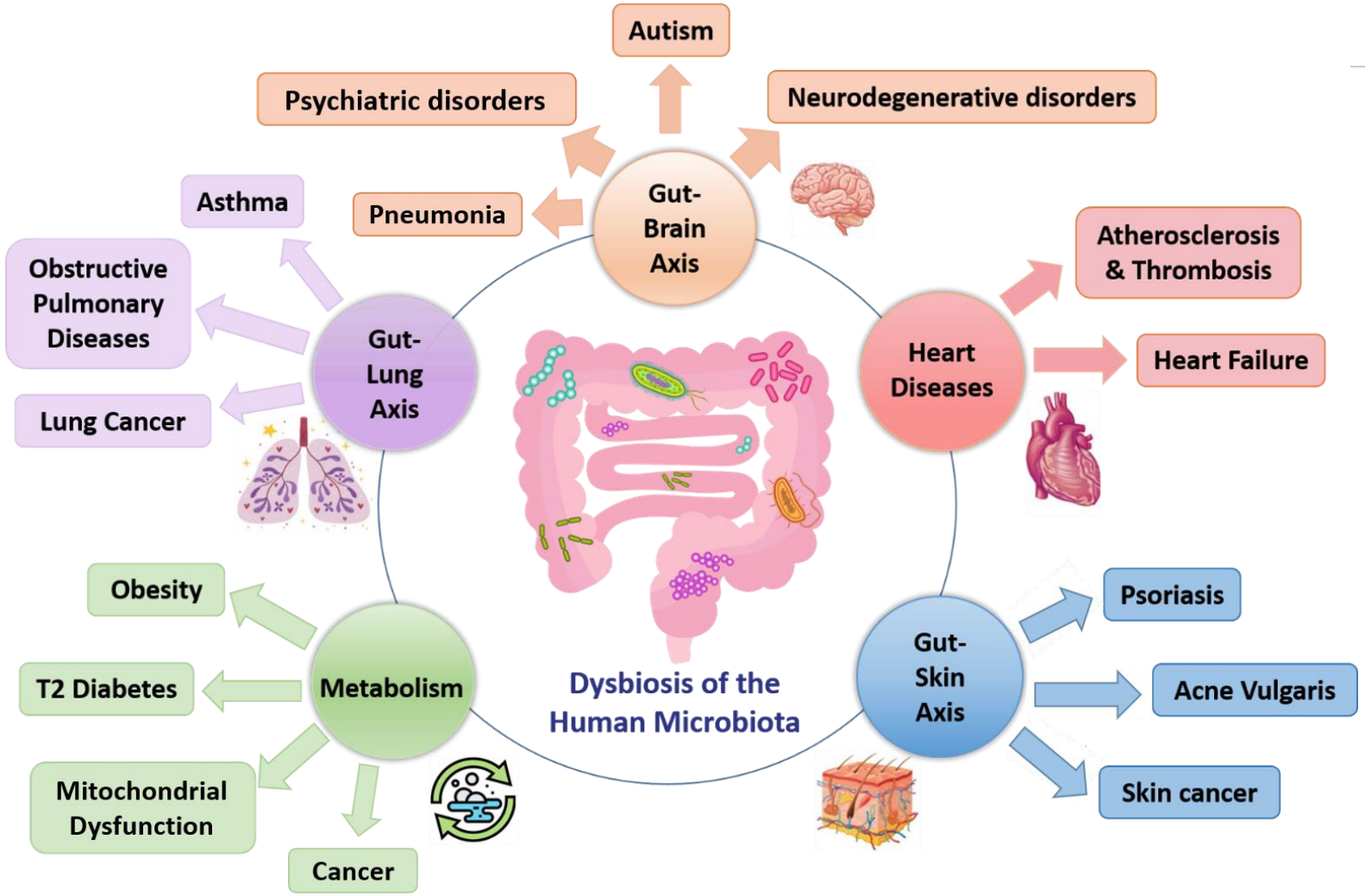


Suchodolski JS - In “Purina Institute - Canine and Feline Clinical Nutrition Handbook, 2023 edition”

Types of dysbiosis



Related diseases in people



Gebrayel, P, *et al. J Transl Med* **20**, 111 (2022)

Intestinal dysbiosis in inflammatory bowel disease

Nirmal Kaur,[1,†] Chun-Chia Chen,[2,†] Jay Luther[1] and John Y. Kao[1,*]

Review

Gastrointestinal Microbiota and Type 1 Diabetes Mellitus: The State of Art

Marilena Durazzo *, Arianna Ferro and Gabriella Gruden

Review

Role of gut microbiota in type 2 diabetes pathophysiology

Manoj Gurung[a,1], Zhipeng Li[a,1], Hannah You[a,1], Richard Rodrigues[b], Donald B Jump[c], Andrey Morgun[b,*], Natalia Shulzhenko[a,*]

Review: The Role of Intestinal Dysbiosis in Parkinson's Disease

Yiying Huang[1†], Jinchi Liao[1†], Xu Liu[1], Yunxiao Zhong[1], Xiaodong Cai[2] and Ling Long[1*]*

Circulation Research

REVIEW

Gut Microbiota and Cardiovascular Disease

Marco Witkowski, Taylor L. Weeks, Stanley L. Hazen

Related diseases in dogs & cats

Antibiotic therapy

Exocrine pancreas insufficiency (EPI)

Chronic inflammatory enteropathies

Food indiscretion/acute enteropathies

Obesity

Diabetes mellitus

CKD

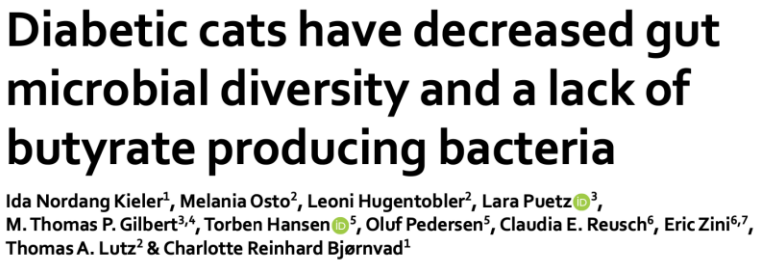
Atopic dermatitis


TOPIC HIGHLIGHT

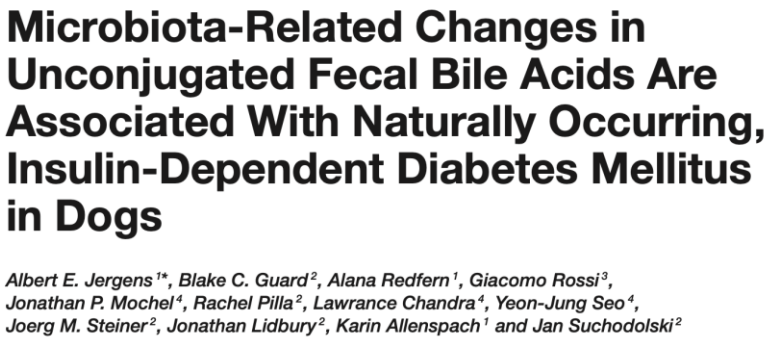
WJG 20th Anniversary Special Issues (17): Intestinal microbiota

Microbiota alterations in acute and chronic gastrointestinal inflammation of cats and dogs

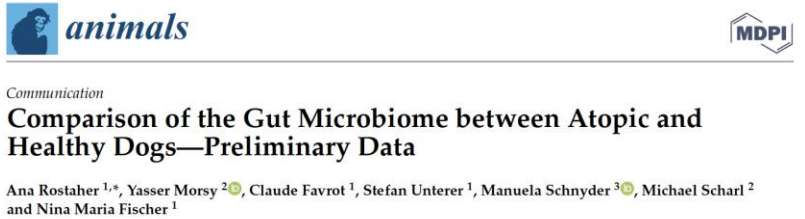
Julia B Honneffer, Yasushi Minamoto, Jan S Suchodolski


Diabetic cats have decreased gut microbial diversity and a lack of butyrate producing bacteria

Ida Nordang Kieler[1], Melania Osto[2], Leoni Hugentobler[2], Lara Puetz[3], M. Thomas P. Gilbert[3,4], Torben Hansen[5], Oluf Pedersen[5], Claudia E. Reusch[6], Eric Zini[6,7], Thomas A. Lutz[2] & Charlotte Reinhard Bjørnvad[1]


Microbiota-Related Changes in Unconjugated Fecal Bile Acids Are Associated With Naturally Occurring, Insulin-Dependent Diabetes Mellitus in Dogs

Albert E. Jergens[1], Blake C. Guard[2], Alana Redfern[1], Giacomo Rossi[3], Jonathan P. Mochel[4], Rachel Pilla[2], Lawrance Chandra[4], Yeon-Jung Seo[4], Joerg M. Steiner[2], Jonathan Lidbury[2], Karin Allenspach[1] and Jan Suchodolski[2]*


animals

MDPI

Communication

Comparison of the Gut Microbiome between Atopic and Healthy Dogs—Preliminary Data

Ana Rostaher [1,*], Yasser Morsy [2], Claude Favrot [1], Stefan Unterer [1], Manuela Schnyder [3], Michael Scharl [2] and Nina Maria Fischer [1]

Diagnosing dysbiosis in practice

TEXAS A&M UNIVERSITY
Gastrointestinal Laboratory

IDEXX

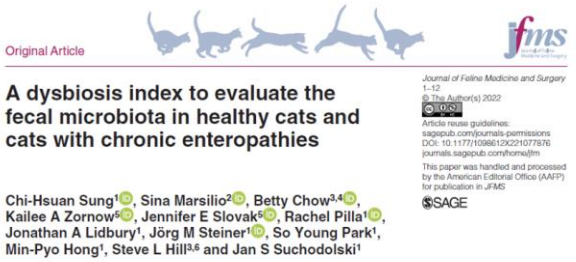
	Function	normal in Dogs	normal in Cats	Change in dysbiosis
Faecalibacterium	anti-inflammatory, production of SCFA	3.4 – 8.0	3.8 – 8.4	↓
Turicibacter	production of SCFA	4.6 – 8.1	4.4 – 9.0	↓
Blautia	production of SCFA	9.5 – 11.0	not measured	↓
Fusobacterium	production of SCFA	7.0 – 10.3	not measured	↓
Bifidobacterium	production of SCFA	not measured	3.2 – 8.7	↓
Bacteroides	production of SCFA	not measured	4.0 – 7.5	↓
Clostridium hiranonis	conversion of primary to secondary bile acids	5.1 – 7.1	4.5 – 7.1	↓
Streptococcus	overgrowth associated with dysbiosis	1.9 – 8.0	1.6 – 5.2	↑
E. coli	pro-inflammatory	0.9 – 8.0	1.4 – 7.0	↑

Validated in dogs and cats!

RESEARCH ARTICLE

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 Minamoto[1], M Markel[1], JA Lidbury[1], JM Steiner[1], E Serpedin[2] and JS Suchodolski[1,*]



Original Article

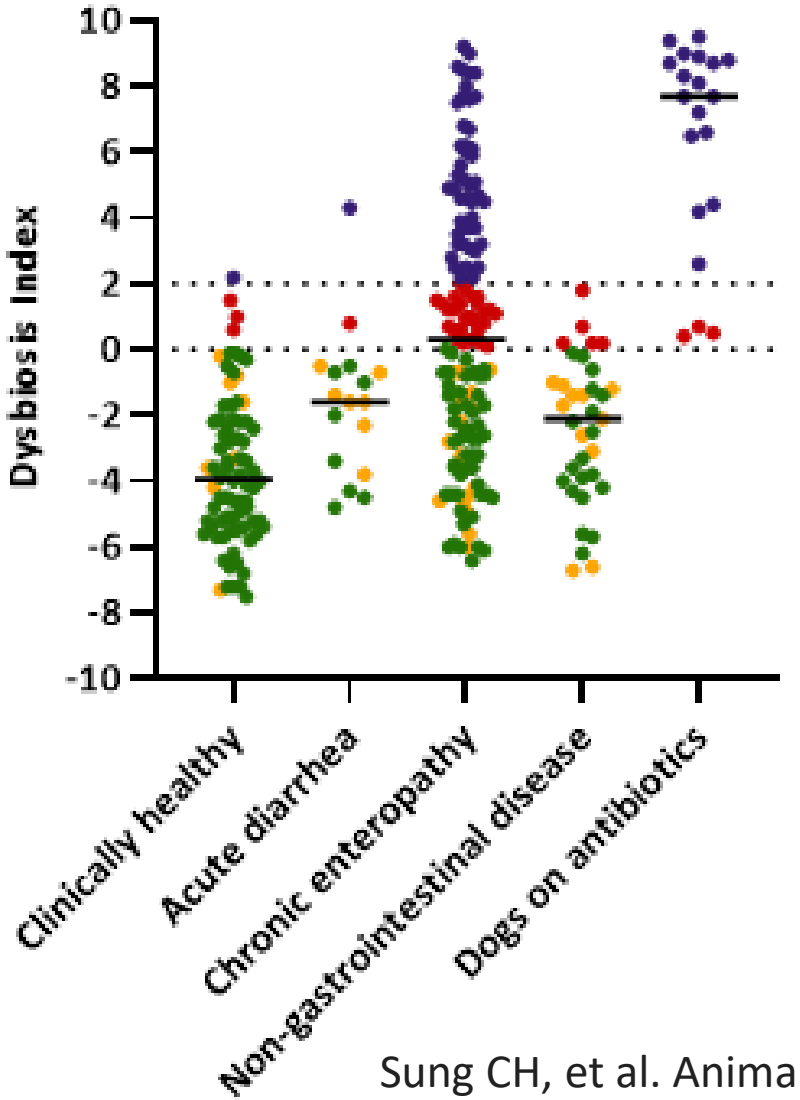
A dysbiosis index to evaluate the fecal microbiota in healthy cats and cats with chronic enteropathies

Chi-Hsuan Sung[1], Sina Marsilio[2], Betty Chow[3,4], Kailee A Zornow[5], Jennifer E Slovak[5], Rachel Pilla[1], Jonathan A Lidbury[1], Jörg M Steiner[1], So Young Park[1], Min-Pyo Hong[1], Steve L Hill[3,6] and Jan S Suchodolski[1]

Journal of Feline Medicine and Surgery

Fecal DI – in practice

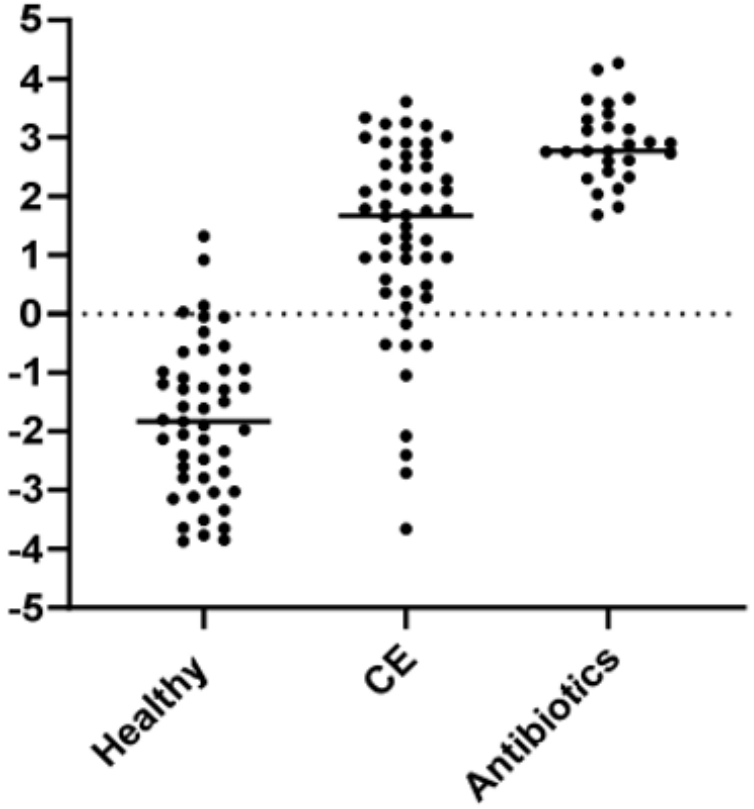
Dogs



TEXAS A&M UNIVERSITY
Gastrointestinal Laboratory

IDEXX

Cats



https://vetmed.tamu.edu/gilab/

Sung CH, et al. Animals (Basel). 2023 Aug 11;13(16):2597.

Potential uses of fecal DI

Identifying sub-clinical dysbiosis in patients at risk

Identifying persistent antibiotic-induced dysbiosis

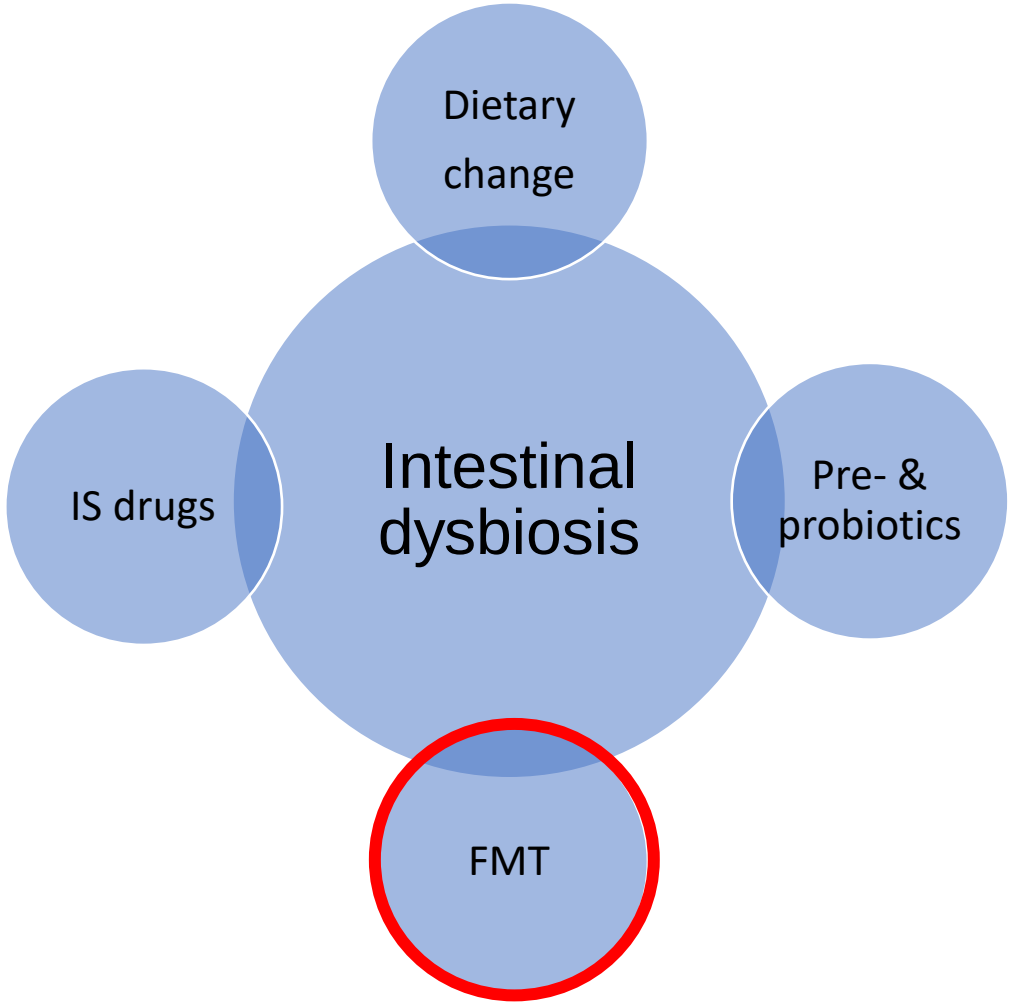
Based on severity and pattern (i.e. loss of *P. hiranonis*)

- Increase likelihood of chronic enteropathy in patient with recurrent/acute on chronic GI signs (especially cats)

Predict long-term response to FMT

Screen for healthy fecal donors

Managing intestinal dysbiosis



Choice of strategy will depend on type/cause, duration and severity of dysbiosis

Multimodal versus sequential approach

Target (clinical remission versus cure) will depend on cause of dysbiosis

Treatment option	Mechanisms of action	Potential limitations
Diet	• Improved digestibility - less substrates for bacterial growth • Reduced immunogenicity	• Palatability, cost
Prebiotics/fibers	• Stimulates growth of beneficial bacteria • Binds toxic metabolites	• Excess might cause clinical signs
Probiotics	• Improve barrier function • Immunomodulation	• Minimal effect on total microbiota composition
Antibiotics	• Reduction in total and mucosa-adherent bacteria • Reduced toxic metabolites	• Negative impact on microbiota diversity and beneficial species • GI toxicity • Limited effect in the long term • Antimicrobial resistance
Fecal microbiota transplantation	• Modification of luminal microbiota and metabolites • Reduction of enteropathogens	• Minimal effect on mucosal adherent microbiota • Limited duration of effect if underlying intestinal inflammation still present

Fecal microbiota transplantation (FMT)

Infusion of **fecal matter** from a healthy donor into the gastrointestinal tract of a patient (to introduce or re-establish a stable microbial community) in order *to treat a dysbiosis-related disease*

Super poo: the emerging science of stool transplants and designer gut bacteria

Rawf8/Getty Images/iStockphoto

Major indication in people

Recurrent *Clostridiodes difficile infection* (CDI)

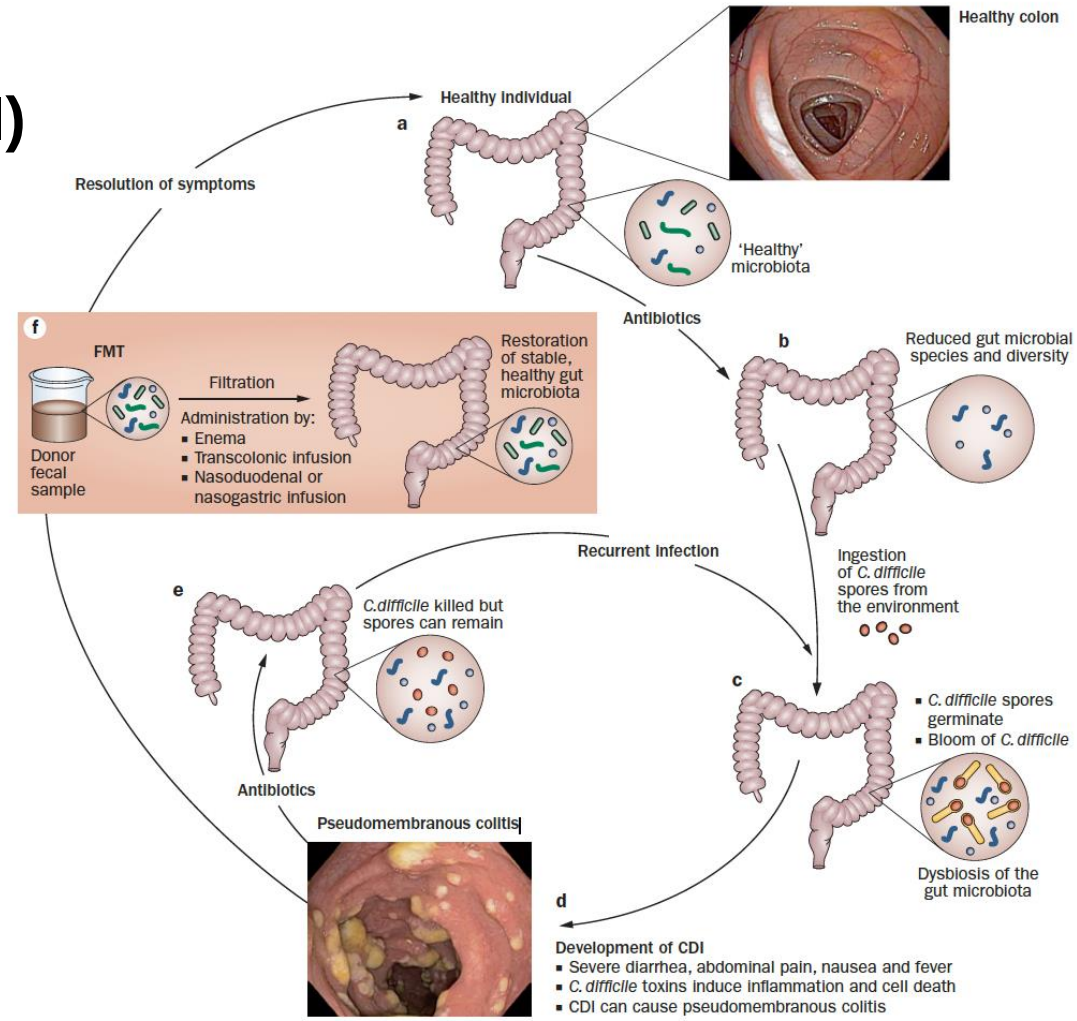
Acquired after antibiotic use + ingestion of environmental *CD* spores

Risk of relapse 20%
Chronic long-lasting CDI (antibiotic refractory)

Annual burden > 80,000$/patient

FMT therapeutic success rates > 90%

Very high safety profile



Borody TJ et al, Nat Rev Gastroenterol Hepatol. 2011: 20;9(2):88-96

Milestone

FDA NEWS RELEASE

FDA Approves First Fecal Microbiota Product

Rebyota Approved for the Prevention of Recurrence of Clostridioides difficile Infection in Adults

FDA Approves First Orally Administered Fecal Microbiota Product for the Prevention of Recurrence of Clostridioides difficile Infection

Ongoing trials in people

Inflammatory bowel disease (IBD)

Irritable bowel syndrome (IBS)

Decolonisation from MDR organisms

Obesity

Metabolic syndrome

Neurological disorders

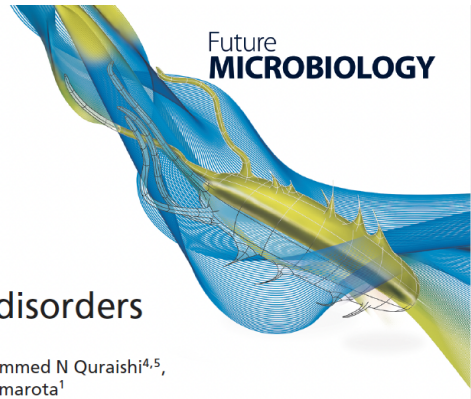
Autoimmune syndromes

Atopy and allergy

Liver disease and hepatic encephalopathy

Cancer

Chemo- and immunotherapy related GI signs



Review

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Fecal microbiota transplantation in gastrointestinal and extraintestinal disorders

Gianluca Ianiro*[,1], Jonathan P Segal[2], Benjamin H Mullish[3], Mohammed N Quraishi[4,5], Serena Porcari[1], Ginevra Fabiani[1], Antonio Gasbarrini[1] & Giovanni Cammarota[1]

Efficacy of FMT in dogs and cats

Infectious diarrhea (*Parvovirus)* - dogs

Acute uncomplicated diarrhoea – dogs

Antibiotic-induced dysbiosis and diarrhoea – dogs, cats

Chronic GI signs refractory to diet/fibre - dogs, cats

SRE and NRE as adjunctive therapy (multimodal therapy) – dogs, cats

Retrospective
Under-powered
Uncontrolled studies
Clinical experience

Canine parvoviral enteritis

Pereira et al, 2018

66 puppies with CPVI

33 STD vs 33 STD + FMT

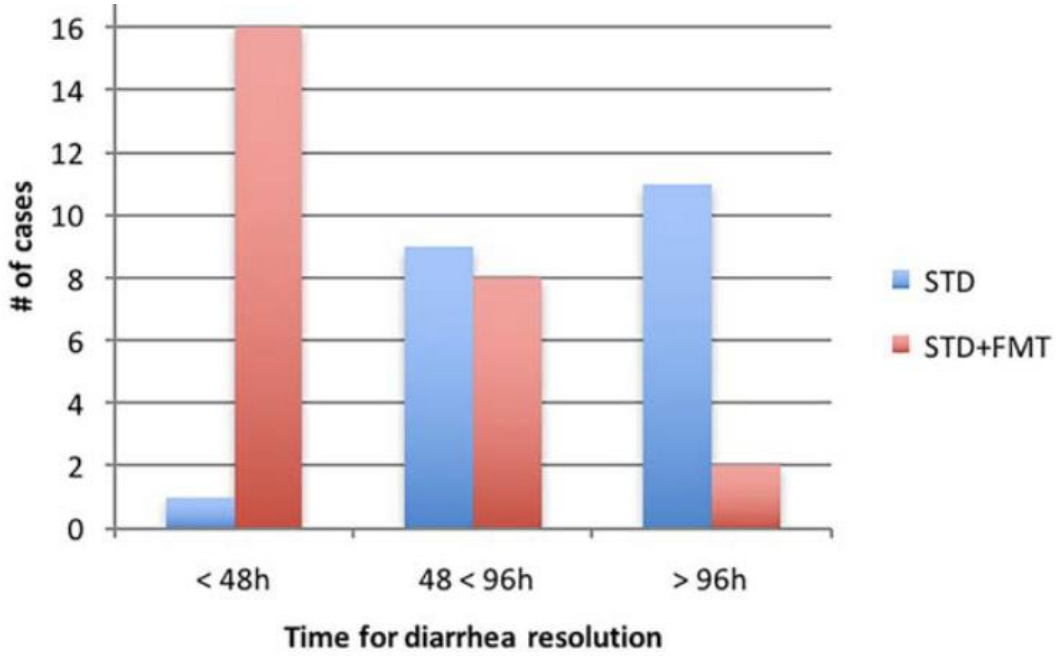
Faster resolution of diarrhoea in FMT

Shorter hospitalisation time

3 vs 6 days

No statistical difference in survival rates

For FMT, 10 g of feces from a healthy dog diluted in10 mL of saline were administered rectally 6-12 hours post-admission



Pereira GQ, et al. J Vet Intern Med. 2018 Mar;32(2):707-711

Canine chronic enteropathy (CE)

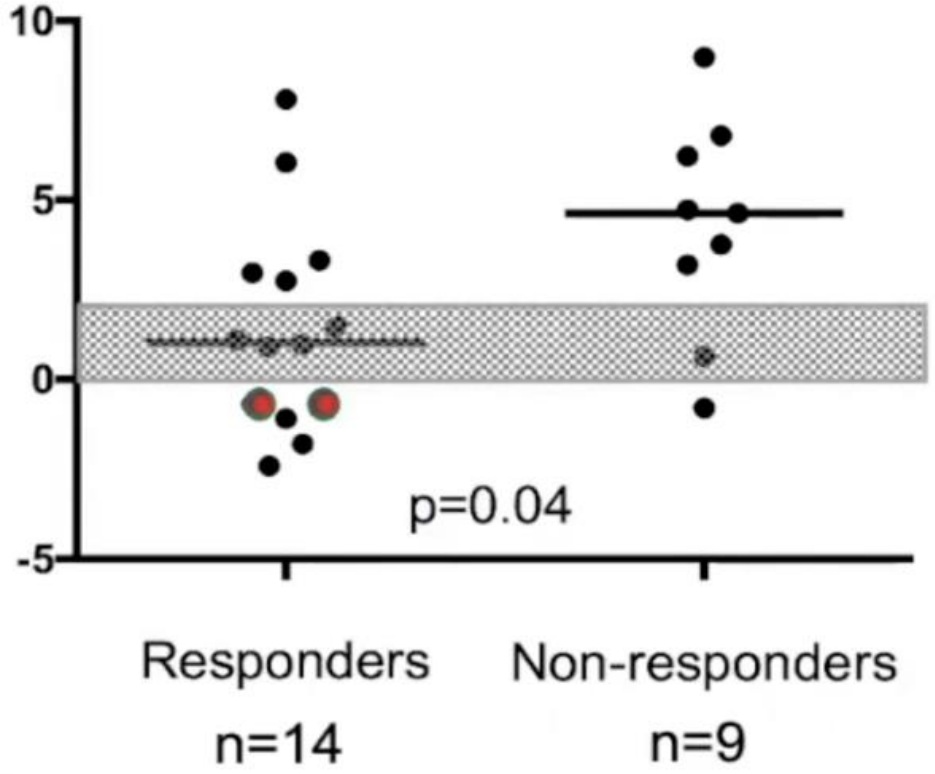
Toresson et al, 2022

Retrospective study
41 dogs with SRE

Treated via – retention enema
Median 3 FMTs 14 days apart

72% of dogs showed satisfactory clinical response

Degree of dysbiosis (DI) associated with response to FMT



Toresson L, et al. *Veterinary Sciences*. 2023; 10(4):271

Canine food refractory CE

AniCura
OSPEDALE VETERINARIO
I PORTONI ROSSI

ALMA MATER STUDIORUM
UNIVERSITÀ DI BOLOGNA
DIPARTIMENTO DI SCIENZE MEDICHE VETERINARIE

Vecchiato C et al (ECVIM Congress 2023) – in press

20 dogs with idiopathic chronic GI signs

No response to 2-weeks trial with hydrolysed or single protein home cooked diet

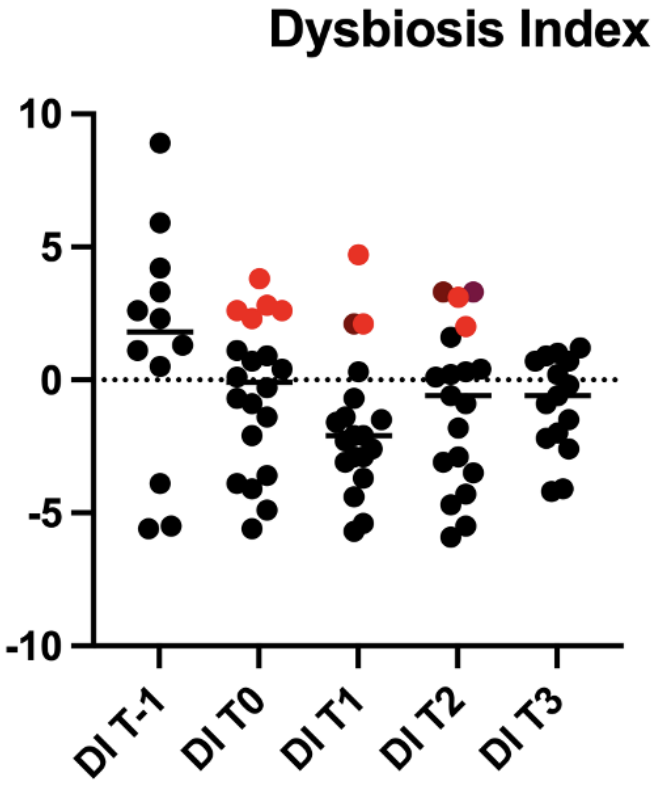
8 x 1 FMT - 12 x 2 FMTs

Clinical response in 20/20

FCS from 4 (1-7) to 2 (1-5) at 60 days

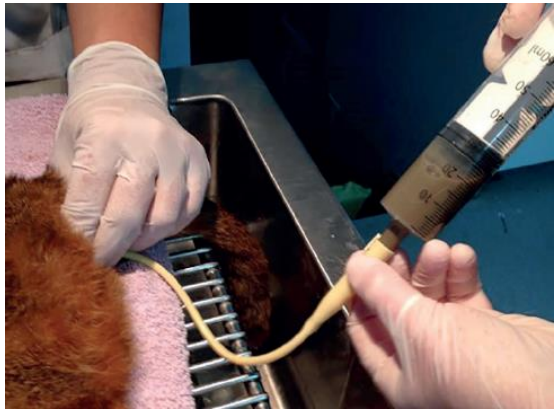
CIBDAI from 5 (1-9) to 1 (0-3) at 90 days

DI from 0.1 (range -5.6 to 3.8) – 2.1 (range -5.7 to 4.7)



First Case Report of Fecal Microbiota Transplantation in a Cat in Israel

Furmanski, S.[1,*] and Mor, T.[2]

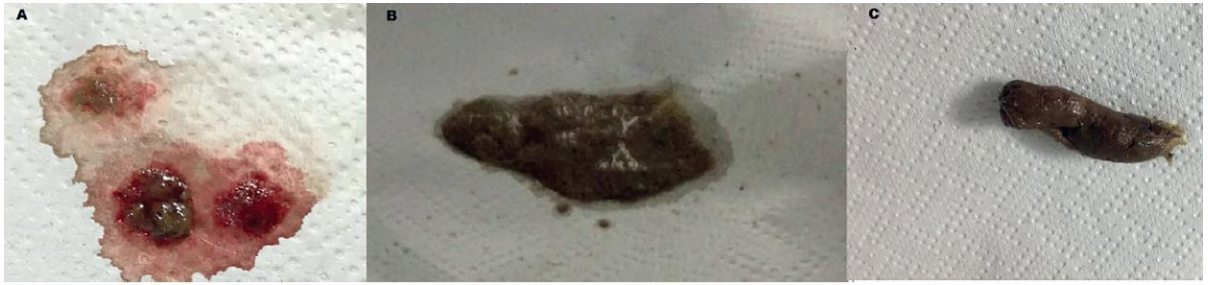


FMT (enema) as a last therapeutic option for cat before euthanasia

Immediate improvement in fecal texture, odor and color

Second FMT was performed 5 weeks later for relapse
Over a 3-month period gradual return to normal stools

11 months after 2nd FMT cat in remission



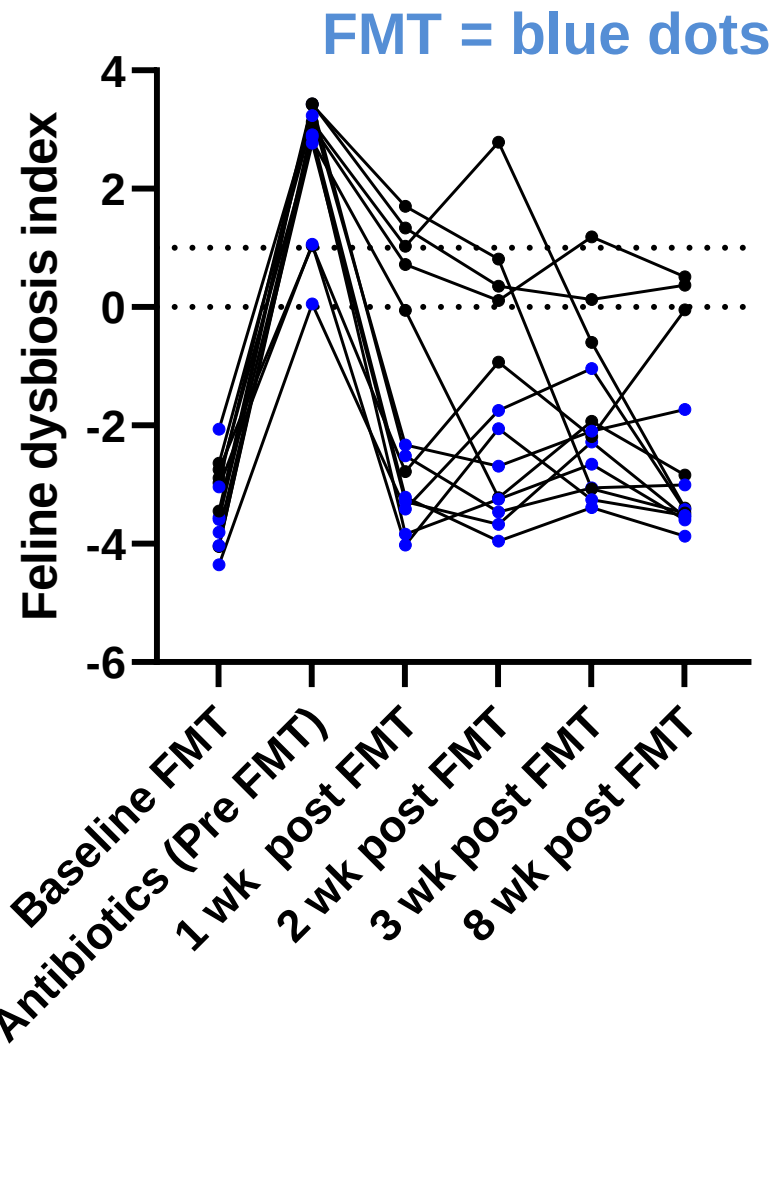
Furmanski S. and Mor T. Israel Journal of Veterinary Medicine Vol. 72 (3) 2017; 35-41

Feline antibiotic induced dysbiosis

Jamie Hui et al, *ACVIM abstract 2022*

Healthy cats treated for 10 days with amoxyclav

FMT via enema (**blue**) or placebo (**black**) after last day of antibiotic



Clinical guidelines

Companion Animal FMT Consortium

FMT Guidelines for Clinical Practice

- Donor Screening & Selection
- FMT Preparations
- FMT Dosing & Clinical Applications

ARTICLE IN PRESS

Advances in Small Animal Care ■ (2024) ■–■

ADVANCES IN SMALL ANIMAL CARE

Clinical Guidelines for Fecal Microbiota Transplantation in Companion Animals

Jenessa A. Winston, DVM, PhD, DACVIM (Small Animal Internal Medicine)[a,*],
Jan S. Suchodolski, DrMedVet, PhD, DACVM, AGAF[b],
Frederic Gaschen, DrMedVet, Drhabil, DACVIM (Small Animal Internal Medicine), DipECVIM-CA[c],
Kathrin Busch, DVM, Dr Med Vet, DECVIM[d],
Sina Marsilio, Dr med vet, PhD, DACVIM (Small Animal Internal Medicine), DipECVIM-CA[e],
Marcio C. Costa, DVM, DVSc, PhD[f], Jennifer Chaitman, VMD, DACVIM (Small Animal Internal Medicine)[g],
Emily L. Coffey, DVM, DACVIM (Small Animal Internal Medicine), PhD[h],
Julien R.S. Dandrieux, BSc, Dr Med Vet, PhD, DACVIM (Small Animal Internal Medicine)[i],
Arnon Gal, DVM, MSc, PhD, DACVIM, DACVP[j],
Tracy Hill, DVM, PhD, DACVIM (Small Animal Internal Medicine)[k], Rachel Pilla, DVM, PhD[b,l],
Fabio Procoli, DVM, MVetMed, DACVIM, DipECVIM-CA, MRCVS[m],
Silke Salavati Schmitz, Dr Med Vet, PhD, DipECVIM-CA, FHEA, FRCVS[i],
M. Katherine Tolbert, DVM, PhD, DACVIM (Small Animal Internal Medicine, Small Animal Nutrition)[b],
Linda Toresson, DVM, PhD[n], Stefan Unterer, DVM, Dr med vet, Dr habil, DECVIM-CA[o],
Érika Valverde-Altamirano, DVM[p], Guilherme G. Verocai, DVM, MSc, PhD, DACVM (Parasitology)[q],
Melanie Werner, Dr Med Vet, Dipl ECVIM-CA (Internal Medicine)[r], Anna-Lena Ziese, Dr Med Vet[s]

Preparation

Fresh (within 2-6 hours from voiding)

Fresh-frozen (processed as soon as possible after voiding

- can be kept refrigerated at 4°C for up to 2 days before)

Addition of cryopreservant before freezing (glycerol 1:10)

Processing can be done in aerobic environment

My method

2.5-5 gr feces /kg b.w. of recipient

Blend in 1:1 or 1:2 with 0.9% NaCl solution by hand in a zip bag

Filtered on fine kitchen sieve

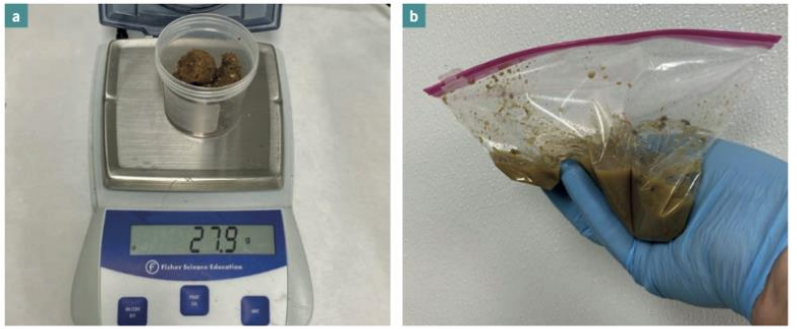
Freeze after adding glycerol 1:10 for later use

Administer after thawing with 20-60 cc syringe through wide bore soft rectal catheter (12 Fr)

With or without sedation (usually needed in cats)

No food and no walk for 4-6 hours (dogs)

Keep in hospital for 4-6 hours (cats)



Repeat 1-2 weeks apart

Some real life case examples

Meet Chloe

5 yrs old FN Maltese cross

Refractory/non-responsive chronic enteropathy

Life long intermittent GI signs
Continuously over last 2 months

Previously:
Fiber enriched diet & novel protein diet trials
Metronidazole

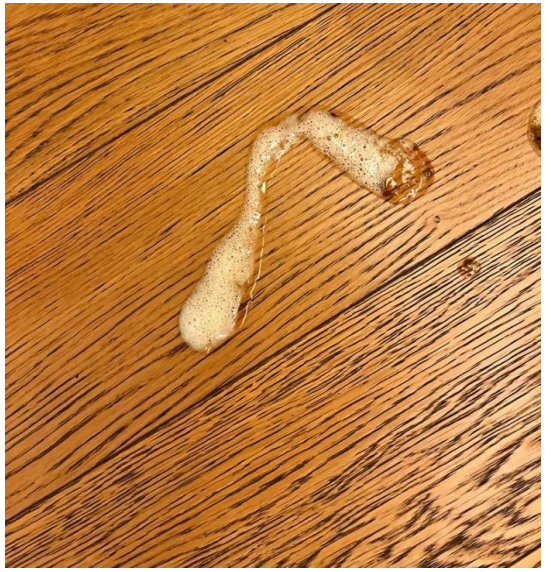
Advised endoscopy for GI biopsies and glucocorticoids trial

At the time of presentation

Daily vomiting (mostly bilious)
Liquid feces with frank blood and mucus (PFS 5-7/7)
& tenesmus

Nocturnal swallowing fits
Selective appetite
Fed on chicken or pork based home cooked diet

Stable weight, BCS 5/9



Diagnostic and clinical staging

Severe clinical disease activity (CIBDAI score 9)

Fecal flotation - negative

CBC - mild eosinophilia
Serum biochem - Mild ALT and DGGR lipase activities increase
cTLI and basal cortisol ruled out EPI and HypoA

Serum cobalamin < 150 ng/L

Abdominal ultrasound: indicative of non-specific mild chronic enteropathy

Initial treatment strategy

Awaiting - fecal DI

Eliminate all extras from daily diet

Hydrolysed soy diet

Multistrain high dose probiotic

Oral cobalamin 0.5 mg PO q 24 hours

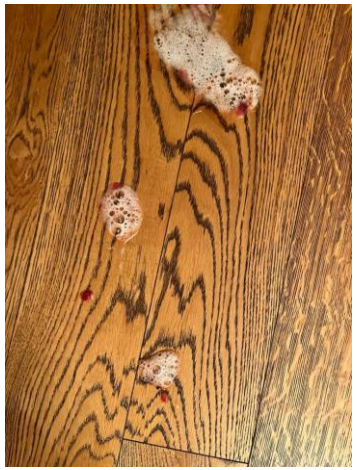
Two weeks follow-up

Partial response

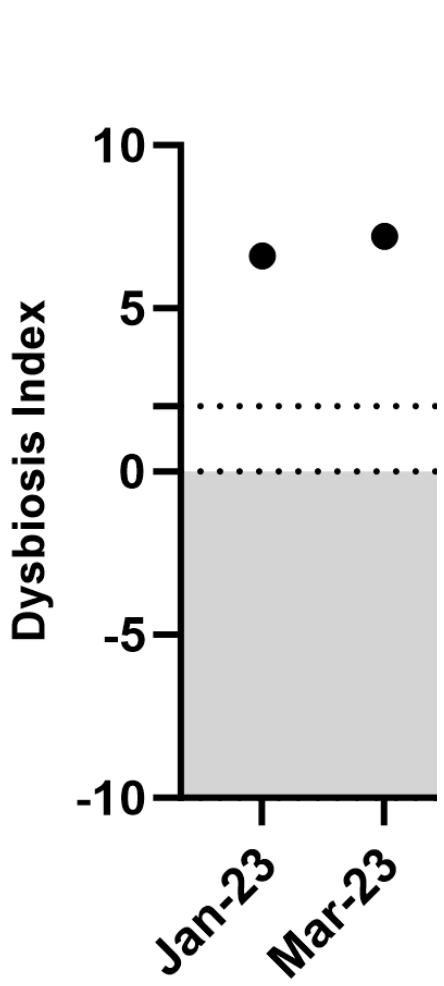
CIBDAI 3

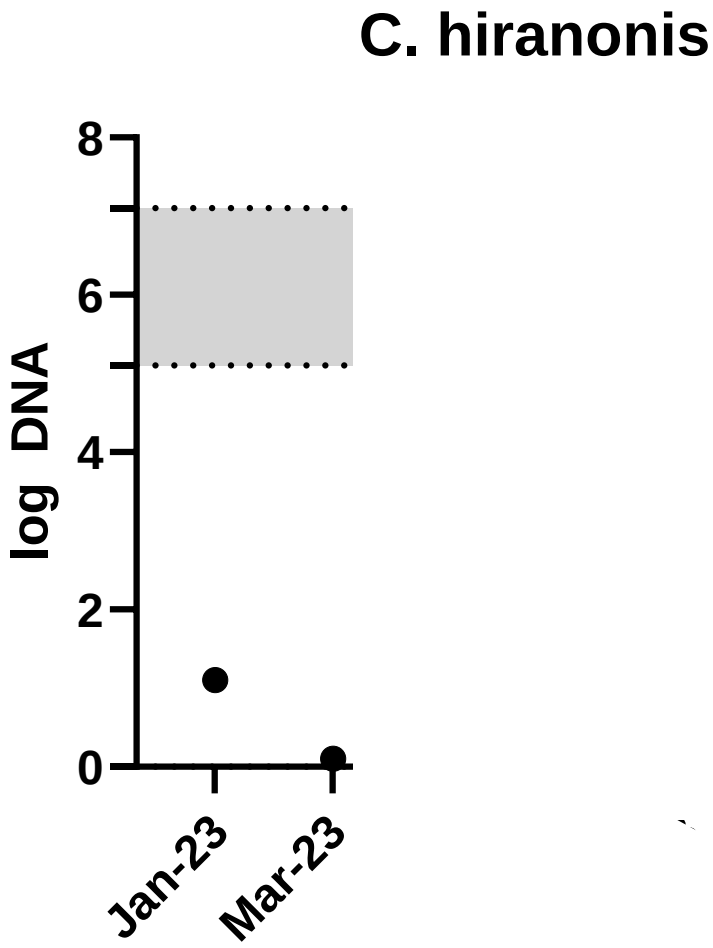
Purina fecal score 3/7

Occasional bilious vomiting + colitis



Fecal DI


DI
Dysbiosis Index
10
5
0
-5
-10
Jan-23
Mar-23


C. hiranonis
log DNA
8
6
4
2
0
Jan-23
Mar-23

Post FMT follow-up

Complete remission

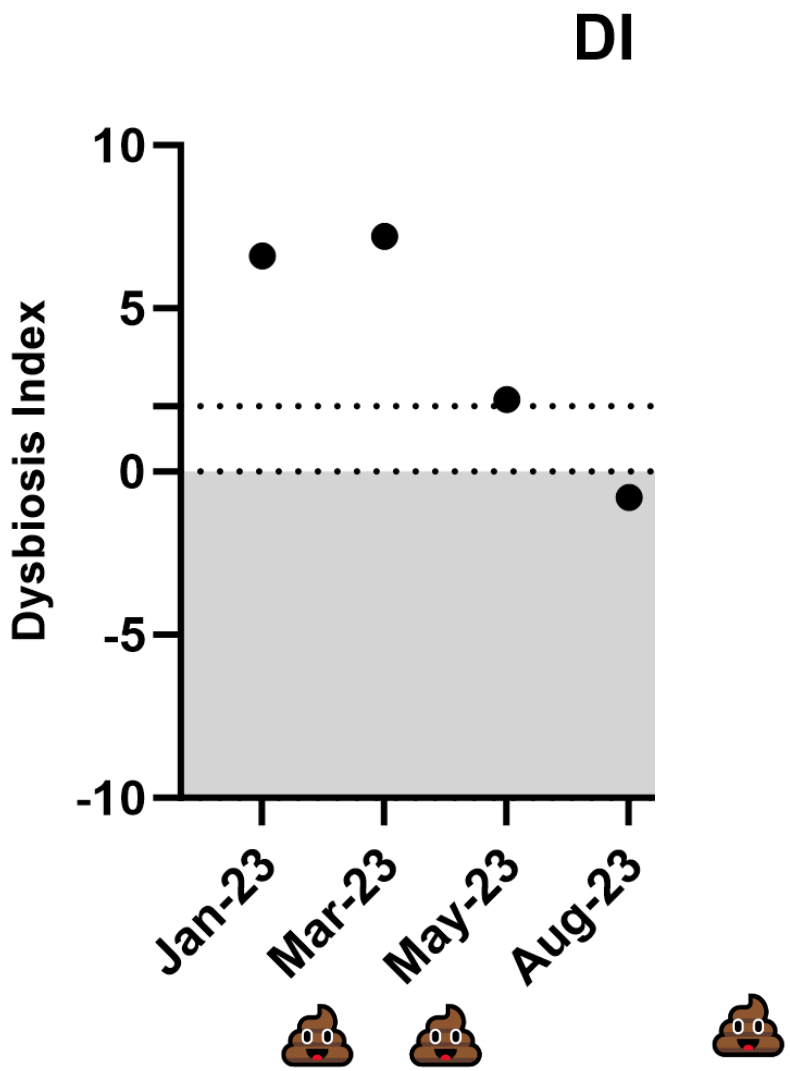
CIBDAI 0

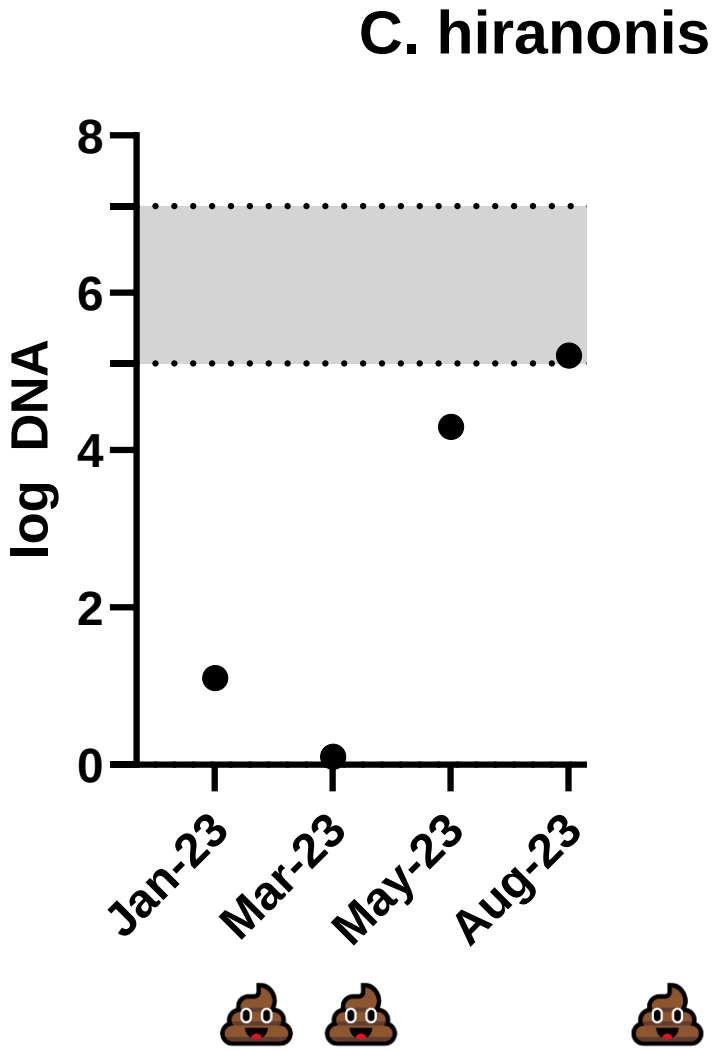
Purina fecal score 2/7

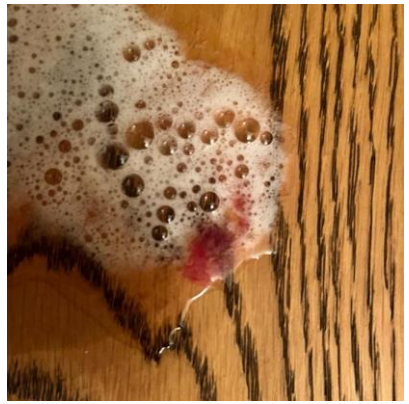
Weight gain

No more vomiting episodes

Follow-up DIs







Skoll

3 yrs old ME Alaskan Malamute

Referred for refractory chronic mixed bowel diarrhoea – 3 months duration

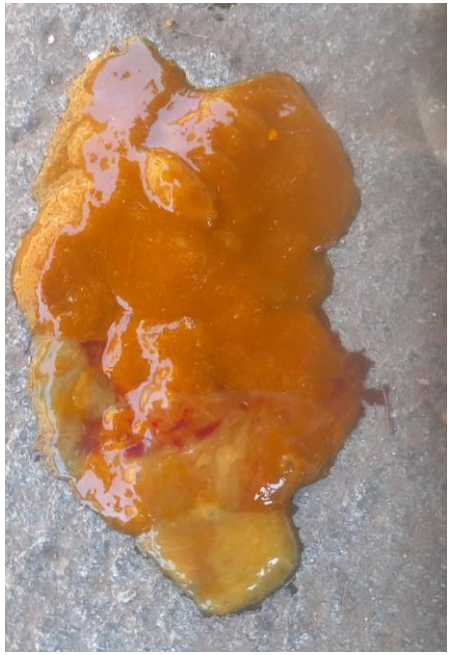
Failed hydrolysed (soy) + single protein (horse) home cooked diets trials

Gastroduodenal-colonoscopy + H&E: mild to moderate lymphoplasmacytic enterocolitis

Minimal response to glucocorticoids + probiotics (still receiving)

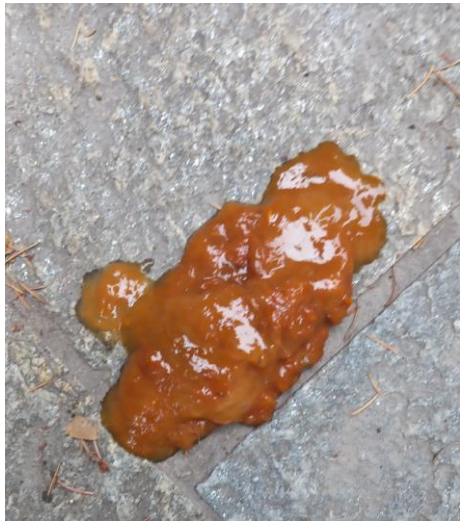
At the time of presentation

Severe mixed bowel diarrhoea (FS 7/7)
Hematochezia + mucus
Increased number of defecation



Dysorexia
Rare vomiting episodes

Weight and muscle loss
BCS 4/9



Polyuria, polydipsia, poor exercise tolerance

Staging

Severe clinical disease activity (CIBDAI score 11)

CBC: within normal limits

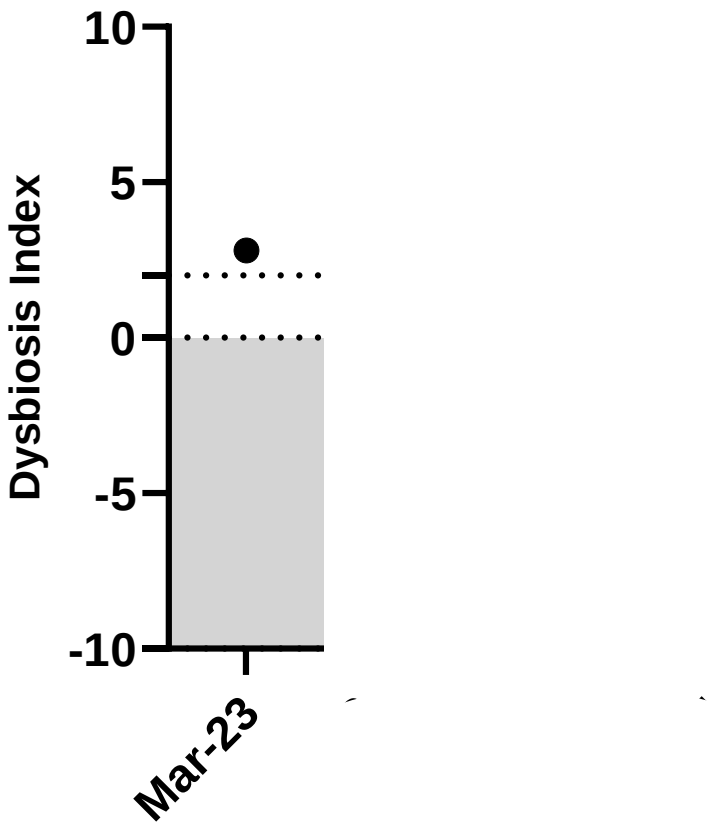
Biochemistry: moderate ALT and ALP increase, marked DGGR lipase increase, mild CRP increase

cTLI: 33 ug/L
Serum cobalamin: 588 ng/L

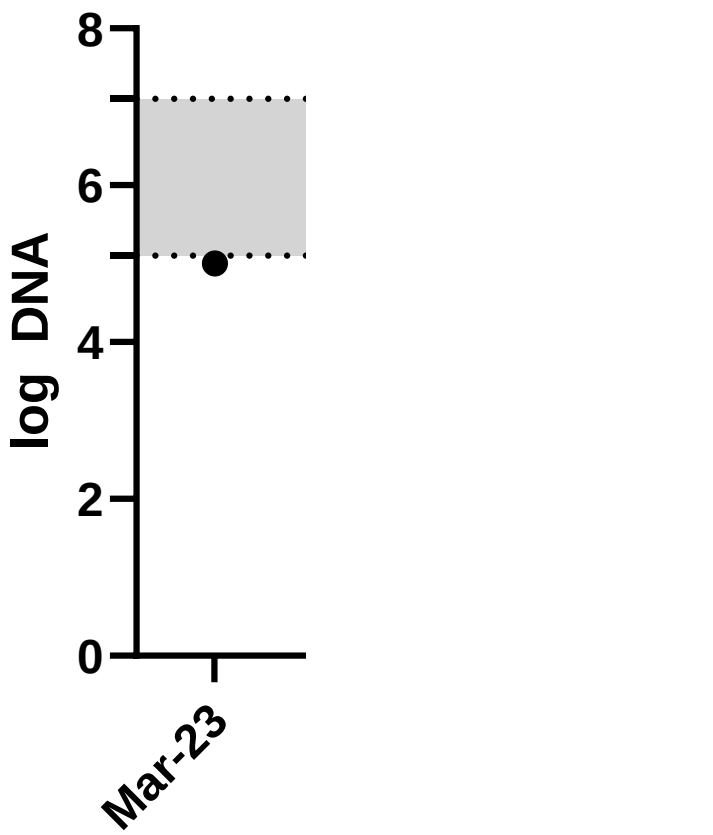
Abdominal ultrasonography: small sized adrenal glands, vacuolar (steroid) hepatopathy, mild chronic enteropathy

Baseline DI

DI



C. hiranonis



Initial treatment plan

Highly digestible low residue fiber enriched diet

Taper down glucocorticoids

Continue high dose multistrain probiotic

Follow-up

Off glucocorticoids

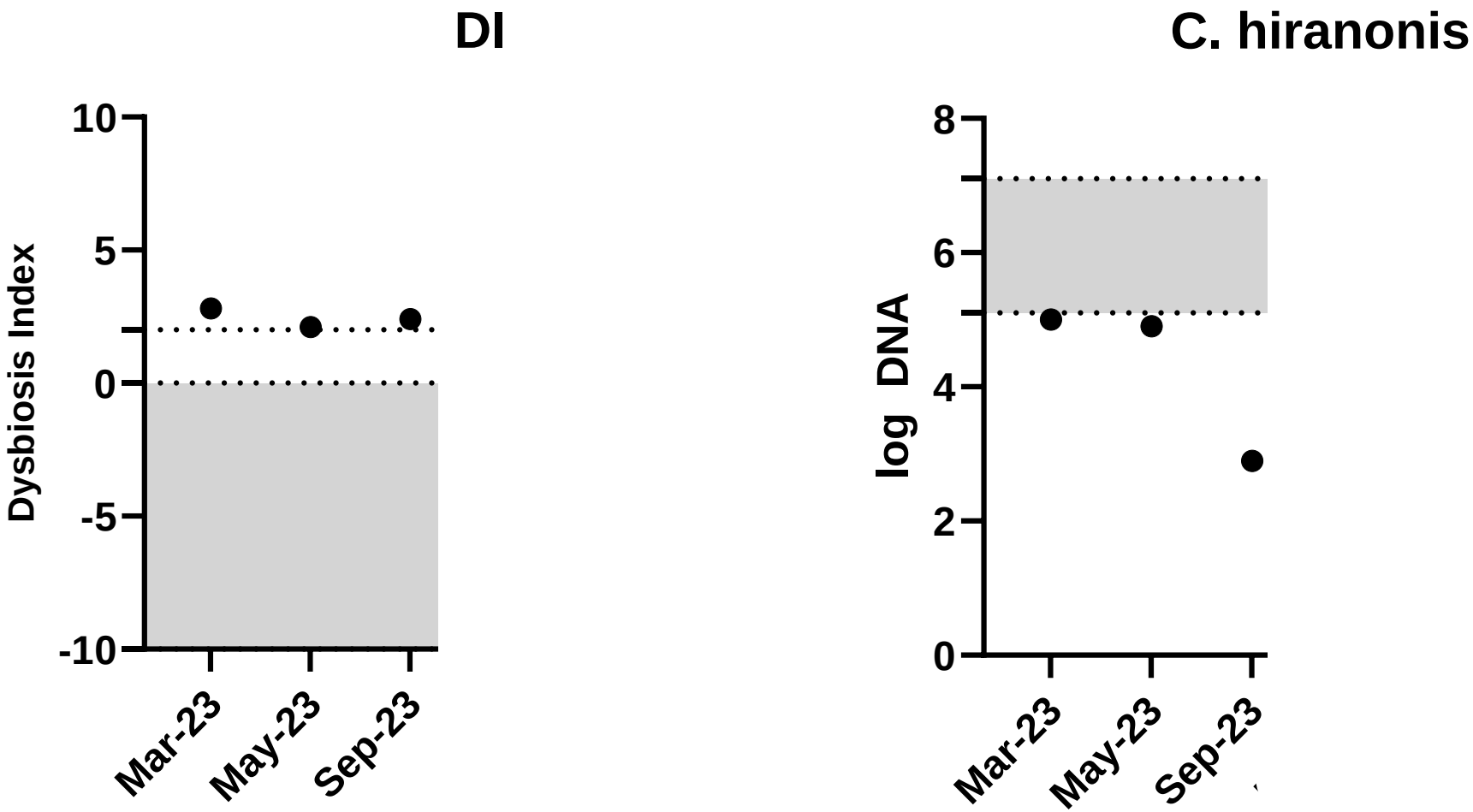
CIBDAI 5 (mild disease activity)

FS 5/7
Occasional hematochezia and mucus
Frequency of defecation reduced

Improved appetite and exercise tolerance
Weight gain

PU/PD only mild

Follow-up DIs



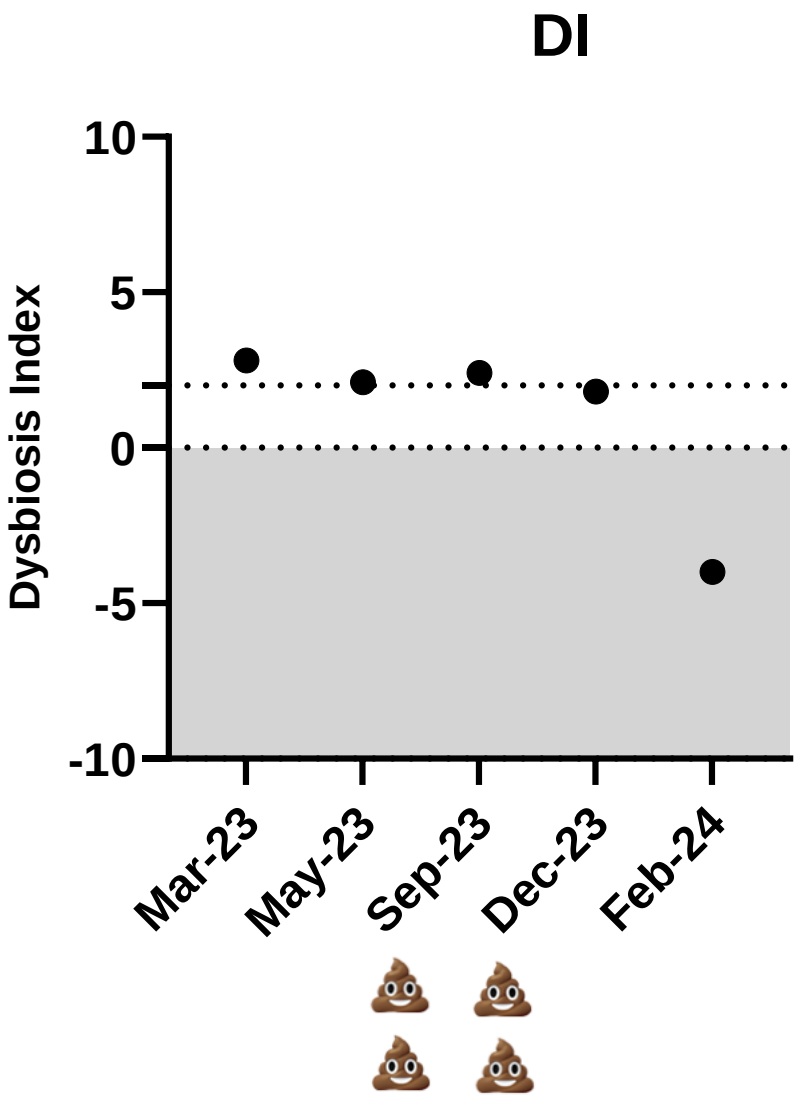
After FMT

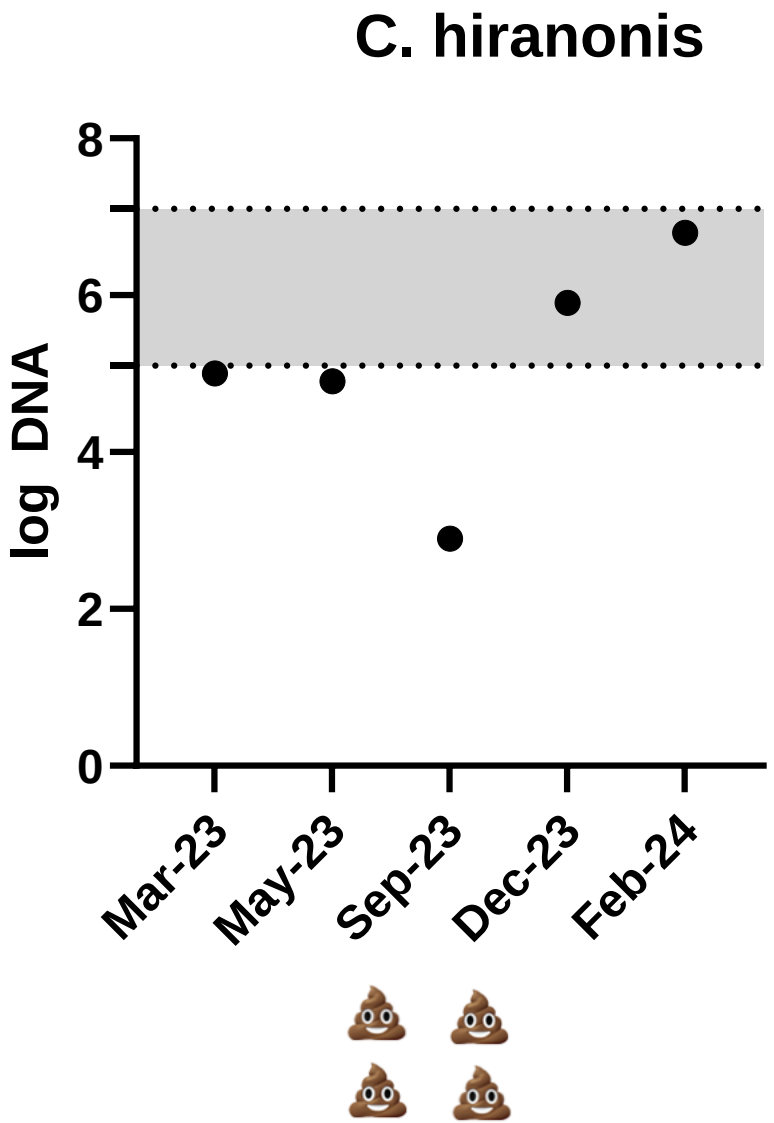
Off glucocorticoids

CIBDAI 0
FS 2-3/7
No other clinical signs

Excellent appetite
2 kg body weight increase
PU/PD resolved

Follow-up DIs





Lupin

2 yrs old MN DSH

Chronic small intestinal diarrhea, 2-3 times a day

No identifiable cause

Refractory to fiber enriched-, highly digestible, hydrolyzed diets and probiotics

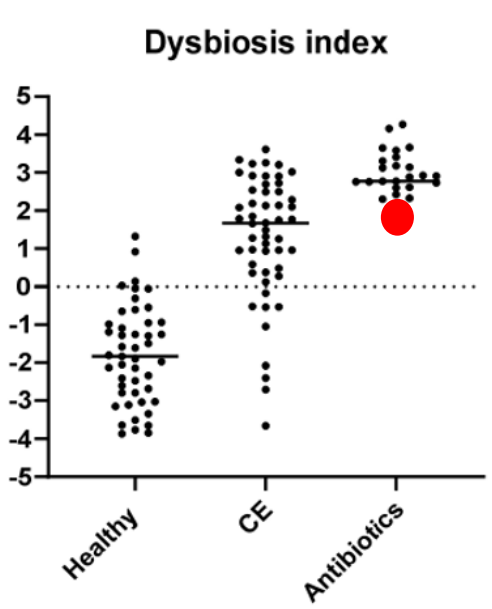
Responsive to amoxicillin clavulanate

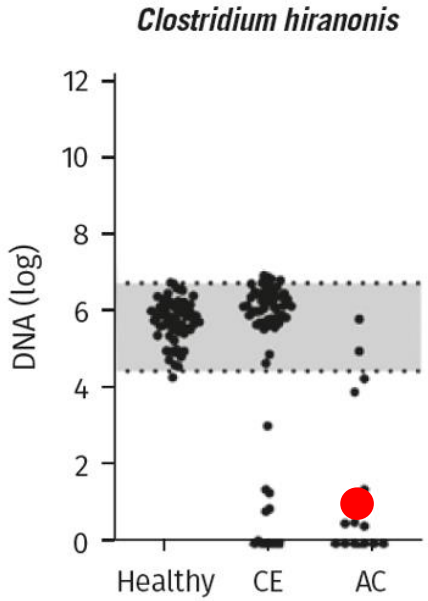
Gradual return to liquid stools when discontinued

Lost responsiveness with time

Fecal DI – 1 month off antibiotics

DI	2.2	< 0
Clostridium hiranonis	**0.8**	4.5-7.1
Bacteroides	5.9	4.0-7.5
Bifidobacterium	6.2	3.2-8.7
Turicibacter	4.8	4.4-9.0
Faecalibacterium	3.9	3.8-8.4
Streptococcus	2.8	1.6-5.2
E. coli	3.9	1.4-7.0





https://vetmed.tamu.edu/gilab/

1 + 4 weeks post FMT

Pre- and post-FMT Dysbiosis index

DI	2.2	0.8	< 0
Clostridium hiranonis	0.8	4,4	4.5-7.1
Bacteroides	5.9	5.3	4.0-7.5
Bifidobacterium	6.2	7.1	3.2-8.7
Turicibacter	4.8	6.4	4.4-9.0
Faecalibacterium	3.9	4.0	3.8-8.4
Streptococcus	2.8	2.2	1.6-5.2
E. coli	3.9	5.4	1.4-7.0

Take home messages

Treatment strategies for intestinal dysbiosis should depend on the underlying cause and will often require a multimodal approach

Cure is possible in mild cases (provided the eliciting cause is eliminated) or in antibiotic-induced dysbiosis (as sole treatment)

Clinical remission is a reasonable target in CE-associated dysbiosis (multimodal strategy)

Based on current available evidence, a dietary trial should be attempted first in dogs and cats with chronic GI signs and should always be part of multimodal treatment strategies

Take home messages

Besides inducing antimicrobial resistance, antibiotics are detrimental to gut and microbiome health

They should not be routinely used for the diagnostic approach and treatment of GI signs

FMT appears to be efficacious especially in young dogs and cats with mild dysbiosis or antibiotic-induced dysbiosis and associated GI signs

The use of FMT in CE appears promising for clinical remission, especially in the context of a multimodal approach

Thank you very much for the attention!

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I PORTONI ROSSI

IDEXX

Questions?