Prescription Poop: The Microbiome, Dysbiosis and How To Perform FMT

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VMX 2025 VETERINARY MEETING & EXPO

Conflict of Interest Disclosure:

I have financial interest, arrangement or affiliation with:

Gastrointestinal Laboratory, TAMU	Employee
IVC/Evidensia	Employee (sabbatical), research grant
Purina	Speaking honorarium,
Dechra	Speaking honorarium
Royal Canin	Speaking honorarium
VETgirl	Speaking honorarium
AMVAC	Speaking honorarium
UNISVET	Speaking honorarium
VETACAD	Speaking honorarium
SCIVAC	Speaking honorarium

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Conflict of Interest Disclosure:

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Name of Organization	Relationship
IDEXX	honorarium for this lecture

.

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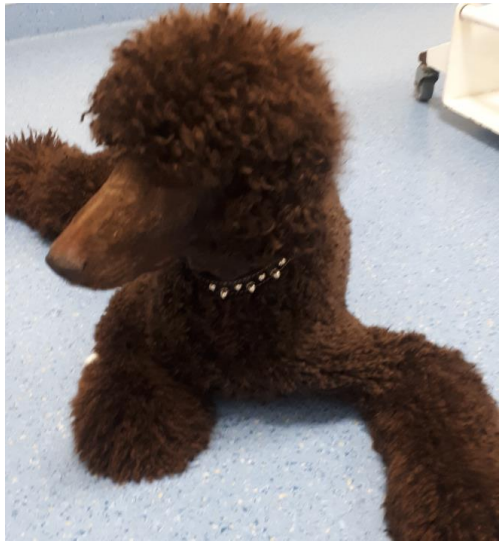
”Harley”, 7 mth old intact male standard poodle

- 3rd novel protein source
- Prednisolone 1.25 mg/kg + probiotic SLAB51 – poor effect



- Olsalazine + loperamide – no effect
- Melena - metronidazole → no melena, still diarrhea
- 8th visit for diarrhea, anorexia, now vomiting, appears to be in pain
- Moderately depressed, moderately dehydrated, BCS 4/9, tense abdomen, painful on palpation
- If no response within a few days - euthanasia

Dogs w acute or chronic diarrhoea- exclude bacterial infection of the GI tract with culture?

= very limited information

Received: 14 September 2020 | Accepted: 20 November 2020
DOI: 10.1111/jvim.15982

STANDARD ARTICLE

Journal of Veterinary Internal Medicine Open Access
ACVIM American College of Veterinary Internal Medicine

Diagnostic value of fecal cultures in dogs with chronic diarrhea

Melanie Werner[1] | Jan S. Suchodolski[2] | Jonathan A. Lidbury[2] | Jörg M. Steiner[2] | Katrin Hartmann[1] | Stefan Unterer[1]

Impossible to differ dogs w. CE from healthy dogs w. fecal culture

Intestinal microbiota

- Very complex eco system
- 5% detected with conventional culture!!

- Consists mainly anaerobes (e. g. Faecalibacterium – up to 16% - very difficult to culture)

- Modern molecular tools (16s rRNA etc) ➔ up to 450 different bacterial species in the jejunum

- Gastroenteritis ➔ pathogen ➔ antibiotics

Dysbios in acute and chronic gastroenteritis

- **Most significant alterations compared to healthy dogs:**

- Less diverse microbiome – depletion, fewer bact. species

- Significant reduction of beneficial microbes - ↓ short-chain fatty acid producing bacteria

(*Blautia* spp., *Faecalibacterium* spp., *Turicibacter* spp *Fusobacterium spp)*

OPEN ACCESS Freely available online

PLOS ONE

The Fecal Microbiome in Dogs with Acute Diarrhea and Idiopathic Inflammatory Bowel Disease

Jan S. Suchodolski[1]*, Melissa E. Markel[1], Jose F. Garcia-Mazcorro[2], Stefan Unterer[3], Romy M. Heilmann[1], Scot E. Dowd[4], Priyanka Kachroo[5], Ivan Ivanov[5], Yasushi Minamoto[1], Enricka M. Dillman[5], Jörg M. Steiner[1], Audrey K. Cook[5], Linda Toresson[6]

1 Gastrointestinal Laboratory, Small Animal Clinical Sciences, College of Veterinary Medicine and Biomedical Sciences, Texas A&M University, College Station, Texas, United States of America, **2** Facultad de Medicina Veterinaria, Universidad Autónoma de Nuevo León. Gral. Escobedo, Nuevo León, México, **3** Clinic of Small Animal Medicine,

Good vs bad party in the gut

Diversity – lots of different bacterial taxa

Buffer – good vs ”bad” ones

Food – SCFA energy source colonocytes

Nice (antiinflammatory) atmosphere –
SCFA, indole, secondary BAs

No leakage – SCFA + indole enhances barrier function and tight junctions

Healthy motility – SCFA

Control of proliferation of negative bacteria – 2nd BAs

Efficient cleaning up – *Cl. hiranonis* converts primary BAs to 2nd BAs

Good vs **bad** party in the gut

Less diversity – less buffer capacity

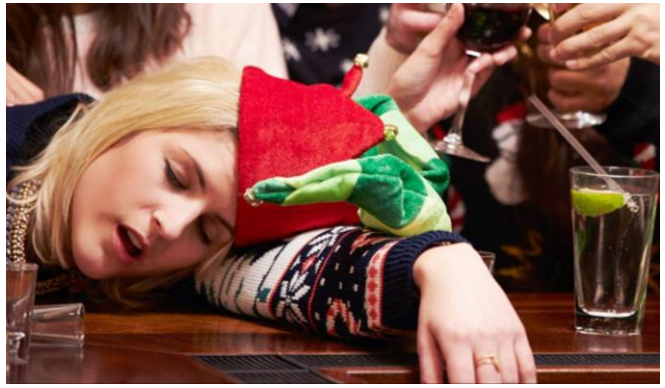
Lack of food – ~~SCFA~~

Toxic atmosphere – proinflammatory –
~~SCFA, indole, secondary~~ BAs

Leakage – ~~indole, SCFA~~

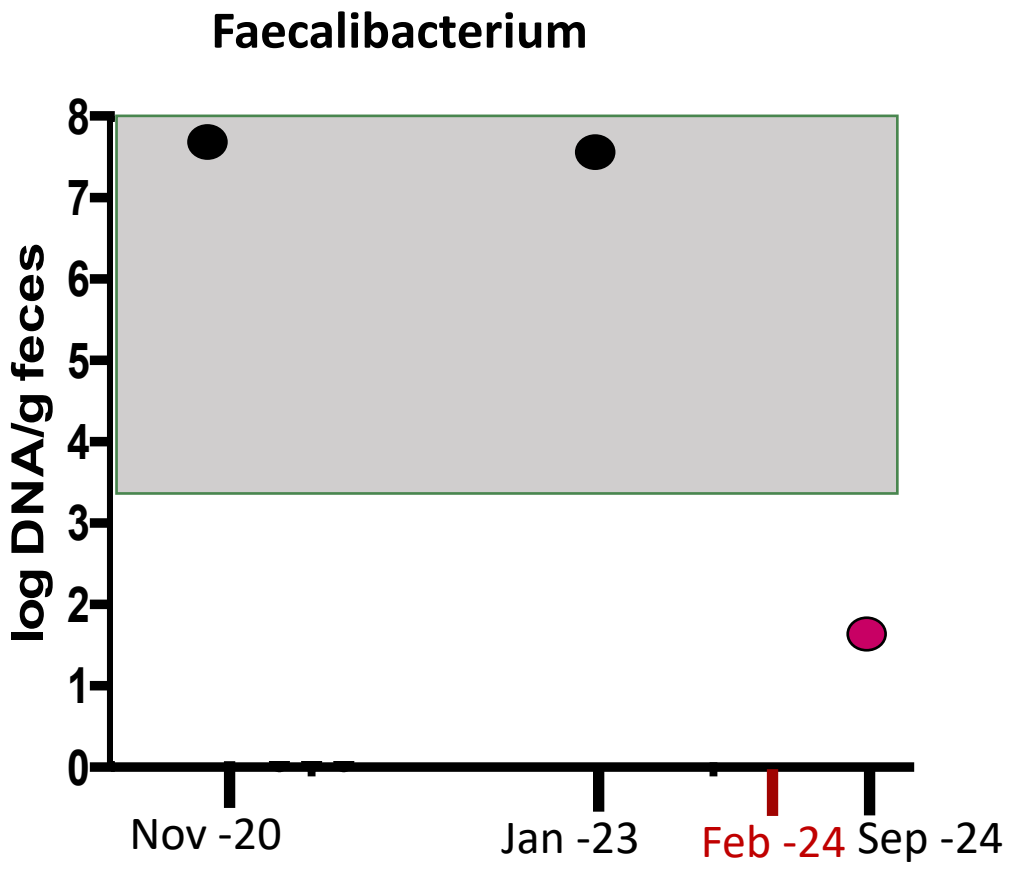
Accelerated motility - SCFA ↓, Primary bile acids ↑

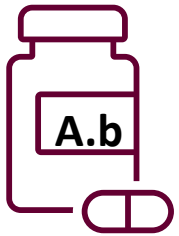
Increased proliferation of *E.coli. Cl perfringens, Cl. difficile*



”Sol”, intact female NSDTR, 5 Y/A

Healthy fecal FMT donor





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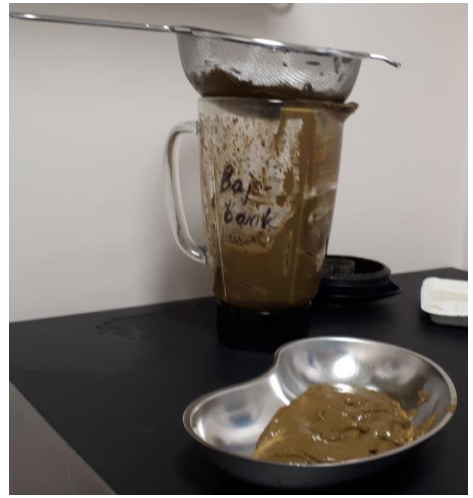
”Harley”, 7 mth old intact male standard poodle

- FMT - rectal enema; 5 g/kg BW
- Frozen feces thawed and blended w NaCl



- Started eating within 12 hours, very alert within 24 hours, diarrhea stopped
- Sent home the day after; scheduled to come back for repeated FMT
- Weaned of metronidazole, under treatment single protein diet + prebiotics + methylprednisolone + chlorambucil EOD 3 years later

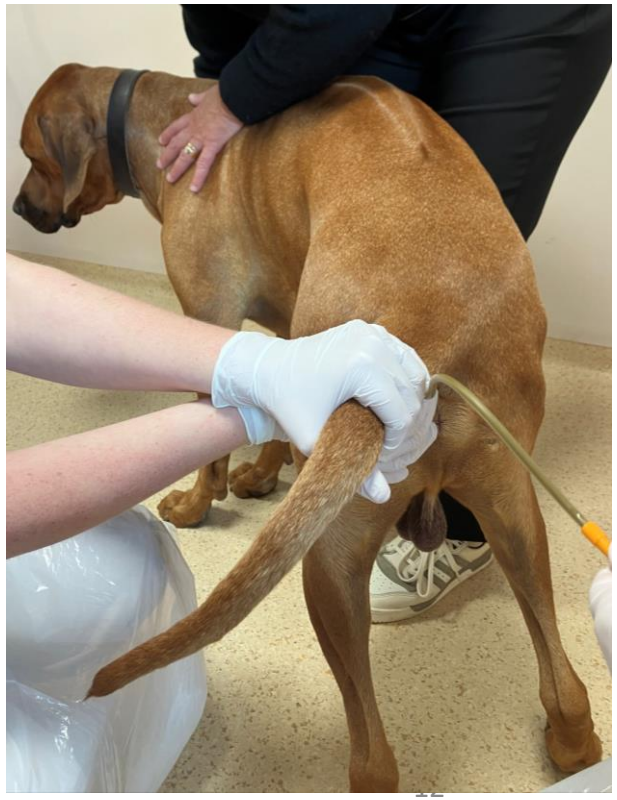
Fecal microbial transplantation (FMT)

FMT → transfer microbiota from healthy donor to recipient with a disease

→ improve the microbiome/decrease disease activity

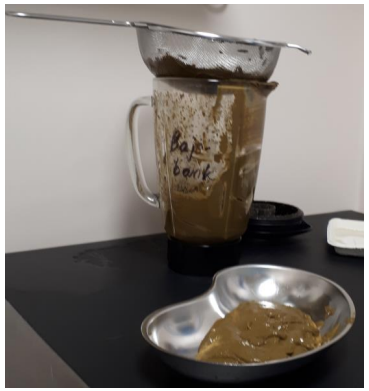
+

+



FMT in people:

Mentioned in a Chinese textbook of emergency medicine in 320 A.D (Hong Ge)



Excellent effect in chronic recurrent *Clostridiodes difficile* inf. – better than antibiotics

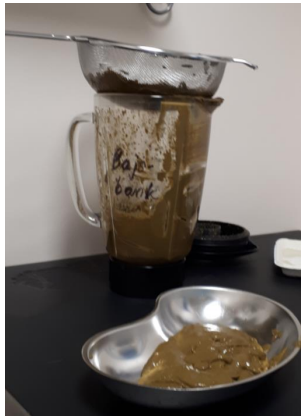
Grade 1 evidence in treating ulcerative colitis and Crohn's disease
(Paramsothy et al 2017; Cheng et al 2021)

Fresh or **frozen feces** from healthy donors **equally effective**

Can be deposited in the colon, duodenum or po - **equally effective**

=fertilizer

=new grass seeds



=new eco system

FMT protocol; Evidensia Specialist Animal Hospital, Helsingborg

1. Use fresh or fresh frozen feces, 5 gr/kg BW of recipient, dogs> 25 kg BW - 3 gr/kg BW

2. Remove visible grass etc, blend feces w NaCl in blender to suitable texture. Filtrate w sieve!

3. Aspirate in 60 ml syringes

4. Recipient – walked for 30 minutes prior to transplantation, (no food 6-8 hrs prior to procedure)

5. (Sedation optional) – we often use a low dose of ACEP (0.1 mg/kg)

FMT protocol; Evidensia Specialist Animal Hospital, Helsingborg

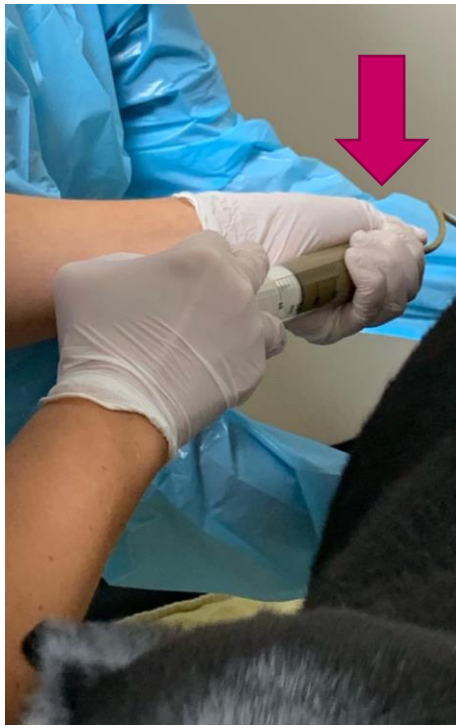
Measure the catheter – from the tip to the level of the last rib

Attach the catheter to the syringe, fill the catheter w. the transplant

Insert the catheter after lubrication

+

Position – standing dog or lying on the abdomen



Hold one hand on the connection between the catheter and the syringe, give the transplant. Remove the catheter

Let the dog owner drive home slowly, no walks or food for a few hours

Cryopreservatives?

10% glycerol can be added to fecal slurry before freezing (1:10)

Improved viability in some bacterial species upon thawing

No studies showing comparing efficacy off fecal slurry with/without glycerol

Multiple studies and case reports on FMT showing good effect without adding glycerol

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STANDARD ARTICLE

Journal of Veterinary Internal Medicine Open Access

ACVIM American College of Veterinary Internal Medicine

Fecal microbiota transplantation in puppies with canine parvovirus infection

Giorgio Q. Pereira[1] | Lucas A. Gomes[1] | Iago S. Santos[1] | Alice F. Alfieri[2] | J. S. Weese[3] | Marcio C. Costa[4]

Standard tx + FMT

Parvovirosis n=66

Standard tx= a.b, i.v fluids

Day 3

7/33 (21%)

Sent home

Mortality

Day 6

12/33 (36%)

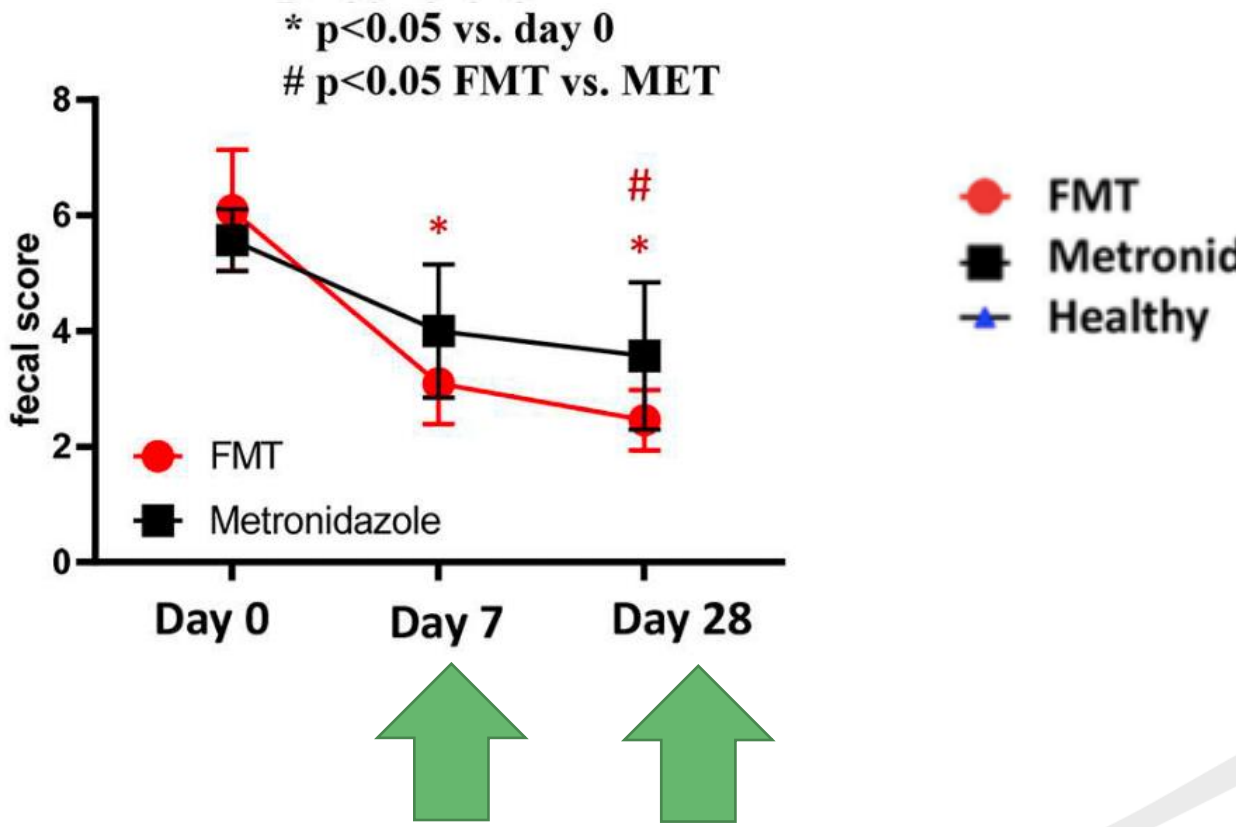
frontiers in Veterinary Science

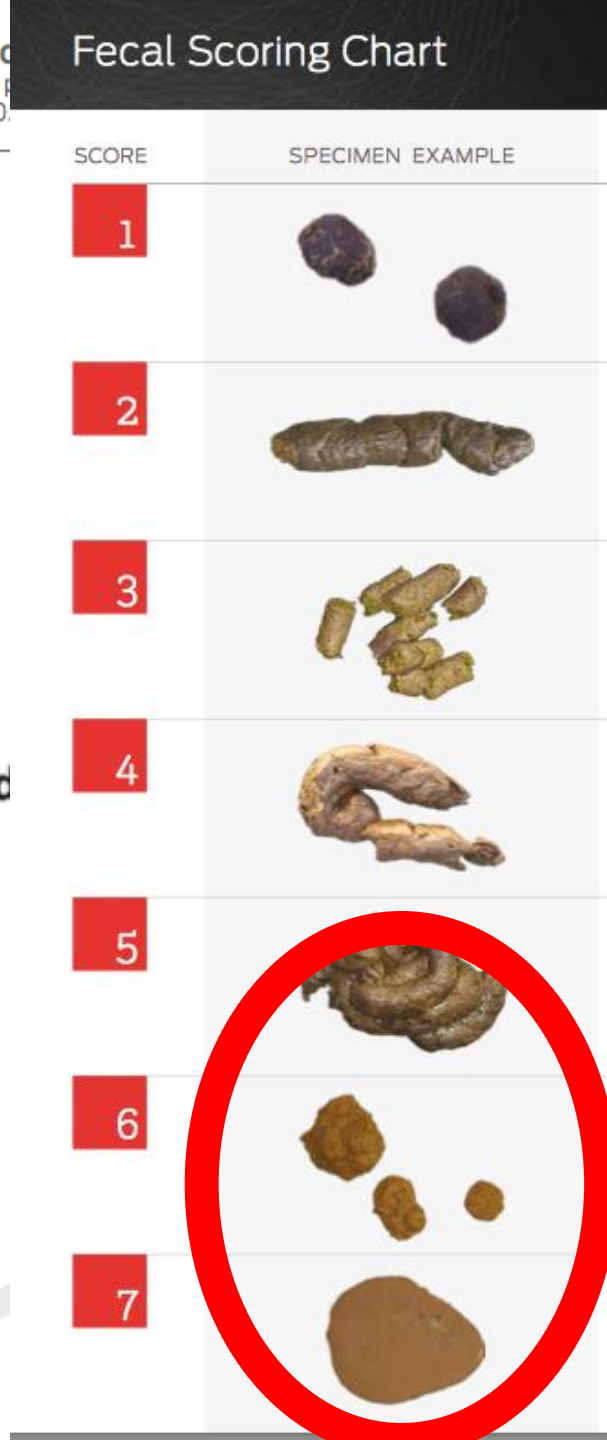
doi: 10.

Fecal Microbial and Metabolic Profiles in Dogs With Acute Diarrhea Receiving Either Fecal Microbiota Transplantation or Oral Metronidazole

Jennifer Chaitman[1], Anna-Lena Ziese[2], Rachel Pilla[3], Yasushi Minamoto[3],*

n=18
1 x FMT=11
7 d Mtz=7





frontiers in Veterinary Science

ORIGINAL RESEARCH
published: 16 April 2020
doi: 10.3389/fvets.2020.00192

Fecal Microbial and Metabolic Profiles in Dogs With Acute Diarrhea Receiving Either Fecal Microbiota Transplantation or Oral Metronidazole

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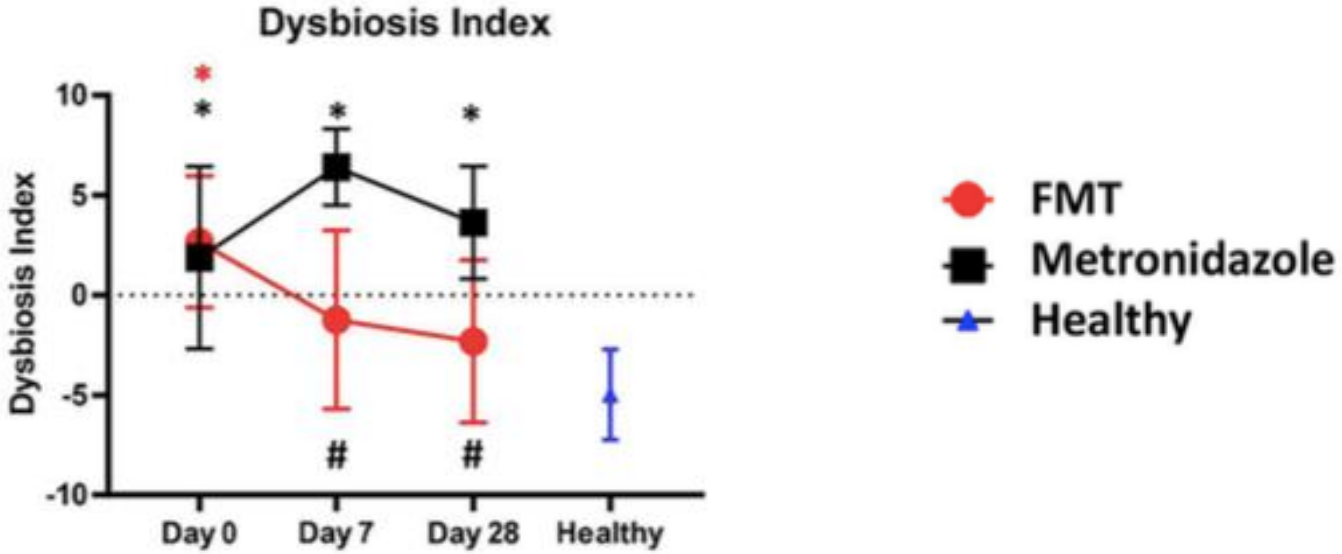

Antibiotics - DI ↑, *C. hiranonis* ↓, normalizes after several weeks - but not in all dogs (Manchester et al 2019, Chaitmann et al 2020)

veterinary sciences

MDPI

Article

Clinical Effects of Faecal Microbiota Transplantation as Adjunctive Therapy in Dogs with Chronic Enteropathies—A Retrospective Case Series of 41 Dogs

Linda Toresson [1,2,*], Thomas Spillmann [1], Rachel Pilla [3], Ulrika Ludvigsson [2], Josefin Hellgren [2], Gunilla Olmedal [2] and Jan S. Suchodolski [3]

- Retrospective study based on a computerized data base search, Feb 2019 - July 2022 (Evidensia Specialist Animal Hospital; SWE)

- Compare disease activity based on Canine IBD Activity Index (CIBDAI) pre-and post FMT in dogs with chronic enteropathies (CE)

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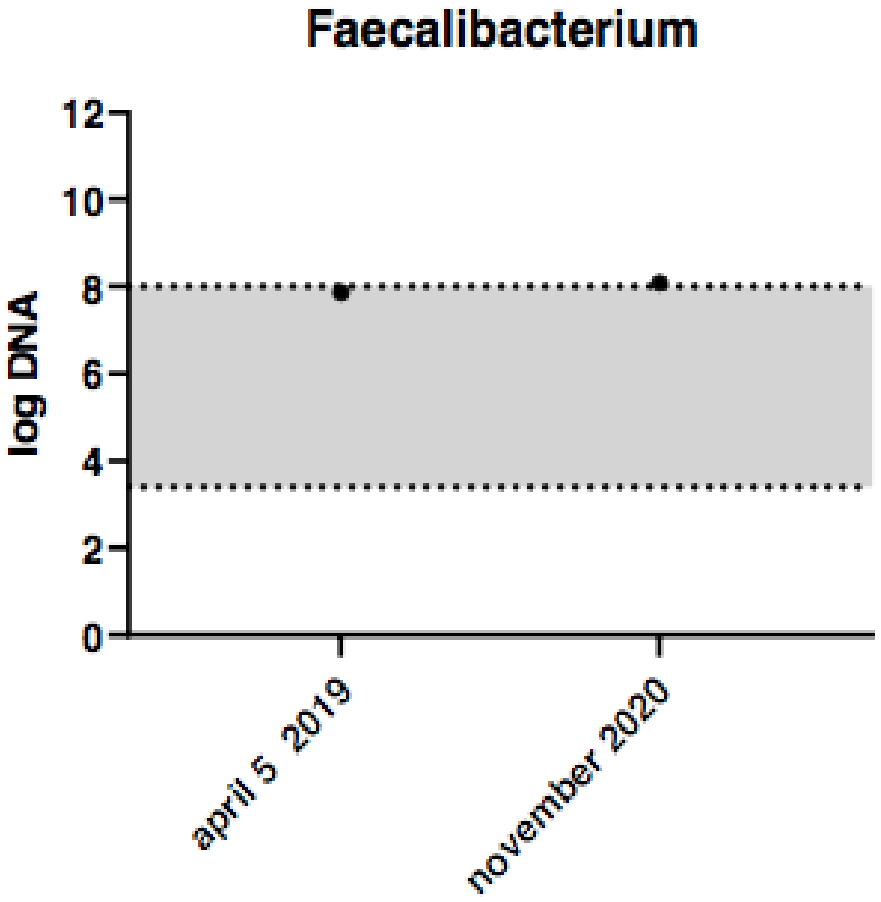
Materials and methods I

- Inclusion criteria:
  - Dogs with CE not responding satisfactorily to evidence-based treatment protocols, treated with FMT
  - Follow-up available for at least 3 months

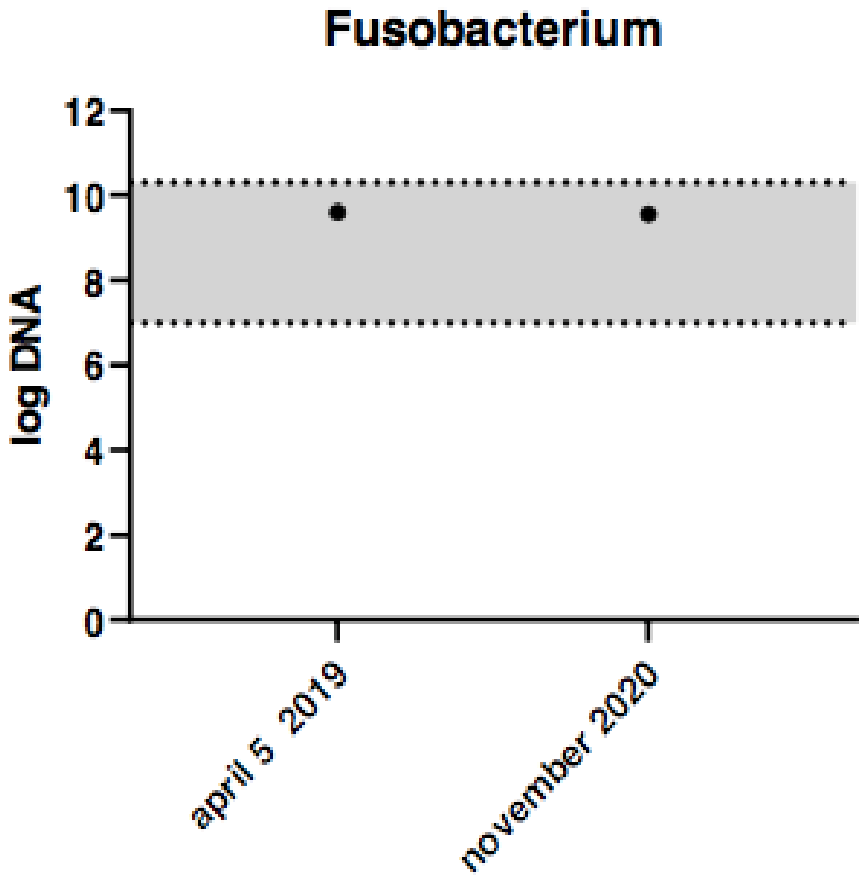
- Exclusion criteria:
  - Starting new immunosuppressive treatment or diet in parallel with FMT
  - Increasing the dose of current maintenance therapy
  - Intestinal parasites

Materials and methods II

- FMT - rectal enema; 5 g/kg BW recipient, BW>30 kg – 3 g/kg
- Frozen feces blended w NaCl



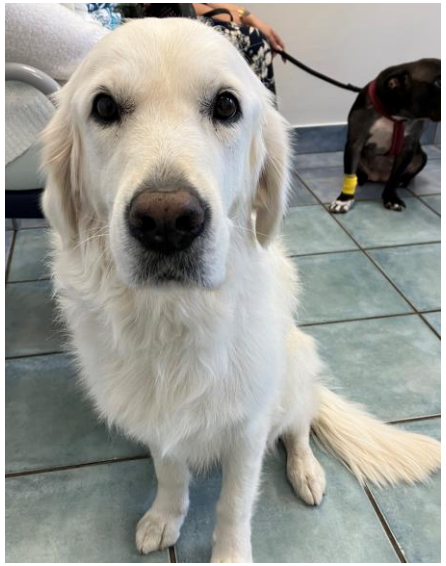
normal



Results – baseline data

- 41 dogs, 7-156 (median 76) months of age included
- 29 different breeds; GSD (4/41), Golden retr. (3/41), mixed breed (3/41)

  Treated for CE 1-110 months (median 20)



- 34/41 histologically verified CIE various severity (WSAVA)
- The majority (24/41) had partially immunosuppressant-responsive enteropathy (P-IRE)

Results – baseline data

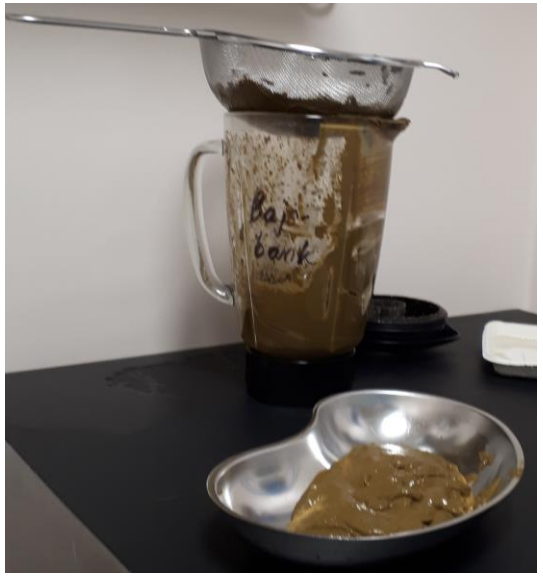
- Main complaints: diarrhea (32/41), lethargy (18/41), side effects of/difficulties tapering corticosteroids/needing antibiotics (17/41), +/- signs of pain/abdominal discomfort (13/41)

- Majority of dogs on a hydrolyzed protein diet¨

- 38/41 on corticosteroids, 23/41 2nd line immunosuppressives
  - MMF 8, CSA 7, chlorambucil 6, azathioprine 2

Results – FMT

- 1- 5 FMTs (median 3) given w 10-20 days interval
- 30/41 dogs (71 %) received 3 FMTs; 2 non-responders 1 FMT

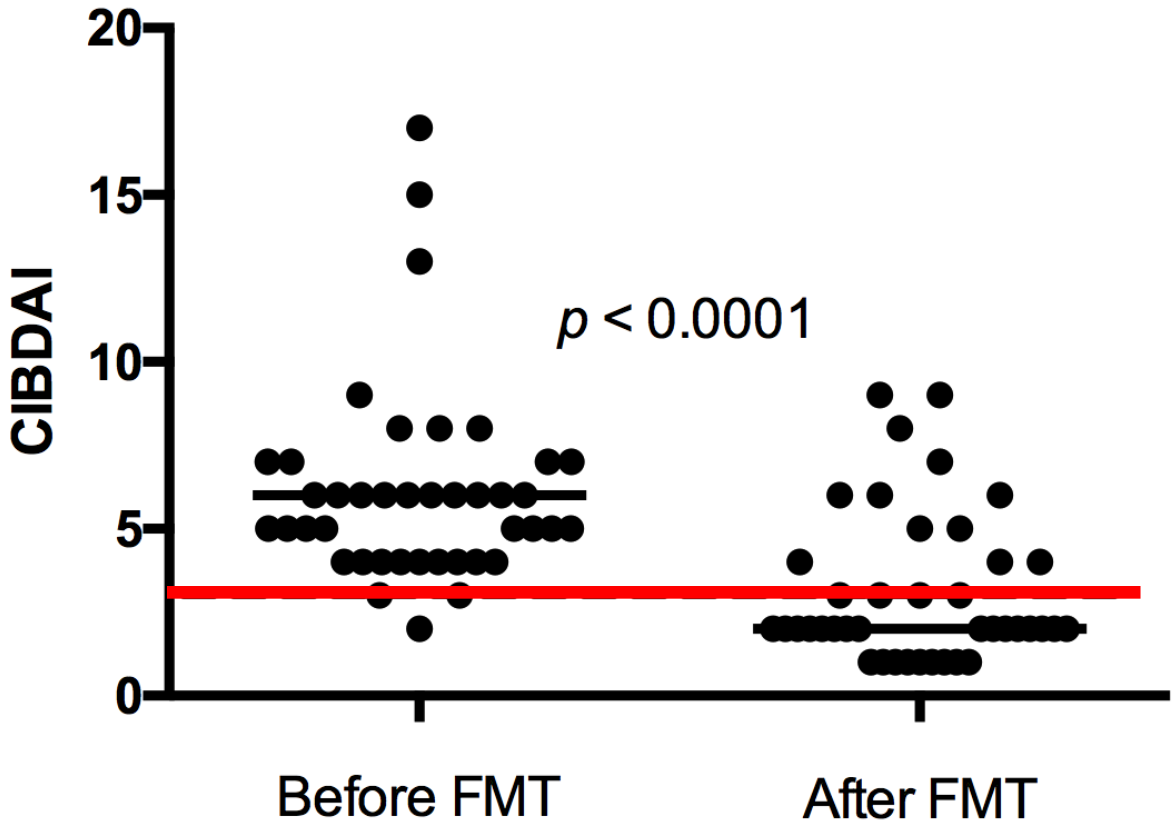


- Clinical improvement 31/41 dogs (76 %)
  - 26 good response, 5 short-lasting response, 10 dogs no response
- 23/31 responders further improvement after FMT 2 and/or FMT 3
- If no clinical response seen after FMT 2, no response to FMT 3

Results – CIBDAI before and after FMT

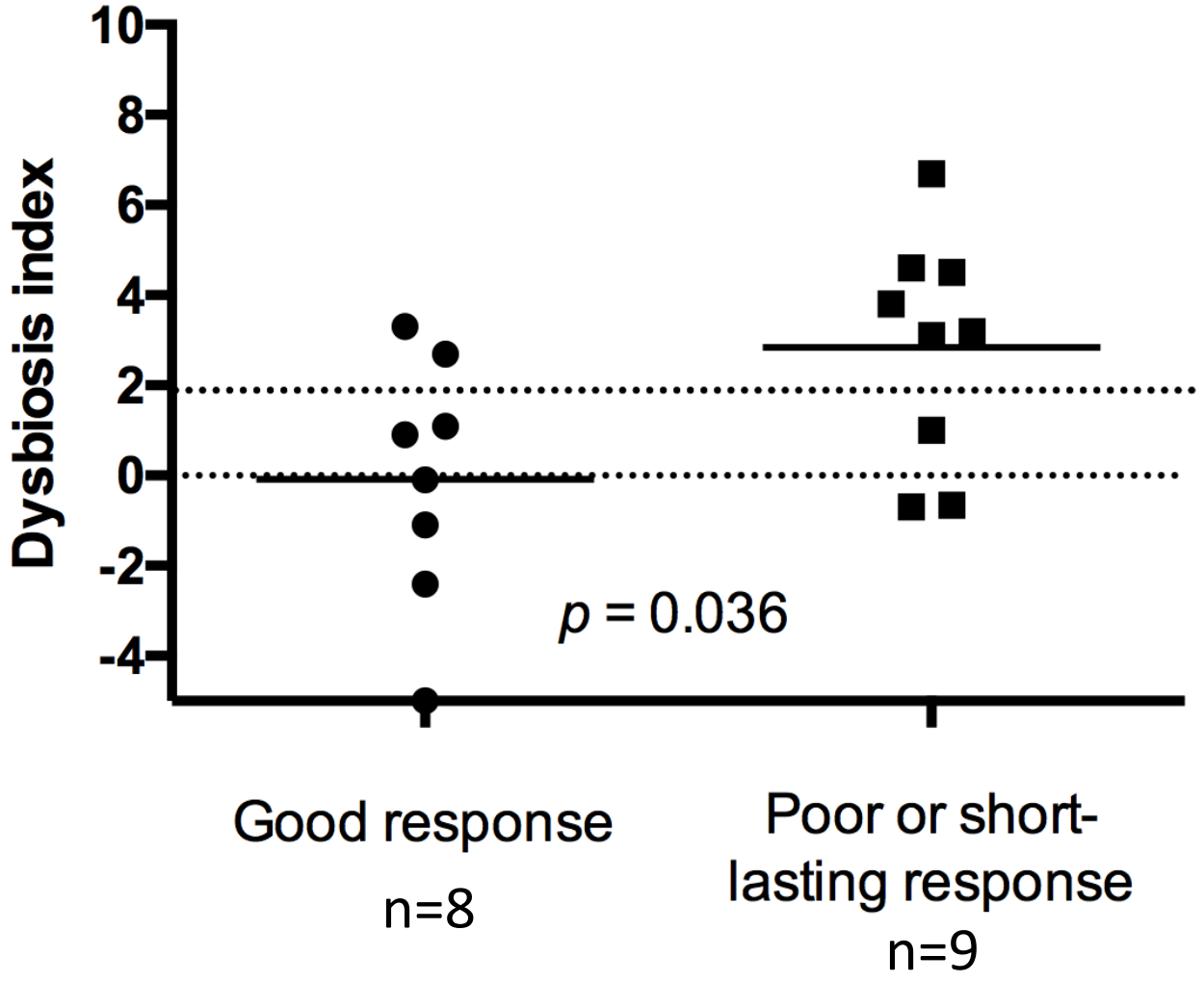
(Wilcoxon matched signed rank test)

	Pre	Post
Range	2-17	1-9
Median	6	2



Dysbiosis index at baseline in responders vs non-responders (Unpaired t-test)

	R	Non-R
Range	-5 - 3.3	-0.7 - 6.7
Mean	0.4	3.4



Results – FMT

Improved

activity level 24/41

fecal scores 24/41

BCS 8/41

appetite 6/41

Decreased

Corticosteroids 10/41

Stopped/avoid repeated antibiotics

3 dogs

Increased activity level

- 8/24 dogs w. increased activity level post FMT not reported as lethargic before

- Expressed as:
  - Taking more initiatives to play/interact owner and/or other dogs
  - More active during walks, longer walks, walking in front of the dog owner instead of behind, more social/inquisitive
  - Spending less time sleeping during daytime

- Placebo?
  - Often mentioned unrelated people (doggy day care, distant friends/relatives)

Adv Ther (2020) 37:97–112
https://doi.org/10.1007/s12325-019-01151-w

REVIEW

Hindawi Publishing Corporation
Gastroenterology Research and Practice
Volume 2015, Article ID 517597, 5 pages
http://dx.doi.org/10.1155/2015/517597

Research Article

Fecal M ... **lity of**

Self-assessed quality of life ↑ ↑ for 3-6 months post FMT

Fatigue ↓ ↓ up to 6 months post FMT

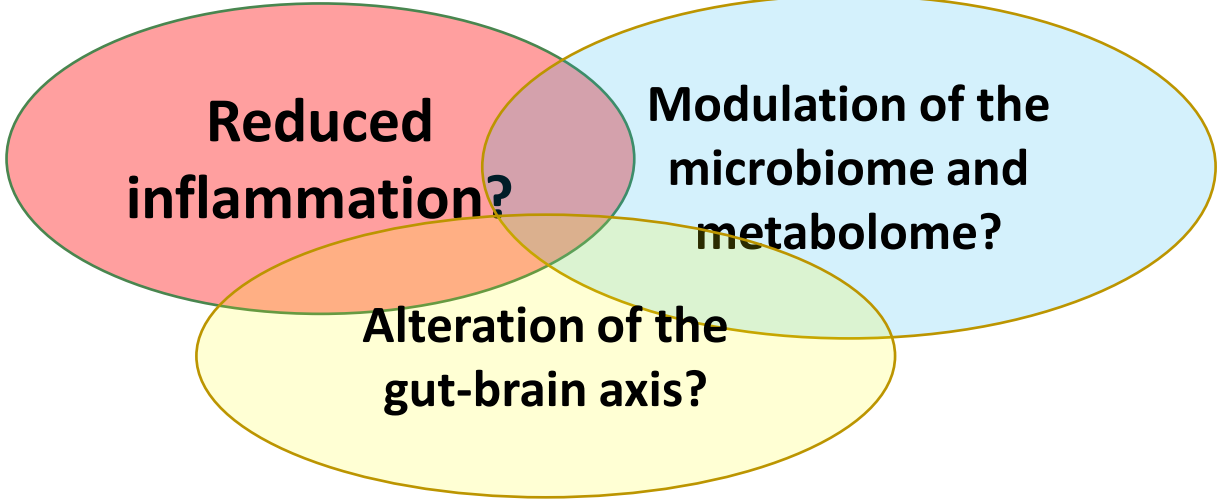
ELSEVIER

Research paper

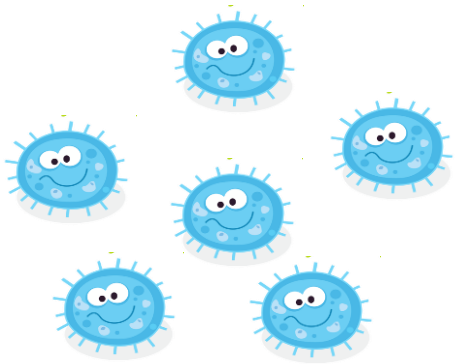
The effect of fecal microbiota transplantation on IBS related quality of life and fatigue in moderate to severe non-constipated irritable bowel: Secondary endpoints of a double blind, randomized, placebo-controlled trial

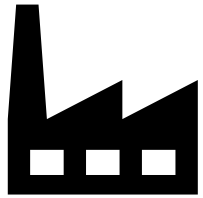
Peter Holger Johnsen[a,e,*], Frank Hilpüsch[b,d], Per Christian Valle[a], Rasmus Goll[c,e]

Check for updates



SCFA





- γ-amino butyric acid (GABA)
- glutamate
- noradrenaline
- dopamine

Gao et al

Advances in Nutrition

Volume 11, Issue 3, May 2020, Pages 709-723

“Moltas”, intact male GSD, 5 Y/A, NRE/IRE/ARE

- Chronic, partially refractory, diarrhea all his life + atopic dermatitis, pyodermia & chronic otitis

Somewhat stable on high doses of corticosteroids

No effect of azathioprine, cyclosporine or multiple dietary trials

Responds to tylosin or mtz during flare-ups

Clinical improvement after chlorambucil added 2.5 y previously

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“Moltas”, intact male GSD, 5 Y/A, NRE/IRE/ARE

Re-check April 2020: doing worse, monthly flare-ups diarrhea, regurgitations, lethargy. **Three courses of Tylosin in 4 mths**

Tx: Budesonide 3 mg EOD, methylpred. 4 mg EOD, chlorambucil 3 mg EOD, cobalamin 1 mg/w

Phys. ex.: Marked abdominal pain

Clin chem: Alb 28 g/L (30-45), TP 51 g/L (61-75), B12 221 pmol/L (180-708) (- Alb 2.8 g/dL (3.0-4.5); TP 5.1 g/dL (6.1-7.5))

Fecal parasites: not found

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“Moltas”, intact male GSD, 5 Y/A, NRE/IRE/ARE

3 FMTs:

- Regurgitations stopped after FMT 1
- Feces improved + more playful after FMT 2
- FMT 3: no diarrhea or palpable abdominal pain

Normalization albumin/protein/B12

January 2022: Mild flare ups every 3rd mth, lasting 1-2 days

Serum biochemistry WNL, no abdominal pain

Relapse after 19 months – responded to repeated FMT

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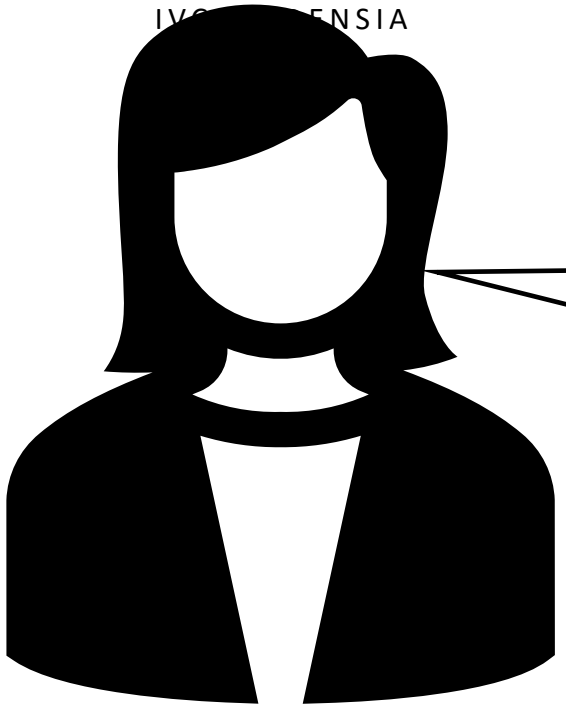
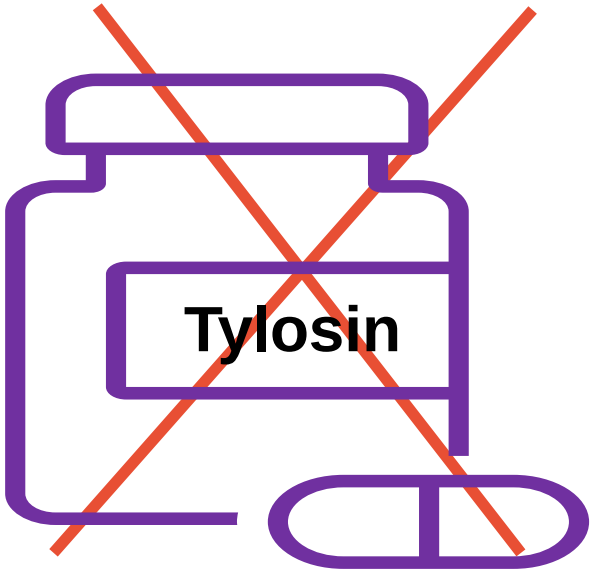
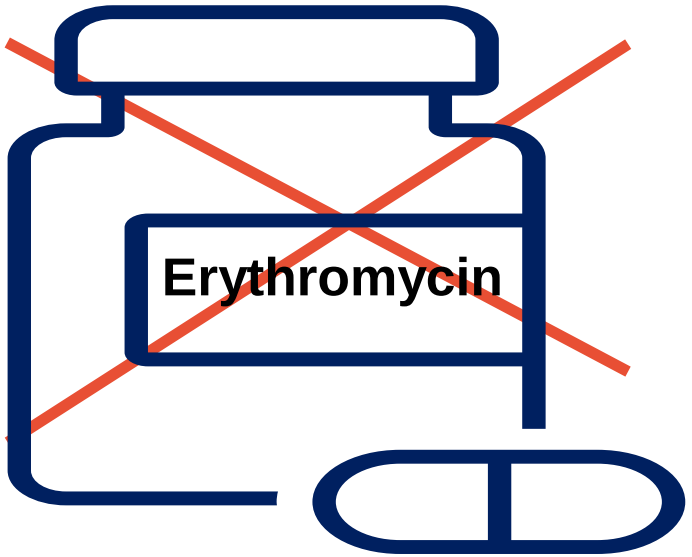
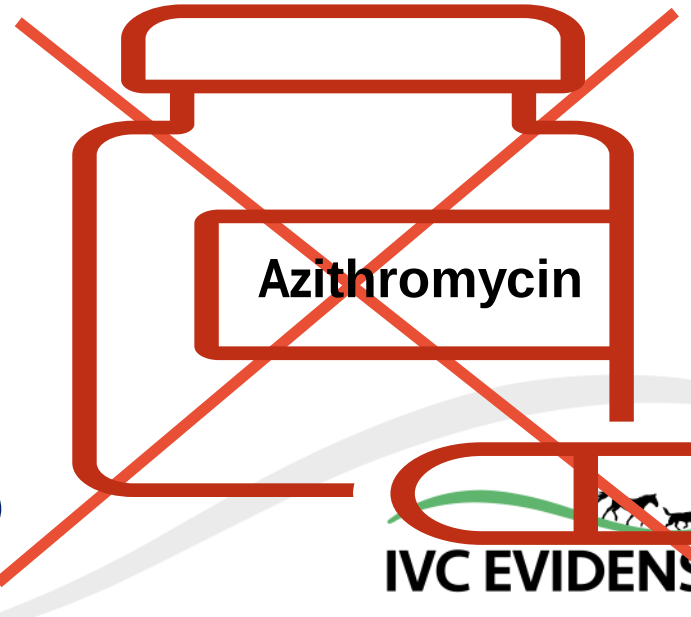
Common argument:



Just give Tylosin – it isn't used for human consumption, so antimicrobial resistance is not a problem





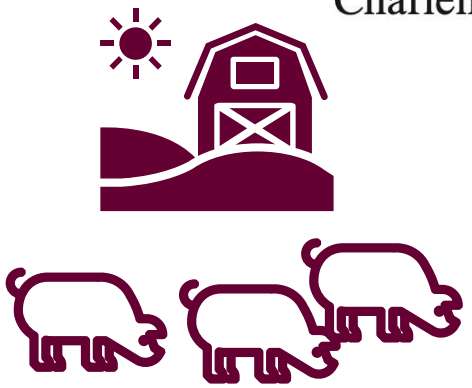


IVC EVIDENSIA

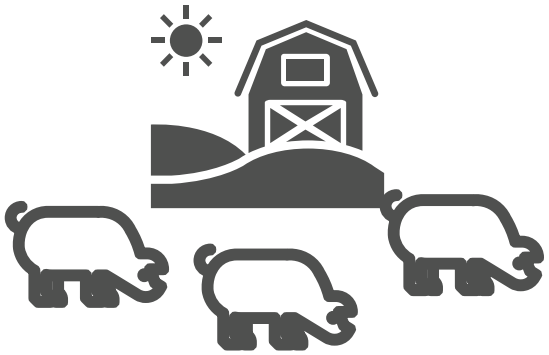
APPLIED AND ENVIRONMENTAL MICROBIOLOGY, July 2004, p. 4205–4210 Vol. 70, No. 7
0099-2240/04/$08.00+0 DOI: 10.1128/AEM.70.7.4205–4210.2004

Effects of Tylosin Use on Erythromycin Resistance in Enterococci Isolated from Swine

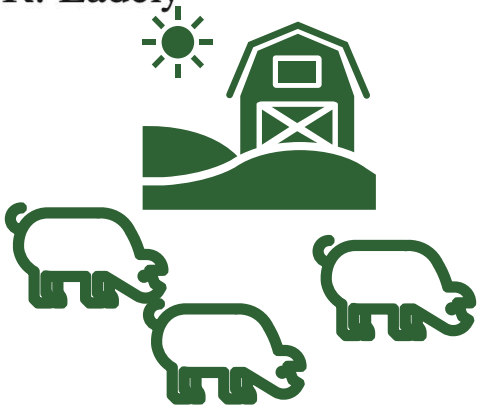
Charlene R. Jackson,* Paula J. Fedorka-Cray, John B. Barrett, and Scott R. Ladely



Farm A
Tylosin used as growth promoter



Farm B
Tylosin used to treat diseases



Farm C
Tylosin not used at all

n=1187 *Enterococci* isolates

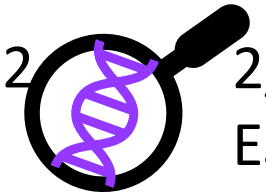
% erythromycin resistant fecal samples:

2%

Documented risk of household sharing of AMR genes

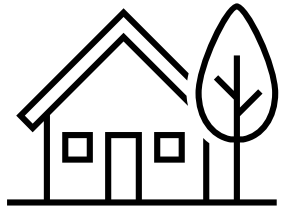
Ljungquist et al 2016:

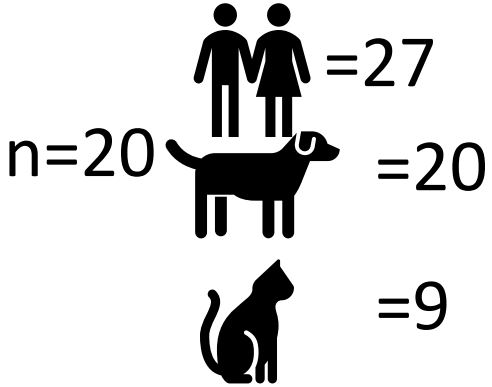
ESBL+/AmpC + Enterobact.

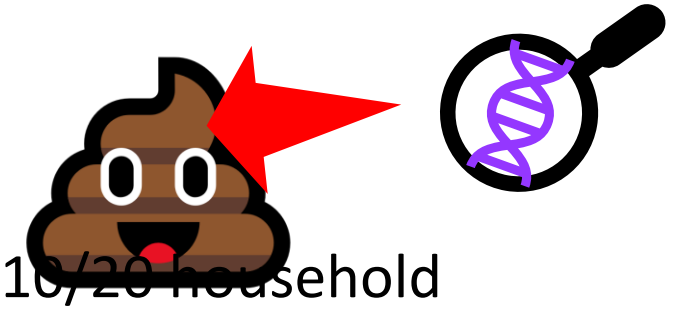


2/22 households sharing of AMR: ESBL or AmpCBL producing Enterobact.

Belas et al 2020:







10/20 household sharing of AMR

Toombs-Ruane 2020:

2/23 households sharing of AMR: ESBL or AmpCBL producing *E. coli*

FMT donor screening – preliminary recommendations

Age/signalment/environment

- minimum 12 months to middle aged
- clinically heathy (no abnormalities found on clinical examination or history)
- CIBDAI < 3
- acceptable body condition score (BCS 4-6/9)
- CBC + serum biochemistry WNL
- No raw food diets
- No antibiotics (min. 6 mths)

- Indoor cats from single households ➡minimize risk of infections
- Cats - minimum 6 weeks in the household

IVC EVIDENSIA

FMT donor screening – preliminary recommendations

Screening (recommended)

- Normal Dysbiosis Index
- *Salmonella*
- *Campylobacter jejuni*
- *Giardia* and *Cryptosporidium*
- other intestinal parasites with centrifugal fecal flotation
- Cats +
  - *Tritrichomonas foetus*
  - Enteric coronavirus (PCR recommended; once for cats in indoor single-cat-household)
  - FIV and FeLV

Frequency

- Minimum every 6 months, potentially more frequent based on risk /environment

Advances in Small Animal Care 5 (2024) 79–107
ADVANCES IN SMALL ANIMAL CARE

Clinical Guidelines for Fecal Microbiota Transplantation in Companion Animals

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Jan S. Suchodolski, DrMedVet, PhD, DACVM, AGAF[b],
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Linda Toresson, DVM, PhD[n], Stefan Unterer, DVM, Dr med vet, Dr habil, DECVIM-CA[o],

Indications for FMT

- Parvovirosis
- Acute gastroenteritis
- Young animals with chronic diarrhea
  - after infections or antibiotic use
  - not responding to dietary trials
- Dogs with CE not responding optimally
  - often require parallel treatment for underlying GI inflammation

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“Nikita”, intact mixed breed female, 7 Y/A, AHDS

- Previously healthy ➔ acute diarrhea 3 days ➔ watery diarrhea ➔ melena, vomiting, anorexia, lethargy. Vaccinations up to date
- Clin ex: Mod. depressed, 5% dehydration, painful abdomen, temp. 100.6 F
- Admitted for hospital care
- CBC+ clin chemistry: Mild hemoconcentration, mild hypokalemia, mild hypernatremia
- Ultrasound scan: Fluid-filled colon and stomach, no signs of ulcerations/FB, the rest WNL

TEXAS A&M UNIVERSITY
Gastrointestinal Laboratory

“Nikita”, intact mixed breed female, 7 Y/A, AHDS

- AHDS without signs of sepsis – supportive care 1st treatment of choice, not antibiotics
- Tx: Supportive care with i.v fluids, semfortan, maropitant, PPi
- After 24 h: almost rehydrated, stressed, mucoid liquid feces w fresh blood oozing from the anus

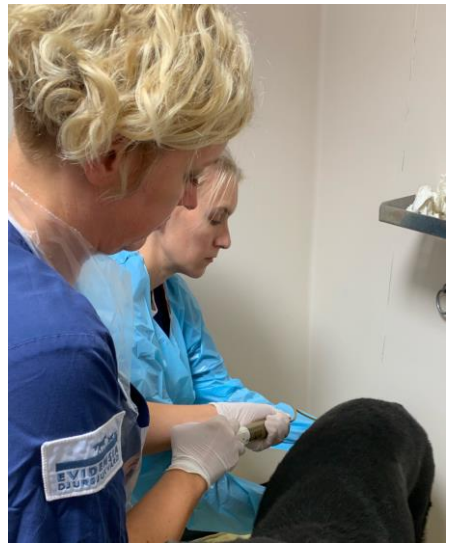
J Vet Intern Med 2011;25:973–979

Treatment of Aseptic Dogs with Hemorrhagic Gastroenteritis with Amoxicillin/Clavulanic Acid: A Prospective Blinded Study

S. Unterer, K. Strohmeyer, B.D. Kruse, C. Sauter-Louis, and K. Hartmann

“Nikita”, intact mixed breed bitch, 7 Y/A, AHDS/HGE

- FMT: mild sedation w. Acepromazine, lots of lubricants+ lidocain
- Difficult - blood clots clogging the catheter several times, placed ”half-way”
- Very effective – no more diarrhea, sent home the day after



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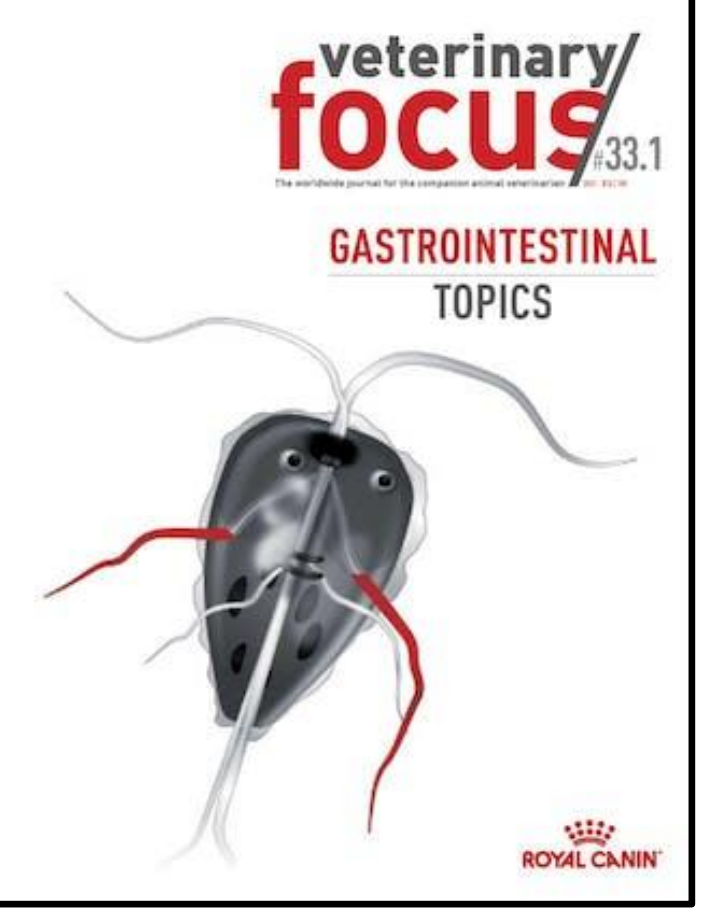

Thank you!

Questions?

More on FMT:

https://vetfocus.royalcanin.com/en/authors/linda-toresson

Clinical tools: Utilizing FMT in practice

TEXAS A&M UNIVERSITY
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