Changing the narrative

Tools for reducing use of antimicrobials for GI conditions in companion animals

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GreyWolf ANIMAL HEALTH

DISCUSSION GOALS…

- Recap of webcast on acute GI Upset
- A case - what would you do?
- Chronic enteropathy and Large Bowel Diarrhea (colitis)
- Alternatives to antimicrobials for chronic enteropathy

The "Roadmap"

.

RECAP…THE ROADMAP: ACUTE ENTEROPATHY

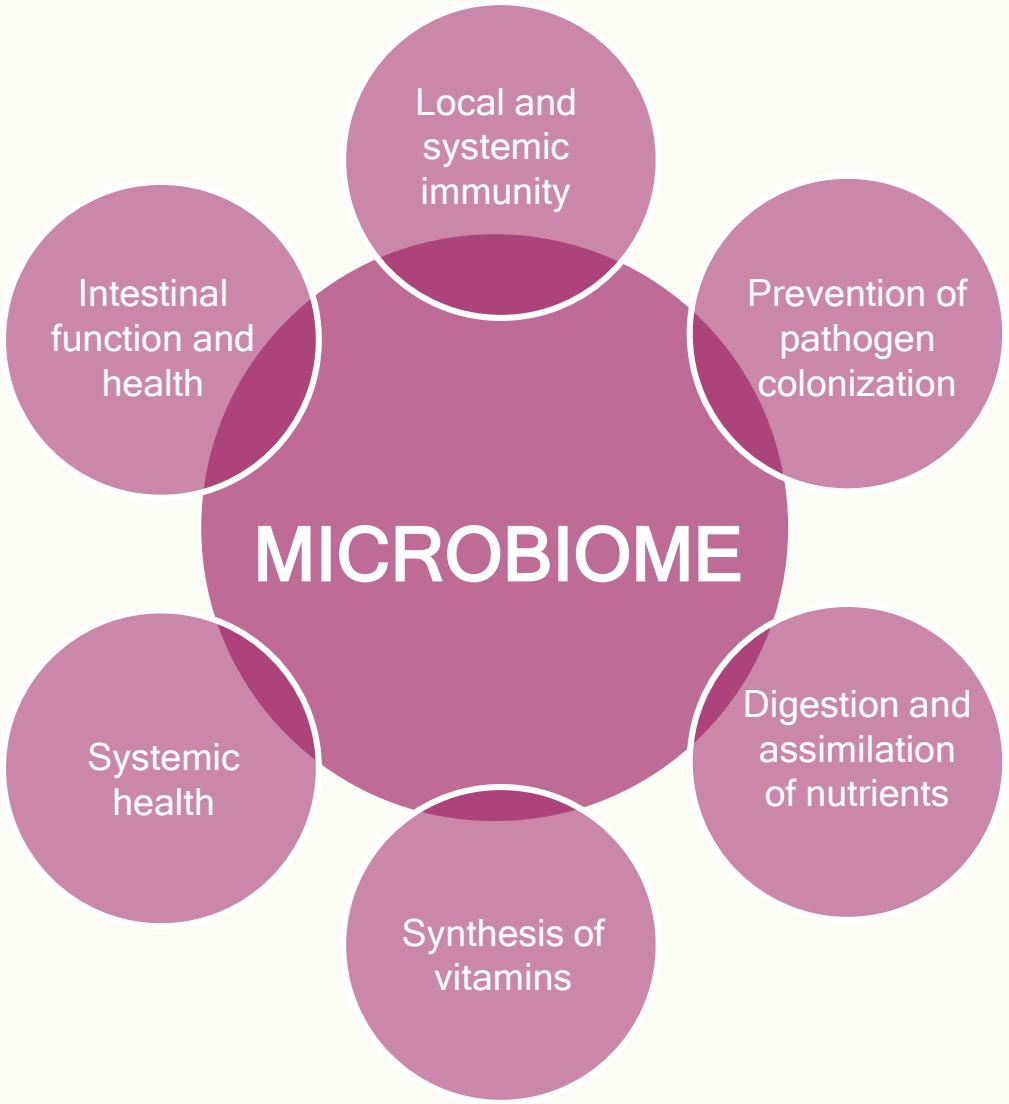
March 2022, we partnered with CommuniVet to provide a CE-accredited webcast,
"Pet parents have come to expect and even demand antimicrobials for mild acute GI upset – how can we change the narrative?"

https://www.communivet.com/en/ca/education/webcasts/antimicrobials-for-mild-acute-gi-upset

THE MICROBIOME

- Host benefit
- Why we care
- Risks of other diseases

Antibiotics in canine GI disease: when to use and when to ditch. February 19, 2020; Grimes and Lidbury, dvm360, March 2020, Volume 51, Issue 3.



THE FACTS: EFFICACY?

ANTIMICROBIALS ARE LARGELY UNNECESSARY IN ACUTE DIARRHEA

> 3,000 dogs, primary practice, acute diarrhea.
Only diet and nutraceuticals associated with resolution.
Antimicrobials made **no difference.**

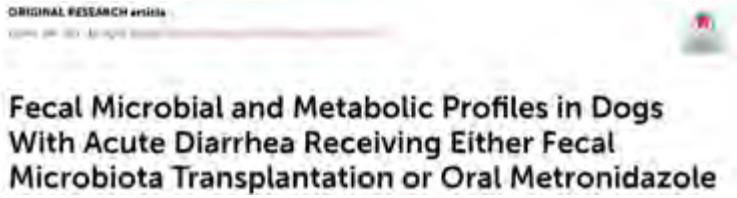
60 client owned dogs, acute uncomplicated diarrhea.
No difference commercial probiotic vs oral metronidazole:
Dogs presenting with acute diarrhea achieved acceptable fecal consistency after 3.5 ± 2.2 days when receiving probiotic, 4.6 ± 2.4 days with metronidazole, and 4.8 ± 2.9 days with placebo, (p = 0.17).

Frontiers in Vet Sci. 2019, Singleton

Frontiers in Vet Sci. 2019, Shmalberg

THE FACTS: HARM

ANTIMICROBIALS CAN HAVE A PROFOUND NEGATIVE IMPACT ON THE MICROBIOME


ORIGINAL RESEARCH article

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

- **Metronidazole**
  - Dogs treated with metronidazole vs. fecal microbiota transplant vs. controls
  - Altered microbial and metabolic profiles still present at day 28 compared to other groups


Journal of Veterinary Internal Medicine ACVIM

STANDARD ARTICLE Open Access

Effects of metronidazole on the fecal microbiome and metabolome in healthy dogs

Rachel Pilla, Frederic P. Gaschen, James W. Barr, Erin Olson, Julia Honneffer, Blake C. Guard, Amanda B. Blake, Dean Villanueva, Mohammad R. Khattab, Mustafa K. Alshawaqfeh, Jonathan A. Lidbury, Jörg M. Steiner, Jan S. Suchodolski

First published: 28 August 2020 | https://doi.org/10.1111/jvim.15871 | Citations: 21

- **Tylosin**
  - Dysbiosis in healthy dogs
  - Re-establishment of native microbiota possible, but not guaranteed, even 2 months after discontinuation


Journal of Veterinary Internal Medicine ACVIM

STANDARD ARTICLE Open Access

Long-term impact of tylosin on fecal microbiota and fecal bile acids of healthy dogs

Alison C. Manchester, Craig B. Webb, Amanda B. Blake, Fatima Sarwar, Jonathan A. Lidbury, Jörg M. Steiner, Jan S. Suchodolski

First published: 31 October 2019 | https://doi.org/10.1111/jvim.15635 | Citations: 25

THE SOLUTIONS FOR ACUTE GI UPSET

STEP 1: MEDICAL GRADE CLAYS

✓ The use of a clay containing paste can be extremely beneficial
✓ Helpful in resolving acute mild GI upset quickly

STEP 2: SYNBIOTICS

✓ Do you use a probiotic? It is not “just because” an antibiotic is used

STEP 3: OTHER

✓ Hydration Support
✓ Diet

MONTMORILLONITE SUPERIOR CHARACTERISTICS

	MONTMORILLONITE	ATTAPULGITE	KAOLIN
CRYSTALLINE STRUCTURE	2:1	Ribbon structure	1:1
CATION EXCHANGE CAPACITY	100 meg/100 g	30-50 meg/100 g	2-10 meg/100 g
WATER UPTAKE	High	Medium	Low
BINDING	High	Medium	Low

* ENTERO AID +GI™
MONTMORILLONITE

* ADVANCED GI
ATTAPULGITE

* PROSOOTHE
KAOLIN

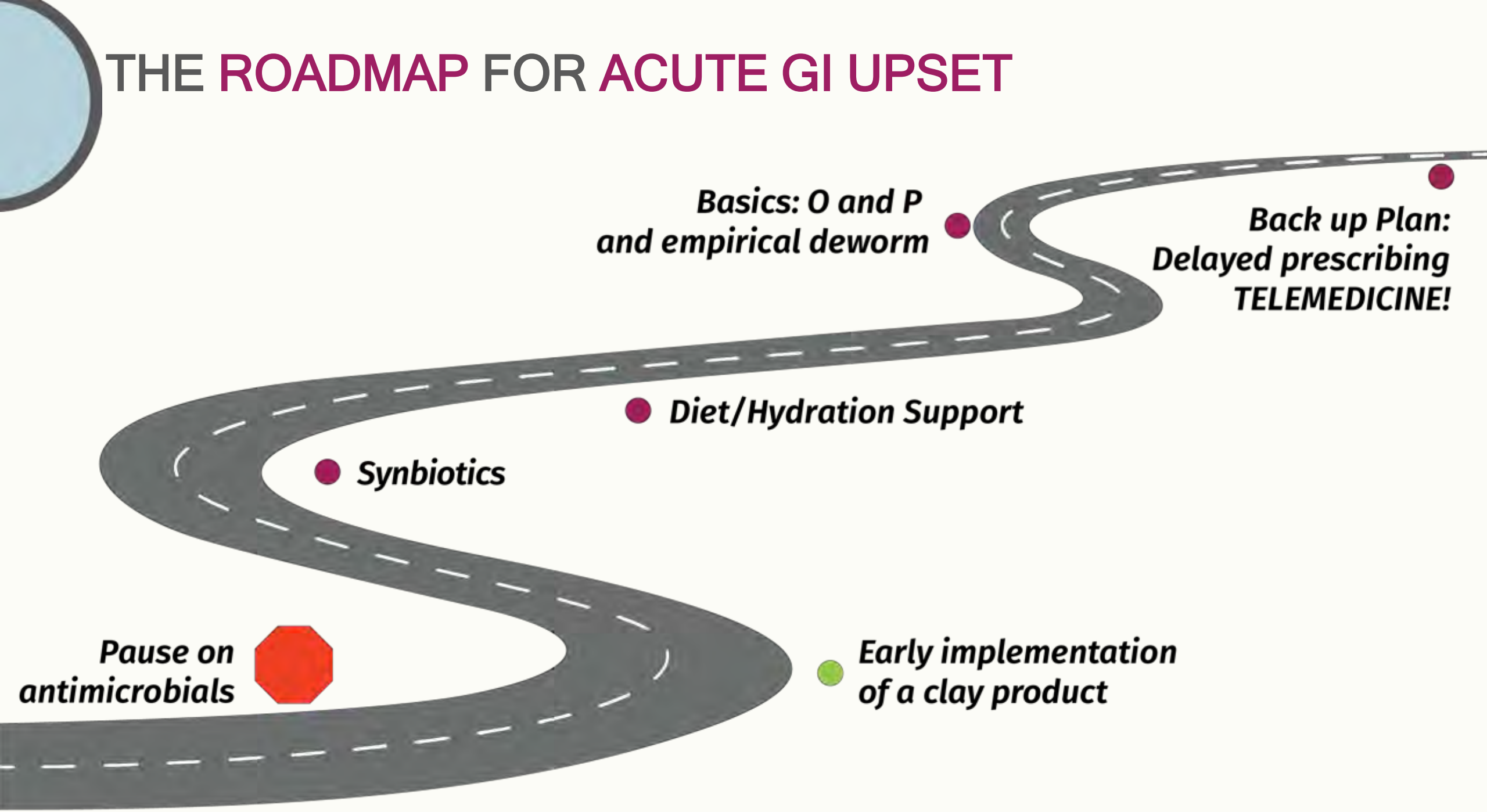
ENTERO AID +GI™

- Montmorillonite clay with probiotic (*E. faecium*) and prebiotic (MOS)
- **10-15 times more effective** than kaolin
- Begins to **work within hours** → resolution of diarrhea more quickly
- Contains
  - L-glutamine
  - Electrolytes
  - No animal protein
- Hypoallergenic
- Health Canada approved

FOR DOGS AND CATS

Restores microbiome and gut function WITHOUT HARM from antimicrobials

THE ROADMAP FOR ACUTE GI UPSET



CHRONIC ENTEROPATHY

LUNA

- 11-month-old, female, intact, labradoodle
- Bright and alert, playful
- Normal BCS & PE
- **Chronic, intermittent diarrhea for several months, without vomiting**
  - No specific pattern documented
- Hx of
  - Several positive fecal tests (*Giardia* and *Toxocara*)
  - Multiple courses of metronidzole for *Giardia*
  - Frequent diet changes, including gastrointestinal diets
  - Intermittent use of probiotics

Current Rx

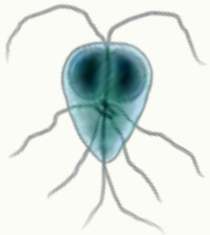
- Monthly heartworm/parasite prevention
- Regularly treated with tylosin
- High protein, low CHO diet

What would you do for Luna?

COMPLEX CONSIDERATIONS FOR LUNA

Age - diets approved for growth

DO NO HARM to microbiome (long term implications)



Parasitism

Fibre needs

THE DEFINITIONS

Chronic, intermittent large bowel diarrhea (colitis) - what is it?

- Food / fibre responsive
- Some immune suppressive
- Other - infectious disease

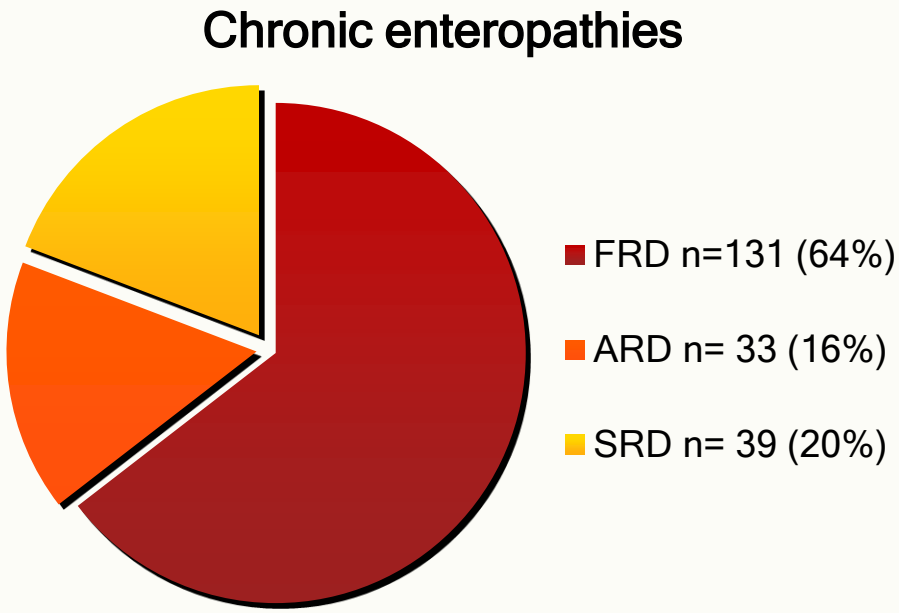
THE DEFINITIONS

Chronic enteropathy – what is it?

Various definitions

- 2 weeks, 3 weeks, 2 days/week x 4 weeks

- Categories:
  - "Inflammatory bowel disease"
  - Food responsive (FRD)
  - Immune suppressive drug responsive (SRD)
  - Antimicrobial responsive (ARD)
  - PLE



Retrospective study, RVC: 203 dogs
Allenspach, et al., Vet Rec 2016

SUMMARY: 33 DOGS WITH ARD

GSD or other large breed dogs

Young!
Median two years

Respond QUICKLY to metronidazole or tylosin

Relapse when antibiotics are discontinued

ARD dogs consistently have the worst outcome after one year

Allenspach, et al., Vet Rec 2016; 178:368. doi: 10.1136/vr.103557.

WHY DO ANTIMICROBIALS SEEM TO HELP?

- Tylosin
- Metronidazole
- Hypothesis: Reduction of bacterial numbers and inflammatory molecules at GI barrier

REf

THE SOLUTIONS FOR CHRONIC GI CONDITIONS

MEDICAL GRADE CLAYS

✓ The use of a clay containing paste can be extremely beneficial
✓ Helpful in resolving acute flare ups in CE

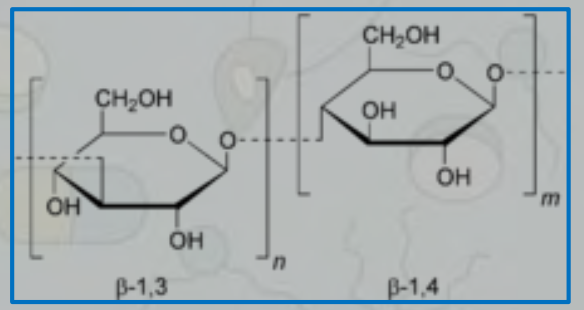
SYNBIOTICS

✓ Used for both acute and chronic enteropathy. It is not "just because" an antibiotic is used (benefit to microbiome/AM sparing)

DIET MODIFICATION/MIXED FIBRE SOURCES

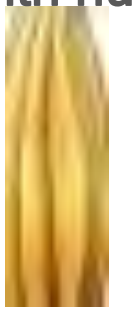
✓ Hydrolyzed
✓ Single protein
✓ Diets and mixed fibre supplements

WHAT IS FIBRE?

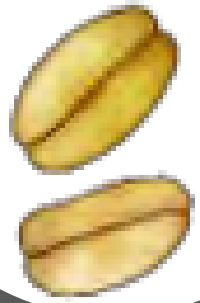


Oat plant

Oat grain with hull



Dehulled oat grain



Oat hull

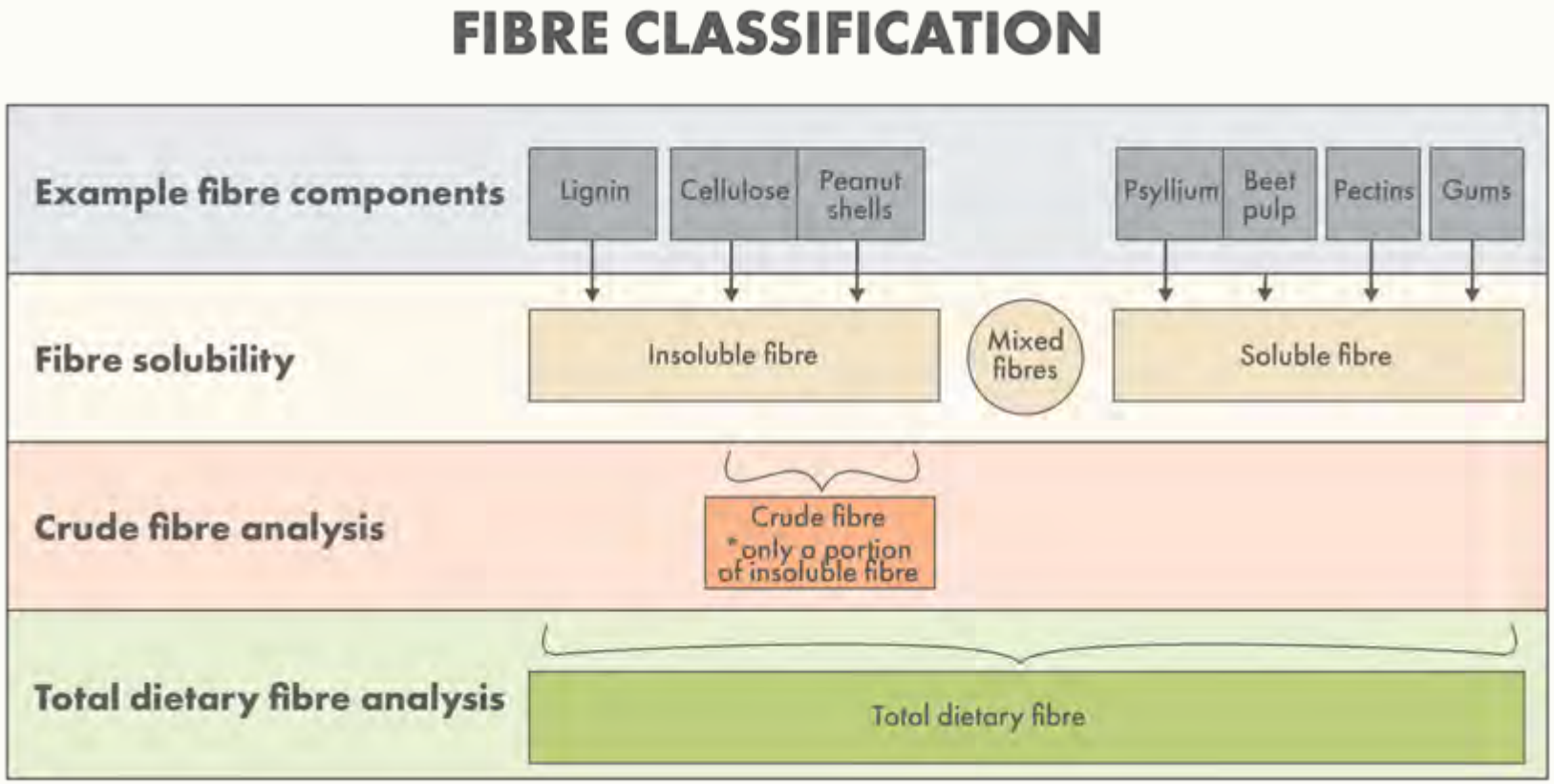
Soluble Fibre

Insoluble Fibre

https://pubs.rsc.org/en/content/articlehtml/2018/fo/c7fo02006f

FIBRE TYPES and AMOUNTS

- Soluble versus Insoluble



Adapted from Rudinsky, et al. (2018). Nutritional management of chronic enteropathies in dogs and cats. JAVMA 253(5), 570-578.

FIBRE SOURCES

SOLUBLE FIBRE SOURCES	INSOLUBLE FIBRE SOURCES	PREBIOTIC FIBRE SOURCES
• Beet pulp • Pectin • Psyllium • Guar gum	• Bran • Cellulose • Hemicellulose • Peanut/Soybean hulls	• Fructooligosaccharides • Inulin • Mannan-oligosaccharides (MOS)

- Definition of mixed fibre source
- **Mixed fibre source is generally ideal**

FIBRE AND DIET CONTENT

TDF versus Crude Fibre

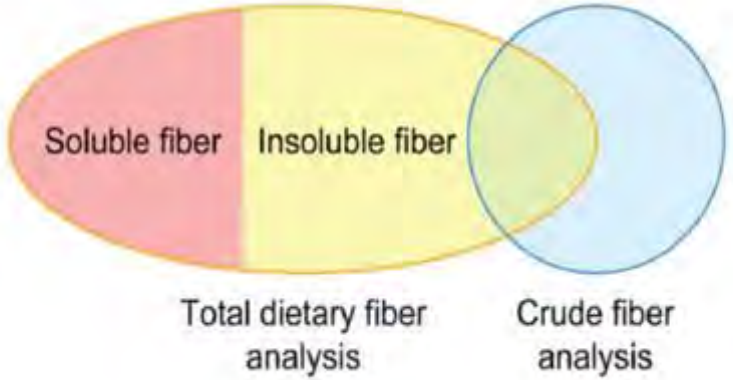
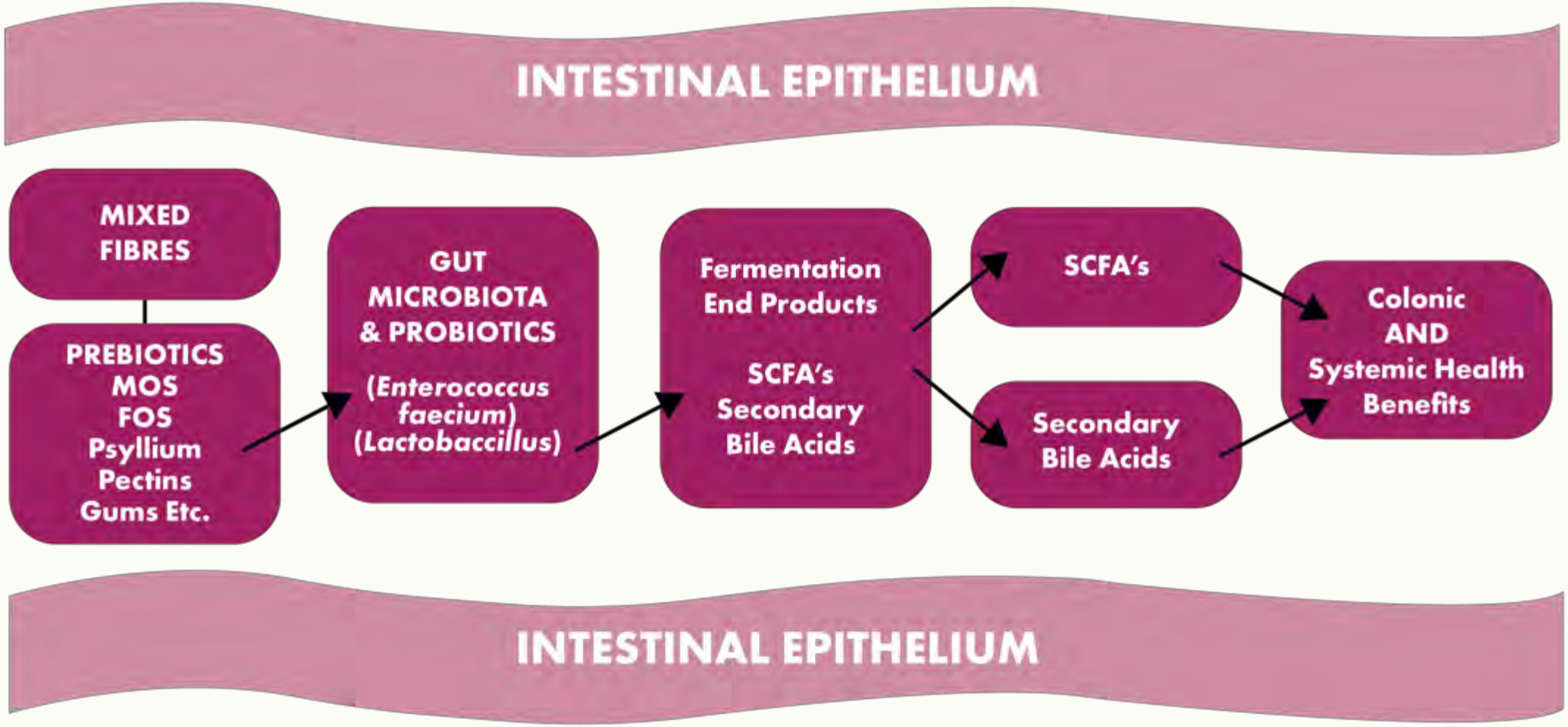


Figure 1. Schematic depiction of the relationship of total dietary fiber, crude fiber, insoluble fiber, and soluble fiber.

	GRAMS PER 1000 KCAL ME
Protein	69
Fat	32
Carbohydrate	140
Crude Fibre	17
Total Dietary Fibre	54

10.2460/javma.253.5.570 - confim ref

BENEFITS OF FIBRE



Adapted from: https://api.intechopen.com/media/chapter/42107/media/image3.png

RECOMMENDED TYPES OF FIBRE – GI DISEASES

CONDITION	FIBRE TYPE
Acute gastroenteritis	Mixed
Chronic enteropathy/ inflammatory bowel disease	Mixed
Colitis	Mixed
Chronic constipation	Mixed, mostly soluble

- Fibre type can be mainly soluble, mainly insoluble, or mixed soluble/insoluble.

Adapted from: Lenox C. E. (2021). Nutritional Management for Dogs and Cats with Gastrointestinal Diseases. The Veterinary clinics of North America. Small animal practice, 51(3), 669-684. https://doi.org/10.1016/j.cvsm.2021.01.006

EVIDENCE FOR FIBRE USE - Colitis

Fritsch 2022, BMC: Mixed fibre diet, 31 client dogs; Improved fecal score and reduced inflammatory markers

Lappin 2022, JVIM: Mixed fibre diet, 52 shelter dogs; Improved fecal score and reduced frequency

Alves 2021, BMC Res: Psyllium, 22 working police dogs; Improved stool quality, weight gain

Leib 2000, JVIM: Psyllium, 37 client dogs; Fecal score improved

Improved stool quality

DISCUSSION FOR FIBRE USE in CE…. 2022

NEW

- Purina Institute Round Table
- ACVIM specialist course - Microbiome
- ACVIM Forum 2022

ROLE OF THERAPEUTIC DIETS

- Content (some proprietary)
- Diets and mixed fibre sources

FIBRE SUPPLEMENTATION TO AN EXISTING DIET

- Availability of diets
- Acceptance
- Patient context
  - Growing dogs, often large breed
  - Owner preference: raw, non-therapeutic
  - Allergic disease
  - Other co-morbidities
  - Home formulation
- Dose is to effect, gradual introduction

WHAT ABOUT…
ADDING PUMPKIN AND OTHER FOODS ?

Ingredient	Amount	Total fiber
Psyllium husk	2 tbsp	~20 grams
Canned pumpkin	3 cups	
Green beans	8 cups	

ACVIM Microbiome course; table courtesy of Dr. Valerie Parker, DVM, DACVIM-SA, DACVN

FIBRE SUPPLEMENTS

- Mixed fibre sources
  - Content varies (soluble versus insoluble)
  - May be useful as adjunctive therapy
  - Addition of fibre to a current diet that cannot be changed

FIBRE BOOST +GI™

FOR DOGS AND CATS

- **Mixed fibre:** oat fibre and psyllium seed husk
- **Synbiotic:** probiotics *(E. faecium and L. acidophilus)* and prebiotic (MOS)
- **Montmorillonite** clay

Also contains

- **B glucan**
- **L-glutamine**

Vegan/Hypoallergenic

Health Canada approved

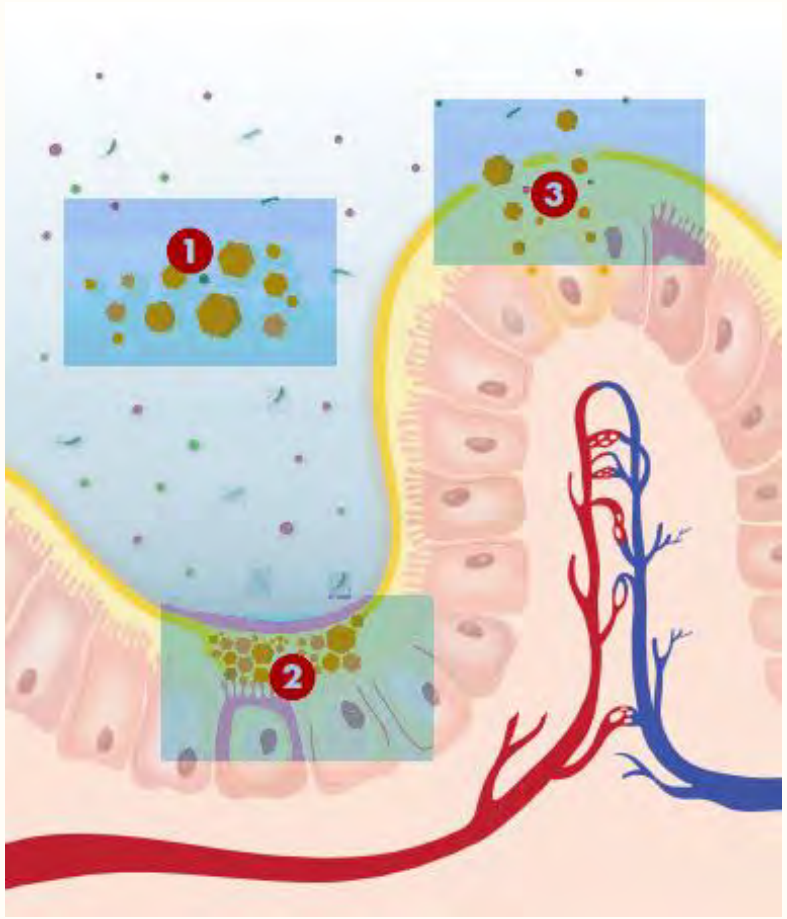
Restores microbiome and gut function **WITHOUT HARM** from antimicrobials

ADDED BENEFIT: MUCOSAL PROTECTION

MONTMORILLONITE (DIOSMECTITE) SAFELY CONTROLS SYMPTONS DURING DISORDERS ASSOCIATED WITH CHRONIC DIARRHEA in HUMANS

- **Advances in Therapy (2021)**
  - Adults with chronic diarrhea have improved stool frequency and consistency.
  - Reduces abdominal pain, bloating, and flatulence.
  - Safe, with few adverse events.

- **BMC Microbiology (2022)**
  - Five-week administration of diosmectite on the fecal microbiota of 35 adults with functional chronic diarrhea.
  - No microbiota-related physiological alterations with long-term treatment.



FIBRE SUPPLEMENT PRODUCTS

	Fibre Boost +GI®	Glandex®	Vetasyl®	Fortiflora SA®	Metamucil® (psyllium)
Fibre	Mixed	Mixed	Primarily Soluble	Primarily Soluble	Primarily Soluble
Soluble Fibre	Psyllium	Apple pectin	Psyllium	Psyllium	Psyllium
Insoluble Fibre	Oat fibre	Pumpkin seed			
Prebiotic	√	√	√	√	√
Probiotic	√	√		√	
Medical clay	√				
Flavour	Vegan	Vegan	Vegan	Hydrolyzed Animal Digest	Vegan

FIBRE SUPPLEMENT PRODUCTS (detailed)

	Fibre Boost +GI®	Glandex®	Vetasyl®	Fortiflora SA®	Metamucil®
Fibre	Mixed	Mixed	Primarily Soluble	Primarily Soluble	Primarily Soluble
Soluble Fibre	Psyllium	Apple pectin	Psyllium	Psyllium	Psyllium
Insoluble Fibre	Oat fibre	Pumpkin seed			
Other Prebiotic	MOS			Brewers yeast	
Probiotic	E. faecium L. acidophilus	E. faecium		E. faecium	
Medical clay	Montmorillonite				
Other Key Components	Beta glucan L-glutamine	Quercetin Bromelain		Vitamin C Vitamin E	
Flavour	Vegan	Vegan	Vegan	Hydrolyzed Animal Digest	Vegan

REMEMBER LUNA?

Consider pausing antimicrobials

- Ova & Parasite and deworm
- Diet trial / mixed fibre
- Synbiotics

WHEN DO YOU USE ANTIMICROBIALS IN GI DISEASE?

ANTIBIOTICS INDICATED	ANTIBIOTICS NOT INDICATED
✓ Parvovirus infection with neutropenia	✗ Uncomplicated acute diarrhea
✓ AHDS with signs of sepsis	✗ AHDS without signs of sepsis
✓ ARD trial ➢ After *appropriate work-up* ➢ After strict diet trial ➢ In an appropriate patient	✗ ARD trial ➢ In lieu of work-up ➢ Before diet trial
✓ E. coli-associated granulomatous colitis ➢ Based on FISH +/- culture and susceptibility testing of colonic tissue	✗ Chronic large bowel diarrhea ➢ In lieu of workup
✓ Enteropathogenic bacteria with signs of systemic illness	✗ Enteropathogenic bacteria in nonclinical cases or mild, self-limited disease

AHDS = acute hemorrhage diarrhea syndrome, ARD = antibiotic-responsive diarrhea, FISH = fluorescence in situ hybridization.

Antibiotics in canine GI disease: when to use and when to ditch. February 19, 2020. Grimes and Lidbury , dvm360 March 2020, Volume 51, Issue 3.

https://event.on24.com/wcc/r/3612856/D2C845949AE61A0D762781138C8CD0C3. 2022; Practical Approach to the Management of AHDS, Dr. Stan Marks

THE BIG PICTURE
WHY SHOULD YOU CARE?

CANADIAN VETERINARY MEDICAL ASSOCIATION
L'ASSOCIATION CANADIENNE DES MÉDECINS VÉTÉRINAIRES

Antimicrobial Use Guidelines now available

Firstline

https://savi.canadianveterinarians.net/en/firstline/

2022 AAFP/AAHA Antimicrobial Stewardship Guidelines

View printable PDF of guideline

On a mobile device? Scroll down for the navigation menu.

Introduction

The Antimicrobial Stewardship Guidelines in companion animals are designed to aid practicing veterinarians in choosing appropriate antimicrobial therapy to best serve their patients and minimize the development of antimicrobial resistance and other adverse effects. The Guidelines were developed by an expert task force and provide a recommended framework for judicious antimicrobial use in companion animals.

AAHA welcomes endorsement of these Guidelines by the American Association of Feline Practitioners (AAFP).

NEW

Therapeutic antimicrobial use should be confined to appropriate clinical indications.

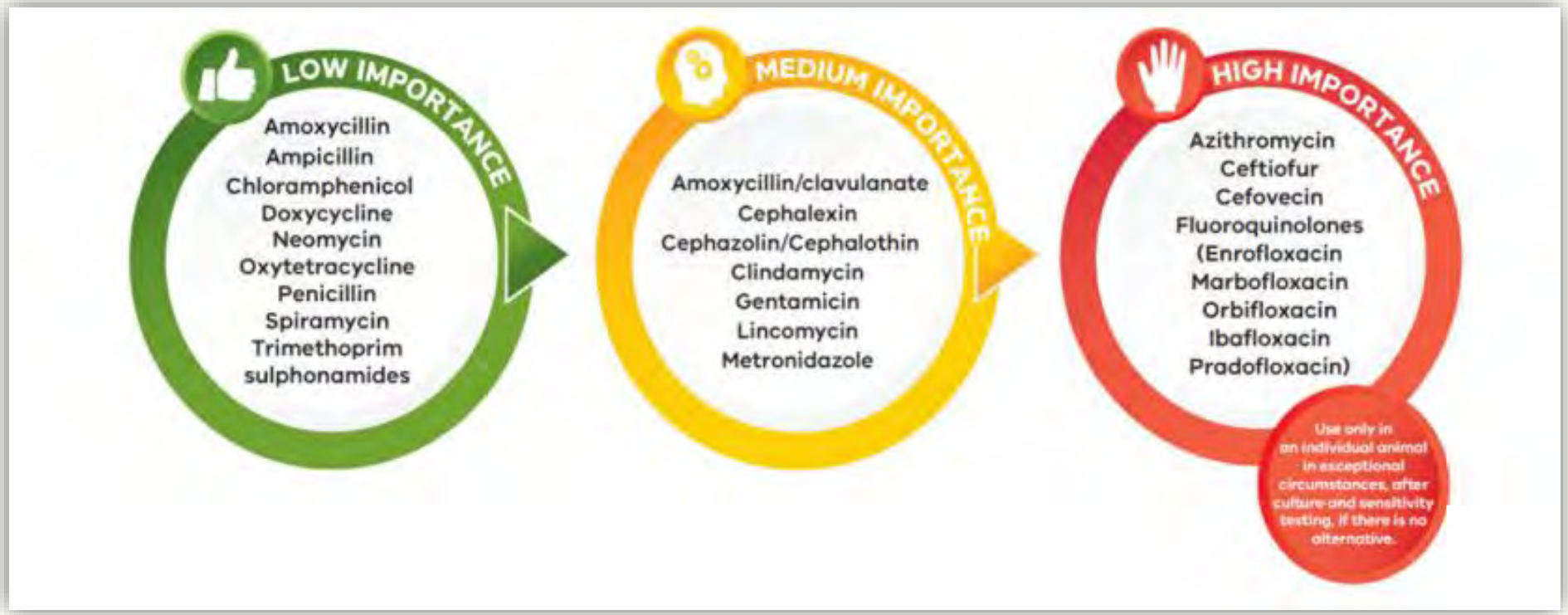
- Most cases of acute diarrhea are not due to pathogenic bacterial infections or are self-limiting, so antimicrobials are not indicated, do not hasten time to clinical resolution, and may cause further dysbiosis.[10–13]

https://www.aaha.org/aaha-guidelines/2022-aafpaaha-antimicrobial-stewardship-guidelines/home/

PEARLS …

Implement traffic light system

Antimicrobials held in the pharmacy **colour coded** based on antimicrobial importance rating



JAC-Antimicrobial Resistance, Volume 4, Issue 1, February 2022, doi.org/10.1093/jacamr/dlac015

PEARL #2: DELAY, DELAY, DELAY

...

WAIT. You won't get antibiotics for your pet today. Your veterinarian believes your pet's illness may resolve on its own. Follow the 2 steps below to ensure your pet gets better:

Step 1

Firstly, follow your veterinarian's advice to help your pet feel better without antibiotics and continue to monitor the symptoms over the next few days.

To help your pet's symptoms:

- Keep your pet warm.
- Ensure access to plenty of fresh water.
- For gastrointestinal signs: offer a diet as recommended by your Greencross vet.
- For cats with urinary signs: monitor urination closely.
- Other: _____

Step 2

If your pet hasn't improved in _____ days, or if things get worse, go ahead and pick up the medication from our clinic*.

If your pet has improved, they do not need antibiotics.

Waiting to see if your pet really needs an antibiotic can help us to use antibiotics only when they are actually necessary. Antibiotics can cause side-effects like diarrhoea, vomiting, and more. Antibiotics can also kill your pet's good bacteria and leave your pet more susceptible to infections.

Not every infection needs to be treated with antibiotics. Antibiotics kill bacteria but not viruses and some bacterial infections can get better without antibiotics. Bacteria can adapt to become "resistant" so that an antibiotic no longer works. Antibiotic resistant bacteria can spread from humans to animals, and animals to humans.

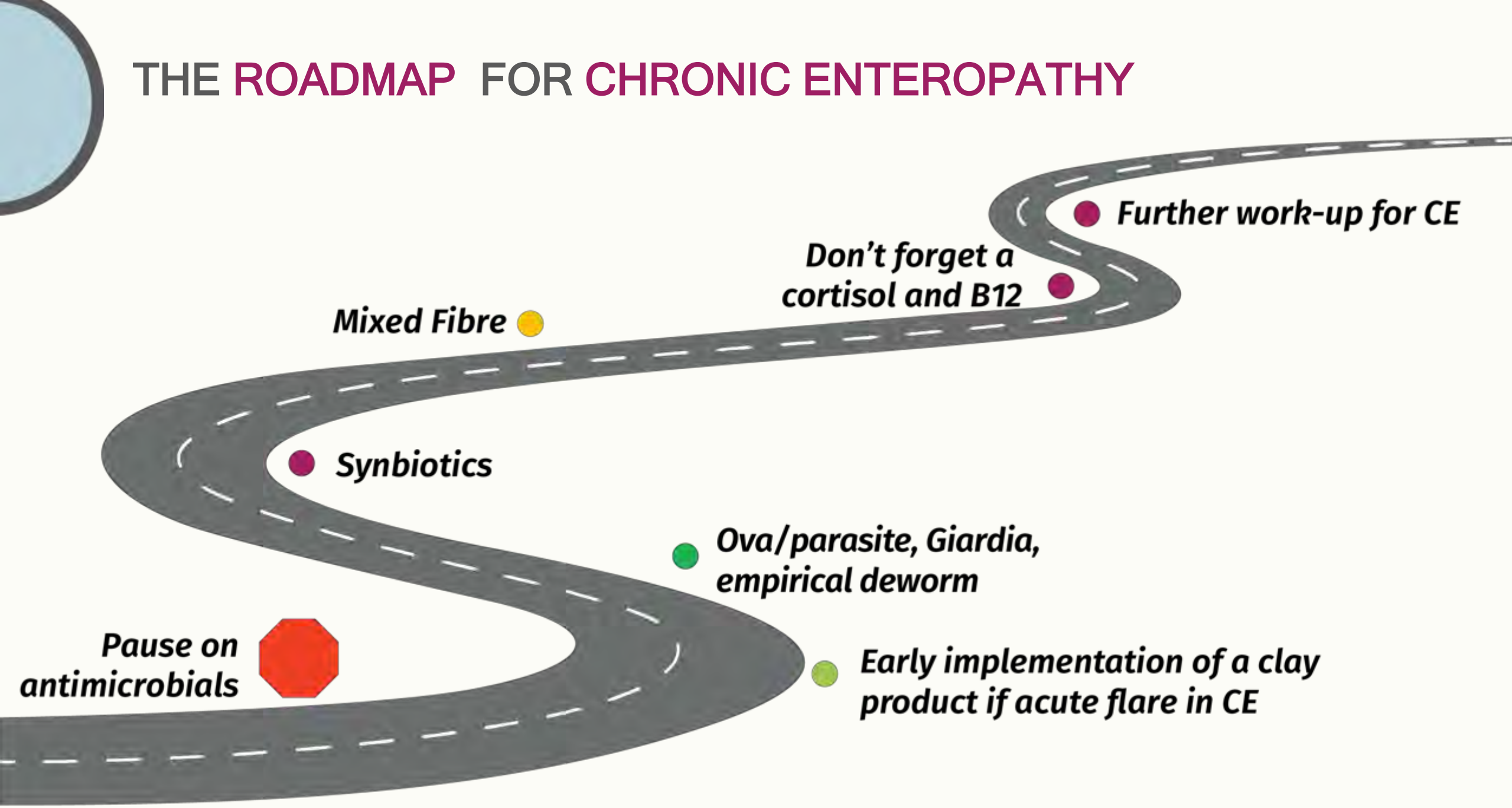
Common Condition	Common Cause		Recovery Time	Are antibiotics needed?
	Bacteria	Virus		
Draining cat abscess	Yes		2-4 days	No
Cat flu	Maybe	Yes	2-3 weeks	Maybe
Feline urinary disease	Maybe		2-7 days	Rarely
Kennel cough	Yes	Yes	10-14 days	No
Ear infection	Yes		1-4 weeks	Topical
Diarrhoea/Vomiting	Maybe	Maybe	3-7 days	Rarely
Skin infection	Maybe[b]		2-4 weeks	Maybe (topical)[a]

[a] Topical antibacterial therapy considered 1st choice
[b] also yeast or fungus

59% of vets **used delayed prescribing**

90% said **delayed prescribing** was a **useful** way of **reducing unnecessary antimicrobial use**

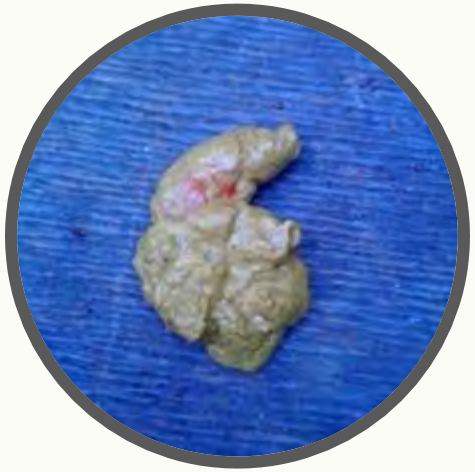
THE ROADMAP FOR CHRONIC ENTEROPATHY



"Fibre can be a solution to many GI issues.

- *Colitis*
- *Chronic enteropathy*

Try fibre before reaching for antimicrobials."



Photos: Dr. Lisa Carioto

Thank you!

Happy to take your questions

GreyWolf ANIMAL HEALTH