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Clinical Considerations for Managing Chronic Enteropathy Patients:

### Why Improving GI Microbiome Health Matters

The intestinal microbiome is a complex ecosystem. What comprises a healthy microbiome versus an unhealthy one?

A I like to describe the composition of the healthy intestinal microbiome as a "good party" and dysbiosis as a "bad party" that takes place in the gut. Consider the following characteristics of each:

Dysbiosis (the "bad party")
Less buffering against unwelcome "guests" (harmful bacteria)
No beneficial microbes producing SCFAs to feed colonocytes
Loss of immunologic control, toxic, pro-inflammatory atmosphere due to the lack of beneficial microbes and its metabolites
Intestinal leakage into the bloodstream
Accelerated motility due to increased numbers of primary bile acids
Proliferation of E. coli, Clostridium perfringens and Clostridium difficile

Oculture and sensitivity testing of fecal samples is commonly conducted with chronic enteropathy (CE) patients to determine which antibiotic will eliminate the suspected pathogen. What is problematic about this approach?

A Veterinarians gain limited information from conventional fecal cultures, as the intestinal microbiome mainly consists of anaerobes. As strict anaerobes are very difficult to culture with standard methods, only a minor part of the bacterial species in the fecal microbiome can be identified. One study compared fecal culture results from healthy dogs versus from dogs with chronic diarrhea at three different commercial laboratories. The cultures failed to distinguish between diseased and healthy dogs and two of the three labs reported an abnormal fecal microbiome in more healthy dogs than dogs with chronic diarrhea.

# Given the role of dysbiosis in dogs with CE, which tools can positively affect the intestinal microbiome?

A Studies have been conducted to evaluate various tools and their value in managing canine patients with CE. The bottom line is that strategies that treat the underlying condition can improve disease activity and the microbiota.

- **Diet.** Several different types of diet, such as elimination diets, hydrolyzed protein diets and fiber-rich diets, can lower disease activity and improve the intestinal microbiota and metabolome in dogs with FRE.<sup>2,3,4</sup>
- Anti-inflammatory medication. A study conducted on dogs with steroid-responsive enteropathy showed that steroid therapy eliminated clinical signs of disease after 8 weeks, but recovery of the fecal microbiome and metabolome was slower—it took one year after treatment.<sup>5</sup>
- Probiotics. There has been some evidence that probiotics can reduce inflammation and foster the growth of beneficial bacteria such as faecalibacterium; however, such results are probiotic-dependent and should not be generalized.
- Prebiotics. While most studies have been conducted in healthy animals, there is evidence that prebiotic fibers can improve stool quality and microbiome diversity.<sup>4</sup>
- Fecal microbiota transplantation (FMT). In one study, dogs with inflammatory bowel disease had a lower proportion of Fusobacterium (a beneficial bacterium that produces butyric acid, an SCFA) versus healthy dogs; however, this was altered with a single FMT.
- Antibiotics. Antibiotics are not a good way to positively affect the microbiome. Broadspectrum antibiotics such as metronidazole can create dysbiosis even in healthy dogs. While dogs with diarrhea may initially respond to an antibiotic, many dogs have been reported to relapse within a 2-month period. Antibiotic therapy has been linked to increased risk of developing chronic gastrointestinal disease later in life in people. Do

# Are there other reasons that use of broad-spectrum antibiotics should be reconsidered in CE patients?

Decisions to use antibiotics in companion animals are not without consequence. A recent study in Portugal looked at 20 households with humans, dogs and cats—all healthy. In 50% of the households, human/animal sharing of at least one gene for antimicrobial resistance (AMR) was documented.<sup>11</sup> A common belief is that tylosin is not used in humans and thus is safe for use in dogs; however, its administration is associated with AMR to erythromycin—a drug that is important to people.<sup>12</sup>

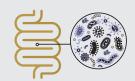
Antibiotic stewardship is an extremely important issue; as veterinarians, we must be careful about making decisions to use antibiotics in a patient. When we do, we should be aware that the decision could affect the pet's family and advise them accordingly.

### Exploring the Gut Microbiome and its Role in Your Patients' Health

The gastrointestinal tract is primarily known as the system responsible for digestion and nutrient absorption. But it also plays a remarkable role in overall health—both for humans and pets.

#### The gut is home to:

of the immune system, protecting the body from harmful (pathogens) or foreign substances (antigens).1



A complex microbial ecosystem with trillions of microorganisms and their genetic material known as the gut microbiome.

#### How is the Microbiome Linked to Health?

#### The microbiome can impact a pet's overall health in many ways:2

- Energy balance
  - Metabolism •
- Immune response •
- Vitamin and mineral synthesis •
- Endocrine signaling
- Gut function
- Neurobehavioral development through the gut-brain axis

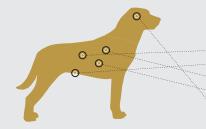
#### Why is Microbiome Balance So Important?

Because the microbiota in the gut help support overall health, it is important to maintain a balance between beneficial and potentially pathogenic bacteria. An imbalanced or maladapted microbiota is called dysbiosis.

#### What can lead to dysbiosis?







#### Dysbiosis is associated with a variety of health conditions:2

- Chronic Inflammatory Enteropathy
- Cardiovascular disease
- Immune-mediated conditions
- Neurodevelopmental conditions

#### How Can You Help? Promote Microbiome Balance with Nutrition



#### PROBIOTICS

Live microorganisms that, when consumed in adequate amounts, confer a health benefit on the host.3

Probiotics are strain-specific and dose-dependent, meaning that different strains have different effects and they must be given in specific amounts.



#### **PREBIOTICS**

Some soluble fibers are prebiotics substances that are selectively utilized by the host microorganisms resulting in a health benefit. 4 This can result in increased microbial diversity and the production of short-chain fatty acids that nourish colonocytes.

Probiotics that contain both prebiotics and probiotics are called synbiotics.



Contains bioactives and antibodies that initiate a beneficial immune response and help to stabilize intestinal microflora.5

Studies show that when fed diets supplemented with bovine colostrum bio-actives, both kittens<sup>6</sup> and adult dogs5 have stronger responses to vaccinations.



### Explore the gut microbiome...and beyond

What comprises the gut microbiome? How can the brain influence gut microbiota? What other microbiomes exist beyond the gut? There are many aspects to this topic and the Purina Institute has them covered. Just click on one of 10 areas to take a deeper dive into each. Visit https://www.purinainstitute.com/microbiome-forum/ microbiome-fundamentals or scan the QR code to start exploring.



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## Prebiotic Fiber: Fueling the Production of Beneficial Bacteria



Dietary fiber significantly influences microbiome health. The characteristics of fiber (i.e., solubility, fermentability, viscosity) determine how a fiber will behave in the gastrointestinal tract and any benefits a dog or cat will derive from the fiber source.

What effects do prebiotic fibers have on gut health? Here's a snapshot of how they work, the benefits they can confer on the microbiome and the types of patients who could benefit from prebiotic intake.

# What are prebiotics and how do they work?

Prebiotics are often referred to as the "fuel" or "food" for beneficial bacteria. They are nondigestible and selectively fermented by beneficial bacteria in the colon, where they help support the growth and activity of health-promoting bacteria in the gastrointestinal (GI) tract.¹

These beneficial bacteria produce short-chain fatty acids (SCFAs), which have positive effects on gut health, such as helping protect the mucosal epithelium and mucosal barrier, promoting immune function and combating inflammation.<sup>2</sup>

Intestinal cells use SCFAs, especially butyrate, as an energy source for colonocytes.<sup>1-3</sup> This enables the intestinal cells to grow and multiply, which helps to maintain the intestinal barrier function and inhibit the growth of pathogenic bacteria. When fermented by beneficial bacteria, wheat aleurone—found in certain pet foods such as Purina® Pro Plan® Veterinary Diets EN Gastroenteric® canine dry formula—is an excellent substrate for producing butyrate.

Psyllium, found in Purina® Pro Plan® Veterinary Supplements FortiFlora® PRO, is a soluble and slowly fermentable fiber source with prebiotic effects. Fiber derived from psyllium has a high water-holding capacity that may help promote normal stool quality in pets.5-7

# What patients could benefit from prebiotics?

Patients with conditions such as acute or chronic large intestinal diarrhea could benefit from prebiotic supplementation to regulate intestinal motility, reduce inflammation and allow beneficial bacteria to compete with potentially harmful gut bacteria. Purina® Pro Plan® Veterinary Diets EN Gastroenteric® Canine Formulas each contain a select prebiotic fiber to support GI microbiome balance and digestive health.

# Do prebiotics benefit healthy patients?

Fiber supplementation can be beneficial for promoting a healthy microbiome, regardless of health status. Not only can healthy pets benefit from supplemental fiber in their diet to **improve stool quality**,

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but prebiotics also help pets **maintain** intestinal health.

However, anytime we supplement a diet with fiber, we must ensure the pet can tolerate the fiber that's being supplemented. Some animals tolerate added fiber very well while others do not. This intolerance, which is usually dose dependent, can be the result of short-chain fatty acid production from fermentable fibers and subsequent osmotic effects in the gut.

# Total dietary fiber versus crude fiber

Current guidelines from the Association of American Feed Control Officials (AAFCO) require pet food companies to include the amount of **crude fiber** in a diet on the packaging. However, some pet food companies have recognized that **total dietary fiber** offers a better representation of the types of fibers present in a diet.

A crude fiber analysis measures only insoluble fiber, but does not include all insoluble fiber sources. Total dietary fiber analysis includes insoluble fiber and most soluble fiber sources to provide a more complete and accurate picture of a diet's fiber content.

Ascertaining exactly what types of fiber in what amounts are present in a diet will help you make informed nutritional recommendations that can help promote a healthy microbiome in your patients. Product guides from various companies may provide this additional fiber analysis; if not, veterinarians can contact pet food makers to determine if additional fiber analysis information is available.

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### Key Takeaways

- Implementing strategies to improve GI microbiome health is a vital component of managing patients with intestinal disease.
- All strategies that reduce GI inflammation—with the exception of antibiotic use—can be associated with recovery of the microbiome.
- Prebiotics help support the growth and activity of beneficial bacteria in the GI tract. These beneficial bacteria produce short-chain fatty acids, which help protect the mucosal epithelium and mucosal barrier, promote immune function and combat inflammation.

