Managing Antibiotic-Induced Diarrhea

Righting the Balance of Good and Bad Bacteria

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Diarrhea is a common side effect associated with antibiotic use in both humans and pets. What do we know about antibiotic use and its effects on good bacteria, as well as bad?

Antibiotics administered orally can cause gastric irritation and vomiting, as well as diarrhea associated with changes to the composition and function of the gastrointestinal microbiota. Antibiotics such as amoxicillin-clavulanate and clindamycin are among those associated with GI side effects.

Just as some people have trouble tolerating antibiotics while others don't, not every dog or cat given antibiotics develops nausea, vomiting or diarrhea—and the effects from different antibiotics can also vary. Why this occurs is not fully understood.

Can "good" bacteria be restored by feeding a probiotic? Does it matter which probiotic is fed?

Administration of a probiotic (non-pathogenic bacteria that may have a beneficial effect on the host) can potentially increase numbers of "good" bacteria in the gastrointestinal tract. At the same time, probiotics can reduce the number of pathogenic ("bad") bacteria that may be associated with the development of diarrhea. It's likely these effects are specific to certain strains of probiotics.

At Colorado State University, we recently conducted a study in cats to look at the effects of *Enterococcus faecium* strain SF68 on GI clinical signs associated with amoxicillin-clavulanate, an antibiotic medication frequently associated with diarrhea, vomiting and, occasionally, inappetance. Our goal was to investigate the incidence of GI side effects associated with the antibiotic's administration, as well as potential beneficial effects from the SF68 probiotic strain.

What was the study protocol and what were the results?

The study[1] was double-blinded and placebo controlled. Thirty-four young adult, healthy, mixed-sex cats were randomized into two rooms and caged so that clinical findings could be monitored daily for appetite, attitude, hydration, vomiting and fecal score, using a scale of 1 to 7 for fecal scoring (1 = hard and dry; 3 = normal; 7 = watery puddles).

The cats in the study underwent a 10-day equilibrium period to screen for and eliminate cats predisposed to stress diarrhea. The remaining cats were administered amoxicillin-clavulanate (Clavamox®, Zoetis) at 62.5 mg/cat PO twice a day for 7 days. Both groups were fed a canned diet sprinkled with either SF68 (equivalent to FortiFlora® Feline Probiotic Supplement, Purina® Pro Plan® Veterinary Diets) or the palatability enhancer contained in the probiotic supplement two hours prior to amoxicillin-clavulanate administration. Clinical scoring continued for the 7 days of treatment and an additional 5 days after the antibiotic was stopped.

The results of the study suggested that amoxicillin-clavulanate can cause gastrointestinal symptoms and that the concurrent administration of SF68 may decrease the severity of diarrhea associated with this antibiotic in some cats (see Table 1).

What kind of probiotic regimen should be considered in veterinary patients on antibiotic therapy?

Minimal studies have been conducted on probiotics and antibiotic-induced diarrhea, and there are no standard protocols for this use. In our study, we chose to administer the probiotic prior to giving the antibiotic in the hope that the probiotic would keep the antibiotic from inactivating the probiotic's effects. If the antibiotic does not inactivate the probiotic, it may be possible to administer them concurrently, as we did successfully in the treatment of non-specific canine diarrhea with metronidazole, with and without FortiFlora®.[2]

Table 1

SF68 vs. Placebo in Amoxicillin/Clavulanate-Treated Cats
Fecal Scores

	SF68-treated cats (n=13)	Placebo-treated cats (n=14)
	% of cats	% of cats
Fecal score ≥ 5	84.6	85.7
Fecal score ≥ 6	61.5	85.7
Fecal score = 7	--	21.4
	% of total samples	% of total samples
Fecal score ≥ 5	43.8	68.4

1 *Torres-Henderson C, et al, Proceedings of the 2015 American College of Veterinary Internal Medicine Annual Forum*

2 *Fenimore L, et al. Proceedings of the 2012 American College of Veterinary Internal Medicine Annual Forum.*

Talking to Clients: Are All Probiotics Created Equal?

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While many clients are familiar with human probiotics, questions about how probiotics can benefit their pets are common.

It may sound obvious, but not all probiotics are equal and interchangeable, and it's important to make that distinction to owners. The following three questions can be helpful in explaining why a specific probiotic is being recommended.

Is the probiotic safe?

This is an important priority with sick or immunocompromised patients. It's essential that the probiotic selected to help a pet carry no risk of causing further disease or worsening symptoms, particularly by permeating the intestinal barrier and translocating bacteria into circulation. If a pet has a condition that can damage the intestinal lining (parvovirus is an example), probiotics may be contraindicated, due to the potential for bacteremia development.

Will the probiotic have a positive impact?

Transient colonization is a key characteristic of effective probiotics. As I explain to clients, this means the bacteria will stick around in the GI tract and then pass when supplementation ends. The gut is a rapidly changing environment that must be able to adapt, so permanent colonization of probiotic bacteria is not desirable.

Along the same lines, the probiotic can't compete with the good organisms in the gut. I tell my clients we want the probiotic to live in peace with beneficial bacteria, promoting the production of short chain fatty acids and antibodies that benefit the pet's gut and immune health. For example, Purina® Pro Plan® Veterinary Diets FortiFlora® contains the probiotic *Enterococcus faecium* strain SF68, which has been demonstrated to help restore intestinal health and balance in dogs and cats.

Over-the-counter probiotics, including yogurt, may have unpredictable bacterial strains and counts, making efficacy less predictable.

Can the probiotic survive long enough to be effective?

Two challenges are associated with the resiliency of probiotic bacteria. Veterinary probiotics are dispensed in an office and then stored in the home, sometimes for an extended period of time, so it's important that the product be shelf stable. Second, once ingested, the bacteria need to be able to survive the harsh, acidic environment of the stomach. A probiotic that can't survive long enough to reach the GI tract won't provide any benefit to a pet in need.

FortiFlora is microencapsulated to withstand handling, processing and storage to aid in the bacteria's survival (see Figure 1). It also carries clear package dating so clients can trust the potency of the product they're feeding.

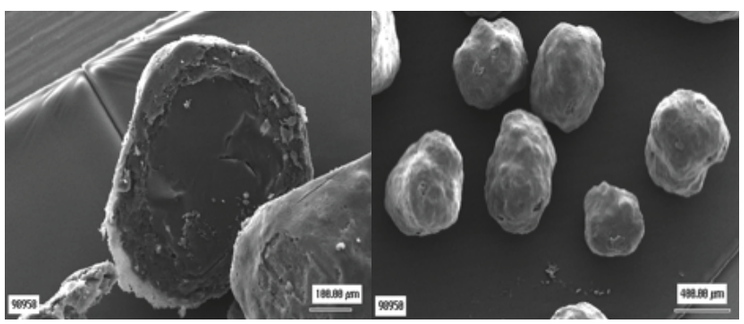
If they've ever taken probiotics themselves—or at the least heard them advertised—clients may have some limited understanding of what a probiotic is. It's up to the veterinarian to educate owners more fully, so they understand how and why their pet may benefit from probiotic supplementation, as well as why the veterinarian is recommending they feed a specific product.

1-2-3s of Probiotic Assessment

1. **Safety -** No risk of causing or worsening symptoms
2. **Beneficial -** Promotes gut and immune health
3. **Stable -** Survives long enough to provide benefit

FIGURE 1

Microencapsulated *Enterococcus faecium* SF68



E. facium SF68 in microencapsulated form offers increased stability and viability.

Evolving the Use of Probiotics

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Any approach my clients think will improve their pets' health or quality of life without requiring medication is likely to interest them. More and more, owners are seeking alternative approaches to their pets' nutrition and health management. For that reason, probiotics have become an important offering in our clinic.

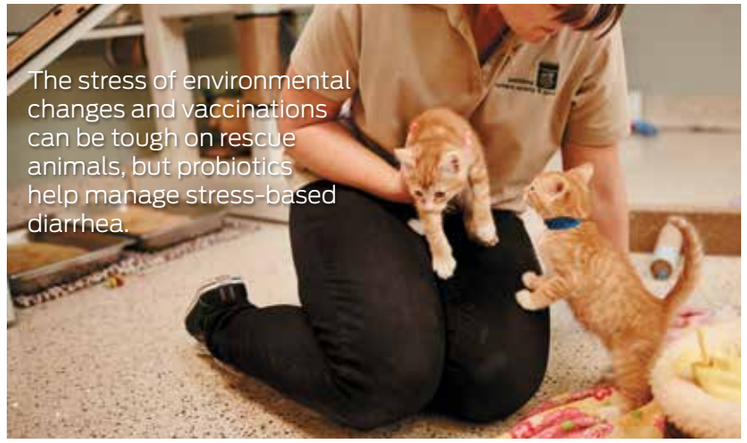
Probiotic use started with chronic diarrhea management

For years, combining a high-quality diet and Purina® Pro Plan® Veterinary Diets FortiFlora® has been an important component of our approach to the management of pets with chronic diarrhea. In pets, this condition is often chalked up as a "sensitive stomach" with recurring rounds of reactive therapy that can be very frustrating for pets and owners, particularly in chronic episodes.

For acute cases, I recommend 10-14 days of FortiFlora added to the diet. However, chronic cases warrant long-term probiotic use, which has proven successful in my experience.

Clinic finds new use for FortiFlora in shelter pets

Our success using probiotics to help manage pets with chronic diarrhea has inspired our clinic to find new cases, and our work with a local humane shelter has been the perfect opportunity. We see a number of recently rescued dogs and cats with GI issues, and probiotic supplements have helped these pets get back on their feet by promoting a strong immune system.



The stress of environmental changes and vaccinations can be tough on rescue animals, but probiotics help manage stress-based diarrhea.

These rescue animals are going through a lot of stress, both psychologically and physically. Vaccinations and spay/neutering can take a toll on any animal's health, particularly those with weakened immune systems. I advise the shelters to keep the pets on probiotics throughout the vaccination schedule to help manage soft stools and stress-induced diarrhea. If symptoms do occur, I recommend maintaining probiotic supplementation until a week after signs resolve.

Probiotics have proven to be an effective tool for pets with GI and immune health issues. With our clients' enthusiastic support, we've been able to find a variety of uses for an effective, easy nutritional supplement.

> Our success using probiotics to help manage pets with chronic diarrhea has inspired our clinic to find new cases.

Key Takeaways

- Probiotics are believed to help to reduce the severity of antibiotic-induced diarrhea by increasing numbers of beneficial bacteria in the GI tract while reducing numbers of pathogenic bacteria. It is believed these effects are probiotic-specific.
- The efficacy of the SF68 probiotic strain in helping to reduce the severity of diarrhea associated with antibiotic use was demonstrated in an independent study conducted at Colorado State University.
- Choosing the right probiotic for patients is important, as probiotics may differ in terms of efficacy and ability to survive in the harsh environment of the GI tract.