

Treatments for diarrhoea: the good, the bad and the unknown

Author : Silke Schmitz

Categories : [Clinical](#)

Date : August 3, 2016

ABSTRACT

The use of antibiotics and probiotics in acute and chronic diarrhoea in small animals is controversial. Even the correct definition of a probiotic in the context of veterinary medicine can be challenging. In contrast to human intestinal disorders, much less is known about the potential benefit of single probiotic strains or their combination. In addition, an added benefit of prebiotics or the use of a combination of probiotics and prebiotics – so called synbiotics – has not been investigated thoroughly in small animals.

This article summarises the indications of probiotics and highlights where antibiotics might or might not be useful in cases of diarrhoea in dogs and cats. It also provides an insight into potential probiotic mechanisms of action and touches on an evidence-based workup of chronic diarrhoea in small animals.

Diarrhoea is believed to be one of the most common reasons for a dog or cat to be presented to a practice. The causes are plentiful and clinical presentation can be variable.

Infectious/inflammatory, dietary, metabolic, endocrine, and many other diseases inside and outside the gastrointestinal tract (GIT) have to be considered. Animals can be otherwise well in themselves, but also be suffering from debilitating dehydration, hypovolaemia/shock or present with a more chronic history that also includes weight loss.

Depending on initial findings, the diagnostic tests and treatments required can also range widely. This can include simple measures, such as a faecal parasitology examination followed by an improvement in deworming protocols, or short-term dietary changes.

It can also mean aggressive fluid administration to restore losses and a variety of diagnostic tests – laboratory assessments and/or diagnostic imaging – to identify affected organ systems and relevant treatment.

Not so obvious

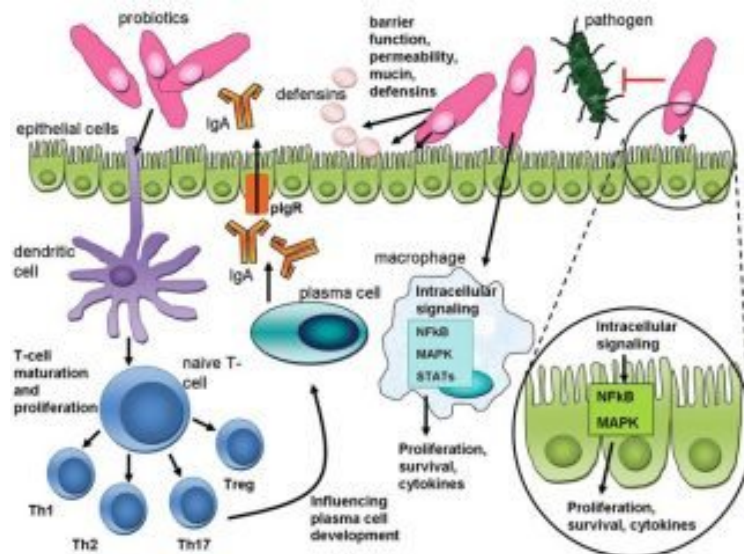


Figure 1. Proposed mechanisms of action of probiotics (click to zoom).

In cases where life-threatening diseases need immediate intervention (for example, GIT obstruction), but involvement of organs outside the GIT (acute or chronic renal disease, pancreatitis, hepatic failure, endocrinopathies such as Addison’s disease and neoplasia) and specific infectious causes, such as *Giardia* infection, have been ruled out, there is often a lack of clear-cut diagnoses and treatment protocols.

In addition, the empirical use of antibiotics in both “idiopathic” acute and chronic diarrhoea in dogs and cats is more questioned in an age where bacterial resistances are increasing.

It is likely antibiotic usage is going to be more restricted and regulated, and will need to be justified more strictly in individual animals in future. In view of this, and the fact owners have become more sceptical towards the use of antibiotics and might ask for alternative options, practices choose other treatments for diarrhoea, probiotics being an example.

But what are probiotics and what is the evidence for their use in acute and chronic diarrhoea in dogs and cats? Where do antibiotics still have their place and where should they no longer be used? Are there any other treatment alternatives? This article will focus on answering these questions by looking at publications and using a number of diseases as examples.

Definition of probiotics

Probiotics are defined by the World Health Organization to be “live microbes, which, when administered in adequate amounts, confer a health benefit on the host”. They are frequently commensal bacteria (the normal “flora” of mucosal surfaces of the body, also called the microbiota or microbiome), but can be yeasts (for example, *Saccharomyces boulardii*) or other microorganisms.

Most frequently, lactic acid-producing bacteria are used – for example, lactobacilli, bifidobacteria or enterococci – and most products available for dogs and cats in the UK contain *Enterococcus faecium*.

Commercially available products can contain the pure living probiotic bacterial strains, but frequently include additional ingredients that are either supposed to optimise growth conditions for the probiotics (so called prebiotics – often carbohydrates such as fructooligosaccharides) or other substances allegedly beneficial to the gut (for example, medicinal clay or short-chain fatty acids). The combination of prebiotics and probiotics is referred to as synbiotics.

Proposed mechanisms of probiotic action

Probiotics can potentially compete with pathogens by interfering with their adherence to the intestinal mucosa or by induction of mucus production¹. In addition, they can produce antimicrobial substances – for example, fatty acids, lactic acid and acetic acid². Some *Lactobacillus* species can decrease toxin production by *Salmonella*, *Escherichia coli* or *Clostridium perfringens*, or inactivate toxins³.

Immune modulation at the level of the local gut immune system might also occur through microbial cell wall components, their metabolites or bacterial DNA⁴. These effects can include maintenance and fortification of the intestinal barrier and the induction of regulatory lymphocytes (so called regulatory T-cells; Tregs) that prevent inflammation and induce local production of immunoglobulins, mainly IgA4 (**Figure 1**).

However, it needs to be stressed effects of probiotics on the intestine and its immune system have mostly been studied in humans and rodent models of human disease. More limited data is available for small animals.

Treatment of acute diarrhoea with probiotics and antibiotics

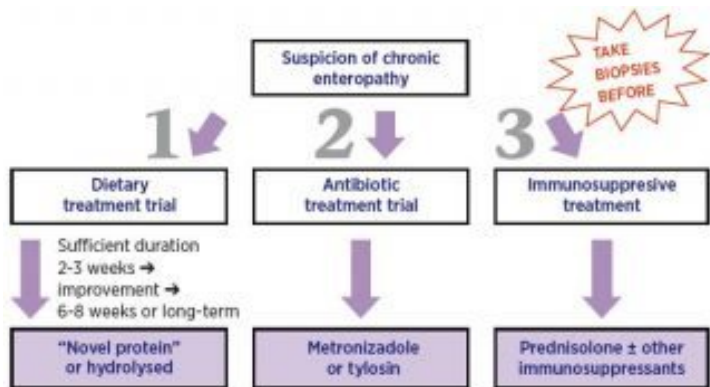


Figure 2. Sequential treatments when chronic enteropathy is suspected and all other potential causes of chronic GI symptoms have been ruled out (click to zoom).

The vast majority of acute diarrhoea cases in dogs and cats are believed to be self-limiting and likely due to dietary factors (intolerance of a food ingredient or ingestion of unsuitable material) or possibly acute infections that might be difficult (and probably unnecessary) to prove.

That implies if any therapeutic intervention is required at all, this can likely include supportive measures (ensuring hydration, meaning antiemetics will be required if vomiting is also present) and a short switch to a bland easy-to-digest diet.

No evidence exists that antibiotics have any positive effect on the severity or duration of clinical signs associated with acute diarrhoea in dogs and cats, hence they have no place in its treatment.

Even in acute haemorrhagic diarrhoea syndrome (formerly called haemorrhagic gastroenteritis) – a severe form of bloody diarrhoea of still undetermined cause, where dogs can potentially lose a lot of circulating volume/blood in a short time and require aggressive treatment – it has been shown addition of broad-spectrum antibiotics, such as amoxicillin/clavulanic acid, have no additional positive effect and these dogs are not at any higher risk of developing infectious or septic complications whether they are treated with antibiotics⁵.

Interestingly, there is some benefit of probiotics in acute infectious and non-infectious diarrhoea. Administration of the probiotic mixture VSL#3 (a probiotic preparation licensed for humans containing nine different bacterial strains) to puppies with confirmed parvoviral enteritis leads to an increased percentage of surviving dogs (90% in the probiotic group versus 70% in the non-probiotic group), and a more rapid improvement of clinical scores and leukocyte/lymphocyte counts⁶.

Similar results could not be achieved for the treatment of canine giardiasis with *E faecium*: after six weeks of treatment no differences in cyst shedding, faecal antigen shedding, faecal IgA or leukocyte phagocytic activity was observed between treated and untreated dogs⁷.

In contrast, kittens with *Giardia* infection treated with *E faecium* were less likely to need additional

supportive treatment (9.5% of cases) than placebo-treated kittens (60%).

The same was observed for infections with *Tritrichomonas foetus* in cats⁸. Also, kittens with acute diarrhoea from a *Campylobacter* outbreak shed less of the bacteria when treated with probiotics.

In stress-associated diarrhoea (kennelling stress), several lactic acid-producing bacteria (but not *E faecium*) led to improved faecal scores and shorter times of diarrhoea episodes in dogs and cats⁹.

Role of probiotics and antibiotics in chronic diarrhoea

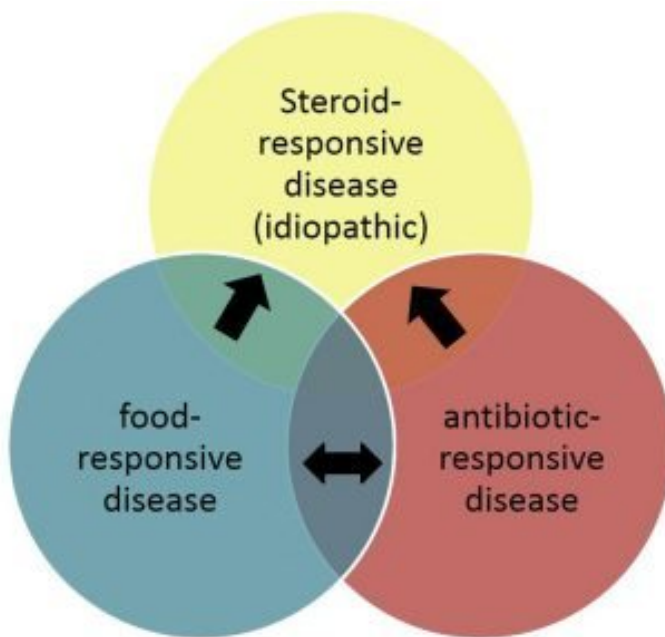


Figure 3. The three forms of chronic enteropathy in dogs. Arrows indicate separation of these forms might not be complete, but dogs can potentially switch between forms (click to zoom).

The cause of most chronic inflammatory GIT diseases in dogs and cats is unknown.

Usually, diagnosis is made retrospectively based on response to treatment. This means dietary trials, antibiotic trials and the administration of immunosuppressants are performed in sequential orders to assess whether clinical improvement occurs (**Figure 2**).

Recently, the umbrella term of chronic enteropathy (CE) has been coined for these diseases, with their respective sub-categories of food-responsive disease, antibiotic-responsive disease and steroid-responsive disease, also termed inflammatory bowel disease (IBD¹⁰; **Figure 3**).

In humans and small animals, the intestinal microbiota is implicated in the development and maintenance of inflammation in CE.

Studies have shown alterations of the composition and abundance of the intestinal microbiota in diseased animals compared to healthy controls. This dysbiosis can potentially be addressed by probiotics and antibiotics.

Antibiotics most frequently chosen in the context of CE are metronidazole and tylosin, and seem to have a direct effect on the microbiota¹¹. Several probiotics have also been administered to small animals with CE.

E faecium had no effect on clinical activity score, histology scores or intestinal expression of inflammatory or anti-inflammatory compounds in dogs¹². More promising results could be achieved by using the probiotic mixture VSL#3 in comparison to treatment with metronidazole and prednisolone.

Clinical activity, duodenal histology scores and lymphocyte numbers in the intestinal tissue decreased post-treatment in both groups. However, beneficial Treg lymphocyte cells only increased in the dogs treated with probiotics, and the composition of the microbiota normalised somewhat¹³.

Saccharomyces boulardii yeasts have also been administered to dogs with IBD in a small clinical trial and compared to standard treatment. Clinical scores improved significantly and serum albumin values improved¹⁴.

Only a few studies assess the effects of probiotics in cats with CE and the clinical sub-categories seem less clear than in dogs. In one study, clinical signs improved in 30% of cats treated with *E faecium*, whereas none of the placebo-treated cats showed an improvement (unpublished, personal communication with Karin Allenspach).

Future outlook

Administering probiotics can lead to faster resolution of clinical signs in small animals with acute idiopathic diarrhoea and is preferred over antibiotics, which have limited indications in acute and even haemorrhagic diarrhoea (for example, in patients where sepsis is suspected).

In more complex chronic enteropathies, such as IBD – where genetic and environmental factors seem to be interacting and are equally responsible for the clinical picture than the disturbance of the intestinal microbiota – no single probiotic organism has, so far, been identified that can lead to significant improvement of clinical signs.

However, there is some promise in probiotic mixtures. More research into the strains of microorganisms that might be beneficial in specific forms of intestinal inflammation is needed, as not only are the characteristics of the specific strains required, but the individual animals that may benefit from this treatment also need to be determined.

In chronic enteropathies, the use of antibiotics is usually restricted to very few drugs applied in an empirical manner. Especially, broad-spectrum antibiotics or fluoroquinolones are not indicated in chronic diarrhoea in small animals.

- Some drugs mentioned in this article are used under the cascade.

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