Probiotics in veterinary practice

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Probiotics are defined as “live microorganisms which when administered in adequate amounts confer a health benefit on the host.” Ideally, probiotics administered to clinically affected patients should originate in the species being treated and should be nonpathogenic, resistant to digestion by gastric acid and intestinal enzymes, able to adhere to the intestinal epithelium, and capable of influencing host immune responses.

The human gastrointestinal tract contains > 100 trillion organisms comprising approximately 500 species, many of which have not been identified. These bacteria are parasites, commensals, or mutualists. Within hours after birth, the gastrointestinal tract is populated with numerous bacterial species, but bifidobacteria predominate in humans. The change to a more complex diet after weaning allows the microbial population to diversify. Critical differences exist between resident bacteria of humans and other animals.

Each organism strain appears to be associated with specific effects on other organisms and on the host, and specific cytokine profiles and biological effects result from these interactions. Gastrointestinal bacteria have coevolved with their host and have become highly specialized over time. Composition of fecal microbiota in individual humans is unique but stable over time. Each host has a unique genetic platform (which expresses disease uniquely) and a unique mixture of indigenous flora that can be considered a fingerprint for that host.

Probiotics have luminal and mucosal effects. Mucosal effects include interactions with immune cells, enterocytes, and goblet cells via cell receptors and cytokine responses. Luminal effects include chemical changes in ingesta and mucus as a result of probiotic activity.

Specific Effects of Probiotics on Hosts

Animals can live without gastrointestinal microbes, but in germ-free animals, certain dietary deficiencies result in more substantial clinical signs than are evident in clinically normal animals. Lactobacilli synthesize B vitamins (niacin, pantothenic acid, pyridoxine, biotin, and folic acid) and certain lipolytic and proteolytic digestive enzymes, which improves digestibility of food components. Lactobacilli and other enterobacteria also synthesize folate coenzymes that are similar to dietary folate. High concentrations of Bacteroides spp may lower serum cobalamin concentrations. Clostridium spp, Bacteroides spp, Bifidobacterium spp, and Eubacterium spp deconjugate bile acids efficiently, and high concentrations of these organisms potentially contribute to steatorrhea.

Ten percent of the daily energy requirements in humans is supplied by microbial activity through anaerobic fermentation. Microbial fermentation contributes little to the metabolic energy of cats and contributes only approximately 2% to 7% of maintenance energy in dogs.

Survival within the gastrointestinal tract varies among species and even strains of organisms. A self-regulating population of gastrointestinal bacteria is maintained through competition, amensalism (ie, a symbiotic relationship between 2 organisms whereby 1 organism is unaffected but the other is negatively affected), parasitism, and predation. Specific mechanisms of interaction with other microbes include production of antimicrobial factors, competition for adhesion sites, and production of antitoxins (such as bacteriocin) and decreases in luminal pH.

In calves, pigs, and poultry, probiotics have increasingly been used to help prevent infection by enteropathogens, such as Salmonella spp and enterotoxigenic Escherichia coli. Lactic acid–producing bacteria may help control enteropathogenic organisms by producing organic acids within the lumen of the gastrointestinal tract or may compete for attachment sites on the intestinal mucosa.

The gastrointestinal tract is the largest immune organ of the body. Germ-free animals have sparse amounts of inactive immune tissues. Probiotic organisms interact with the host immune system in a number of ways. and activation of immune receptors drives nonspecific responses as well as immune responses. Immune cells in the gastrointestinal tract recognize probiotic species types through Toll-like receptors, which leads to specific signal transduction. Cytokine responses characteristic of a specific probiotic species lead to proliferation of responses characteristic of those for T-helper 1 or T-helper 2 cells and modify immu-
nologic tolerance and responsivity. Enhanced humoral immunity, IgA production, and responses to vaccines are examples of these interactions. Probiotics also may play a role in the pathogenesis and management of immune-mediated diseases, such as allergies.

Probiotics may affect the epithelial barrier as well as influence the production of mucus. They can increase brush-border membrane activity, promote epithelial restitution, prevent epithelial apoptosis, protect tight junctions during inflammation (reducing permeability), suppress electrolyte secretion during enteropathogen infection, increase expression of mucin glycoproteins, provide enzymes that may enhance host digestion of dietary nutrients, and shorten gastrointestinal transit time.\(^{12,34}\)

### Prebiotics

Prebiotics are short- or long-chain oligosaccharides that are not digestible by mammalian digestive enzymes but are fermented in the colon by microorganisms. One example of a prebiotic incorporated into some pet foods is inulin, which is found in the roots of certain plants. Prebiotics reduce pH in the colon because of production of SCFAs as a by-product of the fermentation process; the fermentation process also yields hydrogen and carbon dioxide gases. Prebiotics appear to increase bifidobacteria counts.\(^{23}\) When not fermented, prebiotics will lead to water reabsorption in the colon. One SCFA, butyrate, is the preferred energy source for colonic cells, but the SCFAs probably also have other activities in the colon. Effects of SCFAs include increasing sodium absorption, salvaging energy, increasing mucosal blood flow, regulating cellular proliferation, influencing cell differentiation and carcinogenesis, modulating immune function, and decreasing blood cholesterol concentrations.\(^{32}\)

Provision of prebiotics is generally believed to increase numbers of beneficial bacteria.\(^{26}\) However, the ecology of the gastrointestinal tract, which depends on a stringently regulated nutritional and chemical environment, is probably also controlled by other rate-limiting nutrients. These nutrients include iron, small organic molecules, amino acids, lipic acid, and fatty acids.\(^{3}\)

Dietary elements (such as oligosaccharides) strongly influence the growth and replication of bacterial populations in the gastrointestinal tract. Diets high in protein and fat support the growth of \(Bacteroides\) spp., peptidococci, and clostridia, whereas a carbohydrate-rich diet supports the growth of bifidobacteria, lactoba­cilli, eubacteria, and yeasts.\(^{3}\) Several investigators have found that dogs eating dry, grain-based diets have better fecal bacterial profiles (fewer clostridia and more lactic acid–producing organisms), lower fecal pH with higher SCFA concentrations (presumably reflecting higher colonic SCFA concentrations), lower bacterial enzyme activity, and lower concentrations of the putrefactive compounds ammonia, sulfide, and indole.\(^{7-30}\) Canned and possibly low-carbohydrate and grainless raw diets may not support optimal growth of beneficial gastrointestinal bacteria. Dietary supplementation with pre­biotics has been evaluated in cats and dogs; however, a thorough review of those studies is beyond the scope of this report.

### Role in Disease

Many disease states have now been associated with altered gastrointestinal microbiota, both in predisease and comorbid conditions. In humans, there is good support for the use of probiotics in the treatment of pouchitis and ulcerative colitis,\(^{2}\) inflammatory bowel disease,\(^{24}\) antimicrobial-associated and nosocomial diarrhoea,\(^{31}\) and infectious diarrhea.\(^{32}\) There is preliminary evidence to suggest that certain probiotics may help prevent the development of allergies in susceptible children,\(^{33-36}\) improve immune function,\(^{37,38}\) and prevent recurrent urinary tract infections.\(^{39}\) Studies have been conducted to determine whether some probiotics prevent bladder cancer,\(^{40}\) calcium oxalate uroliths,\(^{41}\) pancreatitis,\(^{42,43}\) and pharyngotonsillitis.\(^{44}\)

### A Study in Healthy Cats

Cats and dogs both have high numbers of bacteria in the proximal portion of the gastrointestinal tract, which are higher than the numbers in the gastrointestinal tract in humans. Cat feces contain high numbers of anaerobes, which are considered abnormal in dogs and humans.\(^{45}\) Of interest in cats, bacterial metabolism of taurine and cobalamin can have relevance in chronic small intestinal disease.

The effects of \(Lactobacillus acidophilus\) DSM13241 in 15 healthy adult cats have been evaluated.\(^{46}\) In that study, cats were fed a probiotic-supplemented kibble or plain kibble during separate feeding periods (each cat served as its own control animal). The concentration of bacteria in the kibble equated to an intake of approximately \(1.2 \times 10^9\) CFUs to \(2.8 \times 10^9\) CFUs daily. The organisms were sprayed onto the extruded kibble, which was packaged to maintain stability; it was confirmed that there were viable bacteria in the kibble at the conclusion of the study. Mean ± SD fecal pH decreased significantly (\(P = 0.017\)) from 6.73 ± 0.34 at baseline to 6.48 ± 0.41 after ingestion of the probiotic-supplemented kibble, and total populations of fecal bifidobacteria decreased significantly (\(P = 0.036\)) from 0.16 ± 0.07% to 0.09 ± 0.04% during feeding of the probiotic-supplemented kibble. \(Clostridium\) spp decreased significantly (1.27 ± 0.06%; \(P = 0.003\)) when cats were eating the probiotic-supplemented kibble, compared with a value of 4.03 ± 1.98% after feeding of the supplemented kibble.\(^{5}\) Similarly, \(Enterococcus\) faecalis populations decreased significantly (0.15 ± 0.09% before feeding of the probiotic-supplemented kibble to 0.05 ± 0.06% during feeding of the supplemented kibble; \(P = 0.001\)) with use of the supplemented kibble. Clostridial and bifidobacteria numbers increased again after feeding of the probiotic-supplemented kibble ended. Serum immunoglobulin concentrations were unchanged, but granulocyte phagocytic activity (measured by use of fluorescence) increased significantly (from 44.81 ± 126.08 nm at baseline to 780.33 ± 131.61 nm after feeding of the probiotic-supplemented kibble; \(P = 0.001\)) and lymphocyte numbers decreased significantly (4.89 ± 1.81 × 10^7 cells/L at baseline to 4.05 ± 1.69 × 10^7 cells/L after feeding of the probiotic-supplemented kibble; \(P = 0.043\)). Eosinophil numbers also increased significantly (\(P = 0.002\)). Erythrocyte fragility decreased significant-
ly (from 17.14 ± 11.32% at baseline to 11.83 ± 9.66% after feeding of the probiotic-supplemented kibble; \( P = 0.028 \)). Plasma endotoxin concentrations were also reduced during feeding of the supplemented kibble.

**Studies in Healthy Dogs**

In 1 study, investigators isolated a strain of *Lactobacillus fermentum* (AD1) from a dog and found that after experimentally providing this strain to dogs, serum protein concentration was significantly (\( P < 0.001 \)) increased by a mean of 1.27 g/dL and serum lipid concentration was significantly (\( P < 0.01 \)) increased by a mean of 0.15 g/dL. Blood glucose concentration was significantly (\( P < 0.01 \)) decreased by a mean of 0.7 mmol/L.

There were no significant differences in serum cholesterol concentration, alanine aminotransferase activity, or urea concentration. Probiotic bacterial numbers in the feces were significantly (\( P < 0.001 \)) increased by 3.3 log\(_{10}\) CFUs/g for lactobacilli and by 1.6 log\(_{10}\) CFUs/g for enterococci. In another study, investigators cultured 40 strains of enterococci (most of which were strains of *Enterococcus faecium*) from dog feces, tested them for potential probiotic activity, and determined that *E faecalis* EE4 and *E faecium* EF01 were candidates for further study.

*Lactobacillus fermentum* LAB8, *Lactobacillus salivaricus* LAB9, *Lactobacillus rhamnosus* LAB11, *Lactobacillus mucosae* LAB12, and *Weissella confusa* LAB10 have been cultured from dog feces. These organisms were administered for 7 days to dogs with permanent jejunal fistulas. The administered strains disappeared within 7 days after discontinuation of the supplemented diet, but there was a sustained change in the population of indigenous lactic acid–producing bacteria in jejunal contents, with native *L. acidophilus* strains predominating.

The ability of lactic acid–producing bacteria to interfere with adhesion by enteropathogens was evaluated by use of the intestinal mucus from dogs with permanent jejunal fistulas. The administered strains disappeared within 7 days after discontinuation of the supplemented diet, but there was a sustained change in the population of indigenous lactic acid–producing bacteria in jejunal contents, with native *L. acidophilus* strains predominating.

The ability to colonize the intestines and remain viable in the feces are claimed to be prerequisites for determining whether an organism has probiotic properties in a species in which it is not native. In 1 study, investigators fed *L. rhamnosus* GG to Beagles at 4 doses. Only at the highest dose (\( 5 \times 10^{11} \) CFUs/d) was 100% colonization and fecal recovery detected. This dose is considerably higher than that required in humans (\( 6 \times 10^{9} \) CFUs to \( 1 \times 10^{11} \) CFUs).

No adverse effects were evident in any of the 4 groups of Beagles. One popular human product contains only \( 2 \times 10^{10} \) CFUs of *L. rhamnosus* capsule, which is a high amount when compared with the content in many other over-the-counter products.

**Clinical Indications**

Inflammatory bowel disease—In diarrheal diseases, the putative mechanisms of benefit from probiotic administration include production of antimicrobial substances (including hydrogen peroxide and acids), competition for nutrients, competitive inhibition of receptor binding, antitoxin activity, and immune stimulation. Dogs with enteropathy for a mean ± SD of 11 ± 3 months were identified at a secondary veterinary medical center and scored by use of the Canine Inflammatory Bowel Disease Activity Index. Endoscopic biopsy specimens were cultured with probiotics of canine origin (*L. acidophilus* NCC2628, *L. acidophilus* NCC2766, and *Lactobacillus johnsonii* NCC2767), a combination of these 3 probiotics, or a control substance (placebo).

When used alone, the probiotic strains had no significant effect on cytokine concentrations. However, the combination of the 3 probiotics led to changes in proportions of regulatory and proinflammatory cytokines in ex vivo cultured biopsy specimens. In biopsy specimens obtained from sick dogs, interleukin-10 protein concentrations increased significantly (\( P < 0.05 \)) when culture medium was stimulated with the probiotic combination (from 70 ± 22 ng/mL in control medium to 161 ± 58 ng/mL in probiotic-stimulated medium). For control dogs, probiotic stimulation of the culture medium resulted in a mean protein concentration of 25 ± 2 ng/mL, which was increased from a mean of 20 ± 11 ng/mL in the control medium.

Fecal and endoscopic biopsy samples were collected from 21 client-owned dogs with food-responsive diarrhea. Dogs were then treated with a probiotic cocktail of *L. acidophilus* NCC2628, *L. acidophilus* NCC2766, and *L. johnsonii* NCC2767 or a control substance (placebo), and duodenal cytokines and gastrointestinal microbial populations were examined. All dogs improved clinically on an elimination diet because canine Inflammatory Bowel Disease Activity Index scores decreased from 5 before placebo treatment to 1 after placebo treatment and from 7 before probiotic treatment to 0 after probiotic treatment.

Numbers of enterobacteriaceae decreased significantly (\( P < 0.05 \)) in placebo- and probiotic-fed dogs, but investigators were unable to associate specific cytokine changes with clinical responses or with probiotic treatment.

**Diarrhea**—One potential benefit from probiotic treatment of animals with diarrhea is to decrease infection by *Clostridium difficile*, *Salmonella* spp., and *Campylobacter* spp. Studies in food animal species suggest that probiotics can reduce shedding of enteropathogenic bacteria, possibly reducing signs and duration of diarrhea.

Dietary supplementation with *E. faecium* SF68 can be beneficial in adult cats and kittens with chronic diarrhea. Thirty-one kittens in a colony developed diarrhea. Approximately half were treated with the probiotic, whereas the others were not. Only 9.3% of the kittens administered the probiotic required additional treatment, compared with 60% of the kittens not administered the probiotic that required additional treatment; these proportions differed significantly (\( P < 0.05 \)). Diarrhea in the kittens fed the probiotic also resolved sig-
nificantly (P < 0.05) faster, compared with resolution in the control kittens. Probiotic treatment led to an increase in fecal bifidobacteria, decrease in Clostridium spp, and increases in blood concentrations of IgA, compared with results for control kittens.

Lactobacillus acidophilus DSM13241 significantly reduces shedding of Campylobacter organisms in infected cats and also reduces reinfection, which reduces the potential for zoonotic transmission. 88 In that study, 50 cats with clinical signs of infection were administered cephalosporin for 10 days, then given food with or without probiotic (1 x 10^8 CFUs) for 4 weeks. The increase in Campylobacter organisms as a percentage of total fecal bacteria was significantly (P < 0.05) smaller in cats administered the probiotic (12.2% in probiotic-treated cats vs 19.7% in untreated cats). At the end of the study, probiotic-treated cats had eliminated significantly (P < 0.05) more Campylobacter organisms (as a percentage of total bacterial population) than did control cats (3.94% vs 14.06%, respectively).

Effects of a product containing E faecium NCIB 10415 (also known as E faecium SF68) on numbers of fecal Salmonella spp, Campylobacter spp, and Clostridium spp were evaluated in 12 client-owned dogs. 97 The daily dose was 9.2 x 10^8 CFUs, which was administered for 18 days, regardless of each dog's body weight. Although bacterial counts varied widely among dogs, there was a pattern for increases in Salmonella spp and Campylobacter spp when dogs were provided with the E faecium product (counts on some dogs were higher, whereas counts in other dogs were lower). However, numbers of clostridial organisms were significantly (P < 0.05) decreased. 97 In baby pigs, this strain of E faecium can decrease the pathogenic effects of E coli with no effect on fecal E coli counts. 97

General immune function—Results of studies 88-91 conducted by use of different organisms in a variety of laboratory animals and humans suggest that many probiotic species can influence immune function. Administration of E faecium SF68 (5 x 10^8 CFUs daily) to puppies from time of weaning to 1 year of age had effects on immune function. Fourteen puppies were allocated into 2 groups and fed a commercial diet, with or without the probiotic, for 1 year. 95 Total fecal IgA concentration typically was higher, but not significantly so (P = 0.056), in the dogs administered the probiotic in their diet, compared with results for dogs fed the diet alone. Beginning when the dogs were 18 weeks old, plasma IgA concentration was higher in the dogs fed the probiotic in their diet, whereas plasma IgG concentrations did not differ between the groups. Response to distemper vaccination (measured as canine distemper virus–specific IgG and IgA content) was significantly (P < 0.05) stronger in the treatment group. There was also a greater proportion of mature B cells in dogs fed the probiotic (mean ± SD, 16 ± 1.6% vs 11.5 ± 1.5% in the treated and control dogs, respectively), whereas T-cell populations were not different between the 2 groups. Amounts of food-specific IgE were not different between probiotic and control groups, which suggested that the effects on immunoglobulins and B cells were not attributable to immune dysregulation. The investigators determined that these effects were attributable to immunomodulation by E faecium SF68, as opposed to changes that were attributable to manipulation of the bacterial population. 83

Chronic renal disease—Uremic toxins diffuse passively from the blood into the lumen of the gastrointestinal tract. Urease-producing probiotic species hydrolyze urea and maintain a concentration gradient that favors diffusion of urea from the blood to the gastrointestinal tract lumen. Studies in rats 84,86 and pigs 49 that involved use of a patented product (a combination of Enterococcus thermophilus, L acidophilus, and Bifidobacterium longum) revealed that administration of the product reduces uremia and number of fatalities. A case series of 7 azotemic cats at a private clinical practice was reported. 89 After administration of a probiotic for 60 days, all cats had a decrease in BUN concentrations and 6 of 7 had a decrease in serum creatinine concentrations. Concurrent treatments varied among the cats, and the medical history of each cat was not reported. Only 1 cat apparently received probiotic administration alone; that cat was fed a commercial food and did not receive parenterally administered fluids. Although the serum creatinine concentration was reduced from 2.6 to 2.2 mg/dl, the cat lost weight (0.23 kg [0.5 lb]) 65.

Pancreatitis—Translocation of gastrointestinal bacteria during pancreatitis can lead to septicemia and substantially worsen a patient's prognosis. Results of studies 81,82 conducted in humans and other animals by use of Lactobacillus plantarum 299, Saccharomyces boulardii, and combinations of probiotics and prebiotics suggest that probiotic administration may be of benefit in patients with acute necrotizing pancreatitis. Probiotic organisms appear to improve the intestinal barrier, which prevents bacterial translocation, and lactic acid–producing bacteria can suppress the inflammation that makes systemic inflammatory response syndrome such a deadly condition in patients with acute pancreatitis.

Investigators have conducted studies 71,72 in dogs with experimentally induced severe pancreatitis. Affected dogs have been provided nutrients parenterally as well as elemental enteral nutrition or dietary supplementation with probiotics. In 1 study, 71 increases in serum activity of amylase, alanine aminotransferase, and aspartate aminotransferase and plasma concentrations of endotoxin, as well as pancreatic and ileal histopathologic changes, were significantly (P < 0.05) suppressed with probiotic administration. The degree of bacterial translocation was significantly (P < 0.05) decreased with probiotic administration, which suggested that this probiotic combination (described as 40 mg of Lactobacillus spp and 40 mg of Bifidobacterium spp) enhanced gastrointestinal barrier function. 71 Investigators in another study 72 obtained similar results.

Safety

Authors of a review 73 published in 2004 found 23 probiotic species of Lactobacillus involved in 89 severely ill humans with lactobacilli bacteria. Predisposing factors were immunosuppression, prior prolonged hospitalization, and prior surgical interventions. On the other hand, a randomized, double-blind, placebo-con-
controlled trial in critically ill humans revealed that the patients were not more prone to adverse effects from probiotic administration, they had significant increases in systemic IgA and IgG concentrations, and their intestinal permeability was decreased. Lactobacillus rhamnosus GG has been associated with bacteremia after administration to a child with short gut syndrome. It has also been suggested that Lactobacillus spp produce organic acids that may lead to decalcification of dental matrix.

A number of cases (92 cases as of 2005) of invasive infection in humans attributable to S. boullardi (a subspecies of Saccharomyces cerevisiae) have been reported, usually when the S. boullardi was administered to patients with diarrhea. Intravenous catheter placement and antimicrobial treatment are common features in these patients. Septicemia attributable to ingestion of a probiotic strain of Bacillus subtilis was reported in a 73-year-old person with leukemia.

To the author’s knowledge, septicemia following dietary supplementation of companion animals with probiotic organisms has not been reported. Caution is advised if dietary supplementation is considered in severely immunosuppressed or critically ill animals or in animals in which marked compromise of the intestinal mucosa is suspected.

**Quality Control of Probiotic Products**

Commercial probiotic products have large variations in quality control. Problems may range from visibility issues to inclusion of species not listed on the label.

In 1 study, health food store products labeled for use in humans in Canada commonly contained (in addition to the organism on the label) a strain of Lactobacillus spp not listed on the label. An analysis of over-the-counter brands of probiotic found that of 13 human products sampled, 4 did not contain the amount listed on the label and 4 did not contain the generally accepted effective dose of at least 10^9 organisms. None of the 13 human products had microbial contamination. Of 3 over-the-counter products formulated for use in domestic animals, 1 did not contain the amount claimed on the label, 2 did not contain the recommended 10^9 organisms/daily dose, and 1 was contaminated with mold.

In another study, 23 over-the-counter probiotic products formulated for use in animals and 21 products formulated for use in humans were evaluated to determine their adherence with label claims. Bacterial species were misspelled (in up to 25% of products), and bacterial species were frequently misidentified (outdated names of organisms or names of nonexistent organisms). Only 5 of the veterinary products provided information about the intended number of probiotic organisms, often without clarification as to the date on which that number should be expected. Because of the deficiencies identified in that study, practitioners and consumers should expect a probiotic product label to include the organisms (included down to the strain level), correct spelling and identification of all organisms in the product, and number of live organisms expected on the expiration date. In another study, analysis of the labels for 5 products on the European market yielded similar results.

Holistic commercial diets formulated for dogs and cats sometimes list probiotics among their ingredients. Thirteen commercial diets for dogs and 6 commercial diets for cats, all of which claimed to contain probiotics, were analyzed for the content of species listed on the labels. Twelve diets did not list a live organism (which is needed to be consistent with the claim to contain a probiotic); instead, they listed probiotic fermentation products. The FDA recommends labeling probiotics as feed ingredients with the term bacterial fermentation products; however, this term does not indicate whether organisms are viable. Only 7 of the diets contained at least 1 of the listed species, and none contained all of the probiotics listed on their labels. Lactobacillus acidophilus was listed in labels of 13 of the diets but was not cultured from any of them. Bifidobacterium spp, which are anaerobic organisms, were not cultured from any product that claimed to contain them. The diets contained < 1.8 × 10^9 CFUs/g, which suggested that approximately 5.5 kg (12.1 lb) of diet would need to be consumed daily to reach dose amounts believed to be necessary to provide clinical probiotic effects. The survival of Bacillus CIP 5832 was investigated. Investigators in that study found that extrusion significantly reduced the number of viable spores, although coating the food with a powder of the probiotic after extrusion better preserved the viability.

Investigators in 1 study added L. acidophilus to dog food. Initial recovery was 71%, with recovery of 63% 8 weeks later. In that study, dogs of various breeds and ages were fed a control food without probiotics for 2 weeks, then given the supplemented food for 4 weeks, and finally given the control food again for an additional 2 weeks. The daily dose was 10^9 CFUs, which was incorporated into the food by adding freeze-dried organisms in oil after extrusion of the kibble. During the period when they ate the supplemented food, the dogs had increased numbers of fecal lactobacilli and decreased numbers of clostridia, changes that were reversed when the control diet was again administered. Feeding of the supplemented diet led to significant increases in RBCs (from 6.22 ± 0.61 × 10^12 cells/L when fed the control food to 6.79 ± 2.39 × 10^12 cells/L when fed the supplemented food [P = 0.033]), and monocytes (from 0.34 ± 0.13 × 10^9 cells/L when fed the control food to 0.52 ± 0.29 × 10^9 cells/L when fed the supplemented food [P = 0.012]). Hematocrit increased significantly (P < 0.001) from 0.45 ± 0.004 L/L when dogs ate the control food to 0.50 ± 0.003 L/L when dogs ate the supplemented food. Hemoglobin concentrations increased significantly (P = 0.003) from 14.97 ± 1.17 g/dL when dogs ate the control food to 15.97 ± 0.88 g/dL when dogs ate the supplemented food. Concentrations of IgG increased significantly (P = 0.010) from 18.2 ± 4.2 mg/mL when dogs ate the control food to 21.4 ± 5.0 mg/mL when dogs ate the supplemented food. Nitric oxide concentration decreased significantly (P < 0.001) from 13.98 ± 8.36 mM when dogs ate the control food to 3.67 ± 2.39 mM when dogs ate the supplemented food. Finally,
RBC fragility decreased significantly (P < 0.001) from 56.6 ± 26.6% when dogs ate the control food to 39.1 ± 31.4% when dogs ate the supplemented food. The investigators processed the food for minimal moisture content (2%), stored it in aluminum bags, provided the food to the dogs in dry form without adding water, and minimized exposure to moisture while it was available to the dogs, thus maximizing the dose.

Debate exists about the value of nonviable probiotic bacteria. In 2 recent clinical studies,44,45 it has been suggested that nonviable organisms do not have probiotic effects. Nonviable bacteria, bacterial DNA components, and media from probiotic cultures have had beneficial effects in animals with induced colitis and in knock-out mice predisposed to colitis.2 On the other hand, a study46 in which investigators used heat-inactivated L. rhamnosus GG was terminated prematurely because of adverse effects on the gastrointestinal tract.

Conclusions

Probiotic products are subject to variations in quality control, and the safety profile is still under investigation. The regulatory situation is similarly unclear because the FDA considers probiotic products labeled with medical indications for animals to be unapproved drugs.

However, it is increasingly clear that manipulation of the ecology of the gastrointestinal tract has powerful systemic effects. Use of probiotics clearly enhances immune function in a number of species, including dogs and cats, and appears to have a role in the treatment of animals with certain gastrointestinal conditions. Other clinical effects (such as prevention of recurrent urinary tract infections, prevention and treatment of allergies, and treatment of pancreatitis, oxalate urolithiasis, and other conditions) have been investigated in humans, which suggests a range of potential benefits in veterinary patients.

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