

DERMATOLOGY PEARLS

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Dermatology Clinic for Animals

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Probiotics in Veterinary Dermatology

Probiotics are microorganisms which, when ingested, exert beneficial health effects beyond that of their nutritional value. Examples include strains of *Lactobacillus*, *Bifidobacterium*, and some strains of *Enterococcus*.¹ Prebiotics are food substances (such as inulin or fructooligosaccharides/FOS) which are not digestible by the host but are fermented by gut bacteria to influence the composition of the gut microbiome to favor the beneficial bacteria; a synbiotic is a combination product containing both a prebiotic and a probiotic.² Probiotic bacteria may help control enteropathogenic organisms by production of organic acids within the GI tract lumen, or may compete for attachment sites on the intestinal mucosa. The mechanism of health effects of probiotics is not well understood, but likely involves interactions of the GI bacteria with GI epithelial and immune cells, food product fermentation, digestion and nutrient absorption, bacterial vitamin B and folate synthesis, and immune system modulation.^{1,2} The GI tract is the largest immune organ in the body, and probiotics interact with toll like receptors on immune cells in the GI tract to elicit cytokine responses characteristic of a specific probiotic species, modulating immune tolerance and response.¹ The ideal probiotic is a bacterial strain which occurs naturally in the same species as the intended host, is non-pathogenic, retains viability during production, storage and passage through the GI tract, adheres to and colonizes the GI epithelial mucosa and is demonstrated to have a beneficial effect on the host.^{1,2} Health effects from probiotic administration are dose, strain, and disease specific, and have not been well-studied, making rational selection of a probiotic difficult in clinical practice. Additionally, probiotic supplements are not FDA regulated, and can suffer from poor quality control in manufacture and storage. In one study, an analysis of 13 OTC human probiotics found that 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.³ In another study, 23 OTC probiotic products formulated for use in animals and 21 products formulated for use in humans were evaluated for label claims; probiotic bacterial species names were often misspelled or misidentified, and only 5 of the veterinary products provided important information such as number of probiotic organisms and expiration date.⁴ Veterinary probiotic products which have been analyzed to meet label claims² include Provable-DC (synbiotic capsule with FOS and *Bifidobacterium bifidum*, *Enterococcus faecium*, *Enterococcus thermophilus*, *Lactobacillus acidophilus*, *Lactobacillus bulgaricus*, *Lactobacillus casei*, *Lactobacillus plantarum*, total bacteria min. 5.0×10^9 CFU/capsule; Nutramaxlabs), FortiFlora (*Enterococcus faecium* SF68, 1×10^8 CFU/g, contains animal digest; Purina), and ProStora (*Bifidobacterium animalis*, min 1×10^8 CFU/g, contains milk; Iams).

Probiotics studied in dogs: The normal canine GI microbial population varies in bacterial species and number depending on location within the GI tract (stomach, upper GI, colon), and the GI mucosal flora is also different than the flora found in intestinal content and feces.⁵ Strains of bacteria which have been isolated from dog feces and studied for probiotic potential include *Lactobacillus reuteri*, *L. animalis*, *L. fermentum*, *L. acidophilus*, *Enterococcus faecalis* EE4, *E. faecium* EF01, and *Bifidobacterium animalis*; all were found to survive passage through the intestinal tract and were recovered in feces, though were usually undetectable 1-2 weeks after supplementation was ceased.⁶⁻¹⁵ *Lactobacillus rhamnosus* strain GG (LGG) was fed to dogs at a dose range of $0 - 5 \times 10^{11}$ CFU/day for 5 days; the probiotic was detected in the feces of 50-63% of dogs receiving lower doses (1×10^9 , 1×10^{10} , 5×10^{10} CFU), and in 100% of dogs receiving the highest dose.¹⁶ Freeze dried canine origin *L. fermentum* was fed to dogs at doses ranging from 1×10^7 CFU to 2×10^8 CFU daily and treated dogs had reduced coliform and clostridial fecal bacteria and reduced fecal pH.¹³ Another study of *L. fermentum* given to 15 healthy dogs (1×10^9 CFU daily for 7 days) showed increases in total protein and total lipid and decreased glucose in treated dogs, suggesting nutrient absorption and metabolism was altered by probiotic supplementation.⁷ *Bifidobacterium animalis* AHC7 administration to dogs reduced fecal carriage of clostridial organisms.¹⁵ A synbiotic containing a mixture of seven probiotic strains (5×10^9 CFU) and a blend of FOS and arabinogalactans as prebiotics was administered daily for 21 days to 12 healthy cats and 12 healthy dogs; the probiotic species were detectable in the stool of 10/12 dogs and 11/12 cats during supplementation indicating successful GI passage, however no changes in GI function or immune markers were observed.¹⁴ Puppies fed a diet supplemented with 5×10^8 CFU/day of *Enterococcus faecium* SF68 from weaning to one year of age had higher fecal IgA and serum distemper vaccine Ig titers as well as increased B cells compared to control pups.¹⁷ In a different study, *E. faecium* NCIB 10415 was fed to 12 dogs (9.2×10^9 CFU daily for 18 days); post treatment stools contained higher counts of *Salmonella* and *Campylobacter* but lower *Clostridium spp.* counts.¹⁸

Probiotics in dog foods: Many dog foods claim to contain probiotics, but are inconsistently controlled. In one study of a Waltham food supplemented with $>10^9$ *L. acidophilus*, 15 dogs were fed the food or a control diet for 2 weeks and fecal/blood samples were compared pre and post treatment.⁹ Recovery of *L. acidophilus* from the supplemented food was 74% and 63% at the start and end of the study, respectively, indicating that the bacteria were able to survive manufacture and storage. Administration of the probiotic supplemented food was associated with increased numbers of fecal lactobacilli and decreased numbers of clostridial organisms. Additionally, there were increases in HCT, neutrophils, monocytes and serum IgG. The probiotic bacterium was not detectable in the feces 2 weeks post cessation of the supplemented food.⁹ In another study, 19 commercial pet foods which had label claims of probiotic or bacterial fermentation products were cultured; no product contained all organisms listed on the label, in 10/19 diets, one or more listed organism was isolated, and 5 diets did not grow any relevant organisms. *Lactobacillus acidophilus* was listed on the labels of 13 of the diets but was not cultured from any of them, nor was *Bifidobacterium* spp. cultured from any of the products claiming to contain it. Average bacterial growth ranged from 0 to 1.8×10^5 CFU/g, which suggests that 5.5kg of food would need to be consumed daily to reach dose amounts believed to be necessary to provide clinical probiotic effects.¹⁹

Probiotics for allergies in humans: A review was performed of 13 randomized placebo controlled trials, 10 of which evaluated probiotics as treatment and 3 as prevention for atopic dermatitis.²⁰ Four studies suggested a statistically significant decrease in severity of clinical signs after probiotic administration for 1-2 months in infants or children with atopic dermatitis, and in 2 other studies clinical signs were reduced after treatment with Lactobacilli only in children with IgE-associated atopic dermatitis. In 4/6 of these studies, clinical improvement was also associated with changes in some inflammatory markers. In 3 studies, clinical signs were no different between probiotic treated and untreated children with atopic dermatitis, with the exception of lower clinical signs in a subset of food sensitized children. In most studies, inflammatory markers were unchanged after probiotic administration compared to placebo.²⁰ Studies evaluating prevention of atopic dermatitis involved pregnant mothers who received *Lactobacillus rhamnosus* GG with or without other probiotics perinatally, followed by treatment of their infants with the same probiotics for the first 6 months of life. In 2 clinical trials, infants at high risk for atopy who received probiotics developed atopic dermatitis significantly less frequently during the first 2 years of life compared to the placebo group, however in the third study there was no difference in severity or frequency of development of atopic dermatitis, and the probiotic treated group had an increased rate of recurrent episodes of wheezing bronchitis.^{20,21} Similar inconsistent findings are present in studies of probiotics for food allergy in humans; differences may be related to different study populations, probiotic strains and probiotic doses.

Probiotics for allergies in dogs: Two small studies have looked at probiotics for the prevention or treatment of atopic dermatitis in dogs. In the first study²², 2 adult atopic Beagles (sire and bitch) were bred twice, a year apart; the first litter was the untreated control group (n=7). *Lactobacillus rhamnosus* GG (LGG) was administered to the bitch during the second pregnancy (200×10^9 CFU orally daily starting at week 3 of the second pregnancy and continuing throughout lactation) and to the puppies from the second litter (n=9) from 3 weeks to 6 months of age (100×10^9 CFU orally daily). All puppies were sensitized to housedust mites at 3 weeks of age, serum samples were obtained q 6 weeks for measurement of housedust mite IgE, and at 6 months of age the pups were intradermally allergy tested for, and environmentally challenged with, housedust mites. The probiotic exposed puppies had a significantly lower titers of allergen specific IgE and milder reactions to intradermal testing compared to the untreated control litter, however clinical scores post housedust mite exposure did not differ between litters.²² In the second study²³, the same Beagle puppies were then followed up 3 years after discontinuation of LGG to evaluate severity of clinical signs and measure allergen specific IgE and IL-10 and TGF- β production after allergen stimulation. Results showed that the clinical scores post housedust mite challenge were higher (ie. more severe) in the non-probiotic exposed litter, the control litter had higher IL-10 levels than the probiotic exposed dogs (IL-10 levels in probiotic exposed dogs were close to levels present in normal Beagles), and allergen specific IgE and TGF- β did not differ between litters.²³ The reduced severity of clinical signs post allergen exposure in probiotic treated dogs is similar to studies of probiotics in children at high risk of atopic dermatitis, which showed a 50% reduction of occurrence of atopic eczema at 2 and 4 years of age.²⁴ While the probiotics did not protect from sensitization, the beneficial effect on clinical signs was persistent in this group of dogs, and warrants further study.

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