# **Probiotics: What to Expect or Not**

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Probiotics are "live microorganisms when consumed in sufficient quantity; provide health benefit on the host" (Bourlioux 2003). They appear to provide their benefits through interaction with the host's immune and defense mechanisms.

Microbiota: 300-500 bacterial species with 2 million genes. There are 10 times more bacterial cells in the gut than in the human body (Quigley 2012).

## Probiotic organisms include

- Lactobacillus species (rhamnosus, rhamnosus GG, casei, reuteri, plantarum, acidophilus)
- Bifidobacteria species (infantis, longum)
- Enterococcus species: (faecium)
- Saccharomyces species: (cerevisiae)
- Bacteroides species (thetaioataomicron, fragilis)
- Streptococcus species
- Escherichia species

## **Probiotics in practice**

- Potential benefits
- Efficacy depends on
  - Quality control
  - Dosing
- Clinical Studies too few

## What are the benefits?

- Physical
- Immunological
- Nutritional

## Physical Effects on the GI

- Effects on the mucosal barrier Protect tight junctions
- Reduce intestinal pH Production of short chain fatty acids
- Increase production of mucus
- Improve host digestion
  - Increase brush border membrane enzyme activity
  - Certain lipolytic and proteolytic digestive enzymes

## Immunological Effects on the GI - Interactions with host immune system include:

## Humoral immune system

- Stimulates IgA and increase nitric oxide prod
- Inhibit IgE
- Modulate cytokine response

## Cellular immune system

- Stimulate macrophage and natural killer cell function
- Promotes growth and regeneration of mucosal cells

## Stimulating adaptive immunity

- recognition of bacterial
- production of cytokines that determine tolerance or responsively

## Microbial interactions with other microbes include (Marteau 2003)

- Production of antimicrobial factors
- Production of antitoxins
- Competition with pathogens for adhesion
- Decrease lumen pH

## **Potential conditions**

- IBD /IBS
- Stress diarrhea (weaning, boarding, psychogenic)
- SIBO
- Some food reactions

## Nutritional

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- Lactobacilli synthesize vitamins
  - 6 diff B-vitamins
  - $\circ$   $\quad$  Questionable value when fed a complete and balanced diet already
  - Bacteroides, bifidobacteria, lactobacilli, and clostridia deconjugate bile acids

Product Quality Control - Commercial probiotic products are subject to large variations in quality control.

## Practitioners and consumers should expect to see on a product label/literature

- correct spelling and identification of all organisms
- all organisms included down to the strain level
- number of live organisms expected on the expiration date

## Quality control problems - ConsumerLab.com analysis of over the counter brands

- 1. 3 animal over-the-counter products tested
  - a. 1 did not contain the amount claimed on the label
  - b. 1 was contaminated with mold
  - c. 2 did not contain the recommended 10^9 per daily dose
- 2. 13 human products sampled
  - a. 4 did not contain the amount listed on the label
  - b. 4 did not contain the generally accepted effective dose of at least 10^9 organisms
- 3. Analysis of 23 over-the-counter animal probiotic products and 21 human products (Weese 2002)
  - a. Species were frequently misidentified or misspelled.
  - b. Number of viable organisms were incorrect.
- 4. Analysis of 19 pet foods claiming to have probiotic supplementation (Weese 2003)
  - a. None contained all of the probiotics listed on their labels.
  - b. Lactobacillus acidophilus was not cultured from any product making such a claim.
  - c. Bifidobacterium was not isolated from any product making such a claim.
  - d. All diets contained less than 1.8 X 10^5 CFU/g.

## Dosing probiotics required for a clinical effect will vary:

- species of organism
- species of host
- clinical condition

## Beagles fed L. rhamnosus at 4 different doses (Weese 2002)

- Colonization occurred only at the highest level 5 X 10^11 CFU per day
- Considerably higher than that required in humans.

Probiotic safety: Sepsis in humans due to probiotic bacteria administered orally has been described. Review found 23 probiotic species of Lactobacillus involved in 89 severely ill humans with lactobacillus bacteremia. (Salminen 2004, Land 2005)

## Predisposing factors to consider in Vet Med

- Immunosuppression
- Lost of mucosal layer Parvo
- Short bowel
- Neonates

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## Clinical studies - Some of the best documented benefits of probiotic use is the management of diarrheas

- ~ 20 yrs in people: rotavirus-induced and C. difficile related diarrheas (Quigley 2012)
- ~5 yrs in pigs, dogs and cats

## Diarrhea in a colony of kittens (Czarnecki-Maulden 2007)

- Design: 31 kittens (8 -14 wks) fed same dry kitten diet and in the same environment. Half were fed E. faecium SF68 probiotic for 1 yr. At 3 months; an outbreak of naturally occurring diarrhea in the colony.
- Results: Only 9.5% of probiotic treated kittens vs. 60% in control required medical treatment for symptoms. Resolution time in probiotic fed kittens was 18 d vs. 45 d in controls (p<0.05).

## Cytokine expression in ex vivo culture of canine IBD cells (Sauter 2005)

- Design: Biopsies from 12 IBD vs. 4 healthy dogs were cultured with probiotics of canine origin
  - o 3 lactobacilli spp
  - mix colony
  - neg controls

- Results: Assayed cell culture for 7 different cytokines
  - Increase in anti-inflammatory cytokines (p<0.05)
  - Decrease of pro-inflammatory cytokines (p < 0.05)

## Does feeding the same diet yield the same microbiome? (Spencer et al 2011)

- Design: 15 women were fed the same diet in a control hospital situation for 62 days [10 days for a base line, 42 days experimental choline deficient diet,10 days experimental choline repletion diet].
- Fecal samples were collected 6 times. PCR amplified the V1-V2 regions of 16S ribosome -> operational taxonomic units (OTUs).
- Results: Does feeding the same diet yield the same microbiome? .... No. The diet did change the microbiome within each person but no two people had a similar microbiome composition).

## Probiotics and companion animals - Can we use human probiotic products in dogs and cats?

- Dog and cats have higher numbers of bacteria in the proximal GI tract than people
- Cat feces contain higher numbers of anaerobes considered abnormal in dogs and people
- Can human strains colonize animal GI tract?
- Probably not due to different strains within a species
- Dosing some preliminary data available

#### In my opinion

- 1. Probiotics have potential but not yet realized because of too many variables
- 2. Microbiome in each individual is so distinct could be used as fingerprinting in people so how can we effectively change the unknown canine or feline microbiome ... in a diseases process?
- 3. Best results to date occur in stress related diarrheas.
  - a. Dog and Cat best studies in shelters/colony -> stress
- 4. Rarely harmful except in immunosuppressed patients

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