Probiotics, Prebiotics & Synbiotics: Good Bacteria?

Stacie L Penkova, PharmD, MHSA, BCPS
Acclaim Pharmacy Benefits Manager | Connected Care Partners Project Manager
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Disclosures

- I, Stacie L. Penkova, PharmD, MHSA, BCPS, do not have a financial interest/arrangement or affiliation with one or more organizations that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation.

- Special thanks to Hillary Hardwick for assisting me in compiling and condensing the material for this and my other presentations you will see today.
Objectives
Definitions

- **Probiotics** - a usually dairy food or a dietary supplement containing live bacteria that replace or add to the beneficial bacteria normally present in the gastrointestinal tract.

- **Prebiotics** - natural substances in some foods that encourage the growth of healthy bacteria in the gut.

- **Synbiotics** - synergistic combinations of pro- and prebiotics.

- **CFUs** - stands for colony forming unit and is the way probiotics are measured.
Definitions

- **Genus, Species & Strain** - The genus is the first word in a bacterium’s name; it’s the large group to which the bacteria belongs. The species is the type of individual bacteria. Some bacteria have several strains, or differentiations of the species, and this is identified by the last part of the name. Here is an example:
  - *Lactobacillus acidophilus DDS1*
  - *Lactobacillus* is the genus, *acidophilus* is the species; and *DDS1* is the strain

- **Dysbiosis**: This is the medical term for when the good and bad bacteria in your body get out of balance.
Gut Microflora

- The human gut is dominated by several bacterial phyla including Bacteroidetes, Firmicutes, and Actinobacteria.

- The term “microbiota,” “microflora,” or “normal flora” is used to designate this vast host of microbes which coexist with the host.

- It is estimated that the human microbiota contains as many as 10^{14} bacterial cells, a number that is 10 times greater than the number of human cells present in our bodies.

- Virtually every surface of the human body starting from the skin surface to the genitourinary tract, oral cavity, respiratory tract, ear, and the gastrointestinal tract is colonized heavily by various species of bacteria.
“the microbiota can be viewed as a metabolic organ exquisitely tuned to our physiology that performs function we have not had to evolve on our own”

Backhed et al. 2004. PNAS 101:15718-15723

Figure 1: The Human Body and number of bacteria present in the total microflora.
Actions of the GI Tract

- The human gastrointestinal environment, including the microflora, has a significant role in the health of its host.

- The gut microflora, which includes both potentially beneficial and potentially harmful bacteria, is important in maintaining a healthy intestinal tract and helps the intestine act as an effective barrier; allowing nutrients to be absorbed, and keeping out toxins and pathogens (foreign bacteria or viruses).

- The gut microflora breaks down vitamins and also ferments fibers and carbohydrates that are not digested in the upper GI tract.

- This breakdown produces fatty acids that are important for supporting a healthy intestinal barrier (particularly in the lower GI tract) and also inhibits the growth of harmful bacteria.
Actions of Probiotics in the GI Tract

- Consumption of probiotics, particularly certain species of Bifidobacteria and Lactobacilli, can help “balance” the flora, increasing the number of helpful, and reducing (inhibiting the growth of) harmful bacteria, in the intestine.

- Consumption of probiotics can also modify the gut immune response and improve its barrier function. For example, specific probiotic species can shorten or reduce the risk of certain infections, particularly those of the GI tract, such as intestinal viruses.

- More recently, probiotics have also been shown to modulate/adjust the activity of the immune system, helping to control or reduce the development of certain allergies.
Actions of Prebiotics in the GI Tract

- The principal characteristic and effect of prebiotics in the diet is to promote the growth and proliferation of beneficial bacteria in the intestinal tract, and thus, potentially yield or enhance the effect of probiotic bacteria.

- Prebiotics have also been shown to increase the absorption of certain minerals (such as calcium and magnesium).

- Prebiotics may also help inhibit the growth of lesions, such as adenomas and carcinomas in the gut, and thus reduce the risk factors involved in colorectal diseases.
Figure 3: Diseases influenced by gut microbial metabolism. The variety of systemic diseases that are directly influenced by gut microbial metabolism and its influence on other mammalian pathways, such as the innate immune system, are shown. Specifically highlighted are the metabolic pathways involved in drug metabolism and obesity that are directly influenced by the gut microbial content. Ags, antigenic C. difficile, Clostridium difficile DGS, dendritic cells; SCFA, short-chain fatty acids; TLR, toll-like receptor. Kimross et al. Genome Medicine 2013 3:14.
Clinical Applications of Various Probiotics, Prebiotics and Synbiotics

- **Antibiotic-Associated Diarrhea** - Many probiotics have been studied for antibiotic-associated diarrhea. Taking a probiotic is thought to replenish the normal, healthy bacteria and therefore prevent over-colonization of pathogenic bacteria.

- **Clostridium difficile** - Overall, research suggests that probiotics are helpful for reducing the risk of Clostridium difficile infection in patients taking antibiotics. In analyses, taking a probiotic along with a course of antibiotics reduces the risk of Clostridium difficile by 66% to 71%.

- **Irritable Bowel Syndrome** - Overall, probiotics seem to moderately improve symptoms of IBS. In one analysis, probiotics significantly reduced overall symptom occurrence by 23%. They reduced the risk of abdominal pain by about 22%.
Clinical Applications of Various Probiotics, Prebiotics and Synbiotics

- **Necrotizing Enterocolitis** - Overall, probiotics appear to reduce the risk of NEC by 65%. Probiotic treatment also significantly reduces all-cause mortality by 58% to 60% and NEC-related morality by 69%.

- **Respiratory Infections** - Overall, probiotics significantly reduced the odds of a respiratory tract infection in infants, children, and adults by about 42%. They also decreased the odds of multiple (3+) infections by 47%.

- **Rotaviral Diarrhea** - A specific strain of *Lactobacillus rhamnosus*, *Lactobacillus GG* (Culturelle), can reduce the duration of the diarrheal phase of rotavirus infection by 1-3 days in infants and young children. *Lactobacillus reuteri* also seems to reduce the duration of acute diarrhea (mostly rotavirus) in hospitalized infants and young children. *Lactobacillus casei* also seems to shorten the course of acute diarrhea in infants and young children.
Clinical Applications of Various Probiotics, Prebiotics and Synbiotics

- **Vaginal Candidiasis (Yeast Infection)** - does not seem to reduce the risk of vaginal candidiasis infection following use of antibiotics

- **Ventilator-Associated Pneumonia** - studies have not found a significant benefit of probiotics in this population
Clinical Applications of Various Probiotics, Prebiotics and Synbiotics

- Gut Microbiota and Obesity - The metabolic equilibrium of the host is maintained by the gut microbes.

- Allergy and Atopic Diseases of Children - Atopic diseases arise from aberrant immune responses to environmental allergens leading to allergic inflammation. Children suffering from AD have higher number of S. aureus and Clostridium in their colon and lower number of Enterococcus, Bifidobacterium, and Bacteroides.

- Hepatic Encephalopathy - The exact pathogenesis of hepatic encephalopathy is still unknown, and the basis for it is still not completely understood; however it is widely agreed that gut-derived-nitrogenous substances and, specifically, ammonia derived primarily from enteric bacteria play a central role.
Clinical Applications of Various Probiotics, Prebiotics and Synbiotics

- **Hypocholesterolemic and Cardioprotective Effects** - Many Lactobacilli, being the natural inhabitants of the intestine, possess bile-salt hydrolase activity. This property has been used for developing probiotic formulations to combat hypercholesterolemia.

- **Cancer Prevention** - As early as 1995, in a controlled, double blind study, with 138 patients a L. casei Shirota preparation was shown to have a preventive effect on the recurrence rate of superficial bladder cancer after surgery.

- **Probiotics and Renal Health** - It has been demonstrated that gut microflora can affect the concentrations of uremic toxins in animals.
Table 1: Properties of an ideal prebiotic (Swennen et al. 2006)

<table>
<thead>
<tr>
<th>Desirable attributes</th>
<th>Properties of oligosaccharides</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active at low dosage</td>
<td>Selectively and efficiently metabolized by <em>Bifidobacterium</em> and/or <em>Lactobacillus</em> sp.</td>
</tr>
<tr>
<td>Lack of side effects</td>
<td>Selectively and efficiently metabolized by beneficial bacteria without producing gas.</td>
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<tr>
<td>Persistence through the colon</td>
<td>Preferably high molecular weight</td>
</tr>
<tr>
<td>Varying viscosity</td>
<td>Available in different molecular weights and linkages</td>
</tr>
<tr>
<td>Acceptable storage and processing stability</td>
<td>Possess 1–6 linkages and pyranosyl sugar rings</td>
</tr>
<tr>
<td>Ability to control microflora modulation</td>
<td>Selectively metabolized by restricted microbial species.</td>
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<tr>
<td>Varying sweetness</td>
<td>Varying monosaccharide composition</td>
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Future Emerging Areas for Probiotic Research

- Myocardial Infarction. Intestinal microbiota has also been shown to promote cardiovascular disease, specifically atherosclerosis, by their catabolism of choline.

- Gut-Brain and Behavior. Exactly how the microbiota influence brain behavior is still unknown but an explanation could involve immune-mediated neural or humeral mechanisms.

- Familial Mediterranean Fever. The first genetic disease to be linked to changes in healthy gut flora is Familial Mediterranean fever (FMF). FMF provides evidence that host genotype can dictate the establishment and composition of the intestinal flora.
Future Emerging Areas for Probiotic Research

- Autism. Very little is known about the underlying etiology of autism. Extensive antibiotic use is commonly associated with late-onset autism (18–24 months of age), causing some to hypothesize that disruptions in the normal microbiota may allow colonization by autism-triggering microorganism(s), or promote the overgrowth of neurotoxin-producing bacteria like *Clostridium tetani*. 
spenkova@nmhs.net