Clinical Advantages to Restoring Gut Health
By Kimberly Lord Stewart

The future of personalized medicine may lie in the gut. Research shows that changes in human gastrointestinal flora can be manipulated with complimentary probiotics and synergistic prebiotics to promote wellness and health.

Biology used to characterize immunity as white blood cells and lymphocytes, but we now know that the intestine contains more immune cells than our entire body. Since the human microbiota genome is 150 times larger than the human genome, determining the exact cocktail of symbiotics necessary to maintain health is the challenge. And furthermore, the manner in which these microbes work synergistically with the human gut, better known as crosstalk, is only just being explored.

Microflora an Evolving Field of Medicine

The research is evolving at such a pace that many physicians are not yet aware of how to implement this new field of medicine. The intestines have long been ignored, and the recent findings challenge one’s previously conceived perceptions of how the human gut affects health.

A 2010 survey of 37 physicians, who specialize in gastroenterology, shows that most believe:

1. probiotics are 100% safe
2. 98% believe that probiotics play a role in treating gastrointestinal conditions and, 3. 93% of their patients take probiotics
3. Yet in this study, most believe the scientific evidence surrounding probiotics is not yet scientifically validated.

Since this survey was released the pace of new knowledge is rapidly changing. The science of probiotics is evolving into a major cornerstone of health and wellness and how body systems interact.

There is wider agreement on the role of commensal bacteria for nutritive, immune-modulating, and metabolic contributions to health. Research continues to show that if the commensal community is carefully balanced, humans from birth to aging will lead a healthier life. If disrupted, the body enters a state of dysbiosis. This occurs largely from host inflammation, which is caused and aggravated by microbial dysbiosis. This in turn, increases vulnerability to pathogens.

Microbiome Primer

The term probiotics, introduced in 1965 by Lilly and Stillwell, were defined as the antithesis of antibiotics, as microbially derived factors that stimulate the growth of other organisms. Since then, the following definitions have universal acceptance:

Probiotics. Live microorganisms which, when administered in adequate amounts, confer a health benefit on the host.

Prebiotics. Nondigestible substances that provide a beneficial physiological effect for the host by selectively stimulating the favorable growth or activity of a limited number of indigenous bacteria. Prebiotics are a special form of fiber that nourish good bacteria in the gut.

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Synbiotics. Products that contain both probiotics and prebiotics.

Probiotics

For the purpose of improving health, probiotics must be able to be prepared on a large scale using organisms that are generally recognized as safe. They must remain viable and stable during storage. And then when administered, the probiotic must survive the intestinal tract and show positive benefits.

The International Scientific Association for Probiotics and Prebiotics (ISAPP) says a probiotic must:

- Be alive when administered
- Have undergone controlled evaluation to document benefits in the target host
- Be a taxonomically defined microbe or combination of microbes (genus, species and strain level)
- Be safe for its intended use

The advantages to using probiotic therapy in your practice include:

1. Reasonable cost
2. Little concern about antibiotic resistance
3. Multiple inhibitor mechanisms, which reduces the chances of pathogens developing resistance
4. Colonization is relatively fast
5. Well tolerated and safe
6. Few if any adverse effects
7. Restorative effects from antibiotics therapies

Identifying probiotic strains

Probiotics are identified on a label in this order, genus, species and strain. In addition, the number of colony forming units (CFU) is a measure of the living and active bacteria that is capable of surviving in normal circumstances per each unit of measurement (CFU/g or ml).

The most common genus includes Bacillus, Bifidobacterium, Lactobacillus, Saccharomyces and Streptococcus.

The genus is typically italicized, for instance Lactobacillus acidophilus strain A, Lactobacillus acidophilus A or L. acidophilus A. However since the genus is often abbreviated, the letter can stand for any number of genus. In the example, an L can mean Lactobacillus or Lactococcus or Listeria.

The genome in a genus that includes core genes, from which every species in that genome is derived. Probiotics from the same genus have similar properties but do not act identically. The genes vary for every species and strain. It is the variance in strain that defines the health properties and the targeted condition or symptom. To find the right probiotic, one must identify the correct strain. In some cases, the manufacturer does not list the specific strain on the package. You may need to contact them directly. It is also important to seek out a probiotic that contains multiple, non-competing strains. The benefits of each strain are unique and cannot be extrapolated and applied to all desired health outcomes. One study review showed that multistrain probiotics showed greater efficacy than single strains. It is not yet clear whether this a result of synergistic interactions between strains or due to the higher probiotic dose.  

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Enterotypes

The ability to catalog microbial species associated with desired health outcomes various diseases is improving thanks to sequencing technology. The challenge now is to define the biomarkers. Initiatives in Europe (MetaHIT Consortium) and the US (Human Microbiome Projects) are ongoing to characterize human microbes, assess their genomes and appraise their role in health and disease.

This process to identify microbiomes has begun by identifying enterotypes that stratify human individuals based on their gut microbiome. They are identified by the abundance of different microbial groups in the individual. In 2011, *Journal Nature* presented evidence of three robust enterotypes that are not defined by age, gender, body weight, or nationality. Every indicator says that long-term diet influences enterotype.

These three enterotypes include: Type 1, characterized by high levels of Bacteriodes; Type 2 includes high levels of Prevotella (with some Bacteriodes) and Type 3 has high levels of Ruminococcus.

“The enterotypes are mostly driven by species composition but abundant molecular functions are not necessarily provided by abundant species, highlighting the importance of a functional analysis to understand microbial communities. Although individual host properties such as body mass index, age, or gender cannot explain the observed enterotypes, data-driven marker genes or functional modules can be identified for each of these host properties. For example, twelve genes significantly correlate with age and three functional modules with the body mass index, hinting at a diagnostic potential of microbial markers.”

<table>
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<tr>
<th>Disease</th>
<th>Probiotic Culture</th>
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How Microbiota Populate

Infants are born with sterile intestinal tracts, colonization occurs immediately after birth, resulting in dramatic changes in microbiota composition within a few days of birth. Babies born by caesarean section have lower numbers of bifidobacteria and Bacteroides than babies born vaginally. Colonizing microbes can be transmitted horizontally (from surroundings and diet), vertically from the mother to the baby, and each individual may have a unique metagenomic genotype.

Gut microbiota also changes later in life, as a result of age, family or community, disease states, diet, antibiotic use, and geographic location. Elderly in long-term care have significantly less diverse microbiota than that of elderly living in a close-knit community. The loss of community-associated microbiota is correlated with increased frailty.

Diet is proving to be a major factor in how microbiota interact and influence disease. “In adults, diets that have a high proportion of fruit and vegetables and a low consumption of meat are associated with a highly diverse microbiota and are defined by a greater abundance of Prevotella compared to Bacteroides, while the reverse is associated with a diet that contains a low proportion of plant-based foods,” according to a study in Nutrients 2013. Furthermore, it is becoming increasingly clear that the effect of the microbial ecology of the gut goes beyond the local gut immune system and is implicated in immune-related disorders, such as IBS, diabetes and inflammatory aging.

Probiotics: The Healthy Bacteria

The general view of probiotics early in the research led many to believe that probiotics prevented the influx of pathogens, however the latest research shows that probiotics are actively involved in the maintenance of healthy bacteria. Regulation by immune T cells of immunoglobulin A (IgA), an antibody responsible for immunity in the gut, is vital for the maintenance of healthy bacterial communities.

Research shows that the immune system “sees” and responds accordingly to different bacterial communities. A balanced community identifies with itself and induces a swift maturation of the immune system and gut responses through the induction of regulatory T cells and IgA.

“In a healthy person, these microbes in the gut stimulate the immune system as needed, and it in turn talks back,” says Dr. Natalia Shulzhenko, author of the study in Clinical Reviews in Allergy and Immunology. “There’s an increasing disruption of these microbes from modern lifestyle including poor diet, overuse of antibiotics and others,” she says. With each disruption, the conversation breaks down. A poorly functioning bacteria community does not identify with itself and instead tries to eliminate T cells with inflammatory properties and Immunoglobulin G (IgG) and/or Immunoglobulin E (IgE) responses.

This latest understanding of how probiotics function and communicate is leading to a greater understanding of how probiotics can provide therapeutic use. There are three current beliefs in how probiotics affect the body:

1. Probiotic microorganisms act directly within the GI tract through direct interaction with the intestinal microbiota or by enzymatic activities.

2. Probiotic microorganisms interact directly with the intestinal mucus layer and epithelium thereby influencing the intestinal barrier function and the mucosal immune system.

3. Probiotic microorganisms can have effects outside the GI tract such as on the systemic immune system and other organs.

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Clinical Uses for Probiotics
The key to reestablishing a healthy microbe state is to provide probiotics and/or fecal transplantation, as well as correcting the faults in the immune system that are inherited or environmentally disrupted. Multiple strains are proven to be more useful than single strains.

The volume of research on probiotics exceeds the capacity of this article, however, the referenced review in the TABLE above offer the most significant trials that identify specific strains^{17}.

Conclusion
As research continues to look at the role of diversity, composition, and metabolic potential of microbiota in relation to health, diet and lifestyle, they will no doubt play a more significant role in health and disease prevention. It is believed that a greater understanding will evolve in how diet, lifestyle and health are influenced by microbiota and how to positively influence healthy bacteria throughout life.

References:

8. M Arumugam, ibid.
17. S Sakar, ibid.

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