THE IMPORTANCE OF TAKING DIGESTIVE+++

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The Science of Microbiology has expanded over the last several years with new discoveries that relate to the health of the gastrointestinal tract. These are published in Nature magazine and other journal articles. They offer profound knowledge that helps us to understand the medical and ecological importance of keeping our digestive tracts in optimal health

The International Association for Probiotics and Prebiotics (ISAPP) defines probiotic bacteria, as "live microorganisms which when administered in adequate amounts confer a health benefit on the host." Dietary prebiotics are "selectively fermented dietary ingredients that result in specific changes, in the consumption and/or activity of the gastrointestinal microbiota, thus conferring benefit(s) upon host health."

For the digestive tract to function optimally, it also requires the ability to break down nutrients into their simplest chemical forms in order for the body to properly absorb them. The goal of digestion through the stomach and intestines is to convert the food into its simplest chemical structure so that it is ready for absorption across the intestinal barrier. If food is not digested properly it can irritate the intestinal lining and cause other problems in the digestive tract.

Six important concepts have evolved over the last decade concerning the importance and value of pre- and probiotics, digestive enzymes and the microbiology of the human body. They are: 1. The human body is a macrocosm composed of both human and microbial partners. 2. The new science called Neurogastroenterology teaches us about GI health in relation to Brain Function. 3. The Enteric Nervous System is a large network of nerves that controls GI tract functions and influences the brain. 4. Studies indicate probiotic supplementation may help reduce the negative thoughts associated with a sad mood. 5. Probiotics have been found to affect the gut-brain-skin axis, showing that these three organs are tied together. 6. As we age, the pancreas is less effective at secreting enzymes or insulin, resulting in decreased efficiency in absorption. Adding supplemental enzymes may be an effective means of helping the full digestion processes.

The Human Body is a Macrocosm (a human ecosystem)

Traditions established years ago and clinical observations in humans showed that taking fermented or live cultures of safe strains of microbes from foods or dietary supplements seem to infer a level of gut health promoting digestion, balanced elimination, energy, possible immune support (less prone to possible infections and allergy reactions) and possible benefits to mood and memory.

Microbiologists, Computer and Genomic Scientists and Biochemists have collectively become so interested about preliminary data on the health benefits of probiotics (good intestinal microbes) that they wish to delve deeper into the science of the symbiotic union that occurs between humans and their microbes. A project called the internationa **Human Microbiome Project (HMP)** is being launched in the USA, European Union and Asia. It reflects the fact that we are human supraorganisms composed of human and microbial constituents.

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The microbes that live inside and on us outnumber our body cells by an estimated tenfold. Over time our microbial symbionts provided us with traits we have not had to evolve on our own.[1]

HMP will address some of the most inspiring, vexing and fundamental questions in 21st century science. Importantly, it promises to break down the artificial barriers between medical and environmental microbiology. The hope is that in addition to providing new ways for defining health and disease predilection, HMP will provide us with the parameters needed to design, implement and monitor strategies for intentionally manipulating our microbiota so as to optimize its performance in the context of an individual's physiology.[1]

The **Microbiome Project** is undertaken to understand the microbes (including their genes) that coexist with humans and can provide benefits.1 As more information is uncovered we will see more applications to the "tailoring" of human associated microbial communities and how they can have positive effects for health. Physiologic features such as the development of innate and adaptive immunity, relative susceptibilities to infections, immune tolerance, bioavailability of nutrients and intestinal barrier function may be modified by changing the composition and functions of the microbial communities that we ingest.[2]

The study objectives are based on the premise that each individual is a macrocosm similar to an ecosystem. Ecologists study ecosystems of forests, deserts, oceans, grasslands and mountainous regions. They take into account the formation of symbiotic and mutual (beneficial) relationships, parasitic (harmful) relationships, natural predators, vegetation, and climate and how these are balanced. When manipulated or altered via changes, such as severe weather (drought, fires, hurricanes, or floods) then that ecosystem shifts. It also can be changed beneficially with good climate and rain. Dormant seeds may propagate and new vegetation may spur new animals to inhabit the local. Depending on these environmental factors, the system will change. The same is true for the human body. Each individual is composed of a microbial ecosystem. It is now recognized how important this microbial ecosystem may be to our health.

From our biological mother, we inherit our microbes. Our intestinal microbes will be similar to hers based on our close association of biological dependence and sharing the same body for a while. Over time as we grow into adults, our macrocosm will change based on diet, exposures, where we live, our genetics, our lifestyle and cultural behaviors. Human trials have shown the effects of prebiotics and probiotics on improving gut health, supporting immune responses, and helping to maintain general health.[3,4]

A New Science, Neurogastroenterology, teaches us about GI health and Brain Function

Although it is a relatively new science, there is much interest and some preliminary research that shows how important the health of the digestive tract may be to the functioning of the brain. The scientific field is called Neurogastroenterology and it regards the interactions of the central nervous system (CNS) and the gut. Scientists call this the **"brain-gut axis."** The brain-gut axis is a two-way communication system and includes the CNS which is composed of the brain, the spinal cord, and the enteric nervous system, composed of nerves, hormones and other molecules such as neuropeptides and cytokines.[2] The roles of the brain-gut axis are to mediate environmental effects such as hunger, stress and emotions on gut functions. Stress and emotions may be reflected by changes in gut-physiology and gut symptoms.[2]

The gut harbors the largest collection of our microbial partners. Research studies and results have continually

supported the idea that eating well designed pro- and pre-biotics alters the ecosystem of the gut in a healthy way. If good microbes are being introduced into the digestive system, then the growth of unhealthy microbes, yeasts and unhealthy levels of harmful bacteria may be reduced. This is called "competitive inhibition" in other microbial scenarios. The pre-biotic also provides ideal nourishment for the good microbes to survive. Good microbes in turn will have qualities that may optimize the pH of the GI tract and manufacture some vitamins and co-factors important for the GI ecosystem.

A growing body of evidence suggests that microbial dysbiosis (overgrowth of unfriendly microbes or imbalance in the gut flora) is associated with gastrointestinal and metabolic disorders.[2] It is now hypothesized that this may result in unregulated neuro-immune functions impacting behavior.[2] When harmful microbes (pathogens) inhabit the intestinal tract they secrete toxins and damaging by-products. If you have ever had traveler's diarrhea or eaten a spoiled food, you may recollect that you may have also felt bad in other ways (grumpy, moody, sad, depressed, or anxious).

The Enteric Nervous System, "the second brain"

Mood alterations may be due to the close association between the brain and gut. The Enteric Nervous System (ENS) often called "the second brain" is embedded within the wall of the digestive tract and extends between the esophagus and anus. It contains approximately 400 million neurons, more than any other peripheral organ and about the same number of neurons as the spinal cord.[2] It is a part of the peripheral nervous system and a division of the autonomic nervous system, which controls the function of the GI tract. The ENS controls GI motility, sensation, regulates fluid exchange, local blood flow, gastric and pancreatic secretion, GI endocrine functions, defense reactions and reflexes.[2]

Embedded within the wall of the GI tract, the ENS is protected from the toxic luminal content by the intestinal barrier. The functions of the barrier are to keep the harsh chemical reactions of the digestion process separate from the closely associated delicate nerves and tissues. When healthy, the barrier carefully allows only certain constituents and ions to pass over. Sometimes the GI tract becomes inflamed. If there is inflammation in the GI tract, studies have shown that this can create behavioral anxiety. Consuming pre- and probiotics has been shown to reduce GI inflammation in several studies and also reduced the consequential behavioral anxiety.[2]

When the gut is inhabited by unfriendly microbes, the individual can experience anxiety and depression as well as the discomfort of the actual imbalance. Microbes in the gastrointestinal (GI) tract exert numerous effects on the intestinal neuro-immune system and influence metabolic activity, immune response and physiological functions4. The gut microbiota composition and activity is subject to a variety of influences. It depends on each person's unique physiology, immunology, diet, antibiotic usage and internal infection.[4]

Studies Indicate Probiotic Supplementation May Help Reduce Negative Thoughts Associated with a Sad Mood

The oral consumption of probiotics and prebiotics have been studied in clinical trials showing they not only improve gastrointestinal function but also central, psychological symptoms.[1] In a triple blind, placebo-controlled randomized trial, 20 healthy participants without mood disorder received four weeks of a probiotic supplement versus 20 control subjects that received a placebo. Subjects were assessed using a depression sensitivity scale (revised Leiden index). The results showed that the group taking the probiotic supplement had a significantly reduced overall mental reactivity to a sad mood, largely due to less ruminating and aggressive

thoughts.[6] An additional study in mice showed that when a harmful bacteria was consumed, the mice became very anxious eight hours after the infection, which lasted up to a week or more. The harmful bacteria also produced a stress-induced memory dysfunction. When repeating the experiment, if the mice were given a daily administration of probiotics before the introduction of the harmful bacteria, they did not experience the memory dysfunction.[2]

Clinical trials have also indicated a role for the gut microbiota in pain perception and in reducing mild stomach pain in children and teenagers. Children stay home from school and parents miss substantial work days due to a high incidence of stomach "aches" during the school years. It is associated with worse quality of life and has a prevalence of about 8 percent in western countries. When 115 children aged 6-18 received either a prebiotic with probiotic or placebo, the group receiving the probiotic experienced less stomach pain.[2,5] If the flora of the GI tract is producing friendly bi-products rather than toxic ones and the barrier function of the gut is preserved, then nerves will relay balanced signals to the brain and other organs for proper functions such as hormone release, immune response and brain functions, which can have a direct effect for well being, positive mood and calming effects. This is a striking new area of scientific discovery.

Probiotics and the Gut-Brain-Skin Axis

Recurring skin breakouts (acne) is a common condition in developed nations and has increased in frequency in the last half century, particularly among adult women.[8] Acne has long been postulated to feature a gastrointestinal mechanism, dating back 80 years to dermatologists John H. Stokes and Donald Pillsbury (1930's). They hypothesized that emotional states such as depression and anxiety could alter normal intestinal microbiota, increase intestinal permeability and contribute to inflammation of different parts of the body including the skin.[8] Conversely, the link between dermatology and mental health is being further understood by rising evidence that the microbial residents of the intestinal tract may play a role in both skin inflammation and emotional behavior. The work of the dermatologists, Stokes and Pillsbury, lay dormant and unreferenced for eight decades, and was finally revisited only recently by Bowe and Logan in 2011. The historical disappearance of the work was almost certainly because it was published precisely at a time when researchers and clinicians were turning away from the "autointoxication" and "intestinal toxemia" theories that were dominating medical thinking at the time. The central tenet of intestinal toxemia was that gut-derived microbes and or microbial breakdown products (putrefactive substances) may play a role in general health, skin conditions and mental health in particular. Numerous studies have indicated an association that persons with acne frequently experience depression, anxiety, and other psychological ailments[8].

Stokes and Pillsbury's work attributed emotional states (depression, worry and anxiety) to altered gastrointestinal tract function and microbiota, which they theorized in turn promotes local and systemic inflammation. They offered an important linkage between emotional states and inflammatory skin conditions by way of the physiology and bacteriology of the gastrointestinal tract. The authors also suggested that stress induced alterations to microbial flora could increase intestinal permeability, thus setting the stage for systemic and local skin inflammation.[8] An investigation of over 13,000 adolescents showed that those with acne were more likely to experience gastrointestinal symptoms such as mild constipation, bad breath and gastric reflux. Abdominal bloating was 37 percent more likely to be associated with acne and other skin conditions.[8]

Although there are limited studies on oral consumption of probiotic supplements for acne in more recent times,

a study from Italy showed that 20 subjects with acne improved clinical symptoms when taking a probiotic supplement as compared to the group that did not receive the probiotic.[10] A Study from Russia showed faster achievement of significant clinical improvement of acne when taking a probiotic supplement along with standard care than those not receiving a probiotic.[11]

In conclusion, clinical research was limited over the last decades as to possible benefits of probiotic supplementation. Although some cultures, physicians and individuals observed and touted the benefits of probiotic administration, there was little documented research accomplished to test for these benefits. With greater professional, scientific and consumer interest in the use of probiotics, a revolution is taking place in the study of just how important probiotics may be to our health. We are learning that we live together with microbes and that positive manipulation of our individual macrocosm may benefit us in ways we did not heretofore understand. The health and look of our skin, the health and function of our digestive tract, our immunity, our brain functions and emotions are holistically tied together with the microbial environment of our GI tract.

The Need for more Enzymes to Ensure Proper Digestion as we Age

The Digestive tract is a very important organ for the optimal function of other organs. We have learned that the body's systems and organs are interconnected—if we take good care of one organ, it will support the good care of the others. We need to eat good food for our health, as well as for enjoyment!

Our body needs calories to function. We need a variety of foods so our bodies are supplied with the components they need. That is why we have been advised that a "well balanced diet" is best. Different categories of foods provide for various functions. We need this variety of food because all cells in the body will be replaced over time except for some brain and nerve tissues. Some organs such as skin and blood will be replaced in months. Others will take a decade but the body cells are in constant reconstruction to a degree and in constant biochemical motion, doing their functions and needing components to work. In order to rebuild and produce cellular energy, we need raw ingredients, proteins, fats, and carbohydrates. We need minerals—especially calcium as found in dairy products—for bone construction. Fatty acids will maintain strong cellular membranes and participate in other important functions.

We need protein to build muscle, skin and bone as this composes about 80 percent of our body mass. If we are athletic or very active we need more protein as continuous exercise damages muscle cells, which need rebuilding more quickly because they are very large cells. We need carbohydrates for energy in the form of the main energy molecule called ATP. This molecule and its derivatives will provide energy for hundreds of chemical reactions that go on in the cell. Fatty acids will help sustain nerves in the eye, brain, spinal chord and throughout the organs. We need to eat good foods to sustain and maintain our bodies.

Obviously our bodies cannot "use" a head of lettuce or a watermelon or a piece of fish as a whole. These need to be broken down into their simplest chemical forms. After consuming a meal as the food enters the stomach, the pancreas will make and secrete digestive enzymes that clip larger molecules into smaller and smaller ones. The goal of digestion through the stomach and intestines is to convert the food into its simplest chemical structure so it is ready for absorption across the intestinal barrier. The tiny blood vessels winding over the intestinal tract will receive the chemical nourishment and deliver it to the various organs throughout every inch of the body. If food is not digested properly, it can irritate the intestinal lining which may cause other

problems in the digestive tract.

The pancreas not only secretes digestive enzymes but it also is busy making and secreting insulin. It is a hardworking, chemical-producing organ or gland. In some situations and through the aging process, the pancreas is not as effective at secreting enzymes or insulin as it should be. As aging progresses, less absorption occurs. Adding enzymes can be very effective in helping the full digestion processes—proper elimination, less fermentation, helping with bloating and gas and easing gastrointestinal disorders.

Adding enzymes provided in the state-of-the-art DIGESTIVE+++ formula can support the digestive process of breaking down proteins, carbohydrates, and fats into their smallest and most available forms. This provides the nutrition to the cells that make up the body and supports all its activities.

DIGESTIVE+++ contains all the basic digestive enzymes necessary to ensure the proper digestion of foods. These include:

1. **Protease blends** - These provide proteolytic activity across a broad pH range that ensures that protein digestion occurs throughout the digestive tract, both in the stomach and through the small intestine.
2. **Peptidase** - Breaks down proteins by hydrolysis of peptide bonds.
3. **Carbohydrase Enzymes** break down various carbohydrates to simpler sugars
   a. **Amylase** breaks down starch.
   b. **Glucoamylase** (maltase) enzyme breaks down maltose and glucose oligomeres. In the small intestine it works in synergy with sucrose-isomaltase and alpha-amylase to digest the full range of dietary starches.
   c. **Diastase** breaks starch into maltose.
4. **Lactase** - An enzyme found in the small intestine of mammals that catalyzes the breakdown of lactose (milk sugar) into the simple sugars glucose and galactose. In humans, lactase is particularly abundant during infancy. It is produced by cells that line the intestinal walls. Mutations in the gene that encodes lactase may result in inherited lactase deficiency, which manifests as lactose intolerance, or the inability to digest lactose. Lactose that is not absorbed in the gastrointestinal tract undergoes fermentation by bacteria, resulting in the production of gas and intestinal distress.
5. **Alpha-galactosidase** is a glycoside hydrolase enzyme that hydrolyses the terminal alpha-galactosyl moieties from glycolipids and glycoproteins. Alpha-galactosidase helps prevent intestinal discomfort and flatulence
6. **Lipase** performs essential roles in the digestion, transport and processing of dietary lipids (e.g. triglycerides, fats, oils).
7. **Invertase** – Breaks down sucrose (table sugar) into fructose and glucose

LifePharm has been on the forefront of research on the benefits of pre- and probiotics as well as digestive enzymes. **DIGESTIVE+++** is designed specifically to assure a quality product that promotes good GI health.

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References:

1. Turnbaugh PJ, Ley RE, Hamady M, Fraser Liggett C, Knight R, Gordon JI. The human microbiome project: exploring the microbial part of ourselves in a changing world. *Nature* 2007 October 18;449 (7164) 804-810.
2. Saulner DM, Ringel Y, Heyman MB, Foster JA. Bercik P, Shulman RJ, et al. The intestinal microbiome, probiotics and prebiotics in neurogastroenterology. *Gut Microbes* 4:1,17-27. January/February 2013.
3. O'Hara AM, Shanahan F. Gut microbiota: mining for therapeutic potential. *Clin Gastroenterol Hepatol* 2007;5:274-84.
4. Preidis GA, Versalovic J. Targeting the Human Microbiome with Antibiotics, Probiotics, and Prebiotics: Gastroenterology Enters the Metagenomics Era, *Gastroenterology*, 2009 May;136(6):2015-2013.
5. Saneian, H, Pourmoghaddas Z, Roohafza H, Gholamrezaei A. Synbiotic containing Bacillus coagulans and fructo-oligosaccharides for functional abdominal pain in children, *Gastroenterology and Hepatology from Bed to Bench* 2015;8(1):56-65.
6. Steenbergen L, Sellaro R, van Hemert S, Bosch JA, Colzato LS. A randomized controlled trial to test the effect of multispecies probiotics on cognitive reactivity to sad mood. *Brain Behav Immun*, 2015 Apr 7pii: S0889-1591 (15) 00088-4.
7. Silverberg, N.B. and Weinberg JM. Rosacea and adult acne: a worldwide epidemic. *Cutis* 2001 68:86.
8. Bowe W, Patel NB, Logan AC. Acne vulgaris, probiotics and the gut-brain-skin axis: from anecdote to translational medicine. *Benef Microbes* 2014 Jun 1;5 (2):185-99.
9. Zhang H, Liao W, Chao W, Chen Q, Zeng H et al. Risk factors for sebaceous gland diseases and their relationship to gastrointestinal dysfunction in Han adolescents *Journal of Dermatology* 2009, 35 :555-561.
10. Marchetti F, Capizzi R and Tulli A. [Efficacy of regulators of the intestinal bacterial flora in the therapy of acne vulgaris]. *Clinica Terpeutica* 1987, 122:339-343.
11. Volkova LA, Khalif IL and Kabanova IN. [Impact of the impaired intestinal microflora on the course of acne vulgaris]. *Klinical Medicine* (Moscow) 2001, 79:39-41.