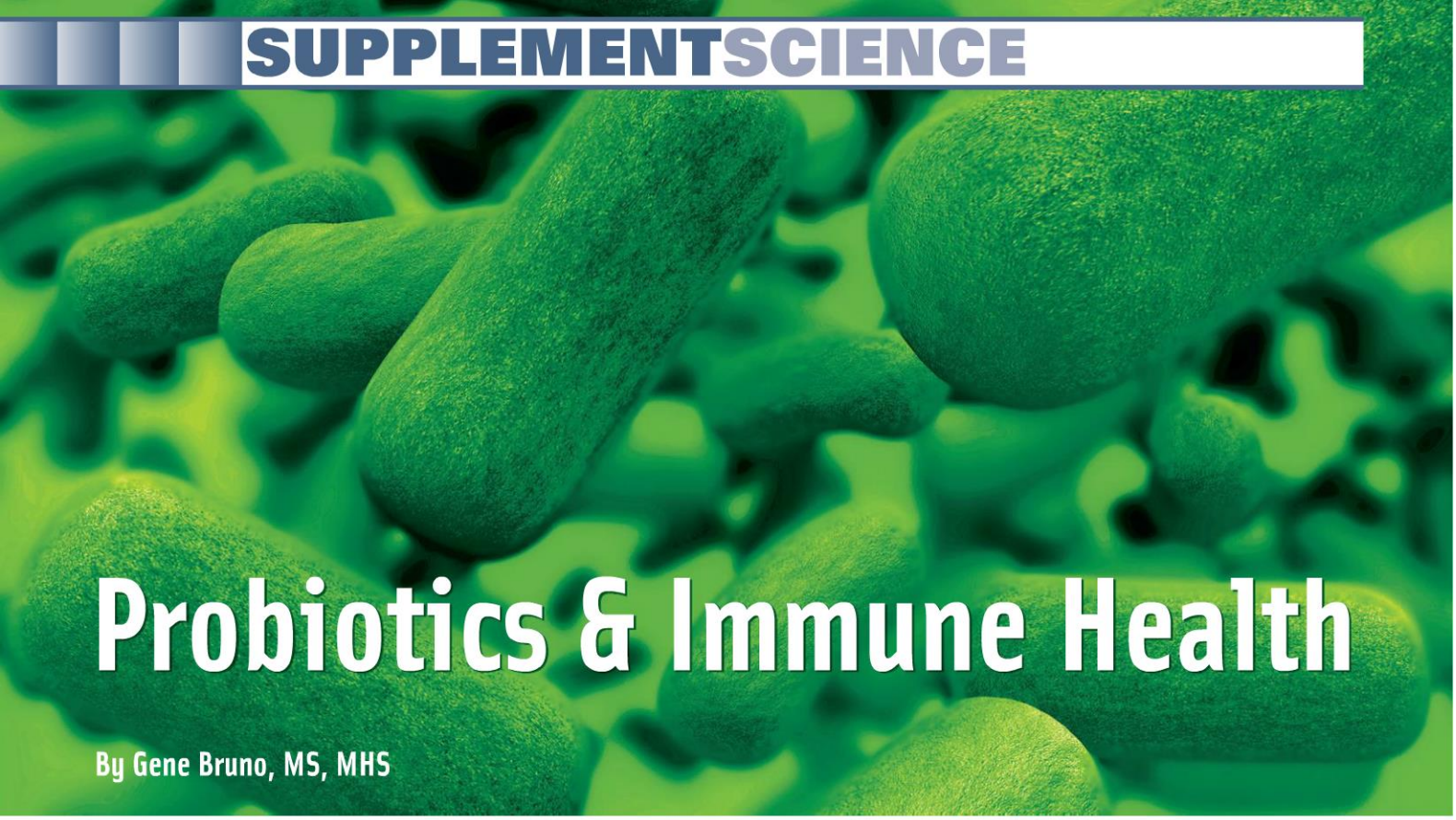

Probiotics & Immune Health

By Gene Bruno, MS, MHS

The Food and Agriculture Organization of the United Nations and the World Health Organization define probiotics as "live microorganisms which when administered in adequate amounts confer a health benefit on the host"[1] (aka, friendly bacteria). Since commercials began extolling the virtues of yogurt for immune health, there has been an increase in public awareness that one of those benefits has to do with the role that probiotics play in immunity.

Probiotic History

Ancient physicians in the Near and Middle East prescribed soured milk containing lactic acid bacteria (probiotics) to manage gastrointestinal health issues.[1] Élie Metchnikoff, a Russian physician, can be partially credited with contemporary interest in probiotics due to his theory that the growth of toxin-producing putrefactive organisms in the gastrointestinal tract could be controlled by the implantation of beneficial cultures in the gut.[2] Concurrently, the French pediatrician Henry Tissier suggested that "bifid" bacteria could be administered to patients with diarrhea to help restore a healthy gut flora.[3]

From these humble beginnings, the popularity of probiotic products has grown significantly, and now the global probiotics market is estimated to reach $31.2 billion in the U.S. this year—growing at a compound annual growth rate of 11.7 percent from 2009-14.[4]

Immunomodulation

The role that probiotics play in immunity varies as a function based on *where* they play the role. Specifically, probiotics may perform their immun-omodulating functions in the intestinal tract, or in and around the oral cavity. The benefits in each of these situations differ.

Intestinal Immunomodulation

Probiotics appear to help create a microbial barrier to infection within the intestine. Specifically, they produce antimicrobial substances that are effective against many harmful gram-positive and gram-negative bacteria.[5,6] Additionally, probiotics such as *Lactobacillus acidophilus* and *Bifidobacterium bifidum* have been shown to influence select aspects of immune function. Such altered function can involve one or several components of an immune response. For example, humoral immune responses (i.e. antibody-mediated) at the mucosal level involve secretory immunoglobulin (sIgA), which mediates immune exclusion of foreign antigens by preventing binding to the epithelial cells and penetration of micro-organisms.[7] Animal and human research has demonstrated that probiotics such as *L. acidophilus* enhanced sIgA production in a dose-dependent manner.[8] Animal research has also shown that probiotics increased the proliferation of spleno-cytes (any one of the different white blood cell types situated in the spleen).[9]

One of the most intriguing aspects of probiotic modulation of immune response is its effects on cytokine production. Cytokines are small proteins that are important in cell signaling, and their regulation of the immune system has been studied intensively.[10-12] Several studies have shown that cytokine production by cells of the immune system can be altered by probiotic use, including the use of *Bifidobacterium bifidum*.[10] In another study, human peripheral blood mononuclear cells (a type of white blood cell) were stimulated with *Lactobacillus* strains. All strains strongly induced interleukins (cytokines expressed by white blood cells).[12] In addition, probiotics have been shown to reverse the age-related decline in the production of cytokines.[13]

From a practical perspective, the use

of probiotics has been found to reduce cold and flu symptoms. In a double-blind, placebo-controlled study[14], subjects receiving *Lactobacillus* and *Bifidobacterium* strains for six months experienced significant reductions in the incidence of fever, coughing and runny nose compared to placebo.

Oral Cavity Immunomodulation

The bacterium *Streptococcus pyogenes* is the cause of some throat infections, including pharyngitis or "strep throat." In human research[15-17], subjects possessing naturally higher levels of certain strains of the oral bacterium *Streptococcus salivarius*, also referred to as bacteriocin-like inhibitory substances (BLIS), were shown to be significantly less likely to newly acquire *S. pyogenes*.

With regard to supplementation, human clinical research[18] demonstrated that prophylactic administration with 5 billion colony-forming units, or CFU (50 mg) of the *S. salivarius* K12 strain (BLIS K12) in adults having a history of recurrent oral streptococcal infections, reduced the number of episodes of streptococcal pharyngeal infections and/or tonsillitis. In this case, the probiotic was not swallowed, but rather provided as a slowly dissolved tablet held in the mouth. Similarly, a study[19] with children found that long-term administration of 5 billion CFU of BLIS K12 reduced the episodes of streptococcal pharyngeal infection by about 90 percent and/or acute otitis media (ear infection) by about 40 percent, calculated by comparing infection rates in the previous year. Other research[20] using 5 billion CFU of BLIS K12 showed that colonization extended beyond the oral cavity to also include the nasopharynx or adenoid tissue, which provides a basis for the positive results in otitis media, including a smaller study in which BLIS K12 reduced the occurrence of otitis media in children.[21]

While examining research on the BLIS K12 strain, it is worth noting that it has shown effectiveness against various species of bacteria involved in halitosis.[22] In fact, in human clinical research[23], the use of 4 billion CFU of BLIS K12 daily in lozenge form was effective in reducing volatile sulfur compound levels in 85 percent of halitosis subjects within one week of treatment, showing suppressed growth of halitosis-causing bacteria. Other research[24] with BLIS K12 showed similar results.

Dosage Forms & Potencies

It is important to use the correct probiotic dosage form for the desired benefit. Specifically, if the goal is throat and ear health, then 5 billion CFU (50 mg) of the BLIS K12 probiotic should be delivered as a lozenge or some other dosage form that will allow it to remain in the mouth for a sufficient period of time (e.g. a few minutes), so that colonization in the oral cavity can take place.

If, on the other hand, the goal is to promote immunomodulation within the intestinal tract, then the probiotic should be in a form that will withstand destruction by stomach acids. There are various delivery systems that will help to achieve this. These include enteric-coating[25], alginate coating[26], succinylated β-lactoglobulin coating[27] and BIOtract®. My personal favorite is BIOtract, a patented technology using a type of pectin that protects the majority of a supplement's probiotics from gastric acid, helping to ensure that a significantly higher percentage of microorganisms reach the intestines alive.[28] In laboratory research, data confirmed that the probiotics are afforded protection through acid exposure and continual release through the testing period in simulation of the passage through the human digestive tract.[29,30] Within the range of 5 to 10 billion cells or CFU is common, and higher doses of probiotics are not necessarily better unless a specific medical need is being addressed. A combination of *Lactobacillus* and *Bifidobacterium* species is preferred. **VR**

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