

IMMUNO-SYMBIOTIC = PROBIOTICS + PREBIOTICS

Dear Doctor,

Raise your hand if you knew that nearly ...

75% OF YOUR IMMUNE SYSTEM IS IN THE MUCOSA OF YOUR GI TRACT.

If you are like me, you have long been aware that the mucosal lining of the mouth, throat, esophagus, stomach, small intestine, and colon is fully equipped to serve as ...

YOUR FIRST LINE OF DEFENSE ...

against microbial pathogens. But only in the last few years have I come to appreciate the gut as ...

THE MASTER CONTROL CENTER OF THE IMMUNE SYSTEM:

- initiating the release or inhibition of pro-inflammatory cytokines
- initiating the release or inhibition of anti-inflammatory cytokines
- activating macrophages when the need is perceived
- triggering lymphocytosis when the need is perceived
- saturated with billions of mast cells, the most fundamental component of the innate immune response
- connecting the immune system to the nervous system as mast cells cluster around sympathetic and parasympathetic nerve endings in the gut wall
- shutting down its own motility and secretion in response to a catecholamine (Sympathetic, Glucogenic, Dysaerobic) stress response
- receiving parasympathetic (Adrenal corticoid, Anaerobic, Ketogenic) feedback provoked by the inflammatory cytokine Interleukin-2
- responding with an alarm reaction to the toxins produced by abnormal bacteria, fungi, yeast, or viruses in the GI tract --- triggering the release of the pro-inflammatory cytokines Interleukin-1 and Interleukin-2

So --- if the GI tract regulates the immune system, and the immune system is the keystone in ...

THE IMMUNONEUROENDOCRINE STRESS ...

that underlies all chronic disease and dysfunction --- then, how important is it to restore and maintain ideal gut mucosa structure and function? ----- Asking in other words, who needs to supplement with IMMUNO-SYNBIOTIC?

YOU DO.

--- And so does everyone in your family; and so do all your patients. We all need to go through one bottle of IMMUNO-SYNBIOTIC, 3, twice daily before meals, and should do so at least once every year to maintain INE control. All your patients ⇒

- with Eosinophilic Fungal Rhinosinusitis (as indicated by a non-sneezy boogey head)
- who have demonstrated a dualistic INE stress response as a vacillator-oscillator via NUTRI-SPEC Metabolic Balance Testing
- who show extreme INE stress in having one or more auto-immune diseases (Type I diabetes, Rheumatoid Arthritis, Lupus, Hashimoto's or Grave's Thyroiditis, alopecia, Reflex Sympathetic Dystrophy, Sjogren's, etc.)
- who have immune-related neurodegenerative diseases (Parkinson's, Multiple Sclerosis, ALS)
- who have chronic yeast/fungal infections (vaginal or oral Candida, athlete's foot or jock itch, ringworm, tinea versicolor, eczema/seborrheic dermatitis)

⇒ need IMMUNO-SYNBIOTIC 3, twice daily for one bottle, then 2, twice daily for one bottle, then at least 1, twice daily for a stronger, longer lifetime. ----- Patients with particularly nasty cases of the pathologies listed above will need more than 2 IMMUNO-SYNBIOTIC daily if they are to minimize their INE stress.

In our several month discussion of ImmunoNeuroEndocrine stress, and the introduction of your Doing FINE procedure to restore INE balance, we have mentioned many times the major clinical conditions that are entirely

expressions of an INE system caught in a raging storm --- chronic fatigue syndrome, fibromyalgia, major depressive disorder, post traumatic stress disorder, and multiple chemical sensitivities. Last month's Letter in particular showed the link between the INE stress of these conditions and the immune system activation associated with Eosinophilic Fungal Rhinosinusitis (EFR) --- an immune system in a swirling tizzy in reaction to fungal toxin exposure. We showed that almost all your patients with chronic fatigue and/or fibromyalgia have EFR, and that almost all EFR patients have some degree of chronic fatigue and/or fibromyalgia.

But in addition to mycotoxin exposure there is another chronic microbial exposure serving as an underlying cause in chronic fatigue syndrome and fibromyalgia, and that is the assault on the immune system that derives from the presence of abnormal yeast and fungi and bacteria in the gut. Research shows, for example, that those with chronic fatigue syndrome have a deficiency of normal flora in the colon, yet a bacterial overgrowth in the small intestine, and that that combination of abnormal flora increases pro-inflammatory cytokines --- with a particular Th2-dominant cytokine profile. Probiotic supplementation of chronic fatigue patients supports Th1-driven cellular immunity, and decreases the pro-inflammatory cytokines, while at the same time improving nutrient absorption, decreasing small intestine bacterial overgrowth, and decreasing oxidative stress systemically.

Research also shows that chronic fatigue syndrome patients suffer from leaky gut syndrome --- with increased translocation of lipopolysaccharide (endotoxin) from gram negative bacteria, causing gut-derived inflammation, and a resultant induction of systemic inflammation, along with oxidative and nitrosaline stress. In particular, the breakdown in intestinal mucosal function leads to elevated immunoglobulin A and immunoglobulin M reactions to endotoxin. (--- These are the patients who will respond beautifully to your IMMUNO-SYMBIOTIC if combined with glutamine supplementation.)

The entire gamut of chronic fatigue syndrome immune imbalances --- including elevated inflammatory cytokines, low natural killer cell function, high CD8+ cytotoxic lymphocytes, high CD38 and HLA-DR activation markers, high CD28+ T cells, and low CD11b expression, along with defects in T cell and natural killer cell activation associated with protein kinase C --- can all be of gastrointestinal origin.

I could go on and on and on quoting studies from the scientific literature showing that all the patients you see every day with chronic fatigue, fibromyalgia, depression, PTSD, and chemical sensitivities have aberrant GI function as a major cause of their conditions. So again --- who needs to supplement with IMMUNO-SYMBIOTIC? We all do. Who most desperately needs to supplement with IMMUNO-SYMBIOTIC? Your 1 in 6 patients with INE stress associated with Eosinophilic Fungal Rhinosinusitis (or the other

eosinophilic infiltration diseases such as asthma and eosinophilic esophagitis), all your patients with chronic fatigue, fibromyalgia, depression, PTSD, multiple chemical sensitivities, and all your patients with autoimmune diseases.

How can you be certain that IMMUNO-SYNBIOTIC will have a life-changing impact on your most severely ill patients? The scientific literature shows that without question there are 3 prebiotics and 2 probiotics that stand far above the rest in reducing INE stress. To appreciate the beneficial effects of these 5 ingredients of IMMUNO-SYNBIOTIC, you need to understand that all the structure and function of colon cells, as well as the link between the GI tract and the immune system, is tied in with the proper quantity and balance of ...

SHORT-CHAIN FATTY ACIDS.

Short-chain fatty acids (SCFA) are end-products of the anaerobic colonic bacterial fermentation of carbohydrates. There are 3 SCFA, acetate, propionate, and butyrate, that must exist in the healthy adult colon in the ratio 3:1:1, and play a vital role in maintenance of colon cell integrity and metabolism, and modulate immune system activation.

SCFA constitute two-thirds of the colonic anion concentration. What critical functions do they perform? SCFA:

- acidify the colon
- promote the growth of healthy colonic flora
- decrease solubility of bile acids, thus facilitating the elimination of secondary bile acids
- increase absorption of minerals (indirectly)
- decrease ammonia absorption by the protonic dissociation of ammonia and other toxic amines
- decrease cholesterol and triglycerides
- decrease the intensity of inflammatory responses in general, specifically decreasing inflammatory cytokines

While in adults the critical SCFA are acetate, propionate, and butyrate, in breast fed infants fecal SCFA consists mainly of acetate and lactate. Lactate (lactic acid) is an appropriate SCFA for infants, but not for adults. This distinction between healthy SCFA content of infants vs. adults is critical for you to understand --- and this fact can only be appreciated by NUTRI-SPEC practitioners. --- Adults should not have any more than tiny amounts of lactic acid in the GI tract. The main reason is because by far the most important and beneficial SCFA is butyrate, and lactic acid decreases butyrate production.

So, adults supplementing with the common probiotic *Lactobacillus acidophilus* produce non-physiological quantities of lactic acid, and do so at the expense of butyrate production. Not only does the lactate create an

undesirable intestinal environment, but the lactic acid is easily absorbed, and can be a metabolic stressor for certain patients (particularly those who have an Anaerobic Metabolic Imbalance).

As you are probably aware, *Lactobacillus acidophilus* has been the foundation of probiotic supplementation for decades. All the while alternative healthcare practitioners have been supplementing their patients with *Lactobacillus acidophilus* “to restore normal intestinal flora,” I have taken literally hundreds of patients off *Lactobacillus acidophilus* supplements --- again --- *L. acidophilus* not only creates a toxic environment in the intestinal tract, and causes absorption of toxic levels of lactic acid, but also has indirect damaging effects by decreasing the all-important SCFA butyrate.

Nothing --- absolutely nothing --- will increase the quantity of SCFA, and particularly increase the quantity of butyrate, more and faster than will the 3 prebiotics and 2 probiotics in your IMMUNO-SYMBIOTIC. Here is a concise description of the 3 SCFA you must restore in the GI tracts of your patients ...

Acetate: The acetate formed via colonic fermentation of undigested carbohydrates is readily absorbed from the colon. 50-70% of the absorbed acetate is taken up by the liver. The remainder goes to the peripheral circulation and is ultimately metabolized by peripheral tissues, particularly muscles, as an energy substrate. Acetate is a primary substrate for cholesterol synthesis needed for neuron and hormone anabolism.

Propionate: Like acetate, propionate is largely taken up by the liver. However, it plays an entirely different metabolic role than acetate. Propionate:

- decreases cholesterol synthesis but decreases cholesterol metabolism so that blood cholesterol increases; increases blood triglycerides
- decreases fatty acids in the liver and plasma
- increases insulin sensitivity
- decreases food intake
- is used for gluconeogenesis
- is immunosuppressive (which can be good or bad)
- has beneficial effects on inflammation, increasing the threshold for the inflammatory response in general

Butyrate: Butyrate in particular has trophic properties for both healthy and injured colonic epithelium.

Butyrate’s actions include:

- lipogenesis in colonocytes
- histone acetylation
- detoxification of xenobiotics

- mucus synthesis (--- depends upon butyrate metabolism (and to a lesser degree, upon propionate metabolism))
 - preventing the development of abnormal colonocytes (more efficiently than propionate and acetate)
 - enhancing growth of bifidobacteria and other normal flora
 - decreasing Interleukin 6, a pro-inflammatory cytokine associated with premature aging, fatigue, and altered sleep/wake cycles
 - increasing adiponectin, the adipocyte hormone that decreases body fat percentage
 - decreasing blood levels of free fatty acids
 - gluconeogenesis in the liver
- Deficiency of butyrate results in intestinal inflammation with elevation of many inflammatory cytokines.
 - Abnormalities in butyrate oxidation are involved in the pathogenesis of mucosal inflammation such as ulcerative colitis.
 - Butyrate protects against colon cancer.
 - Butyrate is not produced by the carbohydrate fermentation action of lactic acid bacteria. (Lactobacillus acidophilus is at best useless, and in many patients harmful.)
 - Butyrate protects against Type II diabetes and cardiovascular disease.

Give your patients A GOOD THYME to knock out the common chronic Candida colonization at the root of the tongue and in the esophagus, along with IMMUNO-SYMBIOTIC for total restoration of colonic function --- your powerful one-two punch against INE stress.

IMMUNO-SYMBIOTIC will have a life-changing impact on your most severely ill patients. It will also significantly improve the health of all your patients, as well as your health and that of your family. The scientific literature shows that without question there are 3 prebiotics and 2 probiotics that stand far above the rest in reducing ImmunoNeuroEndocrine stress. As you prepare to learn the beneficial effects of these 5 ingredients of your IMMUNO-SYMBIOTIC, you will first need to recognize that the 5 ingredients do not include ...

LACTOBACILLUS ACIDOPHILUS.

For more than 3 decades, I have been telling my patients to quit eating yogurt (and chiding doctors foolish enough to believe the health food industry propaganda about yogurt). I tell my patients if they want a sugar-laden dairy dessert they are better off eating ice cream than yogurt --- at least the ice cream will give them a little saturated fat to partly balance the gooey gobs of sugar it contains. The health food industry propaganda is so effective that no health nuts want to believe their sugary “health food” is more harmful than ice cream.

“OK!” --- My patients exclaim in their frustration over my harassment --- “I’ll switch to unsweetened yogurt so I can at least get the Lactobacillus acidophilus.”

“Sorry,” I reply, “But you will not be getting any acidophilus bacteria from your yogurt. It is virtually all dead long before you get it to your kitchen. All you will get is the excrement those little critters left behind --- a belly full of lactic acid.”

For nearly 25 years I have been telling all my patients (and any NUTRI-SPEC doctors who will listen) to quit supplementing with Lactobacillus acidophilus. The little bit of good that L. acidophilus does, is done far better by other probiotics, and there is significant harm for many patients in taking it. In last month’s Letter, I made the first “official” (better 25 years late than never) condemnation of L. acidophilus. ----- Wow! ----- After just a few days of our recent NUTRI-SPEC Letter hitting the mailboxes of NUTRI-SPEC practitioners, we were inundated with disparaging remarks from doctors outraged by our stance against Lactobacillus acidophilus. We stir up this kind of uproar every time we slaughter a health food industry sacred cow.

How did L. acidophilus gain icon status among health food store devotees and alternative healthcare practitioners alike? Its success story is easy to understand. Back in the 70s and early 80s, L. acidophilus was the first probiotic easy and inexpensive to produce commercially, and, it yielded some of the benefits its proponents were seeking. L. acidophilus was there in the infancy of our understanding the importance of the intestinal environment to good health.

It was not long before the inadequacies of L. acidophilus became apparent, but by that time the bandwagon was rolling at high speed, as health food nuts were gobbling up yogurt by the truckload, and every supplement peddler had an acidophilus product on the market. For patients with a rotten gut, and particularly for patients who had been on antibiotics, acidophilus, at least short-term, yielded a positive benefit to cost ratio. In other words, it was better than nothing, and there were not many economical alternatives available.

But now, the scientific literature clearly establishes that:

- a. Lactobacillus acidophilus is not a significant part of the normal intestinal flora of an adult human. (It is a significant, but still rather small part of the normal intestinal flora of an infant --- but by age 2 should be almost entirely absent.)
- b. The benefits of lactobacillus acidophilus so cherished by the health food faithful are minimal. Lactobacillus acidophilus will acidify the gut, which gives symptomatic relief to many with constipation. It will help chase

away the overgrowth of certain less than ideal bacteria that tend to populate the gut after antibiotic use. That's it. --- And --- there are several other probiotics (particularly the 2 that are in your IMMUNO-SYNBIOTIC) that confer these benefits far more effectively.)

- c. *Lactobacillus acidophilus* does survive the journey through the human gut. That was part of the reason for its early success. --- Studies demonstrated that *L. acidophilus* supplementation would dramatically increase its population in the colon, so it was celebrated as being "effective." But in so effectively (though temporarily) colonizing the colon, *L. acidophilus* crowds out the beneficial bacteria that produce the essential short chain fatty acids such as butyrate. Excess lactic acid production displaces the production of the more important acetate, propionate, and especially the all-important butyrate. As explained in last month's Letter, it is the SCFAs, particularly butyrate, derived from the presence of healthy intestinal flora, that is responsible for virtually all the benefits of probiotic supplementation. *L. acidophilus* supplementation leads to competitive inhibition of other flora that produce significantly more butyrate.

Lactobacillus acidophilus thus does not contribute significantly to the support of the immune system derived from healthy, natural intestinal flora. --- Remember --- 75% of your immune system is in the mucosa of your GI tract. If you want a tremendous immune system boost and a significant decrease of INE stress, you will get it from your IMMUNO-SYNBIOTIC --- you will not get it from *L. acidophilus* supplementation.

- d. In those with a compromised immune system, particularly those with immune deficiency, or in premature infants, or other children in poor health, *Lactobacillus acidophilus* can actually become pathogenic. For example, in infants and children in low socioeconomic groups, supplementing with *L. acidophilus* actually increases their incidence of lower respiratory tract infections.
- e. And who in the world wants lactic acid, anyway? Lactic acid is toxic. Your body goes to great lengths to eliminate lactic acid. Lactic acid will exacerbate Anaerobic Imbalances, any form of Acid Imbalance, and any form of Alkaline Imbalance. That means that more than half your patients who have Metabolic Imbalances will have at least their symptoms if not their fundamental metabolic state of imbalance exacerbated by the absorbed lactic acid created by *Lactobacillus acidophilus*. --- And, those harmful effects are from l-lactic acid. *Lactobacillus acidophilus*, in some people more than others, also produces d-lactic acid, which is extremely toxic. It is one of the nastiest intestinal-derived toxins in terms of demand placed on both the liver and the immune system.

So now, you've got me in a predicament. My intent is to devote this Letter to singing the praises of your IMMUNO-SYMBIOTIC --- enabling you to share in my celebration of this tremendous new product we have to offer our patients. But so many of you are, in righteous indignation, literally pleading, "Dr. Schenker, say it isn't so. --- We believe in Lactobacillus acidophilus. Your shining the light of truth on our health food dogma is too painful to endure!"

Since the whole point of NUTRI-SPEC is an understanding of objective reality as relates to clinical nutrition, I naturally respond to all these pleas with a promise to provide references from the scientific literature exposing the shortcomings of L. acidophilus. But humbug!!! I do not want to waste an entire issue of this Letter on the negatives of health food mythology, when I would rather be celebrating the positives of your NUTRI-SPEC products. --- So --- I am delivering on my promise, but if you want the several page write-up exposing L. acidophilus, you will have to read the version of this month's Letter on our website.

So now --- back to the celebration --- yet another expanded issue of this Letter singing the praises of a supplement you can find only at NUTRI-SPEC, and its role in your practice. Whether you are offering your patients NUTRI-SPEC Metabolic Balancing, or serving them with your newly revised, easy to use Diphasic Nutrition Plan, IMMUNO-SYMBIOTIC is about to carry you to a new level of clinical success.

If you wanted to pick just one bacterial probiotic to do everything you ever dreamed a bacterial probiotic could possibly do, which species would you choose? In other words, which bacterial probiotic would do all the things you want to believe Lactobacillus acidophilus does, but does not? The winner by a landslide in the bacterial probiotic competition is Lactobacillus reuteri.

Lactobacillus reuteri is the most effective of all the probiotic bacteria. Anything any other probiotic does, lactobacillus reuteri does better, and it demonstrates more profound effects on the immune system.

L. reuteri is one of a limited number of indigenous lactobacillus species occurring naturally in the human intestine.

L reuteri supplementation during late pregnancy reduces breast milk levels of TGF- β -2, and low levels of this cytokine are associated with less sensitization and possibly less IgE-associated eczema in breast-fed infants. The colostrum also contains slightly increased levels of IL-10.

L reuteri may be transferred to the newborn child during birth via vaginal transmission. L reuteri has been experimentally shown to be maternally

transmitted in humans. *L reuteri* is also present in low numbers in human milk, and thus transmission to infants might be facilitated during lactation.

L reuteri restores Th1/Th2 balance in infants with low Th1 and high Th2 accompanied by allergies, eczema or wheeze. [Th2 is highest at birth in all infants since the fetomaternal interface during gestation is surrounded by high Th2-like cytokines. --- Mothers with high IgE produce infants with particularly high neonate Th2, thus increasing the incidence in those infants of allergies and asthma in the first 6 years of life].

L reuteri improves symptoms of infant colic, with 95% of colicky infants responding positively to *L reuteri* supplementation with decreased daily crying times. It is postulated that *L reuteri* may reduce colic symptoms by stimulating gastric emptying.

L reuteri at 10 (8) live bacteria per day, improved infantile colic in 95% of cases (while simethicone only yielded improvement in 7% of patients).

L reuteri suppresses human TNF- α production by LPS-activated monocytes and primary monocyte-derived macrophages from children with Crohn's disease. It also suppresses the MCP-1/CCL-2 in macrophages of children in remission.

L reuteri reduces duration and severity of diarrhea caused by rotovirus in children. It reduces incidence of diarrhea in infants. It also reduces colicky symptoms in 95% of infants. It improves gastric emptying and reduces crying time in premature infants.

L reuteri reduces IgE-associated eczema in 2-year-olds. It reduces levels of TGF- β -2.

In a study of human infants in a daycare setting, children receiving *L reuteri* supplementation had a reduced number of sick days, antibiotic prescriptions, diarrheal episodes, and duration of diarrhea.

Down-regulation of pro-inflammatory cytokines such as TNF- α by *L reuteri* is observed in macrophages, LPS-activated monocytes, and primary monocyte-derived macrophages from children with Crohn's disease.

L reuteri may contribute to an environmental modulation of the intestinal dendritic cell generation toward favoring tolerance toward antigens bearing no "danger signal," while at the same time keeping intact the capacity to respond against pathogens recognized via a danger signal like LPS.

It may be that the inhibiting effect of *L reuteri* on dendritic cells is mediated through interference with TLR 2, causing a universal inhibition toward other

lactobacilli and possibly G gram-positive bacteria, but leaving the LPS stimulation through CD-14 unaffected. (Alternatively, other TLRs activated by bacteria may be involved).

Studies done in the 1960s and 70s show that *L reuteri* was then one of the dominant lactobacilli and regularly detected in the human GI tract. The low prevalence in humans in more recent studies suggests a reduction of the *L reuteri* population size during the past 50 years.

L reuteri can use several external electron receptors (fructose, glycerol, nitrate) to gain additional energy and increase growth rates. However, these nutrients are in low supply in the human colon due to their prior absorption in the small intestine. The ability of *L reuteri* to use 1, 2-propanediol as an energy source might therefore constitute an important colonization factor in the human gut. The enzyme for 1, 2-propanediol utilization, diol dehydratase, is vitamin B12 dependent. This enzyme is also involved in the utilization of glycerol as an electron receptor and reuterin formation.

Several experiments in animals show that indigenous strains of *L reuteri* outperform exogenous strains when competing in the GI tract. The ability of *L reuteri* strains to adhere to gut epithelial cells is, to a large degree, host-specific. CONCLUSION: Human-derived strains of *L reuteri* will confer maximum benefits as probiotic supplements. Host environment is the major factor in evolution of *L reuteri*.

Oral supplementation with *L reuteri* induces significant temporary colonization of the stomach, duodenum, and ileum of healthy humans, and is associated with significant alterations in the immune response in the gastrointestinal mucosa. Gastric mucosal histiocyte numbers were reduced, and duodenal B-lymphocyte numbers were increased. *L reuteri* administration induced a significantly higher amount of CD-4 plus T-lymphocytes in the ileal epithelium.

L reuteri supplementation is particularly effective at controlling rotavirus gastroenteritis and its associated diarrhea. Rotavirus infections are the most common cause of pediatric diarrhea worldwide. Rotavirus infections all leave a lingering adverse effect on the gut microbiota.

L reuteri in an in-vitro study of chronic active colitis in mice had the following effects: Increased IL-10, decreased IL-6, decreased IL-12. Conversely, *E. coli* and *E. faecalis* bacteria associated with chronic active colitis induced the production of pro-inflammatory cytokines TNF- α and IL-12. Macrophages released comparably substantial amounts of reactive oxygen species (ROS) in response to *L reuteri*, while *E. coli* and *E. faecalis* ability to induce generation of ROS was negligible. In contrast to ROS, the production of NO by macrophages activated with all bacterial strains tested was similar. Moreover,

for the first time, it is shown that *L reuteri* induces expression of a stress-inducible enzyme with antioxidant and anti-inflammatory properties.

L reuteri increases IL-10, decreases IL-6, and decreases IL-12 in an animal model of chronic colitis.

L reuteri inhibits colitis in IL-10-deficient mice. The mechanism is up-regulation of nerve growth factor and inhibition of IL-8 induced by TNF- α . *L reuteri* also inhibits IL-8 synthesis induced by salmonella enterica.

Considering the properties observed for *L reuteri*, which from an immunological standpoint are opposite those observed for *L casei*, bacteria with such properties might be beneficial for patients with inflammatory bowel disease. The cytokines IL-12 and TNF- α are both implicated in the enteropathy of these diseases, being increased in patients suffering from diseases like Crohn's, and for administration for TNF- α neutralizing antibodies has been successful therapy. Conceivably, bacteria like *L reuteri* might be a potential treatment effective for down-regulating production of IL-12 and TNF- α while inducing the anti-inflammatory IL-10, thus representing an effective anti-inflammatory therapy.

L reuteri diminishes *Helicobacter hepaticus*-induced inflammatory bowel disease in IL-10 deficient mice.

L reuteri and oat fiber decreases acidic acid-induced colitis in the rat.

L reuteri contributes to immune tolerance in the gut. *L reuteri* suppresses the production of pro-inflammatory cytokines such as TNF- α , IL-12, and IL-6 in macrophages, monocytes, and dendritic cells. The modulation of dendritic cells has been shown to be mediated through the development of T reg cells producing high amounts of IL-10 and TGF- β . This suppression of immune responses is likely to underlie the ability of *L reuteri* to reduce intestinal inflammation in several mirroring colitis models.

Irritable bowel (IB)

- IBS-D = lactobacilli
- IBS-C = bifidobacteria
- IBS = *L plantarum*, *B infantis*, *Strep faecalis*
- IBS pain = *L plantarum*
- Infectious diarrhea:
 - *S boulardii*
 - *L reuteri*
 - *L acidophilus* + bifidobacteria
 - *Enterococcus* LAB

- Traveler's diarrhea:
 - *S. boulardii*
- C diff:
 - *S. boulardii*
 - *L. plantarum*
- Post-antibiotic diarrhea:
 - *S. boulardii*
 - *L. rhamnosus*

L. reuteri (but not *L. plantarum*) primes monocyte-derived dendritic cells to drive the development of T cells. These T cells produce increased levels of IL-10, are capable of inhibiting the proliferation of bystander T cells. *L. reuteri* binds the C-type lectin dendritic cell-specific intracellular adhesion molecular 3-grabbing-non-integrin. This targeting of DC-S IgN by *L. reuteri* explains its beneficial effect in the treatment of a number of inflammatory diseases, including atopic dermatitis and Crohn's disease.

L. reuteri primes monocyte-derived dendritic cells to drive the development of T cells producing increased levels of IL-10, thus benefitting inflammatory diseases including atopic dermatitis and Crohn's disease.

L. reuteri has profound effects on the immune system. It decreases LPS-induced IL-8 and IFN- γ . It is beneficial in atopic and non-allergic dermatitis in children by decreasing IFN- γ and IL-4. It also decreases elevated IFN- γ and IL-4 in asthma patients.

L. reuteri controls the Th2 in atopic patients, and decreases allergic airway response.

L. reuteri decreases atopic and non-allergic dermatitis in children by decreasing IFN- γ and IL-4. (IFN- γ and IL-4 are also elevated in asthma).

Oral supplementation with *L. reuteri* (but not *L. salivarius*) in mice significantly attenuated the influx of eosinophils to the airway lumen and parenchyma and reduced the levels of TNF, monocytes chemo attractant protein-1, IL-5, and IL-13 in bronchoalveolar lavage fluid of antigen-challenged animals. *L. reuteri* (but not *L. salivarius*) also decreased allergen-induced airway hyperresponsiveness. These favorable responses were dependent on TLR9 and were associated with

increased activity of indoleamine 2, 3-dioxygenase. Conclusion: *L reuteri* can attenuate major characteristics of an asthmatic response in a mouse model of allergic airway inflammation.

L reuteri protects against asthma in mice by increasing the percentage and total number of CD4+, CD25+, and FOXP-3+ T cells in spleens. CD4+ and CD25+ cells isolated from *L reuteri*-fed animals also had greater capacity to suppress T-effector cells proliferation. This *L reuteri* potent immunoregulatory action may have therapeutic potential in controlling the Th2 bias observed in atopic individuals and asthmatics.

L reuteri reduces bronchial inflammation in asthmatic children, as it increases IL-10 and decreases IL-2.

L reuteri attenuates the asthmatic response in a mouse model of allergic airway inflammation by decreasing the influx of eosinophils, reduced TNF- α , MCP-1, IL-5, and IL-13.

L reuteri enhances IgG 1 and IgG 2a antibody responses to *Candida albicans*.

L reuteri inhibits yeast growth in women with vulvovaginal candidiasis by up-regulating IL-8 in the vaginal epithelium.

L reuteri has pro-apoptotic effects in myeloid leukemia-derived cells induced by TNF. The *L reuteri* strain down-regulates nuclear factor-kappa B (NF-kappa-B)-dependent gene products that mediate cell proliferation and cell survival.

Oral administration of *L reuteri* induces expression of pro-inflammatory Th-1 cytokines, TNF- α , IL-1- β and IL-2, and also enhances the IgG response.

L reuteri down-regulates NF-kappa-B-dependent gene products that mediate cell proliferation and cell survival in myeloid leukemia-derived cells induced by TNF- α .

L reuteri inhibits TNF- α , IL-6, and IL-12 induction.

IFN- γ is inhibited by *L reuteri*.

L reuteri down-regulates human rotavirus infection-induced monocytes/macrophage activation/recruitment at the systemic lymphoid tissue.

L reuteri has different, and even opposing, effects on immune markers in the GI tract. Dendritic cells play a pivotal immuno-regulatory role in the Th-1, Th-2, and Th-3 cell balance and are present throughout the GI tract. Various species of lactobacillus differently activate dendritic cells. *L reuteri* is a poor

IL-12 inducer, inhibiting IL-12, IL-6, and TNF- α induction by the strong cytokine inducer L casei.

While L reuteri inhibits the L casei induced TNF- α , IL-12, and IL-6, L reuteri does not decrease LPS induction of TNF- α , IL-12, and IL-6 or IL-10.

The differences observed between L reuteri and L casei in the capacity to induce production of key cytokines such as TNF- α , IL-12, and IL-10 and also maturation surface markers, especially B7-2, indicate these bacteria may differentially alter antigen presentation in the gut and thus differentially affect the steady state level of dendritic cell activation.

IL-6 promotes terminal differentiation of B cells into plasma cells and polarizes naïve CD 4+ T cells to effector Th-2 cells. There is a strong capacity to induce IL-6 by most Lactoballicus strains, which not only induce IL-6 but also enhance intestinal IgA responses. One exception is L reuteri, which down-regulates IL-6 expression, and perhaps attenuates IgA responses.

In possessing a capacity to moderately up-regulate maturation surface markers of dendritic cells, and to induce IL-10 but not IL-12 production, L reuteri may contribute to a Th-2 or Th-2 polarization of the dendritic cells, as opposed to L casei, which as a strong inducer of both surface molecules and IL-12, may promote a Th-1 dendritic cell polarization.

L reuteri may have a dendritic cell polarizing capacity distinct from other lactobacilli strains.

Other potent Th-2 dendritic cell polarizing factors, i.e. factors causing IL-12 suppression, in addition to L reuteri include compounds with cAMP-elevating properties such as PGE2, beta-2-agonists, and histamine.

L reuteri reduces TNF- α production in activated macrophages.

L reuteri reduces production of pro-inflammatory cytokines in dendritic cells, and induces T reg cells.

L reuteri activates dendritic cells and induces the production of IL-12 at about the same level as do L johnsonii and L gasseri. L reuteri induction of IL-6 is significant and also matches the activity of L johnsonii and L gasseri. Production of IL-1- β is induced at a much higher level by L gasseri than by L reuteri as is the induction of TNF- α .

L reuteri, L gasseri and L johnsonii all skew T cell activity toward a Th1 response --- to a significant increase in INF- γ . Of the 3 species, only L reuteri induces a significant amount of IL-10, but still favors a Th1 immune response.

L acidophilus and B bifidus and L reuteri all result in expansion of NK cells via dendritic cell maturation and increased NK cell cytotoxic activity. Thus, these probiotics (similar to pathogenic microorganisms and inflammatory stimuli) “license” dendritic cells to signal to NK cells. An enlarged and more cytolytic pool of NK cells would be beneficial prophylactically in healthy individuals, but also therapeutically in many pathologies.

While all 3 probiotic species, L acidophilus, L reuteri, and B bifidus, induce substantial amounts of IL-10, IL-12 production in dendritic cells was strongly induced only by L acidophilus. Other probiotic strains have been found to elicit highly variable levels of these cytokines. Only dendritic cells matured by L acidophilus induced high amounts of IFN- γ in NK cells. It is generally accepted that IL-12 induces IFN- γ production in NK cells, and that IL-12 to IFN- γ relationship is confirmed in this study. IFN- γ production by NK cells is required to induce Th1 responses in lymph nodes, emphasizing the importance of probiotic regulation of IL-12 production in dendritic cells.

The mechanism by which L acidophilus induces IL-12 production in DCs, and subsequently IFN- γ in NK cells, probably involves a cell wall component, likely acting via TLRs on dendritic cells. It is known that IL-10 inhibits IL-12 production in dendritic cells --- but --- IL-10 was not responsible for the inhibition of L acidophilus-induced IL-12 production by B bifidum and L reuteri since this inhibition was also evident in the presence of IL-10 blocking antibody. Therefore, it is unlikely that the secreted components of B bifidum and L reuteri exerting the IL-12 inhibitory effect are merely strong inducers of IL-10. Probably they interact directly with inhibitory receptors on dendritic cells.

Lymph nodes have been identified as one of the sites where NK cells and dendritic cells interact, and it is likely that gut-derived dendritic cells reach mesenteric lymph nodes upon probiotic stimulation, and engage in cross-talk with resident NK cells where concomitant CD4 plus T cell activation takes place. Therefore, NK cells interacting with migrating dendritic cells may regulate T cell responses.

In conclusion, probiotics potentially but differentially initiate NK-dendritic cell interactions via dendritic cell maturation. NK cells then expand and increase their cytolytic potential. The balance between NK cell responses and regulatory responses may be delicately regulated by intestinal probiotics, as NK cell effector functions are subjected to suppression mediated by T regs, and these T regs may also be induced by probiotics, which at the same time sustain NK cell cytolytic activity.

The cytokine balance during autoimmune diseases driven by Th-IL-17 cells in the absence of IFN- γ may be modulated by probiotics by promoting potent Th1 immune responses, desirable in infection and cancer. Similarly, the presence

of certain probiotics early in life will skew the immune system toward a Th1 response, possibly through the intermediate of NK cells, thus aiding in prevention of Th2-mediated allergy. Delicate balance is maintained by the weak IFN- γ -inducing probiotics that are able to suppress the action of IFN- γ -inducing stains while preserving NK cell stimulatory activity.

One study using mouse bone marrow-derived dendritic cells found in induction of Th2 immune responses when dendritic cells were treated with L reuteri. In contrast, human dendritic cells treated with L reuteri induced Th1 polarization. These data suggest that lactobacilli can exert different effects on human immune cells than on mouse immune cells.

One study using mouse bone marrow-derived dendritic cells found an induction of Th2 immune responses when dendritic cells were treated with L reuteri. In contrast, human myeloid dendritic cells treated with L reuteri induced Th1 polarization. Myeloid dendritic cells treated with L reuteri or L johnsonii induced the production of both IFN- γ and IL-10 in CD4+ T cells, but IL-10 was not induced in CD8+ T cells. In contrast, L gasseri induced a clear Th1 polarization pattern in both CD4+ and CD8+ T cells. These data suggest that lactobacilli can exert different effects on human immune cells when compared with mouse immune cells. L gasseri induced high levels of IFN- γ , but a low level of IL-10. In contrast, L reuteri or L johnsonii induced IL-10 in CD4+ T cells.

L reuteri and B bifidum inhibit L acidophilus-induced IL-12 production in dendritic cells, and accordingly decrease IFN- γ production by NK cells.

Dendritic cells were activated with live L gasseri, L johnsonii or L reuteri plus E. coli. Under these conditions, LPS promoted the production of IL-10 only in 11% of dendritic cells, compared with the high (60%) induction of IL-10 with E. coli LPS in the absence of L reuteri. IL-6 was induced in dendritic cells at similar levels whether treated with either of the 3 lactobacilli species or E. coli LPS. IL-1- β was minimally induced in dendritic cells treated with L johnsonii or L gasseri or E. coli LPS, but was induced in dendritic cells treated with L reuteri. IL-1- β , TNF- α production was observed in dendritic cells treated with any of the 3 lactobacilli species or with E. coli LPS.

In a model of murine colitis, L reuteri combined with L paracasei, the pro-inflammatory cytokines TNF- α and IL-12 were reduced as intestinal inflammation was reduced.

Th1 suppressors: L reuteri, L salivarius, B infantis, L casei shirota, E. coli.

The effects of probiotics on LDL cholesterol and an assessment of the potential probiotic intake as a therapeutic lifestyle change dietary option was investigated. Twenty-six clinical studies and 2 meta-analyses were reviewed.

Significant LDL reductions were observed for only 2 probiotic strains when supplemented individually. Those were *L reuteri* and *enterococcus faecium*. Over the probiotics examined, *L reuteri* was found to best meet TLC Dietary Requirements by significantly reducing LDL as well as total cholesterol, and doing so with robustness similar to that of existing TLC Dietary Options. *L reuteri* was also found to improve other coronary heart disease risk factors such as inflammatory biomarkers.

One group of researchers doing studies of probiotic supplementation and obesity discovered that mice given probiotic supplementation routinely had larger testicles and increased serum testosterone compared to their age-matched controls. Further study demonstrated that *L reuteri* was the probiotic having the major benefit on testicular function. Mice consuming *L reuteri* in their drinking water had significantly increased somniferous tubal cross-sectional profiles and increased spermatogenesis and Leydig cell numbers per testes when compared with matched diet counterparts. These results showed that criteria of gonadal aging were reduced after routinely consuming *L reuteri*.

To test whether these benefits typical of sustained reproductive fitness may be due to anti-inflammatory properties of *L reuteri*, it was found that testicular mass and other indicators typical of old age were similarly restored to youthful levels using systemic administration of antibodies blocking pro-inflammatory cytokine IL-17A. This result indicated that uncontrolled host inflammatory responses contributed to the testicular atrophy phenotype in aged mice.

Significantly, reduced circulating testosterone levels have been implicated in many adverse effects in human males and females. *L reuteri* supplementation may provide a viable natural approach to prevention of male hypogonadism and female testosterone insufficiency, and do so absent the controversy and side-effects of traditional hormone replacement therapies. *L reuteri* supplementation for management of disorders typically associated with normal aging suggest a potential high impact for such therapy by imparting hormonal and gonadal features of reproductive fitness typical of much younger, healthy individuals.

Recent epidemiological studies show that eating “fast food” items such as potato chips increases the likelihood of obesity (--- no surprise). There has also been demonstrated in animal models of obesity that the immune system plays a critical role in this process. In both human and mouse models consuming Westernized “fast food” diet, it is found that CD4+ T helper Th-17-biased immunity and changes in microbial communities and abdominal fat with obesity were found after eating the typical Western diet or in the animals eating “Western” chow. Surprising benefits on the obesity-generating effects of “fast food” were found with *L reuteri* supplementation. In fact, *L reuteri* therapy alone was sufficient to change the pro-inflammatory immune cell profile and prevent abdominal fat pathology as well as age-associated weight gain in mice -

-- and do so regardless of their baseline diet. In other words, the effect of L reuteri was so powerful that the development of obesity was inhibited to some degree even when the “fast food” diet was maintained.

Assuming you are now thoroughly convinced of the superior benefits of L. reuteri on the ImmunoNeuroEndocrine stress of your patients, stop to consider this:

L. REUTERI IS THE LEAST IMPORTANT OF THE 5 INGREDIENTS IN YOUR IMMUNO-SYNBIOTIC.

All 4 other ingredients have an even greater effect on the connection between the GI tract and the immune system as the gut:

- initiates the release or inhibition of pro-inflammatory cytokines
- initiates the release or inhibition of anti-inflammatory cytokines
- activates macrophages when the need is perceived
- triggers lymphocytosis when the need is perceived
- initiates and coordinates the action of its billions of mast cells, the most fundamental component of the innate immune response
- connects the immune system to the nervous system as mast cells cluster around sympathetic and parasympathetic nerve endings in the gut wall
- responds with an appropriate alarm reaction to the toxins produced by abnormal bacteria, fungi, yeast, or viruses in the GI tract --- triggering the release of the pro-inflammatory cytokines Interleukin-1 and Interleukin-2.

The 5 ingredients of your IMMUNO-SYNBIOTIC have synergistic effects, giving you power over INE stress that other nutritionists can only dream of. Your NUTRI-SPEC Metabolic Balancing and Diphasic Nutrition Plan give you two incomparable strategies to meet the specific nutrition needs of all your patients.

Actions to take:

- 1) Use your Doing FINE strategy for all your Diphasic Nutrition Plan (DNP) patients who have Chronic Fatigue Syndrome, Fibromyalgia Syndrome, Multiple Chemical Sensitivities, Post Traumatic Stress Disorder, or Major Depression ----- or ----- who have autoimmune disease such as Rheumatoid Arthritis, Lupus, Alopecia, Insulin-Dependent Diabetes, Hashimoto’s or Grave’s Thyroiditis, Crohn’s Disease, Ulcerative Colitis, Sjogren’s, etc.
- 2) Use Doing FINE to Facilitate INE balance --- to calm the raging storm and replenish reserves --- in all your Metabolic Balancing patients who either have the above conditions or who show that they are vacillator-oscillators upon follow-up testing.

- 3) Use IMMUNO-SYNBIOTIC for all your patients who are Doing FINE.
- 4) Have every patient (and yourself and your family) go through a bottle of IMMUNO-SYNBIOTIC, 3, 2X daily before meals, at least once each year.
- 5) Give all your patients with asthma, chronic sinus congestion, allergies, Irritable Bowel Syndrome, GERD, and chronic Candida or other fungal infections of the skin, GI tract, or urinary tract, at least 2 bottles of IMMUNO-SYNBIOTIC.
- 6) Give all your patients with Eosinophilic Fungal Rhinosinusitis (which, by definition, means everyone with recurring sinus congestion) a punch in the nose with BOOGIEY BUSTER, at least 4 times daily. KILL, FLUSH. KILL, FLUSH. KILL, FLUSH. KILL, FLUSH.
- 7) Give your patients A GOOD THYME for Candida in the mouth, at the root of the tongue, or in the esophagus; for Candida or other fungal overgrowth of the gut; for H. pylori infection of the stomach or duodenum; for a more extensive sinus irrigation than can be achieved with BOOGIEY BUSTER.

In your last NUTRI-SPEC Letter we spent 10 pages proclaiming the superiority of L-reuteri (one of the 5 ingredients of IMMUNO-SYNBIOTIC) over all other probiotics. But after making such a strong case in support of L. reuteri supplementation, we finished by exclaiming that ...

L. REUTERI IS THE LEAST IMPORTANT OF THE 5 INGREDIENTS IN YOUR IMMUNO-SYNBIOTIC!

So, for at least a moment the question must have danced through your head --- what is the most important ingredient in IMMUNO-SYNBIOTIC? Below, we will reveal our answer to that question, but first ---

WE SOLICIT YOUR FEEDBACK.

We would like to hear any testimonials you can offer on extraordinary responses to IMMUNO-SYNBIOTIC supplementation. Here are some that we have so far:

- Two cases of astounding weight loss, including one woman who lost 13 pounds in the first 5 days on IMMUNO-SYNBIOTIC.
- Several fibromyalgia cases with dramatically decreased pain within days of starting IMMUNO-SYNBIOTIC

- One stroke victim who has been on the same dose of the blood thinner Coumadin for years, who showed such a surprising improvement in her prothrombin time after 1 week on IMMUNO-SYMBIOTIC she had to have her Coumadin dose lowered, and was called back for a retest the next week. The next week the pro time had improved just as much, and her Coumadin dosage was decreased again; the following week showed an equally dramatic improvement in pro time, and her Coumadin dose was adjusted downward for the third time in 3 weeks.
- An autistic child whose symptoms were clearly improved with IMMUNO-SYMBIOTIC supplementation.
- Zillions of cases of improved GI function --- with decreases in cramping, constipation, diarrhea, bloating, etc.

[On the other hand, there have been a few reports of patients who simply cannot take IMMUNO-SYMBIOTIC. Some of these are those with ulcerative colitis, or with a family history of ulcerative colitis. We have cautioned you that IMMUNO-SYMBIOTIC can increase the already excessive stool frequency in these patients. There have been a few other patients as well who experience such a violent war between the “good guys” promoted by IMMUNO-SYMBIOTIC and the “bad guys” that have been living in the gut for a lifetime, that the discomfort of IMMUNO-SYMBIOTIC supplementation is more than they choose to deal with. --- Let us know about these cases, too.]

You may be thinking that our request for testimonials flies in the face of NUTRI-SPEC principles --- and you are right. After all, the very essence of your NUTRI-SPEC philosophy is objectivity in clinical nutrition --- with nothing but disdain for relying on subjective reports of either improved or exacerbated symptoms. --- But --- when we have 2 supplements that meet the strict criteria to be classified as ...

ADAPTOGENS ...

the subjective responses of our patients are just as meaningful as changes in objective test results. --- And nowhere will you find adaptogens as universally powerful as your ...

ELECTRO TONIC and IMMUNO-SYMBIOTIC.

[See pages 1-3 of your July 2010 NUTRI-SPEC Letter for a clear understanding of the difference between:

- a drug,

- a metabolically specific supplement, and
- an adaptogenic supplement.

The adaptogens IMMUNO-SYNBIOTIC and ELECTRO TONIC will yield gratifying results for nearly all your patients.]

Now, let us explore the extraordinary ingredients of your IMMUNO-SYNBIOTIC. If L. reuteri is the least important, which of the other 4 ...

DOES THE MOST TO REDUCE IMMUNONEUROENDOCRINE STRESS?

Stop and think for a minute --- what is the most critical aspect of reducing the INE stress associated with the 75% of the immune system arising from the GI mucosa? Your most essential consideration is maintaining a high level of Short Chain Fatty Acids (SCFA), especially butyrate. As you learned from last month's Letter, as end products of the anaerobic colonic bacterial fermentation of carbohydrates, the SCFA acetate, propionate, and butyrate (in the ratio 3:1:1) play a vital role in maintenance of colon cell integrity and metabolism --- and L. reuteri is a valuable aid in increasing butyrate. --- But ---

- The probiotic Saccharomyces boulardii is better.
- The prebiotic Inulin is better.
- The prebiotic Glucomannan is better.
- The prebiotic Guar Gum is better.

- Other probiotics are inferior, and potentially harmful.
- Other prebiotics are pitifully inferior.

Last month we exposed the inferiority of the most popular probiotic, Lactobacillus acidophilus. Now, you need to learn more about prebiotics.

Prebiotics are food, primarily carbohydrate, that passes through the small intestine and into the colon in an undigested state. It thus becomes food for the natural flora of the colon. Prebiotic supplements are concentrated sources of undigestible carbohydrate taken for the purpose of increasing the population of beneficial bacteria in the colon, and particularly feeding the bacterial species that are most beneficial. The greater purpose of prebiotic supplementation is the production, through fermentation of the prebiotic by the beneficial bacteria, of increased quantities of short chain fatty acids. The most specific intent is to not only increase the overall quantity of SCFA, but to increase the proportion of butyrate, the most critical of the SCFA.

There can be problems with prebiotic supplementation. Many prebiotics support the growth of pathological bacteria such as Clostridia as well as the beneficial bifidobacteria. Also, some patients respond with extreme GI distress

to prebiotic supplementation --- with flatulence, cramping, bloating, or diarrhea.

Other problems with popular prebiotics include:

- being expensive
- requiring huge quantities to do any good
- binding (thus robbing) mineral nutrients
- adversely affecting liver function or metabolic efficiency

Common prebiotics that illustrate their inadequacy for high-level nutritionists like you include:

Lactitol is a moderately effective prebiotic. Supplementation of 10 grams per day for 7 days will decrease fecal pH, and increase propionate and butyrate. However, lactitol has some undesirable metabolic effects.

Enzyme-treated rice fiber is an effective prebiotic, but the effective quantities are measured in spoonfuls rather than grams, making it less than practical as a prebiotic supplement. Furthermore, even with the gross quantities that must be supplemented, the benefits on intestinal flora and SCFA are inferior to those derived from IMMUNO-SYMBIOTIC.

Wheat bran is much the same as rice fiber as a prebiotic. To benefit from wheat bran supplementation requires a minimum of 30 grams (6 spoonfuls) daily. Again, the benefits on intestinal flora and SCFA production are inferior to those of other prebiotics. And, wheat bran is high in phytates that bind mineral nutrients, rendering them unabsorbable.

Maltitol + polydextrose is a prebiotic combination shown to increase lactobacilli and bifidobacteria, and increase both propionate and butyrate. It is expensive, must be taken in relatively large quantities, and is not as effective as your Inulin, Glucomannan, and Guar Gum.

**JUST HOW SUPERIOR ARE YOUR
INULIN, GLUCOMANNAN, AND GUAR GUM
OVER CHEAP PREBIOTICS
SUCH AS PSYLLIUM, BRAN, AND METAMUCIL?**

--- The far-reaching benefits of these prebiotics on INE stress are evidenced by so many dozens of studies from the literature that we will devote all of next month's Letter to them. --- Then, you can be the judge of which ingredient wins the recognition as #1 INE stress fighter.

But as you continue this month using IMMUNO-SYMBIOTIC as a foundation of the best professional nutrition your patients can find anywhere --- don't forget about the greatest probiotic by far ...

SACCHAROMYCES BOULARDII.

Saccharomyces boulardii, unlike other probiotics, is not a bacterium, but rather a yeast. Unlike the bacterial probiotics, *S. boulardii* does not colonize in the colon; rather, it creates an environment hostile to pathogenic bacteria and quite favorable for the beneficial flora. *S. boulardii* not only decreases bacterial overgrowth; it increases colonic butyrate.

S. boulardii has unparalleled trophic effects on the intestinal mucosa. It increases intestinal brush boarder enzymes; it has immune stimulatory effects far exceeding those of any other probiotic.

(*S. boulardii* is not resistant to stomach acid, so it must be taken on an empty stomach, or, must be encapsulated in a protective coating of alginate microspheres.)

S. boulardii is beneficial and safe for children of all ages, including very young infants. Many of the bacterial probiotics are not safe for the delicate immune system of infants.

S. boulardii is effective in decreasing the intestinal inflammation from any source, and in all cases of irritable bowel disease, by blocking tumor necrosis factor-alpha (TNF-alpha), IL-1 beta, and by decreasing IL-8. It blocks the toxic effects of lipopolysaccharide (endotoxin).

S. boulardii is the most effective probiotic against antibiotic associated diarrhea. It is also effective against traveler's diarrhea, and any case of acute gastroenteritis.

S. boulardii is by far the most effective probiotic against Candida albicans colonization throughout the GI tract. *S. boulardii* decreases *Candida albicans* virulence, decreases *Candida* hyphae formation, and decreases *Candida* adhesion and biofilm development. *S. boulardii* secretes capric acid which decreases the *Candida* hyphae formation and prevents the *Candida* from forming its protective biofilm layer throughout the gut. *S. boulardii* decreases IL-8 expression in *Candida*-infected Caco-2 cells in general, whether in response to *Candida albicans* or pathological bacteria overgrowth, *S. boulardii* decreases damaging pro-inflammatory cytokines.

S. boulardii is effective in eradicating *Helicobacter pylori*, the bacterium that causes stomach ulcers.

S. boulardii releases a protease that cleaves *Clostridium difficile* toxin A, and stimulates antibody production against toxin A.

With a combination of IMMUNO-SYNBIOTIC and A GOOD THYME and BOOGY BUSTER, you can do more for your chronic Candida sufferers than you ever imagined. In fact, NUTRI-SPEC has you ...

PERFECTLY POSITIONED ...

at the top of all clinical nutrition providers, with the power to help dozens and dozens of patients who up 'til now have been wasting their money on health food industry remedies for Candida, chronic fatigue, fibromyalgia, and the devastation of auto-immune diseases such as hypothyroid, diabetes, rheumatoid arthritis, alopecia, Crohn's disease, and lupus. --- Reach out to these many people in need --- with your DIPHASIC NUTRITION PLAN (and Doing FINE) to control INE stress.

Recognize that your IMMUNO-SYNBIOTIC gives you the means to immediately restore a healthy intestinal milieu --- but the benefits are systemic as well. Since 75% of the immune system originates in the gut mucosa, your IMMUNO-SYNBIOTIC has a powerful effect at correcting ImmunoNeuroEndocrine stress. Most of your patients will begin their DNP with 3 IMMUNO-SYNBIOTIC twice daily. Some will need to go through 1 bottle; some will need to go through several bottles; some will need to stay on it indefinitely. For most patients, after the first bottle at 3, twice daily before meals, you can reduce it to 2 or 1 twice daily before meals. For patients who experience a yeast/fungal die off reaction in response to IMMUNO-SYNBIOTIC or, who experience diarrhea, you will want to back off the quantity and recommend only 1 or 2 daily, and gradually build up from there.

To highlight exactly how you are going to ...

HAVE A LIFE-CHANGING IMPACT ...

on even your most severely ill patients, let us resume our discussion of exactly how your IMMUNO-SYNBIOTIC will ...

STRENGTHEN A STRESSED IMMUNE SYSTEM.

You have already learned how your IMMUNO-SYNBIOTIC L. reuteri kills Candida, suppresses *H. pylori*, prevents vitamin B12 deficiency, decreases elevated cholesterol and triglycerides, elevates depressed white blood count, kills a broad diversity of noxious bacteria, restores balance to the cytokines produced by T lymphocytes --- particularly decreasing the inflammatory cytokines TNF- α , IL-6, and IL-12 --- increases the production of health-promoting short-chain fatty acids from prebiotics, protects diabetics from renal fibrosis, and has shown to be specifically beneficial in a broad diversity of

diseases including asthma, atopic dermatitis, and Crohn's disease. --- And --- you have learned that L. reuteri is the least important of the 5 ingredients in your IMMUNO-SYNBIOTIC.

You also learned in last month's Letter that Saccharomyces boulardii is unmatched in its power as a probiotic. S. boulardii is by far the most effective probiotic against Candida, against Helicobacter pylori, against antibiotic-associated diarrhea and all other forms of diarrhea, and that S. boulardii has unparalleled trophic effects on the intestinal mucosa, as it increases colonic butyrate and yields immuno-stimulatory effects far exceeding those of any other probiotic.

You now know all you need to know about probiotics. The 2 probiotics in your IMMUNO-SYNBIOTIC are so far superior to all others, that there is no point wasting your patients' money on anything else. So now, let us sneak a peek at your 3 prebiotics and the health-restoring, age-preventing effects they have.

We have already pointed out the many problems and insufficiencies of the common (cheap) prebiotics such as wheat bran, rice fiber, lactitol, and maltitol. --- A person needs to swallow a truckload to do anything at all, and they are hopelessly inferior to your inulin, glucomannan, and guar gum in feeding beneficial flora and increasing the overall quantity of short-chain fatty acids, as well as the proportion of butyrate to other fatty acids. Furthermore, many prebiotics support the growth of pathological bacteria such as Clostridia, and can cause extreme GI distress.

LET US LOOK AT INULIN ...

Inulin is perhaps the most popular of the prebiotics. It is an undigestible carbohydrate consisting of a broad diversity of undigestible saccharides, including fructo-oligosaccharides (FOS), as well as many longer chain oligofructoses and other saccharides. There is a problem, however, in the shorter chain polysaccharide version of FOS, as it can in some patients lead to GI side-effects such as cramping, bloating, and occasionally diarrhea. Longer chain inulin has the same healthful effects as FOS or oligofructose, but with less GI side effects. As you can well imagine, your NUTRI-SPEC IMMUNO-SYNBIOTIC contains predominantly the longer chain polysaccharide form of inulin.

- Inulin supplementation has been shown in countless studies to increase the population of beneficial intestinal flora. Inulin hydrolyzes to oligofructose and galactooligosaccharides, which specifically feed bifidobacteria.
- Inulin increases the colonic and fecal levels of butyrate better than other sources of fiber, including beet, soy, cellulose, FOS, and multi-

oligosaccharides, and, far better than wheat bran, psyllium, Metamucil, and rice bran.

- Inulin decreases postprandial insulin response but has no effect on fasting glucose nor insulin --- and thus helps Type II diabetics.
- Inulin is beneficial for Crohn's disease by increasing the anti-inflammatory IL-10, and increasing toll-like receptor 8 and toll-like receptor 4 expression. The problem is, that patients with Crohn's disease (as well as those with ulcerative colitis) desperately need the immune-modulating benefits of inulin --- but --- the inulin can increase the already excessive stool frequency in these patients. [Patients with Crohn's disease or ulcerative colitis can be some of our most gratifying triumphs, but they can also be our most frustrating patients. Some of these patients need Oxy D+ and glutamine and histidine to control their symptoms by reducing their immune system stress, and others benefit from taurine and carnitine and either calcium or bicarbonate. But --- regardless of what other supplements they need, these patients will respond much more quickly if you can get inulin from your IMMUNO-SYMBIOTIC into them without excessively increasing gut motility. These patients can be a challenge to manage, but please understand that no one else can offer them any health-promoting physiological approach to their pathology but you. Without you, they are destined to surgery and a lifetime of prednisone and immune-suppressing drugs.]
- Inulin increases GI absorption of magnesium, copper, and calcium.

----- Yes, with IMMUNO-SYMBIOTIC and an amazing array of adaptogens, you've finally got what you want --- your comprehensive and powerful, easy to administer ...

DIPHASIC LONGEVITY PLAN.

Recognize that your Immuno-Synbiotic gives you the means to immediately restore a healthy intestinal milieu --- but the benefits are systemic as well. Since 75% of the immune system originates in the gut mucosa, your Immuno-Synbiotic has a powerful effect in correcting ImmunoNeuroEndocrine stress. Mast cells in particular, are pro-inflammatory little devils residing in the intestinal tissues. They absolutely must be kept under control, and Immuno-Synbiotic does the job.

In your November Letter, we posed the question --- "Which of the 5 ingredients of your Immuno-Synbiotic does the most to reduce ImmunoNeuroEndocrine stress?" Is it the most effective bacterial probiotic in the world, *L. reuteri*? Is it the non-bacterial probiotic *Saccharomyces boulardii*? Both these probiotics have unparalleled trophic effects on the

intestinal mucosa. Both of them dramatically increase colonic butyrate, the short-chain fatty acid with far-reaching immune benefits. Both reduce pro-inflammatory cytokines of an over-reactive immune system. Both help eradicate nasty critters in the gut --- including *Helicobacter pylori* (the cause of stomach ulcers), as well as *Candida albicans*. --- Or --- is the most critical ingredient in your Immuno-Synbiotic one of the 3 prebiotics, inulin, glucomannan, or guar gum? --- The far-reaching benefits of these prebiotics on INE stress are evidenced by so many dozens of studies from the literature that we will devote all of next month's Letter to them. --- Then, you can be the judge of which ingredient wins the recognition as ...

#1 INE STRESS FIGHTER.

Meanwhile, the testimonials raving about Immuno-Synbiotic's benefits keep coming in to the NUTRI-SPEC staff. Many of these rave reviews come from doctors who are not even using NUTRI-SPEC, but just began using Immuno-Synbiotic as a GI "remedy." (--- Maybe some of these doctors will now see the light and begin offering the entire NUTRI-SPEC package to their patients.) Some of the testimonials are coming from patients who contacted NUTRI-SPEC directly because they felt the need to express their enthusiasm over how well they feel.

One additional note on Immuno-Synbiotic is that we tweaked the formulation a bit. We decreased the percentage of inulin, and proportionately increased the amounts of glucomannan and guar gum. It is not that the inulin is to be disregarded as a powerfully effective prebiotic. But we determined that many of the patients who could not take Immuno-Synbiotic because it increased stool frequency were experiencing their negative reaction entirely due to the inulin. You see, inulin is a mix of many saccharides. Patients with disaccharidase enzyme deficiency (an example of which is lactose intolerance) were the ones having difficulty with diarrhea/gas/bloating from Immuno-Synbiotic. If you had a patient or two with such a reaction to Immuno-Synbiotic, we encourage you to take another shot at it. Everyone needs the benefit of these probiotics and prebiotics. You absolutely must use it for your patients with Crohn's disease, ulcerative colitis, and celiac disease.

A MAST CELL IS A FAST CELL AND THE LAST CELL YOU WANT CAST WELL IN THE ROLL OF IMMUNE DEFENDER IF YOU HAVE SUFFERED THE PAST HELL OF A VAST SWELL OF HIVES THAT YOU COULD AT LAST QUELL ONLY AFTER A PHARMACIST'S FAST SELL OF IMMUNO-SUPPRESSIVE DRUGS.

Yes, Doctor, a mast cell is the proverbial Dr. Jekyll and Mr. Hyde. Who needs these quickly activated specialized white blood cells? We all do --- but only occasionally and in strictly limited quantities. Although mast cells, when well-behaved, are an essential component of our immune system, their

activation more often, in more patients than you can imagine, does more harm than good, as they transform into hideous monsters. --- Asthma, dermatitis, sinusitis, hives, sneezing, pain sensitivity, and all sorts of inflammation are associated with excessive mast cell reactivity --- reactivity that can be provoked in many of us by any number of environmental triggers, whether inhaled, touched, or ingested.

Why the big fuss about mast cells? We have made the point repeatedly since introducing your master controller of ...

IMMUNONEUROENDOCRINE STRESS,

your ...

IMMUNO-SYMBIOTIC,

that ...

75% OF THE IMMUNE SYSTEM ORIGINATES IN THE GUT MUCOSA.

Mast cells in particular are pro-inflammatory little devils residing in the intestinal tissues. They absolutely must be kept under control, and Immuno-Synbiotic does the job.

One fascinating and clinically relevant piece of information regarding mast cells and the rest of the 75% of the immune system residing in the GI tract is that those cells tend to congregate around autonomic nerve endings --- both parasympathetic cholinergic nerve endings and sympathetic adrenergic and cholinergic nerve endings. --- Stop and think! We are talking here about the most significant link between the “I” and the “N” of INE stress. The autonomic nervous system (Symp-athetic/Parasympathetic balance within the context of your NUTRI-SPEC paradigm) is the critical link between nervous system function and immune system function --- integrating the two in appropriate (or, as is too often the case in our patients, inappropriate) response to environmental stressors. Can you begin to imagine how integrating the use of your Immuno-Synbiotic with intelligently administered Complex S and/or Complex P supplementation gives you a huge advantage in controlling ImmunoNeuroEndocrine stress in your patients?

There is even more to say about the relationship between the gut mucosa and appropriate vs. inappropriate immune reactivity. While your Immuno-Synbiotic will inhibit excess mast cell reactivity (particularly if used in conjunction with Complex S and/or Complex P), there are many other inappropriate immune responses triggered in the gut, and which you and only you can control in your patients. These inappropriate immune responses are

associated with a broad diversity of pro-inflammatory cytokines. These nasty cytokines are at least facilitators and often primary causative factors in virtually all the chronic diseases and autoimmune conditions responsible for 90+% of the suffering and ultimately death in our civilization. Diabetes, cancer, rheumatoid arthritis, osteoarthritis, cardiovascular disease, asthma, obesity --- you name it --- and pro-inflammatory cytokines are there, kicking your patients in the teeth, as the principle barriers to ...

LIVING STRONGER LONGER.

How effective are the 2 probiotics and 3 prebiotics in your Immuno-Synbiotic at inhibiting excess reactivity of pro-inflammatory cytokines? Following is a summary of just the facts clinically relevant to you and your patients:

First, consider Interleukin-6. Interleukin-6 is one of the nastiest of the nasty pro-inflammatory cytokines. Particularly, Interleukin-6 leads to increases in C-reactive protein, the inflammatory marker of the innate immune response that has been associated with cardiovascular disease, as well as Crohn's disease, ulcerative colitis, rheumatoid arthritis, chronic inflammation in Type II diabetics, elevated cholesterol and triglycerides, and the list goes on and on. Interleukin-6 is associated with all forms of inflammation-associated aging. Interleukin-6 suppresses thyroid function, while stressing the adrenal glands, and is associated with excessive activation of mast cells, basophils, and eosinophils. Interleukin-6 is also a major factor behind the symptoms of both chronic fatigue syndrome and major depression.

What is the major means by which your body prevents excess activation of Interleukin-6? Butyrate. Where does butyrate come from? Butyrate (as you may recall from past Letters) is the most important of the short-chain fatty acids produced in the GI tract. So, if butyrate is the key to controlling Interleukin-6, what is the key to producing abundant butyrate? The 3 prebiotics and 2 probiotics in your Immuno-Synbiotic --- inulin, guar gum, and glucomannan, plus *L. reuteri* and *S. boulardii* --- are far and away the best way to increase butyrate production in the GI tract.

There is another pro-inflammatory cytokine that is involved in even more autoimmune diseases and chronic inflammatory diseases than Interleukin-6. That pro-inflammatory cytokine is Tumor Necrosis Factor-alpha (TNF-alpha). Research shows that no less than 3 of the ingredients of your Immuno-Synbiotic are powerfully effective at suppressing excess TNF-alpha. Those 3 nutrients from your Immuno-Synbiotic are the prebiotic glucomannan, as well as both probiotics, *L. reuteri* and *S. boulardii*. How important is it that your patients have glucomannan, *L. reuteri*, and *S. boulardii* to control TNF-alpha? TNF-alpha suppresses thyroid function by several mechanisms. It activates the pro-inflammatory NF-kappa B. It provokes both catecholamine stress and cortisol stress. It induces the formation of neurotoxic quinolinic acid that

destroys the memory center in the hippocampus of the brain. It is the primary inflammatory cytokine causing the symptoms of Crohn's disease. It is associated with the neurotoxic reactions underlying Alzheimer's and Parkinson's. It is a part of insulin resistance, obesity, and Type II diabetes. It alters the sleep/wake cycle in both fibromyalgia and chronic fatigue syndrome patients. No way, except through you and your Immuno-Synbiotic, can your patients experience the benefits of controlling excess TNF-alpha.

By several mechanisms, both probiotics in your Immuno-Synbiotic decrease inflammatory cytokines. We have already cited the increased production of butyrate that decreases Interleukin-6. Here is a list of specific inflammatory cytokines that research has shown are controlled by your 2 probiotics (and not by the common garbage probiotics most of your patients are buying at the health food store):

L. reuteri inhibits excess inflammation associated with:

- TNF-alpha
- Interferon-gamma
- Interleukin-4
- Interleukin-5
- Interleukin-6
- Interleukin-8
- Interleukin-12
- Interleukin-13
- NF-kappa B
- Eosinophils

S. boulardii inhibits excess inflammation associated with:

- TNF-alpha
- Interleukin-1B
- Interleukin-8

Yes, with your Immuno-Synbiotic, you have the power to ...

ACHIEVE A LIFE-CHANGING IMPACT ...

on even your most severely ill patients. In this month's Letter we are taking the opportunity to complete the story on this incredibly valuable supplement.

You have already learned how your Immuno-Synbiotic's L. reuteri kills Candida, suppresses H. pylori, prevents vitamin B12 deficiency, decreases elevated cholesterol and triglycerides, elevates depressed white blood count, kills a broad diversity of noxious bacteria, restores balance to the cytokines produced by T lymphocytes --- particularly decreasing the inflammatory cytokines TNF- α , IL-6, and IL-12 --- increases the production of health-promoting short-chain fatty acids from prebiotics, protects diabetics from renal fibrosis, and has shown to be specifically beneficial in a broad diversity of diseases including asthma, atopic dermatitis, and Crohn's disease.

You have also learned in past Letters that Saccharomyces boulardii is unmatched in its power as a probiotic. S. boulardii is by far the most effective probiotic against Candida, against Helicobacter pylori, against antibiotic-associated diarrhea and all other forms of diarrhea, and that S. boulardii has unparalleled trophic effects on the intestinal mucosa, as it increases colonic butyrate and yields immuno-stimulatory effects far exceeding those of any other probiotic.

You now know all you need to know about probiotics. The 2 probiotics in your Immuno-Synbiotic are so far superior to all others, that there is no point wasting your patients' money on anything else. --- Now let us bring you up to speed on everything you need to know about prebiotics.

Prebiotics are concentrated sources of undigestible carbohydrate taken as supplements for the purpose of increasing the population of beneficial bacteria in the colon, and particularly feeding the bacterial species that are most beneficial. The secondary purpose of prebiotic supplementation is the production, through fermentation of the prebiotic by the beneficial bacteria, of increased quantities of short chain fatty acids. The most specific intent is to not only increase the overall quantity of SCFA, but to increase the proportion of butyrate, the most critical of the SCFA.

In your December Letter, we gave you the details on inulin. You were informed that inulin supplementation has been shown in countless studies to increase the population of beneficial intestinal flora, and that inulin increases the colonic and fecal levels of butyrate better than almost any other source of fiber. Metabolically, inulin decreases postprandial insulin response but has no effect on fasting glucose nor insulin, and thus helps Type II diabetics. Inulin is particularly beneficial for patients with Crohn's disease and ulcerative colitis. Inulin also increases GI absorption of magnesium, copper, and calcium.

Now, let us complete your understanding of your powerful Immuno-Synbiotic by giving the details on your other 2 prebiotics, guar gum and glucomannan.

Guar Gum is a prebiotic composed of galactose and mannose. Guar Gum produces more SCFA than most any other form of dietary fiber.

Guar Gum benefits patients with irritable bowel syndrome (IBS), including the constipation type, the diarrhea type, the mixed type, and all symptoms such as abdominal pain, flatulence, and abdominal spasm. Guar Gum has more beneficial effects on IBS patients than any other prebiotic. An outstanding feature of Guar Gum is the comparatively small amount required to achieve its prebiotic effects. Only 5 grams per day of Guar Gum is more effective in IBS patients than 30 grams per day of wheat bran. Furthermore, Guar Gum dramatically increases the intestinal population of healthy intestinal flora.

Additionally, Guar Gum decreases elevated LDL cholesterol, without decreasing HDL cholesterol. Guar Gum lowers cholesterol by a mechanism other than that of the other water-soluble fiber sources such as psyllium and pectin, both of which lower cholesterol only by interfering with intestinal absorption of cholesterol and other nutrients. In other words, Guar Gum lowers high cholesterol that is associated with excess sugar and carbohydrate intake, and does so by improving liver and metabolic efficiency.

Guar Gum also decreases elevated triglycerides, decreases elevated glucose, decreases excess insulin production, decreases obesity, and increases insulin sensitivity.

Guar Gum causes a cholecystokinin-mediated decrease in colonic transit time. It decreases bacterial conversion of the primary bile acids to secondary bile acids or their metabolites.

Glucomannan is perhaps the most effective prebiotic in terms of the small quantity required to yield major benefits. Only 4.5 grams daily for 21 days is enough to decrease constipation, increase healthy flora, decrease fecal pH, and increase acetate, propionate, and butyrate. Similar to Guar Gum, Glucomannan increases the HDL to cholesterol ratio, decreases LDL cholesterol, decreases liver cholesterol, decreases elevated glucose, and decreases excess insulin. Both Guar Gum and Glucomannan thus have tremendous benefits in preventing Metabolic Syndrome, with its associated abdominal obesity, Type II diabetes, hypertension, and cardiovascular disease.

Glucomannan has been shown to decrease immunoglobulin E-mediated dermatitis. It not only decreases atopic dermatitis (eczema), it decreases the associated autoimmune antibodies and TNF-alpha.

As part of its anti-inflammatory and cardiovascular-protective effects, Glucomannan decreases fibrinogen. It increases fecal excretion of steroidal stress hormones, and increases fecal excretion of bile acids, and prevents reabsorption of secondary bile acids.

Shall you help your patients **LIVE STRONGER LONGER?** --- Whether administered as part of your DIPHASIC NUTRITION PLAN or your METABOLIC BALANCING, give them Immuno-Synbiotic.

IMMUNO-SYNBIOTIC

(Information & Instructions
for NUTRI-SPEC Practitioners)

- A. All patients need to go through one bottle of IMMUNO-SYNBIOTIC to restore and maintain ideal gut mucosal structure and function, and to reduce INE stress.
1. Take on an empty stomach.
 2. Take 3, twice daily before meals, with a full glass of water.
 3. Repeat at least once every year to maintain INE balance.
 4. Patients with Crohn's disease or ulcerative colitis should not take IMMUNO-SYNBIOTIC without consulting their doctor since it can increase GI motility.
- B. Many patients need to go through more than one bottle of IMMUNO-SYNBIOTIC:
- patients with Eosinophilic Fungal Rhinosinusitis (as indicated by a non-sneezy boogey head)
 - patients who have demonstrated a dualistic INE stress response as a vacillator-oscillator via NUTRI-SPEC Metabolic Balance Testing
 - patients who show extreme INE stress in having one or more auto-immune diseases (Type I diabetes, Rheumatoid Arthritis, Lupus, Hashimoto's or Grave's Thyroiditis, alopecia, Reflex Sympathetic Dystrophy, Sjogren's, etc.)
 - patients who have immune-related neurodegenerative diseases (Parkinson's, Multiple Sclerosis, ALS)
 - patients who have chronic yeast/fungal infections (vaginal or oral Candida, athlete's foot or jock itch, ringworm, tinea versicolor, eczema/seborrheic dermatitis)
1. Take on an empty stomach, with a full glass of water.
 2. Go through one bottle of IMMUNO-SYNBIOTIC 3, twice daily for one bottle, then 2, twice daily for one bottle, then at least 1, twice daily for a stronger, longer lifetime. ---
 3. Patients with particularly nasty cases of the pathologies listed above will need more than 2 IMMUNO-SYNBIOTIC daily if they are to minimize their INE stress.
 4. (Patients with Crohn's disease or ulcerative colitis should not take IMMUNO-SYNBIOTIC without consulting their doctor.)
- C. Some patients, even those who seem reasonably healthy, cannot take the full IMMUNO-SYNBIOTIC recommendation of 3, twice daily at first. The reason is that their intestinal flora is so deranged that their GI tract becomes a battle field between the good guys and the bad guys. There can be a tremendous amount of gas pressure, bloating, sometimes diarrhea, and sometimes cramping. If the die-off of bad critters causes symptoms that are too uncomfortable, the patient should stop entirely for 1 day, then resume at 1, twice daily, and then increase to 2, twice daily, and then finally 3, twice daily as symptoms permit.
- D. Children need IMMUNO-SYNBIOTIC just as much as adults do. Except for children who are either immune deficient or suffering from autoimmune disease, 1 bottle of IMMUNO-SYNBIOTIC is generally all the typical child needs. For children age 10+, the adult dose is appropriate. For younger children, reduce the dose proportionately --- either 2, twice daily or 1, twice daily.

Just as with adults, if uncomfortable symptoms are produced, stop for a day and then come back on at a lower dose.