The Leaky Gut and Allergy Catch 22:

The Underlying Trigger for a Myriad of Health Concerns

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Increased intestinal permeability—otherwise known as leaky gut—is associated with a surprising number of health concerns including seasonal allergies, autoimmune disorders such as rheumatoid arthritis, migraines, depression, and Alzheimer's, among others that I will address later in this article. Athletes and postmenopausal women are also susceptible to impaired intestinal permeability. Yet, unless patients with these conditions have comorbid gastrointestinal issues, they often are not tested for leaky gut or the associated food sensitivities that serve as a red flag for the presence of increased intestinal permeability. In this article, I will discuss the link between leaky gut and food allergies/sensitivity as well as how this correlation may lead to the pathogenesis or progression of several diseases. My clinical philosophy is to test patients when it comes to allergens and sensitivities, to help ensure that indeed the food they are consuming is "Good Medicine and Does no Harm."

Leaky Gut: How and Why It Occurs

The intestinal epithelial lining and factors secreted from it create a barrier to prevent the passage of toxins, antigens, and bacteria in the lumen from entering the bloodstream while allowing for optimal nutrient absorption. When this barrier is compromised, it leads to a leaky gut. The foundation of this barrier consists of only a single layer of specialized epithelial cells joined by tight junction proteins. However, other factors are involved in intestinal barrier support including mucins, antimicrobial molecules, secretory IgA (sIgA), and cytokines.[1]

The most abundant immunoglobulin in the body, sIgA is found on intestinal mucosal surfaces where it interacts with commensal bacteria to protect against pathogens, toxins and other irritants. Every day, the human body synthesizes approximately 3 grams of sIgA into the intestinal lumen.[2] Although other aspects of gut barrier function can sometimes compensate for a decline in sIgA,[2] optimal levels of this immunoglobulin are important for gut health. sIgA also is secreted in other mucous membranes, such as the oral cavity, where it protects against viral, bacterial, and parasitic assaults. In the intestinal tract, sIgA is secreted when there is an immune reaction to foods.[3]

While underproduction of sIgA can result in impaired gut barrier function and increase intestinal permeability, dysregulation of zonulin, a physiological modulator of intercellular tight junctions, also poses a threat to gut barrier integrity.[4] Zonulin plays a role in intestinal innate immunity.[4] It is upregulated in animal- and human-derived intestinal epithelial cells exposed to the wheat protein gliadin, thus impairing gut barrier function and increasing intestinal permeability by weakening tight junctions.[5,6,7]

Zonulin upregulation also is linked to increased intestinal permeability in people with type 1 diabetes and their relatives.[8] Interestingly, in these subjects, zonulin upregulation occurs before disease development, pointing to an interplay between increased intestinal permeability, environmental exposure to non-self antigens, and the pathogenesis of autoimmunity in people who are genetically susceptible.[8]

Factors contributing to the disruptions in intestinal integrity responsible for leaky gut include food sensitivities/allergies, exposure to environmental toxins, chronic psychological stress, a diet high in sugar and processed foods, alcohol abuse, antibiotics, and anything that results in dysbiosis of the gut microbiota. These factors can all act together to compromise gut barrier function. Athletes are also susceptible to increased intestinal permeability with associated gastrointestinal problems.[9] Other factors that may predispose to the development of leaky gut include consuming a low-fiber or high-fat diet.[10,11]

Clinically, I routinely consider supplementation of glutamine and mitochondria support for athletes that present with either decreased performance or increased GI or allergic symptoms. I find that increased intestinal permeability arising from relative depletion of glutamine that is used for muscle, immune and gut integrity is often a key clinical consideration. Additionally, subclinical mitochondria dysfunction may also contribute to some athletes manifesting with intestinal permeability changes and decreased exertional performance.

The Catch-22 of Leaky Gut

Many factors can lead to leaky gut. However, intestinal permeability can also cause those same factors to begin with or make them worse, leading to a vicious cycle. For example, dysbiosis of the gut microbiota contributes to leaky gut.[12,13] Intestinal microbiota assist with the production of short-chain fatty acids (SCFAs), which provide fuel for colonocytes and are important for gut health.[14] At the same time that dysbiosis of the microbiota can result in leaky gut, increased intestinal permeability can exacerbate the imbalance in gut microbiota by encouraging microbial translocation into the systemic circulation and by inducing an inflammatory state,[15] which is associated with dysbiosis.[16]

Likewise, there is a bidirectional interplay between food allergies/sensitivities and leaky gut, which is why I employ IgG/IgA tests in patients at risk for leaky gut for food allergies/intolerances. Impaired gut barrier function leading to leaky gut is involved in the development of food allergies/intolerances. Increased intestinal permeability allows undigested food particles to translocate into the bloodstream, where the immune system launches an assault on what it perceives to be a foreign, harmful substance. Conversely, food allergies/sensitivities play a role in the etiology of intestinal permeability.[17] As I noted earlier in this article, exposure to food components such as gliadin upregulates zonulin. This ability to upregulate zonulin is an indicator that food antigens are involved in tight junction dysfunction.

Leaky gut can lead to deficiencies of nutrients such as zinc,[18] vitamin A,[19] iron,[19] and calcium,[20] creating another vicious cycle whereby intestinal permeability interferes with the absorption of nutrients and lack of nutrients weaken gut function.[18,20,21,22]

Health Conditions Related to Leaky Gut and Food Allergies or Intolerances

An abundance of evidence has found that leaky gut is associated with several health conditions. There is also indication that food allergies or sensitivities may be involved in the pathogenesis of many of these conditions or exacerbate the disorders in a manner that involves intestinal permeability. Moreover, I have observed in my clinical practice that testing for IgA/IgG food sensitivities and then implementing an elimination diet based on the offending foods has resulted in improvements in autoimmune disorders, mental health, and seasonal allergies.

Seasonal Allergies, Atopic Disease, and the Gut

The connection between allergic diseases and the gut has been demonstrated in many studies. Gnotobiotic mice treated with antibiotics were more susceptible to peanut sensitization characterized by increased peanut specific IgE and anaphylactic symptoms with peanut challenge.[23] Antibiotic-treated mice colonized with a Clostridia-enriched microbiota, which is known to influence colonic immunity, were protected against food allergies through a mechanism involving intestinal barrier function.[23] Further adding to the evidence of an association between allergies and gut health are a number of human studies demonstrating that supplementation with probiotics can mitigate allergic rhinitis or atopic disease.[24,25,26]

A common occurrence in people with allergic rhinitis known as oral allergy syndrome also points to the link between allergic diseases and the gut. This syndrome is characterized by a cross-reactivity to certain foods in people who are allergic to pollen from birch trees, ragweed, and grass. Patients allergic to grass pollen may react to peaches, oranges, celery, tomatoes, and melons, while ragweed allergy patients often react to melon, cucumber, banana, and zucchini.[27] Some estimates indicate that as many as 70% of people allergic to birch pollen have allergenic reactions after eating raw fruits.[28,29] Given the contribution of food allergies/intolerances to leaky gut, it is possible that these cross-reactivities may impair gut barrier function in people with seasonal allergies or atopic disease.

Autoimmune Diseases

A leaky gut can lead to the initiation and progression of autoimmune disease, especially in people who are genetically predisposed.[1] Autoimmune diseases associated with increased intestinal permeability include inflammatory bowel disease, celiac disease, autoimmune hepatitis, type 1 diabetes mellitus, multiple sclerosis, and systemic lupus erythematosus (SLE).[30,31,32,33,34] In type 1 diabetes, impaired intestinal barrier function has been shown to occur before the onset of the disease,[1,35] indicating it may play a role in the pathogenesis. Moreover, lipopolysaccharides (LPS), a cell wall component of gram-negative bacteria, can penetrate the intestinal epithelium and translocate into tissues, triggering the development and progression of SLE.[36] The resolution of intestinal permeability through the use of probiotic organisms is a promising approach to supporting the health of people with autoimmune diseases.[1]

Depression

Preliminary evidence suggests intestinal permeability associated with IgG-dependent food sensitivity correlates with the etiology of depression. Overproduction of zonulin is suspected to be triggered by the wheat protein gliadin, thus leading to impairment in the tight junction barrier and an increase in intestinal permeability.[37] This is thought to permit larger molecules to translocate into the bloodstream, leading to IgG-dependent food sensitivity and an associated immune response. This could lead to the synthesis

of proinflammatory cytokines, which may result in the development of depressive symptoms.[37]

This correlation between mood and leaky gut was demonstrated in a study of human patients with severe depression. In this study, researchers measured the serum concentrations of IgM and IgA against LPS of gram-negative enterobacteria in patients with major depression compared with normal controls.[38] Serum IgM and IgA against LPS of enterobacteria were significantly greater in patients with major depression compared to the controls, indicating increased translocation of LPS from gram negative bacteria in the depressed patients.

Autism

There is a correlation between leaky gut and autism spectrum disorder (ASD) as indicated by studies that show increased levels of zonulin in patients with autism compared to controls.[39] Furthermore, gastrointestinal symptoms, including increased intestinal permeability and dysbiosis of the gut microbiota, occur frequently in autistic children.[40] Biopsy specimens derived from the duodenum of 12 ASD and 9 control patients revealed that 75% of the ASD samples analyzed were characterized by lower expression of tight junction components, indicating an impaired intestinal barrier.[41] ASD also is associated with intolerance to the dietary proteins gliadin, cow's milk protein, and soy, as indicated by an abnormal innate immune response against the endotoxin LPS.[42]

Other Conditions Related to Leaky Gut

Metabolic syndrome is another disorder linked to increased intestinal permeability. In a study of 363 people, higher zonulin levels correlated with higher waist circumference, diastolic blood pressure, and glucose concentrations as well as a greater likelihood of being overweight or obese and having hyperlipidemia.[43] Leaky gut and the associated bacterial translocation also have been implicated in Alzheimer's disease.[44] Postmenopausal women are also at risk of impaired gut barrier function. Estrogen protects the intestinal mucous layer against oxidative damage and reduces intestinal permeability.[45] Moreover, low levels of sex steroids in mice increase intestinal permeability, which is involved in inflammatory pathways that cause bone loss.[46] Nephropathy is another condition associated with intestinal permeability as well as the production of IgA type antibodies against gliadin, soy, HAV (salt extracted antigens of oat flour), and ovalbumin.[47]

Likewise, increased intestinal permeability, and the resulting translocation of endotoxins into the bloodstream, are implicated in migraines.[48,49] Given the association between intestinal permeability and migraines, it's not surprising that both IgE-specific food allergies and IgG-mediated food intolerances have been found to aggravate migraine attacks, while an elimination diet reduced headache frequency.[50,51]

The Critical Importance of Testing

Based on the number of health conditions related to leaky gut and the association between food allergies/sensitivities and increased intestinal permeability, IgA/IgG testing for food sensitivities and IgE testing for food allergies is underutilized. The goal is to test patients in any of the high-risk groups mentioned in this article for food allergies/sensitivities then focus on eliminating the offending foods while simultaneously supporting gut healing through supplementation with L-glutamine, probiotics, and other relevant nutraceuticals. After six months on the supplements and the elimination diet, I then retest patients for food allergies/sensitivities. Once the leaky gut is fixed, many allergic and autoimmune burdens should lessen. As I share with my patients, if we are not testing we are guessing. Even the most theoretically advantageous food, such as avocado or beets can be detrimental, as countless times once I have tested patients for food sensitivities or overt allergies.

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