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by Editor

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From Science Fiction to Scientific Fact

Peter Bongiorno, ND, LAc

Anxiety disorders are the most common of the psychiatric illnesses in the United States, with approximately 30% of Americans experiencing anxiety-related symptoms during their lifetime,¹ and 18% having an anxiety disorder.² According to the Centers for Disease Control (CDC), 9.1% of the population currently meets the criteria for depression.³

Evidence shows that bowel disorders are often correlated with poor mood. In fact, 20% of patients with functional bowel disorders such as irritable bowel syndrome (IBS) have diagnosable psychiatric illness.⁴ Almost one-third of patients with IBS have been found to have anxiety or depression.⁵

Is Leaky Gut Real?

For the past few decades, natural medicine practitioners have referred to the unofficial diagnosis of "leaky gut syndrome" to describe a foundational connection between poor digestion and inflammatory disease. While abnormal intestinal permeability (aka leaky gut) is fairly well-recognized in the naturopathic physician community, conventional biomedicine has spurned this concept over the years, calling it "unproven" and the work of "pseudo-scientists." In fact, in 2013, the National Health Service of England⁶ summarized the sentiment of mainstream medicine regarding leaky gut, as follows:

"There is little evidence to support this theory... While it is true that certain factors can make the bowel more permeable, this probably does not lead to anything more than temporary mild inflammation of an area of the bowel... Some scientists and sceptics [sic] believe that people who promote 'leaky gut syndrome' are either misguided and read too much into the theory, or are deliberately misleading the public to make money from the 'treatments' they sell."

If you can endure it, the summary continues on to deride natural medicine overall:

"Generally, it is wise to view 'holistic' and 'natural health' websites with scepticism [sic] – do not assume that the information they provide is correct or based on scientific fact or evidence."

While this is still fairly standard thinking in the majority of the conventional medical world, this opinion seems to fly in the face of medical research. Emerging information suggests leaky gut syndrome is indeed quite real and is a strong contributor to disease, including mood disorders.

Food Allergy/Sensitivity and Leaky Gut – The Evidence

Neurological manifestations in patients with established celiac disease have been reported since 1966.⁷ However, it was not until 30 years later that gluten sensitivity was first shown to manifest solely as neurological dysfunction, such as unexplained neuropathies and ataxia.⁸

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While celiac is an antibody-mediated disease affecting 1% of the population and is generally characterized by gastrointestinal complaints, gluten sensitivities can be subtler in reaction, often without overt gastrointestinal problems, manifesting instead as extra-intestinal neurologic and psychiatric symptoms. In celiac patients, tryptophan stores may be especially vulnerable to malabsorption. Reductions in spinal fluid tryptophan have been shown to increase after 1 year on a gluten-free diet.⁹

Gluten sensitivity may be even more causative of psychiatric illness than overt celiac disease. Gluten sensitivity occur at 6 times the rate as celiac disease and does not generally present with the hallmark villi breakdown or celiac antibodies.¹⁰ Most interestingly, one study showed gluten withdrawal to produce a greater improvement in gut symptoms in non-celiac, gluten-sensitive patients than in patients with celiac disease (75% vs 64.7%, respectively).¹¹

Any food to which a particular person is sensitive can spark immune-related responses in the digestive tract, eliciting inflammatory cascades throughout the body. Stressors will also increase the likelihood of immune response to food by decreasing parasympathetic response and proper enzymatic production. Low digestive enzyme status leads to an inability to digest food, which can then result in undigested macromolecules breaching the intestinal barrier. This, in turn, can provoke inflammatory responses via the mucosa- and gut-associated lymphoid tissue (MALT and GALT).

Leaky gut-induced inflammatory responses in the gut over a long period of time will significantly compromise both the structure and repair mechanisms of the digestive tract. Under this inflammatory fire, tight junctions, known to hold gastrointestinal (GI) cells together, begin to crumble. When these structures break down, material in the lumen of the GI tract has greater access to the bloodstream. This is known by the term of "gut permeability" or what many practitioners and enlightened patients simply call "leaky gut."

Particles that escape from the digestive tract can travel to other parts of the body and trigger global inflammatory effects, contributing to disease. If someone has a predisposition (genetically or epigenetically) to a particular disease, leaky gut and its accompanying inflammation may increase the likelihood that this disease will manifest. For example, in an individual prone to heart problems, inflammation in the coronary arteries will contribute to endothelial dysfunction and blockage. In a person predisposed to autoimmune conditions like rheumatoid arthritis, the inflammation may foster disfigured and painful joints.

Leaky Gut and Mood Disorders

In a similar fashion, people with mood disorders may have a greater tendency to have brain inflammation. When leaky gut and intestinal inflammation are present, transcellularly-leaked particles translocate into the bloodstream where they enter the hepatic portal system and spur upregulation of the hepatic Kupffer cells, thereby triggering microglial inflammation in the brain; this can result in brain degeneration and changes in mood. Perivascular areas of the brain, such as the hypothalamus and limbic system, are especially vulnerable to inflammation and contribute to "sickness behavior" (anhedonia, fatigue, etc). The likelihood of this cascade of events has been shown to be far greater with leaky gut than when the intestinal barrier is intact.¹²

One study measured the serum concentrations of IgM and IgG antibodies against lipopolysaccharide (LPS) of intestinal gram-negative bacteria in patients with chronic fatigue.¹³ Positivity for these antibodies effectively serves as a marker of a leaky gut situation. Forty-one of these patients were given a "leaky gut diet" (ie, low-carb, and milk- and gluten-free) and prescribed natural anti-inflammatory and anti-oxidative supplements such as glutamine, N-acetylcysteine, and zinc. After an average of 10 to 14 months, 24 out of 41 patients showed a significant clinical improvement or remission in mood and fatigue, as well as normalization of the IgA and IgM responses. The author has suggested that the inflammatory response from the translocation of bacteria creates an inflammatory cascade that contributed to a "sickness behavior" that can manifest as psychiatric illness.¹⁴ A study by the same group a few years later in 112 patients with major depression found that serum IgM and IgA against LPS coats of these commensals were significantly higher in chronically depressed patients than in controls.¹⁵ Previous animal studies have also demonstrated the presence of LPS to also cause anxiety-like behaviors, including reduced exploratory behavior and social interactions.¹⁶

There are various ways the body reveals increased levels of inflammation. These may include the presence of skin conditions (rashes, eczema, psoriasis, rosacea, etc) or be more internal (such as autoimmune conditions, cancers, cardiovascular disease, mental health, and inflammatory bowel diseases). Laboratory tests (such as high levels of ESR, CRP, homocysteine, and/or autoimmune markers (eg, ANA, anti-thyroid antibodies, and celiac markers) can also point to inflammation.

Naturopathic Ways to Improve Leaky Gut and Mood:

1. **Meditation / Relaxation/ Mind-body work:** Help to increase parasympathetic response and support circulation to the GI tract
2. **Sleep:** Eight hours of sleep and getting to bed by 11PM at the latest helps balance immune function
3. **Exercise:** At least 3 times a week for 30 minutes helps burn stress hormones, calms the nervous system, and builds muscle to support insulin sensitivity, thus lowering insulin, which is pro-inflammatory

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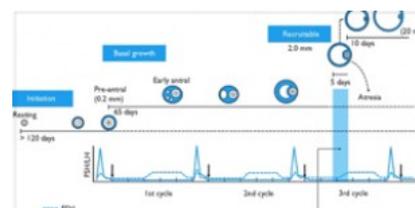
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4. **Diet:** Focus on anti-inflammatory foods and the Mediterranean diet: fish, green vegetables, raw nuts and seeds, and plenty of fiber. Avoid dairy, gluten, and foods cooked at high temperatures (fried, charbroiled, etc).
5. **Supplements:** Help to lower inflammation and heal a leaky gut:
 1. **Fish oil:** At least 1000 mg EPA/800 mg DHA for anti-inflammatory and mood-boosting effects^{17,18}
 2. **Probiotics:** To help heal the mucosal membrane¹⁹
 3. **Zinc:** Studies have shown zinc supplementation to resolve permeability alterations in patients with Crohn's disease and help prevent relapse in remitted patients.²⁰ Typical dose is 15 mg BID of zinc carnosine.
 4. **Curcuma longa (turmeric):** Helps decrease inflammation and oxidative stress in the gut.²¹ Dosage will depend on form and preparation.
 5. **L-Glutamine:** Is a preferred fuel for digestive tract cells and helps with intestinal repair.²² Standard dosage is 1 tsp (~5 g) BID in liquid away from meals.
 6. **Robert's Formula / Bastyr Formula:** Is an old naturopathic formula with anecdotal efficacy for healing the digestive tract; no formal research has been done on this herbal combination. While there are variations, the standard formula usually includes *Althea officinalis*, *Echinacea*, *Ulmus fulva*, *Geranium*, *Phytolacca*, *Hydrastis*, and cabbage powder, which is high in glutamine. Some versions also include niacinamide and pancreatic enzymes. This formula is typically dosed 1 or 2 capsules up to 3 times daily.
 7. **Botanicals for Anti-anxiety / Anti-depression / Digestive Support:** Botanicals which address both digestive health and mood include *Crocus sativus* (saffron) and lavender for depression and digestive issues; also *Scutellaria lateriflora* (skullcap) and *Matricaria* (chamomile) for anxiety with digestive issues.



Peter Bongiorno ND, LAc was a predoctoral fellow in clinical neuroendocrinology at the National Institute of Mental Health before attending Bastyr University for his naturopathic and acupuncture degrees. He has a thriving practice in New York City and Long Island, NY. His latest book, *How Come They're Happy and I'm Not?: Natural Treatments to Heal Depression for Good* (Red Wheel/Weiser), is available on Amazon. Dr Bongiorno can be contacted through his clinic, www.InnerSourceHealth.com, and www.DrPeterBongiorno.com.

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