
Gastrointestinal Integrity and Good Health

Key Nutrients for Maintaining the Balance of Life

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The gastrointestinal (GI) tract is the boundary between the external and the internal world. The GI tract's function is to allow enough of the external world to be absorbed to allow life to be sustained but not so much that homeostasis is disturbed, leading to disease and possible death. The absorptive process of the intestines takes place primarily as a result of diffusion, carrier transport, and endocytosis. When too great or too small a quantity of nutrients and substances is absorbed, the balance of life is challenged. The GI tract's protective role qualifies it as one of the largest immune organs in the body, responsible for protecting the internal milieu.

A Healthy GI Tract's Effect on Overall Health

Many chronic disease states arise from inadequate functioning of the GI tract. Any state of functioning that is less than optimal results in the inability of the body to control its exposure to harmful external factors.

Illness frequently arises when the total load of toxins and external substances accumulates to deleterious levels as a result of increased permeability and parasitic infections. It is critical in the pursuit of health to optimize GI integrity, thus minimizing disruptive xenobiotic and other exposures. (See box entitled Supportive Measures for Protecting GI Functioning.)

Proper Intestinal Permeability

When the intestinal tract is functioning properly, it allows for the transport of sufficient nutrients to nourish the

body yet offers adequate filtration of molecules that can result in harm. Increased intestinal permeability (Leaky Gut syndrome), on the other hand, leads to a myriad of potential health consequences. This arises from the increased absorption of xenobiotics, antigens, immune complexes, intact microorganisms, and endotoxins. Chronic disruption of GI permeability has been associated with a predisposition to developing autoimmune diseases, liver dysfunction, and arthritic and other degenerative diseases. (See box entitled Conditions Associated With Disrupted Intestinal Permeability.)

Causes of Increased Intestinal Permeability

Altered intestinal permeability may arise from any one of many etiologies or combinations thereof. Opportunistic infections can cause disruption of the selective permeability of the intestinal lumen. Among classical culprits are parasitic infections, intestinal candidiasis, bacterial overgrowth, food allergies, and chronic imbalances of the normal intestinal microflora.

Medication-Induced Increased Permeability

Numerous drugs have been associated with increased intestinal permeability. Among these drugs are amphetamines, cocaine, estrogen, therapeutic gold, chemotherapy drugs, nonsteroidal anti-inflammatory drugs, methotrexate, and antibiotics. The increased permeability associated with these drugs can be either direct or indirect.¹

Other Common Causes of Increased Intestinal Permeability

Alcoholism has been associated with increased permeability as a result of the damage to GI mucosa.

Gastroenteritis, whether viral or bacterial in origin, can lead to increased intestinal permeability. Eating during the acute illness phase and ensuring that proper hydration is maintained can minimize this.²

Total parenteral nutrition is associated with increased intestinal permeability and, as a result, increased risk of endotoxemia and bacteremia.

Surgery and radiation have been linked to altered intestinal permeability. It has been proposed that abdominal radiation results in increased reactive oxygen species of flora that damage the intestinal mucosa and can lead to long-term and sometimes progressive disruption of GI functioning.³ A similar disturbance of intestinal permeability has been demonstrated in patients who have undergone cardiac surgery, which leads to elevation of blood endotoxin levels.⁴

Trauma of a severe nature, including blunt and other traumas to the abdomen, as well as severe burns, can result in chronic disruption of intestinal permeability.⁵

Diagnostic Testing

The most common clinical intestinal permeability test is the lactulose/mannitol test. This test makes use of the fact that both of these water-soluble molecules are not metabolized by the body and are eliminated intact via the urinary tract.

Glutamine has proven to be helpful in preventing injury and in facilitating the healing process.

Supportive Measures for Protecting Gastrointestinal Functioning

Reduce exposure to toxins:

- In the diet
- In the environment
- In the patient's lifestyle
- By enhancing GI^a function.

To achieve optimal digestion/motility:

- Maintain adequate digestive enzymes
- Decrease endotoxin production
- Strengthen mucosal lining
- Eliminate GI pathogens
- Protect against oxidative damage
- Maintain normal gastric acidity
- Maintain sufficient mucus
- Ensure proper intestinal flora.

^aGI, gastrointestinal.

Conditions Associated With Disrupted Intestinal Permeability

- Alcoholism
- Ankylosing spondylitis
- Arthritis
- Asthma
- Celiac disease
- Crohn's disease
- Cystic fibrosis
- Eczema
- Food allergy
- Gastroenteritis
- Increased intestinal permeability caused by NSAID^a utilization
- Rheumatoid arthritis
- Ulcerative colitis
- Urticaria

^aNSAID, nonsteroidal anti-inflammatory drug.

Lactulose and mannitol differ in size and in the degree to which they are absorbed in the intestinal tract. Mannitol is a monosaccharide with about half the molecular weight of lactulose and is readily absorbed and excreted in the urine in large quantities. In contrast, lactulose, a disaccharide, is not absorbed well and, as a result, appears in the urine only in small quantities.

The test is simple to administer: After an overnight fast, a urine sample is collected prior to the ingestion of the lactulose and mannitol solution. After the sugar solution is consumed, urine is collected for 6 hours. If lactulose is found in large amounts, it indicates increased intestinal permeability. Mannitol, if found in small quantities, suggests malabsorption.

Nutrients To Support Healthy GI Functioning

Glutamine

Glutamine is the most abundantly available amino acid in the body's free amino-acid pool. Glutamine's concentration in skeletal muscle, the principal organ of glutamine synthesis and storage, is up to 30 times greater than amounts that go into the body's circulation. The

small intestine is the major organ for glutamine extraction from the body's circulation, accounting for 20–30 percent of total glutamine utilization. Glutamine concentrations drop dramatically during serious illness.⁶

Glutamine is the key amino acid used by the enterocytes within the small intestine. The mucosa of the small intestine is one of the most rapidly proliferating tissues in the body. This tissue renews itself once every 48–72 hours.⁷

There has been ongoing debate as to whether glutamine should be considered as a "qualified" essential amino acid for the gut. In the truest sense, however, glutamine must be qualified as being nonessential because it can be synthesized from glutamate in various tissues.

Glutamine functions as the preferred oxidative fuel for enterocytes and as a precursor component for the synthesis of lipids, nucleic acids, and other amino acids. Metabolism of this amino acid to α -ketoglutarate, with subsequent oxidation in the Krebs cycle, yields 30 mol of ATP per mol of glutamine.

This critical nutrient also serves as a precursor for glucosamine synthesis. Mucin synthesis, in turn, requires glu-

cosamine, serving the critical role of being the provider of the mucus coating to the intestinal lining.

What is also critical in the pathway of glutamine metabolism is sufficient glucosamine synthetase essential for the formation of N-acetyl-D-glucosamine. Inflammatory and irritable bowel disease have both been linked, in part, to deficient glucosamine synthetase.⁸

In a study of 20 postoperative patients on total parenteral nutrition, the patients received either parenteral nutrition enriched with glycyl-L-glutamine or the standard parenteral nutrition. Duodenal biopsies were taken prior to, and 2 weeks after, the time the parenteral nutrition was administered. Villous height was unaltered in the glutamine-enriched group as opposed to a decreased villous height in the non-glutamine-enriched group.⁹

When it comes to treating intestinal injury, glutamine also has proven to be helpful in preventing injury and in facilitating the healing process. A study involving whole-abdominal radiation demonstrated that rats receiving glutamine-enriched diets had a 100 percent survival compared to 45 percent of the rats in the non-glutamine-enriched group. In addition, the glutamine-enriched group had diminished bloody diarrhea and bowel perforation.¹⁰

Dietary Fiber

Fermentation of soluble fiber by intestinal bacteria serves as the primary source of short-chain fatty acids, such as butyrate, acetate, and propionate.

Butyric acid is the fatty acid that most nourishes the epithelial tissues of the colon. These fermentation products feed colonic tissue but also support the growth of friendly intestinal flora, decreasing colon pH and helping suppress pathogenic growth. The preferred fibers include oat bran and psyllium, whereas wheat bran does not increase short-chain fatty acids.¹¹

Essential Fatty Acids

Increased consumption of fish oils and certain vegetable oils that are high in essential fatty acids (EFAs) helps to lessen

The use of common sources of flavonoids decreases inflammation.

intestinal inflammation and increased permeability. Biochemically, EFAs help to decrease the inflammatory process of the prostaglandin, leukotriene, and thromboxane pathways.¹²

Flavonoids

One of the greatest confounding variables when addressing increased intestinal permeability is the inflammatory process that perpetuates GI disruption further. However, the use of common sources of flavonoids, such as ginkgo, quercetin, and green tea, decreases inflammation. The antioxidant and membrane-stabilizing properties of flavonoids allow them to help stabilize mast cells that, when triggered to degranulate, release histamine that injures mucosal cells.¹³

Fructo-Oligosaccharides

Fructo-oligosaccharides (FOS) are practically indigestible by the human digestive system. Supplementation increases *Bifidobacteria* and *Lactobacilli* growth, decreases intestinal pH, and enhances fecal short-chain fatty acid levels.¹⁴

Lactobacillus

Lactobacilli have been used traditionally to assist in recolonizing the intestinal tract after postantibiotic treatment. The benefits are not limited to this simple function. These lactic-acid-producing organisms also reduce intestinal pH, produce natural antibacterial substances, support secretory immunoglobulin A production, decrease tumor necrosis factor, and compete for binding sites with pathogens.¹⁵

N-Acetyl-D-Glucosamine

N-acetyl-D-glucosamine (NAG) synthesis in the body begins with the conversion of glutamine to glucosamine-6-phosphate that undergoes N-acetylation to form NAG. This nutrient is a key component in the formation of glycoproteins that are essential for the synthesis of intestinal glycocalyx.

In the case of irritable bowel disease, there is a biochemical defect that prevents this acetylation process. Thus, the normal

protective glycocalyx is diminished allowing the mucosa to be more susceptible to inflammation and irritation. External factors, such as aspirin and alcohol use, can also lead to decreased glycoprotein formation.¹⁶

Phosphatidylcholine

The phospholipid membrane of intestinal cells is enhanced by phosphatidylcholine supplementation.¹⁷ The strengthened intestinal mucosa cells are more resistant to irritation, external insult, and inflammatory processes.¹⁸

Conclusion

The overall health of the GI tract is relevant to major health care problems because catabolic diseases are major causes of death and disability. More specifically, these degenerative processes are characterized by an increase in glutamine metabolism.¹⁹ Involvement of glutamine in maintaining health and well-being is illustrated well by the fact that more of this critical amino acid is required in chronic disease processes.²⁰ □

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