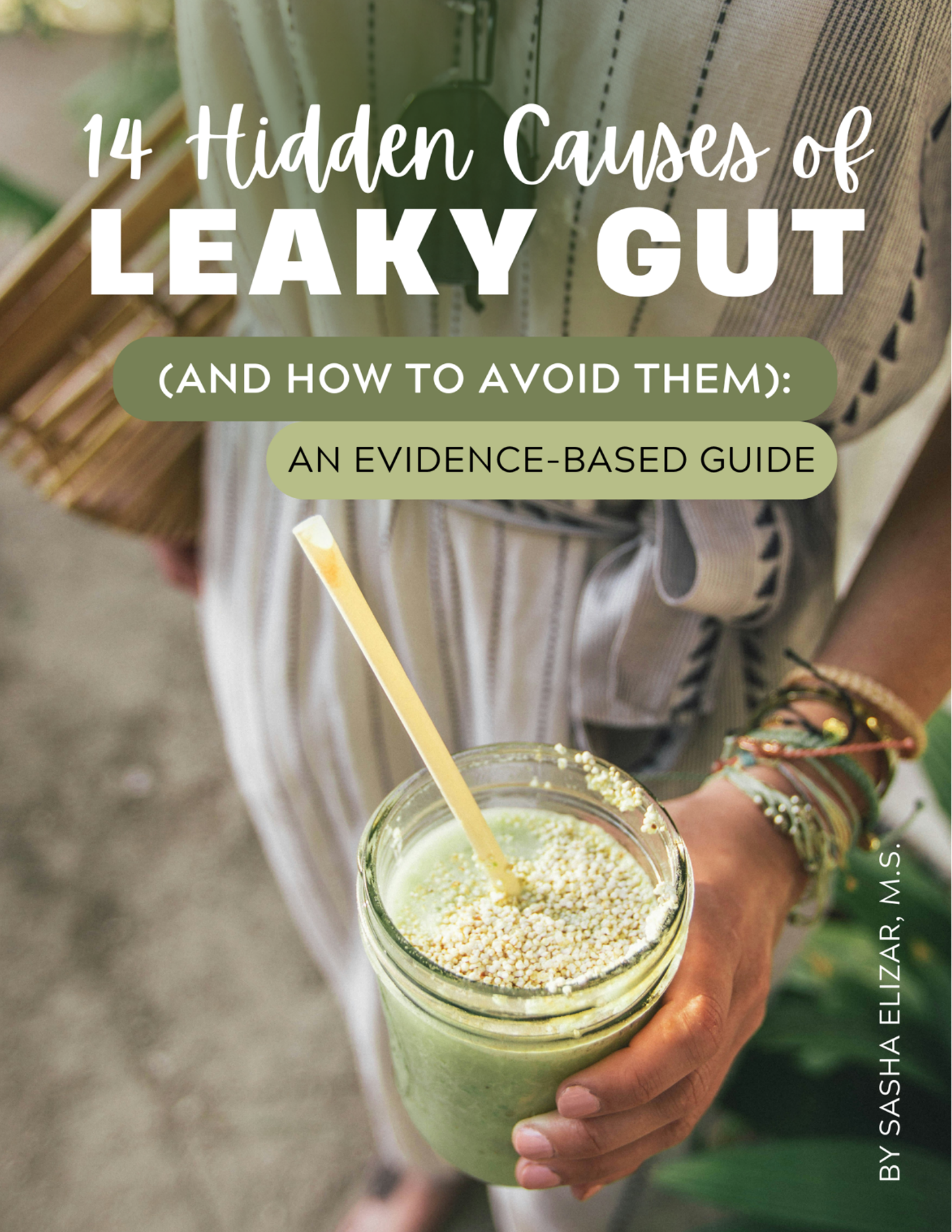


A person wearing a light-colored, patterned shirt and a woven basket on their back is holding a glass jar filled with a green smoothie. The smoothie is topped with a layer of white seeds and a wooden stick is inserted into it. The person's hand is visible, and they are wearing a colorful beaded bracelet.

14 Hidden Causes of **LEAKY GUT**

(AND HOW TO AVOID THEM):

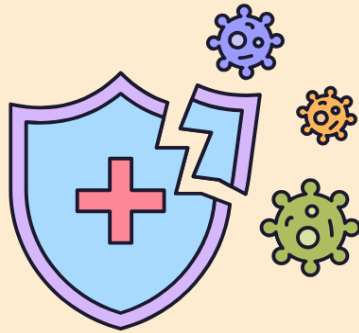
AN EVIDENCE-BASED GUIDE

BY SASHA ELIZAR, M.S.

Causes of LEAKY GUT



AGING



AUTOIMMUNE
DISEASE



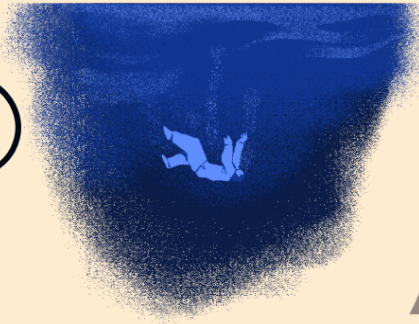
GENETICS



INFLAMMATION &
OXIDATIVE STRESS



STRESS &
TRAUMA
[EMOTIONAL &
PHYSICAL]



DEPRESSION



URBANIZATION
& EXCESS
HYGIENE



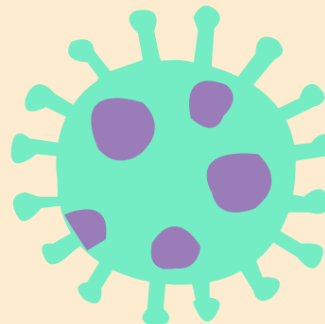
TOXIC
CHEMICALS



DRUGS OF
ABUSE



DIET



TOXINS &
INFECTION



MEDICATIONS
& RADIATION



Introduction

We all know gut health is the foundation of an optimized body. Like soil nourishing the roots and branches of a tree, nutrition feeds the gut and organs of the body. The richer the nourishment, the lusher the leaves: skin, muscles, hair, nails, vision, etc. Thus, supporting the roots (that is, the gut) allows you to absorb more light (i.e., gain more energy, vitality, and clarity, and enjoy more life) and also give more shade to others (i.e., emanate generosity, presence, and make a positive impact). Stronger roots make for a taller tree.

For the past 10 years as a neuroscience researcher, I have been interested in the causes of human pain, suffering, and disease. Though self-regulation and stress reduction (e.g. an information diet) are major aspects of mental well-being, it has become increasingly evident that in long-term, brain function relies heavily on lifestyle factors, particularly nutrition. Nutrition is a particularly bio-hackable and modifiable factor in health: daily choices add up to our body composition, rate of aging, function, and quality of life. Disease is driven by inflammation, and improper nutrition majorly contributes to inflammation.

What's one of the most significant drivers of inflammation? Leaky gut, a condition which is now widely acknowledged within the scientific community. This article explores in depth what causes leaky gut, an important pre-requisite to any discussion about solutions to leaky gut.

Your gut barrier is made up of mucus and a single layer of intestinal epithelial cells. (Learn more about [gut layer anatomy](#).) Leaky gut is a process whereby small gaps in the gut lining allow food contents, microbes, and microbial signatures to “leak” into immune tissue and circulation. Gut inflammation can create a ripple effect beyond the GI tract, affecting the skin, brain, lungs, immune system, metabolism, and the heart, bringing symptoms like pain, anxiety, depression, breakouts, brain fog, fatigue, vitamin deficiencies, asthma, and autoimmune disease.

Disease is often rooted in inflammation; in turn, a major driver of inflammation is leaky gut. We turn our attention now to the root causes of leaky gut. In this feature we will cover the host, psychological, biological, dietary, chemical, and electromagnetic causes of leaky gut. I hope you find this issue as valuable as I did putting it together.

Sincerely,

Sasha Elizar, M.S.

Table of Contents

Signs and Symptoms of Leaky Gut	5
Causes and Effects of Gut Dysbiosis	6
Part 1: Host-related risk factors for leaky gut	7
Aging	7
Autoimmune disease and cross-reactivity	8
Genetics and family history	8
Inflammation and oxidative stress	8
Part 2: Psychological influences and mental health	10
Stress and trauma	10
Depression	11
Physical stress	11
Part 3: Environmental and lifestyle factors	13
Urbanization and excess hygiene	13
Alcohol, cigarettes, opiates, and other psychoactive substances	13
Dietary factors	14
Toxic chemicals	17
Part 4: Biological and iatrogenic factors	22
Infections, toxins in food, and microbial endotoxins	22
Medications: antibiotics, NSAIDs, and more	23
Ionizing Radiation	26
Summary	27
References	28

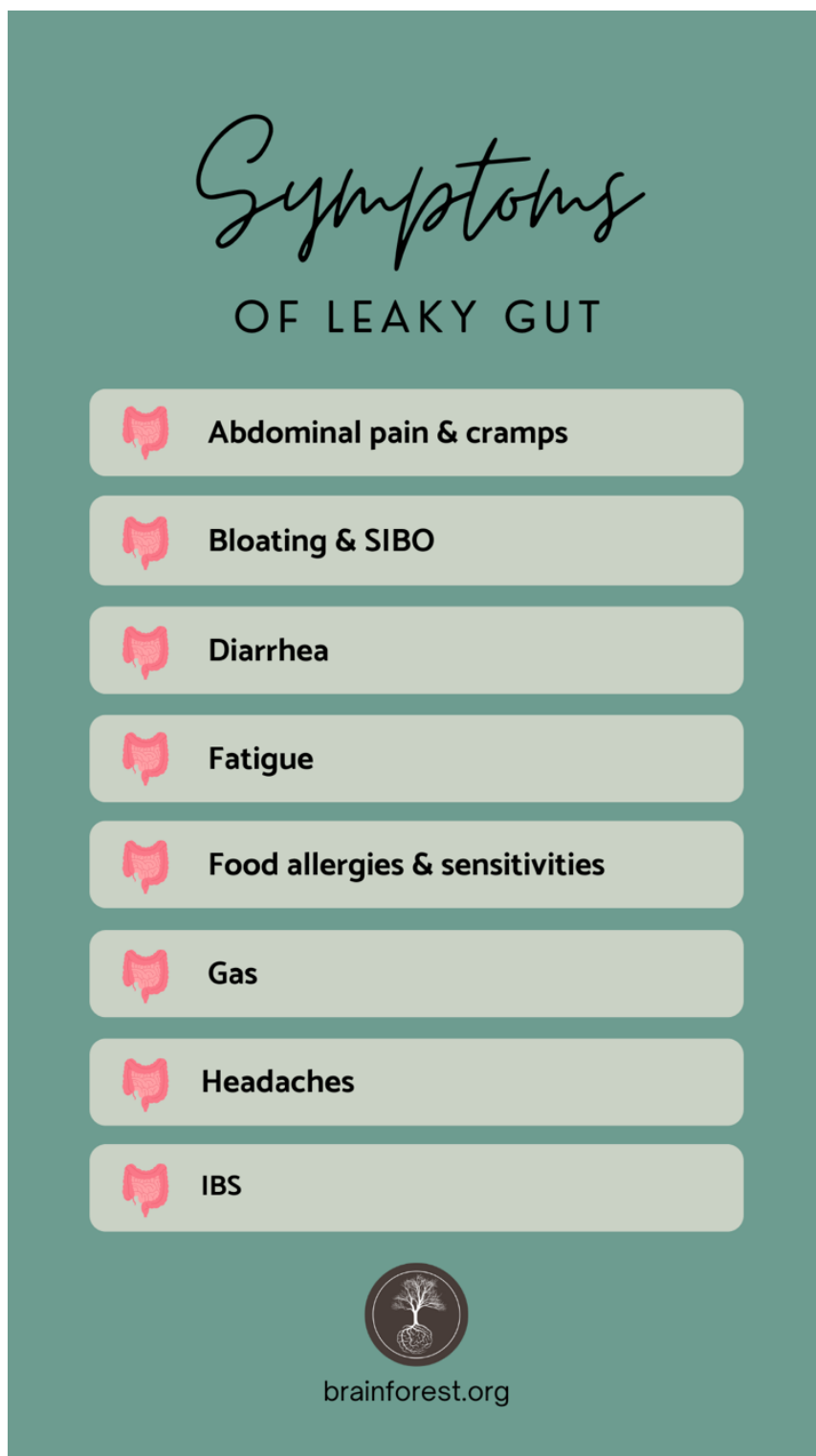
What are the signs and symptoms of leaky gut?

How does one come to suspect they may have leaky gut? Symptoms of leaky gut include:

- Abdominal pain and cramps
- Irritable bowel syndrome (IBS)
- Bloating (often driven by small intestinal bacterial overgrowth, or SIBO)
- Diarrhea
- Fatigue
- Gas
- Headaches
- Food allergies and sensitivities

These symptoms don't necessarily mean someone has leaky gut, but it's worth checking through functional gut panels [1] (see [biomarkers of leaky gut](#)). One of biggest leaky gut red flags is having issues with a variety of foods.

Leaky gut can also have far-reaching effects on other body symptoms, generating hormone disruption, low energy, brain fog, inflammation, dysregulated metabolism, and skin concerns, as discussed more in the [biomarker](#) issue.



What causes gut dysbiosis? What are the effects of gut dysbiosis?

The best way to prevent leaky gut is to prevent gut dysbiosis from happening in the first place, wherever possible, by cultivating a balanced gut ecosystem. Gut dysbiosis is an imbalance in the composition and function of the gut microbiota, towards a more pathogenic, pro-inflammatory phenotype. That is, there is a greater proportion of harmful microbes that secrete deleterious metabolites, which have a negative effect on a host's physiology.

Sometimes, temporary changes in the microbiota are unavoidable, such as dietary changes due to travel or antibiotic use due to infection. However, sustained gut microbial imbalances increase risk of leaky gut.

Causes of gut dysbiosis include:

- Poor diet
 - High-fat diet
 - Nutritional insufficiency (e.g., fiber or tryptophan deficiency)
 - Pesticides on food
- Sedentary lifestyle
- Stress
- Poor sleep [2]
- Antibiotic use [3]. Antibiotics disrupt the gut microbiota (GM), leading to fungal overgrowth. They also decrease short-chain fatty acid (SCFA) production, leading to electrolyte imbalances. The duration of the disruption / shift in the microbiome effects depends on the mechanism of action of the antibiotic. For example, amoxicillin doesn't have long-term impacts on GM, while ciprofloxacin does. Repeated antibiotic exposure can lead to destabilization of gut flora, resulting in antibiotic-resistant pathogenic bacteria outgrowth.

Gut dysbiosis may lead to malabsorption, insulin resistance, and compromised immunity [2, 4]. Eubiosis, indicated by favorable metabolic activity in the gut, goes a long way towards building and maintaining a balanced, healthy body.

Host-related Risk Factors for Leaky Gut

1. Aging

Aging elevates the risk of leaky gut. A study published in Scientific Reports in [2018](#) by Dr. Kylie Kavanagh at Wake Forest University School of Medicine looked at leaky gut and metabolic disease in healthy aged female monkeys versus young monkeys fed an equivalent diet [5]. They found that older monkeys had significantly higher endotoxin levels in the portal vein, which carries blood from the gut to the liver. LBP-1, a [biomarker of leaky gut](#), was five times higher in old monkeys. This suggests that leaky gut occurs due to the natural aging process.

Age-related changes in gut function include:

1. Declines in mucus. The [mucosal barrier](#) protects us from infections, environmental toxins, pollutants, and allergens. Mucus and antimicrobial peptide secretion decline with age.
2. Degeneration of intestinal epithelial cells (IECs), including Goblet cells
3. Decreased ability to fight infection. Immunosenescence in primates is characterized by a loss of naïve T cells with a shift towards memory phenotype cells, loss of T cell diversity, and greater systemic inflammation. Thus, we become less resilient to new infections as we get older.

That being said, immunotherapies (like immunoglobulins or monoclonal antibodies against pro-inflammatory cytokines like TNF-alpha) may not improve barrier function. They treat the symptoms, not the causes. Stopping microbial translocation is paramount. The key target here is restoring the intestinal barrier, as well as fortifying the gut-associated lymphoid tissue (GALT). We know aging is not a linear process, and the rate of aging can be decelerated through by combining specific lifestyle interventions that restore and fortify the gut barrier with those that quell chronic inflammation.

Therapies that reverse immune aging have not been developed yet. [Microbiome rejuvenation](#) therapy is being investigated for its potential to reverse some of the declines in function of the gut with age and as an approach to decelerate aging. This treatment introduces youth-associated, beneficial gut microbiota. However, it has yet to be clinically investigated for improving gut barrier function.

2. Autoimmune Disease and Cross-Reactivity

The immune system constantly evaluates gut bacteria to determine whether they are helpful, neutral, or harmful [6]. Intestinal epithelial cells help maintain immune tolerance by keeping bacteria within approved zones like the gut lumen or mucus layer [6]. Microbes communicate by displaying or secreting molecular signals called antigens, which are typically proteins or sugars.

Problems arise when microbial antigens resemble proteins found in human cells. In such cases, immune cells may mistake self-tissue for foreign invaders, triggering an autoimmune response. Unfortunately, this means that microbes (or food intolerances interacting with genes) can trigger autoimmune disease.

This molecular mimicry can lead to cross-reactivity, where the immune system attacks healthy tissues, contributing to autoimmune diseases. These conditions are often linked to leaky gut, either as a cause or a consequence. When immune responses are deployed, they can open compartments like the gut barrier or even the blood-brain barrier.

In a similar vein, under systemic, chronic inflammation induced by gut microbiota, IFN- γ , IL-17A, and zonulin can promote leaky gut by modulating tight junctions and their associated cytoskeleton. This creates a feedback loop where autoimmune activity worsens gut permeability, which in turn perpetuates inflammation. Identifying the original trigger—be it microbial, dietary, or environmental—is key to breaking this cycle.

3. Genetics and Family History

Asymptomatic close relatives of patients with inflammatory bowel diseases (IBDs) also show compromised barrier integrity [7]. IBS is more common in individuals with a first-degree relative with IBD, and IBS is associated with leaky gut. Indeed, there is an inherited component of leaky gut, but whether it is at the level of genetics or epigenetics is unclear. These distinctions can lead to variation in disease severity and manifestation.

4. Inflammation and Oxidative Stress

Left unresolved, an imbalanced internal habitat will chronically trigger the immune system, eventually leading to oxidative stress, DNA damage, and inflammation.

Inflammatory cytokines (signaling molecules e.g. IFN- γ and TNF- α) contribute to barrier dysfunction [8]. Exactly how is unknown, but some molecular mechanisms are proposed. Cytokines can modulate the

cytoskeleton, activate kinases that phosphorylate tight junctions, disassemble tight junctions, or cause tight junctions to be internalized in vesicles (cargo bubbles) and degraded in the proteasome (a complex that degrades proteins). Proteasome degradation has been seen in IBS [7, 8].

IFN- γ also acts through an AMPK-dependent pathway to downregulate ZO-1 and occludin expression, inducing barrier permeability, irrespective of cellular energy levels [7].

Oxidative stress can also cause leaky gut—reactive oxygen species (ROS) can disrupt tight junction protein interactions and alter membrane integrity [7, 9]. Thus, it's important to detoxify from free radicals, counteract oxidative stress, and cultivate microbial species that lead to cytokine balance. Oxidative stress can be mitigated in part by lifestyle behaviors: check out the environmental causes of [oxidative stress](#).

Psychological Influences & Mental Health

5. Stress and Trauma

The mind-body connection is very real—mental states influence health and disease. Chronic stress modulates inflammation and can drive leaky gut.

How does stress affect the gut and brain barriers?

- Neuroendocrine-immune crosstalk via the hypothalamic-pituitary-adrenal (HPA) axis.
 - Corticotropin-releasing hormone (CRH) secreted from the hypothalamus mediates activation of mast cells, a type of innate immune cell [10]. This was shown in human participants tasked with public speaking and receiving electrical shocks.
 - Human participants with significantly elevated cortisol also had permeability changes [11].
 - Stress hormones cause translocation of LPS, which binds to immune receptors, CD14 and TLR4. This triggers the release of pro-inflammatory cytokines (TNF- α , IFN- γ , IL1b, and IL-6), histamine, and proteases. This immune signaling can, in turn, increase tight junction opening, leading to endotoxemia.
- Changes in blood flow.
 - Stress diverts blood away from the gut and towards the muscles. This siphons off resources and can transiently reduce gut function. A stomachache or diarrhea are commonly reported responses to stressful scenarios. Background stress can make healthy women more susceptible to the impacts of physical stress on leaky gut [12].
- Disruption of the blood-brain barrier (BBB) [10].
 - In another study of US Marines undergoing training, stress did not increase leaky gut, as measured by LBP, but was associated with BBB permeability, as measured by S100B [13].
- Affects the mucus lining of the gut.
 - Physical stress impacts the mucus lining of the gut. Major burns can cause mucosal weakness found in stress disorders [14].
- Speeds up GI motility.
 - CRH secretion in turn can cause enterochromaffin cells to secrete excessive amounts of serotonin (5-HT), which speeds up GI motility [15].
- Affects tight junction gene expression.
 - Early-life chronic isolation increased expression of occludin and ZO-1 and decreased expression of claudin-5 in the small intestines of female rats [16].

The effect on gut function depends on the type and duration of stress. Trauma can also increase risk of IBD. Abuse, family trauma, or emotional trauma can also cause leaky gut. Early life trauma, including maternal deprivation, can increase leaky gut by affecting CRH, mast cells, and nerve growth factor (NGF) [17]. Physical and emotional trauma also open the BBB [18]. Gut microbiota also impact CRH secretion, influencing stress hormone signaling. Thus, stress reduction practices can be paired with gut microbiota modulation, most prominently through diet.

6. Depression

Chronic stress leads to depression, depending on an individual's susceptibility or resilience [19]. Men and women respond differently to stress and develop depression-like behaviors at different time points. Interestingly, progesterone might modulate response to stress, mediated by serotonin-1A (5-HT_{1A}) receptors in the amygdala and periaqueductal gray. Data from rats suggests that time in a menstrual cycle influences responses to stress in low-stress animals. Low-stress animals in proestrus-estrus (corresponding to the follicular phase in women) show higher startle responses compared to animals in diestrus (corresponds to the luteal phase) [19].

Depression likely impacts gut function and vice-versa. Blood samples from women with major depressive disorder (MDD) were found to have upregulated LBP. In addition, MDD has high comorbidity with IBD. Depression also impairs vagus nerve signaling, which influences digestion, absorption, and metabolism. This suggests leaky gut may affect emotional regulation and vice versa: emotional regulation may affect leaky gut [20].

Thus, it may be possible to treat depression (and by consequence leaky gut) through emotion regulation practices and dietary protocols. Of note, microbiota may modulate the impact of stress on the gut. Gut microbiota impact CRH secretion; probiotics have been shown to be beneficial for depression and memory.

7. Physical Stress

Soldiers, firefighters, astronauts, and nightshift workers all undergo varying intensity and forms of physical stress that may cause leaky gut. Physically demanding conditions that can increase permeability of the intestinal epithelial barrier are listed below:

- Blast exposure (particularly in the case of mild TBI)
- Traumatic brain injury [21, 22]
- Major burns

- Spaceflight and microgravity [23-25]
- Disrupted circadian rhythm (shown in mice) [26]
- Intense exercise, which is predicted by fraction of anaerobic threshold (i.e., lactate buildup in blood) rather than VO₂max (maximum oxygen consumption rate) [27]. If you keep yourself cool, you can increase performance and decrease leaky gut [28, 29].
- High altitude [30]
- Heat stress [31-33]
- Prolonged cold exposure [34]

The probiotic bacteria *L. johnsonii* could buffer against the deleterious effects of physical stress on both GI function and memory [35].

Environmental and Lifestyle Factors

8. Urbanization and Excess Hygiene

Exposure to microbes early in life is critical for immune system development. Having a relationship with land allows a healthy immune tolerance to develop, while an excessively sterile environment leaves barren, inviting terrain for autoimmune disease and allergies. Indeed, the rise in autoimmune diseases is attributed in part to excess hygiene. Urbanization and industrialization were implicated in reducing the mucosa barrier and contributing to numerous diseases, as reported by Akdis in a 2021 Nature Reviews Immunology paper [36].

9. Alcohol, Cigarettes, Opiates, and Other Psychoactive Substances

Alcohol is known to cause intestinal permeability and can also cause hormone and neurotransmitter imbalance and contribute to the risk of breast cancer [14]. The ethanol metabolite acetaldehyde also contributes to leaky gut [8].

Chronic alcohol use disorder has been shown to lead to intestinal permeability via microbiota dysbiosis. Not all chronic alcohol misuse leads to leaky gut; it appears that both microbiota dysbiosis and alcohol misuse are necessary to induce intestinal permeability. Within two weeks of abstaining from alcohol, intestinal permeability is restored, but microbiota dysbiosis may persist. This also shows that microbiota dysbiosis can exist without leaky gut [37].

Morphine and fentanyl have also been shown to impair intestinal barrier function [38].

Cigarette smoke and e-cigarettes have also been shown to compromise the intestinal barrier [39, 40]. Smoking also causes gut dysbiosis.

According to current literature, cannabis does not impair intestinal permeability; however, more research is needed on effects of cannabis smoking on the epithelial barrier. Additionally, there is no peer-reviewed evidence that psilocybin impairs intestinal permeability. There is also not enough evidence to conclude whether stimulants such as caffeine, cocaine, or amphetamines cause leaky gut [41].

10. Dietary Factors

The Western Diet, Vitamin and Nutrient Deficiencies, Malabsorption, and the State of American Nutrition

Conventional agriculture practices are depleting our food's nutrition, causing widespread vitamin and nutrient deficiencies and modern malnutrition. Widespread use of pesticides kill soil microbes and fungi and diminish crop nutritional quality. A Journal of the American College of Nutrition study from University of Texas by Donald Davis analyzed the nutritional content of 43 different vegetables and fruits over a 50-year period. They found reliable declines in the amount of protein, calcium, phosphorus, iron, riboflavin (vitamin B2), and vitamin C that Americans consumed from 1950 to 1999. They attributed the decline in nutritional quality to a prioritization of high yield [42] and the widespread use of pesticides, which kill soil microbes and fungi and diminish the nutritional quality of crops. Historically, the most common nutritional deficiencies are iron, vitamin D, iodine, calcium, vitamin B12, vitamin A, and magnesium.

The US Department of Health and Human Services (DHHS) and the USDA released the [2020-2025 dietary guidelines for Americans](#), which identified nutrients consumed below the estimated average requirements. Potassium, dietary fiber, choline, magnesium, calcium, and vitamins A, D, E, and C were on the list. Of top concern were potassium, fiber, choline, calcium, and vitamin D.

Nearly 30% men and 60% of women over 19 years old do not consume enough calcium, and more than 90% do not consume enough vitamin D. A review from the Journal of the American College of Nutrition looking at deficiencies from 2007-2012 confirmed 0% of the U.S. population hit the RDI for potassium, 8% achieved choline requirements, and only 33% were getting adequate vitamin K [43].

General Population Recommendations

According to a CDC study published in [2017](#), around 90% of Americans aren't meeting their daily fruit and vegetable intake. More than 90% of women and 97% of men are not eating adequate fiber. Based on eating patterns, most Americans can stand to follow this general advice:

- Eat more vegetables, fruits, dairy, whole grains, and seafood.
- Consume less refined grains, added sugars, saturated fat, and sodium.
- Men aged 19-31: eat less meat.
- Women on a 2,000-calorie diet: eat more red and orange and starchy vegetables (since they're getting, on average, enough dark leafy greens), 5.5 ounces of protein a day, mostly from meat, poultry, and eggs; 27 grams of oil, and a 240-calorie allowance for outside foods.

Healing the Gut: What to Avoid – Lectins, Gluten, and More

To protect the gut barrier, it is recommended to avoid the following:

- Processed foods and food additives.
 - Food processing generates advanced glycation endproducts (AGEs) from the Maillard reaction. For example, acrylamide is found in potato chips and movie theater popcorn, and it is linked to cancer [44].
 - Preservatives, stabilizers, and fillers: surfactants and emulsifiers [14, 45]
 - Mono- and diglycerides or esters of fatty acids. Conversely, melatonin has been found to help against surfactant-induced increased intestinal permeability [46]
 - Carboxymethylcellulose (CMC) and polysorbate-80 [47] alter gut mucus [48]. They can be found in multivitamins and nutraceuticals, so be sure to carefully read the ingredients before buying. CMC has been linked to SIBO and has been shown to inhibit flavonoid absorption [49]. Polysorbate-20 also damages IECs [50].
 - Thickeners and bulking agents, such as gums [51] – e.g. guar gum, xanthan gum.
 - Manufactured antioxidants: nonylphenols used in manufacturing antioxidants are linked to increased incidence of IBD [52].
- High-fat diet (HFD). It increases bile acids [53], impairs duodenal barrier integrity, and reduces Goblet cells in the large intestine [54, 55]. Excess meat consumption is the most significant contributor to a HFD, and it drives up TMAO production and is linked to heart disease.
- Canola oil and other highly processed oils
- Excess sugar—artificial or natural. Avoid excess sugar [56] and high-fructose corn syrup. Artificial sugars also damage the gut microbiome and change the brain. They trick the tastebuds but confuse the body, making us crave more sugar to meet our body's demands. Even a fructose-rich diet has deleterious effects on the gut barrier [57].
- High-glycemic foods. In mouse models of obesity and diabetes, hyperglycemia drives transcriptional reprogramming of IECs via GLUT2 (glucose transporter 2) and alters tight junctions. Following hyperglycemia, increased serum levels of orally administered FITC-dextran were found, indicating increased intestinal permeability [14, 58]. Thus, eating low-glycemic foods can mitigate gut inflammation.
- Wheat products and gluten, for people with Celiac disease, gluten intolerance, or non-Celiac gluten sensitivity (NCGS), due to trouble digesting gluten. Gliadin, a component of gluten, interacts with the immune system, causing tight junction reorganization and leaky gut [47].
- Lectins. These are antinutrients that can cause bloating and leaky gut. Gluten is just one type of lectin [59]. For most lectin-containing foods, cooking for 5-10 minutes, particularly with wet heat (pressure cooking or boiling), reduces lectin content down to nothing. However, nuts (e.g. cashews), seeds, tomatoes, bell peppers, and A1 cow milk may be consumed raw, so these are the biggest sources of lectins.

- **GMO foods.** Avoid BT-treated corn and potatoes, and buy organic. Some corn has been genetically modified to express an endotoxin from *Bacillus thuringiensis* (BT). BT toxins from insecticide use can poke holes in insects' intestinal cell walls, causing leaky gut. BT endotoxin also pokes holes in human cells [60]. In a BT GM crop, every cell has this effect. BT is also used in potato crops.
- **Excess salt.** Too much salt in the diet is a cause of hypertension. Hypertension promotes microbial translocation and dysbiotic shifts in the fecal microbiome of non-human primates [61].

Gut Health Recommendations: What to Add

Proper nutrition helps intestinal epithelial cells function. For optimal gut barrier integrity, ensure you are intaking adequate levels of:

- **Vitamin A.** Vitamin A deficiency weakens mucosal barrier and epithelial function, compromising immunity against viruses, while vitamin A sufficiency strengthens mucosal barrier function [62]. Indeed, vitamin A strengthens the intestinal barrier [63]. That said, both insufficient and excess vitamin A can lead to fetal abnormalities, so pregnant women should ensure they are intaking enough vitamin A, but not too much, as both can be teratogenic [64, 65]. Vitamin A regulates tight junction proteins, mucosal barrier, and immune cells [66].
- **Vitamin D.** Vitamin D deficiency also compromises gut barrier function [66-68]. In a clinical trial, vitamin D and soy isoflavones improved barrier integrity in women with IBS [69].
- **Zinc.** Zinc deficiency can lead to leaky gut. It was shown to repair mucosal injury in human studies [70]. However, caution must be taken not to over-supplement, as excess zinc also harms the intestinal barrier [71].
- **Fiber.** Fiber deficiency leads gut microbes to shift their consumption to metabolizing the glycans found in the gut mucosa, which compromises the gut barrier [72].
- **Aryl hydrocarbon receptor (AHR) agonists,** such as tryptophan, curcumin, quercetin, and gallic acid [73]. Insufficient tryptophan also causes gut dysbiosis.
- **Omega-3 fatty acids.**
- **L-glutamine.** It improved ileal morphology in animal studies [71] and can help repair damage and heal the intestinal lining.
- **Choline.**
- **Polyphenols.** Anthocyanins, found in berries, modulate tight junction proteins and improve antioxidant status in IECs [71].

11. Toxic Chemicals

The human exposome is expanding exponentially. Over 150,000 synthetic chemicals have been created over the past 50 years, with an estimated 2,000 new ones per year for agricultural and industrial applications. The combination of synthetic compounds and a sanitary lifestyle spent indoors is creating fewer co-evolved microbial relationships and disrupting immune homeostasis.

Industrial chemicals including pesticides, plastics, detergents, household cleaning products, persistent organic pollutants, food contaminants, and air pollution can be added to the list of epithelial barrier-damaging agents we're chronically exposed to, and they are all linked to leaky gut.

Pesticides

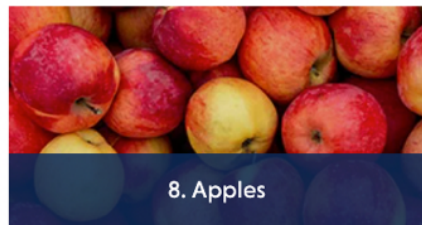
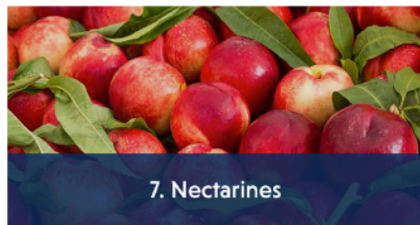
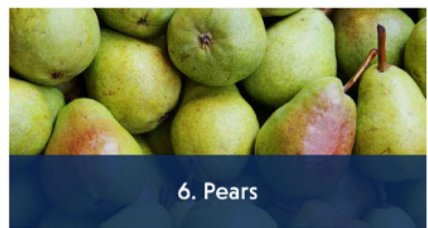
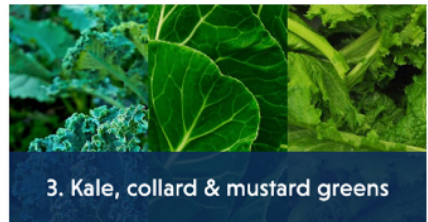
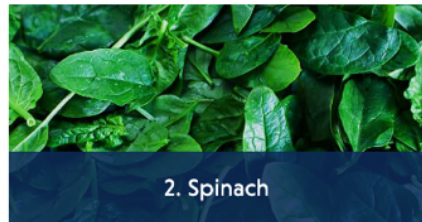
Pesticides are overused in agricultural contexts, contaminating soil and livestock feed. Humans then ingest pesticides, which disrupt the gut barrier [74].

Here are specific pesticides that have been linked with leaky gut:

- Glyphosate. It blocks the shikimate pathway, inhibiting microbial folate production. In humans, it changes vitamin D3 and cholesterol metabolism. It is an endocrine-disrupting chemical, probable carcinogen according to the IARC, and causes liver and kidney damage in animals. It also has been shown to cause leaky gut. Glyphosate moved through a Caco-2 (human intestinal epithelial cell) line, disrupted the actin cytoskeleton, and caused paracellular permeability at a dose over 10 mg / mL [75]. Glyphosate caused dysbiosis and altered mucus secretion, damaging the microvilli. Glyphosate changed immunological, enzymatic, and genetic features of animal models. These animals had damage to their energy, circulatory system, vitamin metabolism, and replication, repair, and protein translation [76]. Glyphosate and microcystin-LR both caused leaky gut in zebrafish [77].
- Paraquat. It loosens microvilli, decreases mitochondrial numbers, and causes apoptosis of ileal cells; it also increased serum FABP and MDA (a biomarker of [oxidative stress](#)) in weaned piglets [78].
- Diquat. It induces oxidative stress and intestinal injury by increasing hydrogen peroxide (H₂O₂) in mitochondria [79-81].
- Atrazine compromised the intestinal barrier in zebrafish and also impaired fertility [82]
- Organophosphorus pesticides are also hazardous to human health, and in a randomized controlled trial, they caused intestinal mucosa injury in patients with acute poisoning [83].
- Chlorpyrifos induces gut dysbiosis and intestinal mucosal permeability in cell culture modeling the intestinal environment [74, 84]. Further, chlorpyrifos allowed MRSA access to circulation [85]. Early life exposure disrupted tight junctions in mice [86].
- Imidacloprid is a neonicotinoid insecticide (very popular class of pesticides that account for over 25% of global pesticide sales). It is neurotoxic, immunotoxic, and reproductively toxic. It induces apoptosis and

inflammation in the liver of mice. It promotes cholinesterase activity and DNA damage in the blood and brain of mice. It also induced inflammation and oxidative stress in carps and caused intestinal dysbiosis in honeybees [87, 88].

Buy organic, especially wheat, grains, soybeans, and wine. Glyphosate has been detected in breastmilk, so be especially cautious if pregnant or breastfeeding.



EWG's 2024 Dirty Dozen list, the list of tested produce with the highest levels of pesticide residues.

Buy organic to avoid many of the contaminant exposures.

Pollution

Air pollution (particularly sulfur oxide, nitric oxide, but also silver iodide, the major compound used in cloud seeding), water pollution (e.g. such as that found in bottled water), and nonylphenols (used in manufacturing laundry and dish detergents) are linked to increased incidence of IBD [52].

Petroleum–Sourced Chemicals

BPA

BPA works through a variety of mechanisms to induce disruptions to homeostasis:

- Intestinal injury: A [2019](#) pathology study showed that BPA caused apoptosis of colonic epithelial cells in mice and increased plasma levels of endotoxin and zonulin. In BPA-treated mice, the number of goblet cells declined, along with mucin 2 gene expression [89]. In a further study, BPA induced intestinal injury and disrupted barrier function [90].
- Liver toxicity: induces liver inflammation and caused fatty liver in mice
- Gut dysbiosis: mice exposed to dietary BPA had higher inflammatory Proteobacteria and lower healthy mucosa-associated *Akkermansia* [91]
- Oxidative stress: BPA increased ROS and decreased the activity of multiple antioxidant enzymes, including superoxide dismutase (SOD), glutathione peroxidase (GPx), and catalase (CAT).
- Inflammation: BPA increased plasma diamine peroxidase (enzyme that breaks down histamine). BPA upregulated the mRNA expression of TLR2, TLR4, myeloid differentiation gene (MyD88), and NF- κ B, key factors of the innate immune system, and the secretion of pro-inflammatory cytokines, including IL-1 β , IL-6, IL-8, and TNF- α , into plasma, as well as greater expression in colonic cells.
- Apoptosis: The team also found significantly greater expression of enzymes involved in apoptosis, like Bax and caspase-3, and lower levels of Bcl2, a pro-survival factor [90]
- Metabolic disruption: BPA increased plasma D-lactate (a biomarker of metabolic acidosis).

BPP

An alternative to BPA, bisphenol P (BPP), found in many tested foods, including American mustard and ginger, has also been shown to disrupt the intestinal barrier in mice [92].

Microplastics and Nanoplastics

Polyethylene microplastics reduce the bioavailability of numerous minerals in the body, including calcium and zinc, by affecting intestinal epithelial barrier permeability [93].

Interestingly, microplastics from the biodegradable biomaterial polyglycolic acid caused intestinal hyperpermeability in zebrafish [94], albeit in the mg / L range, which is much higher than exposure doses that humans would encounter. By comparison, styrofoam nanoplastics in dosages of ug / L were sufficient to induce intestinal permeability, oxidative stress, and microbiome changes in multiple species of fish, including zebrafish [95, 96]. These sort of doses of micro- and nanoplastics (ug / L) lead to severe toxicity in *C. elegans* [97, 98]. In mice, styrofoam microplastics also decreased mucus and downregulated tight junction proteins ZO-1, occludin, and claudin-1 in the colon [99].

Major dietary sources of microplastics include steeping plastic tea bags in hot water, microwaving food in plastic containers, drinking from plastic water bottles, and cutting food on plastic cutting boards.

Persistent Organic Pollutants (POPs): Forever Chemicals and PFAS

Persistent organic pollutants (POPs), also known as “forever chemicals,” are highly resistant to degradation and readily bioaccumulate in human fat, allowing them to persist for decades in the body, write Sandys and te Velde. POPs include polycyclic aromatic hydrocarbons, polychlorobiphenyls (PCBs), brominated flame retardants, polychlorinated-p-dioxins, per- and polyphluoroalkyl substances (PFAS), and many pesticides. The category “PFAS” actually comprises over 4,700 manufactured chemicals. They are so ubiquitous that they are now found in human breastmilk. Humans are exposed via drinking water, food, and indoor and outdoor environments. They are readily absorbed through the GI tract. A 2022 review reports that concentrations of PFAS and perfluorooctane sulfonates in drinking water serving 6 million Americans are above EPA guidelines [51]. (Read about [plastic-free alternatives](#) and see the [plastic-free challenge](#) for ideas on living a low-tox lifestyle.)

Household cleaners: detergents and sodium lauryl sulfate

Preliminary culture work suggests that dishwasher detergents and rinse aids can also cause damage to intestinal epithelial cells [100]. This could create residues on plates that contribute to chronic low-dose GI toxicity.

Sodium lauryl sulfate (SLS) or sodium dodecyl sulfate (SDS) is found in many cleaning and hygiene products, including shampoo, toothpaste, and even shaving cream, according to [EWG](#). Interestingly, 4% SLS administered to shaved skin caused apoptosis of mast cells in the intestinal epithelium, which speaks to the gut-skin connection [101].

Practical tips: industrial chemicals

Below are practical tips to minimize barrier-disrupting industrial chemicals:

- To avoid ingesting plastics, steep unbleached paper tea bags (or free, loose-leaf tea), never microwave food in plastic containers, drink filtered water and blend your own smoothies instead of drinking bottled water and bottled beverages, bring your own hydro-flask and thermoses for hot coffee instead of using plastic-lined paper cups, cut food on wooden instead of plastic cutting boards, use calendula wax silk floss, use silicone-based menstrual cups instead of tampons, avoid single-use plastics (e.g. plastic wrap and sandwich bags), and wear natural fabrics (e.g. cotton, wool, hemp, or cashmere) instead of synthetic fibers (e.g. polyester or nylon).

- For household cleaners, opt for gentle detergents and rinse aids, and opt for sulfate-free shampoos.
- Buy organic, especially wheat, grains, soybeans, wine, and produce on the dirty dozen list. Glyphosate has been detected in breastmilk, so be especially cautious if pregnant or breastfeeding. The 2024 Dirty Dozen list summarizes the tested produce with the highest levels of pesticide residues. Buy organic to avoid many of the contaminant exposures.

Other tips involving toxic exposures naturally found in certain foods:

- Cassava – contains cyanogenic glycosides, which can release cyanide if not properly prepared.
- Tuna, swordfish, and shark – high in mercury
- Rice (brown and white) – arsenic exposure (rinse rice)
- Farmed salmon – PCBs and pollutants
- Processed meats (e.g. sausages, salami, deli meats) – carcinogenic nitrates
- Fried foods (potato chips, fries) – cancer-causing acrylamides

Biological and iatrogenic factors

12. Infection, toxins in food, & microbial endotoxins

Definitions

The word “toxin” is a commonly misused term, so we will define it here as it appears in scientific literature.

- **Toxin** – an agent of biological origin (e.g. bacterial, fungal, viral, archaeal, etc.) capable of causing disease, such as lipopolysaccharide (LPS) or aflatoxin (when people say “toxins in food” they are rarely using the term correctly, instead referring to food dyes and preservatives. They should be using the term “toxicant” for clarity.)
- **Toxicant** – aka, “chemicals.” Any nonliving ingredient in food that causes disease, such as carrageenan or diquat
- **Toxic** – harmful and capable of causing disease, as in ionizing radiation
- **Detoxification** – process whereby the body metabolizes and excretes toxins, toxicants, or other toxic agents

Toxins in food and water can contribute to allergy development. A 2022 paper published in *Frontiers in Allergy* showed that co-exposure to microbial toxins and food allergens sensitizes the immune system to developing food allergies by damaging the epithelial barrier. That is, mycotoxin and cholera toxin had an adjuvant effect in the development of peanut allergies [102]. Aflatoxin, a common food toxin, is found in moldy grains and nuts (peanuts, corn, and wheat). Cassava is also contains toxic unless processed appropriately.

Infections

Specific enteropathogens can harm gut health, including bacteria and eukaryotes (fungi, protozoa, and parasites). Sepsis, an extreme reaction to an infection, also drives leaky gut [103].

Bacteroides fragilis is a major single source of LPS and fragilysin found in the body [8]; these molecules can disrupt paracellular and transcellular barriers, opening tight junctions via intercellular adhesion protein cleavage [104, 105]. Other bacteria have also been linked to leaky gut: *Clostridium difficile* [106], *Listeria*, *Salmonella typhimurium* (causes enterocolitis), *Staphylococcus aureus*, *Shigella*, cholera [105, 107], and *Pseudomonas aeruginosa* [108].

H. pylori infection disrupts tight junctions of gastric epithelium [8] and induces neuroinflammation [109]. It interacts with microglia but interestingly inhibited neuroblastoma growth, suggesting a role for *H. pylori* bacteria in boosting the immune system and inhibiting cancer development. Strangely, *H. pylori* may be protective against IBD [110].

E. coli infection [8] is also implicated in leaky gut. Different *E. coli* strains, both pathogenic (enterohemorrhagic EHEC and enterotoxigenic ETEC) and non-pathogenic (*E. coli* C25) were involved in leaky gut [107, 111]. Conversely, *E. coli* Nissle 1917 (EcN) was found to ameliorate paracellular permeability, so effects of *E. coli* may be strain-dependent.

As for eukaryotes, fungi such as *Aspergillus* and *Penicillium* mold (involved in food spoilage), *Candida albicans*; protozoa including *Entamoeba histolytica*, *Blastocystis* spp., *Giardia* spp., and *Cryptosporidium* [112-114]; and parasites like *Toxoplasma gondii* can wear down the gut lining and open tight junctions [105].

Bacteriophages: Dark Matter of the Gut

Phages are viruses that can infect commensal bacteria and also disrupt the microbiome. Crass-like and Microviridae bacteriophages coexist abundantly with bacterial genera *Bacteroides*, *Prevotella*, and *Faecalibacterium*. An increase in temperate phage number is a specific change in Crohn's disease. Specific bacteriophages have been associated with intestinal barrier permeability. A Metagenomic Gut Virus catalog attempts to inventory the resident viruses of the gut. Interestingly, overall viral richness decreases significantly from adults to elderly individuals in both Western and Chinese cohorts. A lot remains to be discovered regarding the role of phages in host health [18].

13. Medications

Certain medications and over-the-counter drugs carry risk of GI-related side effects.

Medications, including antibiotics, the hormonal contraceptive pill [115] as well as non-steroidal anti-inflammatory drugs (NSAIDs) are known to increase the risk of IBD, likely through altering the commensal flora and/or the intestinal barrier [110, 116, 117].

Proton pump inhibitors also damage mitochondria. Steroids, acid blockers, hormonal replacement, antipsychotic medications, and opioids all damage the gut, cause microbiome problems, and are detrimental to gut barrier function [120].

Hormonal Contraceptive Pill

A meta-analysis of case-controlled and cohort studies revealed that individuals exposed to oral contraceptives had a 24% and 30% increased risk for developing Crohn's disease and ulcerative colitis, respectively, compared with those not exposed to the medication [118]. Meanwhile, normally menstruating women did not have different intestinal permeability than men [119].

Antibiotics

The link between antibiotics and leaky gut is nuanced. Some antibiotics may protect against microbiota-driven leaky gut, while others may cause a compensatory weakening of the barrier due to lack of immune challenge. Evidence has shown that antibiotics may cause gut dysbiosis and increase the risk of antibiotic-resistant bacterial overgrowth and IBD. IECs secrete mucus in response to microbes, so naturally, antibiotic depletion of the microbiome would decrease mucus production. Since antibiotics don't wipe out 100% of the microbiome, some microbes could get through the barrier.

In rats, antibiotics cefotaxime and vancomycin decreased intestinal permeability, while metronidazole treatment increased intestinal permeability, as measured by plasma FITC-dextran levels [121]. Mice with oral combination neomycin and bacitracin also displayed lowered intestinal permeability. Antibiotic-treated mice also had higher levels of expression of tight junction proteins like zonula occludens 1 (ZO-1), junctional adhesion molecule A (JAM-A) and occludin in the ileum, as well as ZO-1, claudin-3, and claudin-4 in the colon [122]. Further, combination vancomycin, neomycin, and polymyxin b protected against experimental acute pancreatitis by reducing bacterial translocation to the pancreas [123].

On the other hand, colostin, an antibiotic used in clinical settings for certain patients in intensive care, could lead to leaky gut [124]. Additionally, mice exposed to either vancomycin or polymyxin B for 7 days showed decreased microbiota diversity, significantly increased colonic mucosal permeability, decreased claudin 4 tight junction protein expression, and significantly increased TNF-alpha and/or IFN-γ cytokine expression. The disruptive effects of polymyxin B were more pronounced overall than those for vancomycin [125].

So the verdict on whether antibiotics drive or deter leaky gut is that it depends.

NSAIDs

In 2001, GlaxoSmithKline demonstrated that indomethacin, flurbiprofen, or diclofenac increased the vascular leakage of radiolabeled albumin in the jejunum, determined 24 hours later [126]. A meta-analysis published in the Journal of Gastroenterology in 2009 showed that NSAIDs increased intestinal permeability [127].

A double-blind, placebo-controlled, randomized crossover trial revealed that acute aspirin challenge (a huge dose of 1,950 mg) significantly increased gastroduodenal permeability.

500 mg/kg acetaminophen also disproportionately caused apoptosis of small intestinal crypt base LGR5+ stem cells. Although these cells were cleared within 24 hours, it's possible that acetaminophen exposure could cause long-term consequences, as indicated by prolonged deficits in gut barrier function. This is particularly observed in the ileum [128]. Additionally, in Winnie mice, which have a single nucleotide polymorphism (SNP) in the Muc2 gene that results in spontaneous colitis, acetaminophen increased intestinal permeability and bacterial translocation to the liver and spleen [129].

Chemotherapy Drugs

Unsurprisingly, chemotherapy drugs are cytotoxic; however, work is being done to advance precision medicine in cancer therapy. As of now, critically ill patients and patients receiving chemotherapy/radiotherapy show severely compromised intestinal barrier integrity [7]. Cyclophosphamide, a chemotherapy drug, also has been shown to cause intestinal barrier injury [130].

Proton Pump Inhibitors

Proton pump inhibitors (PPI) are widely used to treat gastroesophageal disorders. Unfortunately, recent studies pointed to a role for PPI in IBD flares. PPI caused myosin light chain kinase (MLCK) activation via p38 MAPK, resulting in increased tight junction barrier permeability. This leaky gut effect of PPI was shown in two different mouse models – dextran sodium sulfate (DSS)-induced colitis and IL-10 negative enterocolitis [131].

Glucocorticoids

Intestinal epithelial cells have glucocorticoid receptors, and these play a role in gut permeability and systemic response following alcohol and corticosteroid (e.g. hydrocortisone) exposure [18]. Alcohol and corticosteroids have been shown to increase gut permeability.

14. Ionizing Radiation

Ionizing radiation (which comes from X-rays, gamma rays, and some UV light) is used in cancer radiotherapy. In particular, abdominal or pelvic cancer radiotherapy can affect the gut [132-134]. Other sources of exposures to ionizing radiation may include a nuclear plant accident, terrorist attack, or military conflict.

Ionizing radiation causes intestinal injury, GI syndrome, and enteritis. It caused epithelial apoptosis and disrupted tight junctions in Caco-2 human cells [135, 136]. It causes loss of crypt cells by inhibiting mitosis; it also causes microbial translocation and oxidative and nitrosative stress [137]. It also damages DNA and changes gene expression in intestinal epithelial cells [138]. Walnut oligopeptides, IV-administered adipose-derived stromal vascular fraction, pravastatin, baicalein (from Chinese skullcap), arabinoxylan from rice bran, *Tenebrio molitor* peptides, a specially encapsulated controlled-release probiotic, γ -tocotrienol, heparin-binding EGF-like growth factor, and a *Lactocaseibacillus casei* strain showed radioprotective properties, mitigating the damage caused by ionizing radiation in rodents [139-149].

Summary

- **Root Cause:** Gut health is a foundation of body health. Leaky gut is a root cause of inflammation, which is a driver of disease.
- **Modifiable Factors:** Some factors, like aging, genetics, and oxidative stress, are out of our control. Other factors, like stress, depression, sleep, exercise, diet, and drug use, are in our control.
- **Play in the dirt.** A relationship with the land cultivates a robust, diverse microbiome and a tolerogenic immune system.
- **Go green and clean.** To the extent possible, minimize plastic use, choose household cleaners with more natural ingredients, buy organic, and get fresh air. If you live in a city, collect plants, use an air purifier and humidifier, and make it a point to escape the city once in awhile.
- **Supplement.** Take multivitamins and minerals.
- **Eat more whole foods and vegetables,** enough fiber, choline, tryptophan- and L-glutamine-rich protein, omega-3s, as well as antioxidants like quercetin, gallic acid, and anthocyanins.
- **Read ingredients labels on everything before you buy!** Eat less processed food, refined grains, and added sugars.
- **Consult with an allergist** if you suspect you may have a food allergy.

I hope you found this feature valuable. If you did, check out our other articles in the series at brainforest.org. Stay tuned for our next article on leaky gut solutions. Best of luck on your healing journey!

References

1. Frieling, T., et al., Endoscopic laser endomicroscopy and "leaky gut" in patients with functional gastrointestinal symptoms and food intolerance. *Z Gastroenterol*, 2023. 61(11): p. 1465-1471.
2. Ragonnaud, E. and A. Biragyn, Gut microbiota as the key controllers of "healthy" aging of elderly people. *Immun Ageing*, 2021. 18(1): p. 2.
3. Siddiqui, R., et al., The Use of Gut Microbial Modulation Strategies as Interventional Strategies for Ageing. *Microorganisms*, 2022. 10(9).
4. Magalhaes, N.S., et al., Gut Microbiota Dysbiosis Is a Crucial Player for the Poor Outcomes for COVID-19 in Elderly, Diabetic and Hypertensive Patients. *Front Med (Lausanne)*, 2021. 8: p. 644751.
5. Wilson, Q.N., et al., Greater Microbial Translocation and Vulnerability to Metabolic Disease in Healthy Aged Female Monkeys. *Sci Rep*, 2018. 8(1): p. 11373.
6. Peterson, L.W. and D. Artis, Intestinal epithelial cells: regulators of barrier function and immune homeostasis. *Nat Rev Immunol*, 2014. 14(3): p. 141-53.
7. Chelakkot, C., J. Ghim, and S.H. Ryu, Mechanisms regulating intestinal barrier integrity and its pathological implications. *Exp Mol Med*, 2018. 50(8): p. 1-9.
8. Turner, J.R., Intestinal mucosal barrier function in health and disease. *Nat Rev Immunol*, 2009. 9(11): p. 799-809.
9. Di Vincenzo, F., et al., Gut microbiota, intestinal permeability, and systemic inflammation: a narrative review. *Intern Emerg Med*, 2024. 19(2): p. 275-293.
10. Bhuiyan, P., et al., Neuroimmune connections between corticotropin-releasing hormone and mast cells: novel strategies for the treatment of neurodegenerative diseases. *Neural Regen Res*, 2021. 16(11): p. 2184-2197.
11. Vanuytsel, T., et al., Psychological stress and corticotropin-releasing hormone increase intestinal permeability in humans by a mast cell-dependent mechanism. *Gut*, 2014. 63(8): p. 1293-9.
12. Alonso, C., et al., Maladaptive intestinal epithelial responses to life stress may predispose healthy women to gut mucosal inflammation. *Gastroenterology*, 2008. 135(1): p. 163-172 e1.
13. Varanoske, A.N., et al., Stress and the gut-brain axis: Cognitive performance, mood state, and biomarkers of blood-brain barrier and intestinal permeability following severe physical and psychological stress. *Brain Behav Immun*, 2022. 101: p. 383-393.
14. Camilleri, M., What is the leaky gut? Clinical considerations in humans. *Curr Opin Clin Nutr Metab Care*, 2021. 24(5): p. 473-482.
15. Zhang, H., et al., Understanding the Connection between Gut Homeostasis and Psychological Stress. *J Nutr*, 2023. 153(4): p. 924-939.
16. Karailiev, P., et al., Tight junction proteins in the small intestine and prefrontal cortex of female rats exposed to stress of chronic isolation starting early in life. *Neurogastroenterol Motil*, 2021. 33(6): p. e14084.
17. Barreau, F., et al., Pathways involved in gut mucosal barrier dysfunction induced in adult rats by maternal deprivation: corticotrophin-releasing factor and nerve growth factor interplay. *J Physiol*, 2007. 580(Pt 1): p. 347-56.
18. Mou, Y., et al., Gut Microbiota Interact With the Brain Through Systemic Chronic Inflammation: Implications on Neuroinflammation, Neurodegeneration, and Aging. *Front Immunol*, 2022. 13: p. 796288.
19. Sgobbi, R.F., et al., The modulatory role of serotonin-1A receptors of the basolateral amygdala and dorsal periaqueductal gray on the impact of hormonal variation on the conditioned fear response. *Neuroscience*, 2024. 554: p. 118-127.
20. Doney, E., et al., Chronic Stress Exposure Alters the Gut Barrier: Sex-Specific Effects on Microbiota and Jejunum Tight

21. Junctions. *Biol Psychiatry Glob Open Sci*, 2024. 4(1): p. 213-228.
22. Hanscom, M., D.J. Loane, and T. Shea-Donohue, Brain-gut axis dysfunction in the pathogenesis of traumatic brain injury. *J Clin Invest*, 2021. 131(12).
23. Weaver, J.L., The brain-gut axis: A prime therapeutic target in traumatic brain injury. *Brain Res*, 2021. 1753: p. 147225.
24. Liu, Q., et al., Association of Blast Exposure in Military Breaching with Intestinal Permeability Blood Biomarkers Associated with Leaky Gut. *Int J Mol Sci*, 2024. 25(6).
25. Akinsuyi, O.S., et al., Gut permeability among Astronauts during Space missions. *Life Sci Space Res (Amst)*, 2024. 41: p. 171-180.
26. Zhang, H., et al., [Gut microbial dysbiosis under space environment: a review]. *Sheng Wu Gong Cheng Xue Bao*, 2023. 39(10): p. 4075-4084.
27. Summa, K.C., et al., Disruption of the Circadian Clock in Mice Increases Intestinal Permeability and Promotes Alcohol-Induced Hepatic Pathology and Inflammation. *PLoS One*, 2013. 8(6): p. e67102.
28. Edwards, K.H., et al., The influence of exercise intensity and exercise mode on gastrointestinal damage. *Appl Physiol Nutr Metab*, 2021. 46(9): p. 1105-1110.
29. Clark, A. and N. Mach, Exercise-induced stress behavior, gut-microbiota-brain axis and diet: a systematic review for athletes. *J Int Soc Sports Nutr*, 2016. 13: p. 43.
30. Cerda, B., et al., Gut Microbiota Modification: Another Piece in the Puzzle of the Benefits of Physical Exercise in Health? *Front Physiol*, 2016. 7: p. 51.
31. Cheng, J., et al., Research Progress on the Mechanism of Intestinal Barrier Damage and Drug Therapy in a High Altitude Environment. *Curr Drug Deliv*, 2024. 21(6): p. 807-816.
32. Lee, B.J., et al., Anthocyanin-Rich Blackcurrant Extract Preserves Gastrointestinal Barrier Permeability and Reduces Enterocyte Damage but Has No Effect on Microbial Translocation and Inflammation After Exertional Heat Stress. *Int J Sport Nutr Exerc Metab*, 2022. 32(4): p. 265-274.
33. Wallett, A.M., et al., Running at Increasing Intensities in the Heat Induces Transient Gut Perturbations. *Int J Sports Physiol Perform*, 2021. 16(5): p. 704-710.
34. Walter, E., et al., Changes in gastrointestinal cell integrity after marathon running and exercise-associated collapse. *Eur J Appl Physiol*, 2021. 121(4): p. 1179-1187.
35. Guo, J., et al., Role of SIRT2 in intestinal barrier under cold exposure. *Life Sci*, 2023. 330: p. 121949.
36. Wang, H., et al., Psychoactive Effects of *Lactobacillus johnsonii* Against Restraint Stress-Induced Memory Dysfunction in Mice Through Modulating Intestinal Inflammation and permeability-a Study Based on the Gut-Brain Axis Hypothesis. *Front Pharmacol*, 2021. 12: p. 662148.
37. Akdis, C.A., Does the epithelial barrier hypothesis explain the increase in allergy, autoimmunity and other chronic conditions? *Nat Rev Immunol*, 2021. 21(11): p. 739-751.
38. Leclercq, S., et al., The link between inflammation, bugs, the intestine and the brain in alcohol dependence. *Transl Psychiatry*, 2017. 7(2): p. e1048.
39. Muchhala, K.H., et al., The role of morphine- and fentanyl-induced impairment of intestinal epithelial antibacterial activity in dysbiosis and its impact on the microbiota-gut-brain axis. *FASEB J*, 2024. 38(8): p. e23603.
40. Djouina, M., et al., Chronic Exposure to Both Electronic and Conventional Cigarettes Alters Ileum and Colon Turnover, Immune Function, and Barrier Integrity in Mice. *J Xenobiot*, 2024. 14(3): p. 950-969.
41. Gui, X., Z. Yang, and M.D. Li, Effect of Cigarette Smoke on Gut Microbiota: State of Knowledge. *Front Physiol*, 2021. 12: p. 673341.
42. Salavrakos, M., et al., Microbiome and substances of abuse. *Prog Neuropsychopharmacol Biol Psychiatry*, 2021. 105: p. 110113.
43. Davis, D.R., M.D. Epp, and H.D. Riordan, Changes in USDA food composition data for 43 garden crops, 1950 to 1999. *J Am Coll Nutr*, 2004. 23(6): p. 669-82.
44. Wallace, T.C., M. McBurney, and V.L. Fulgoni, 3rd, Multivitamin/mineral supplement contribution to micronutrient intakes in the United States, 2007-2010. *J Am Coll Nutr*, 2014. 33(2): p. 94-102.

44. Guibourdenche, M., et al., Food Contaminants Effects on an In Vitro Model of Human Intestinal Epithelium. *Toxics*, 2021. 9(6).
45. Khoshbin, K. and M. Camilleri, Effects of dietary components on intestinal permeability in health and disease. *Am J Physiol Gastrointest Liver Physiol*, 2020. 319(5): p. G589-G608.
46. Peters, K., et al., Melatonin-Activated Receptor Signaling Pathways Mediate Protective Effects on Surfactant-Induced Increase in Jejunal Mucosal Permeability in Rats. *Int J Mol Sci*, 2021. 22(19).
47. Jaquez-Duran, G. and A.L. Arellano-Ortiz, Western diet components that increase intestinal permeability with implications on health. *Int J Vitam Nutr Res*, 2024. 94(5-6): p. 405-421.
48. Lock, J.Y., et al., Acute Exposure to Commonly Ingested Emulsifiers Alters Intestinal Mucus Structure and Transport Properties. *Sci Rep*, 2018. 8(1): p. 10008.
49. Glade, M.J. and M.M. Meguid, A glance at ... dietary emulsifiers, the human intestinal mucus and microbiome, and dietary fiber. *Nutrition*, 2016. 32(5): p. 609-14.
50. Ogulur, I., et al., Mechanisms of gut epithelial barrier impairment caused by food emulsifiers polysorbate 20 and polysorbate 80. *Allergy*, 2023. 78(9): p. 2441-2455.
51. Sandys, O. and A. Te Velde, Raising the Alarm: Environmental Factors in the Onset and Maintenance of Chronic (Low-Grade) Inflammation in the Gastrointestinal Tract. *Dig Dis Sci*, 2022. 67(9): p. 4355-4368.
52. Abegunde, A.T., et al., Environmental risk factors for inflammatory bowel diseases: Evidence based literature review. *World J Gastroenterol*, 2016. 22(27): p. 6296-317.
53. Liu, H., et al., Taurocholic acid, a primary 12alpha-hydroxylated bile acid, induces leakiness in the distal small intestine in rats. *Food Chem Toxicol*, 2022. 165: p. 113136.
54. Seguela, L., et al., High-fat diet impairs duodenal barrier function and elicits glia-dependent changes along the gut-brain axis that are required for anxiogenic and depressive-like behaviors. *J Neuroinflammation*, 2021. 18(1): p. 115.
55. Miranda, C.S., et al., Time-dependent impact of a high-fat diet on the intestinal barrier of male mice. *World J Methodol*, 2024. 14(1): p. 89723.
56. Ondee, T., et al., High Fructose Causes More Prominent Liver Steatohepatitis with Leaky Gut Similar to High Glucose Administration in Mice and Attenuation by *Lactiplantibacillus plantarum* dfa1. *Nutrients*, 2023. 15(6).
57. Regnier, M., et al., Gut microbiome, endocrine control of gut barrier function and metabolic diseases. *J Endocrinol*, 2021. 248(2): p. R67-R82.
58. Bischoff, S.C., et al., Intestinal permeability--a new target for disease prevention and therapy. *BMC Gastroenterol*, 2014. 14: p. 189.
59. Vanuytsel, T., J. Tack, and R. Farre, The Role of Intestinal Permeability in Gastrointestinal Disorders and Current Methods of Evaluation. *Front Nutr*, 2021. 8: p. 717925.
60. Jneid, R., et al., *Bacillus thuringiensis* toxins divert progenitor cells toward enteroendocrine fate by decreasing cell adhesion with intestinal stem cells in *Drosophila*. *Elife*, 2023. 12.
61. Vemuri, R., et al., Hypertension promotes microbial translocation and dysbiotic shifts in the fecal microbiome of nonhuman primates. *Am J Physiol Heart Circ Physiol*, 2022. 322(3): p. H474-H485.
62. Amimo, J.O., et al., Immune Impairment Associated with Vitamin A Deficiency: Insights from Clinical Studies and Animal Model Research. *Nutrients*, 2022. 14(23).
63. Abdelhamid, L. and X.M. Luo, Retinoic Acid, Leaky Gut, and Autoimmune Diseases. *Nutrients*, 2018. 10(8).
64. Abadie, R.B., et al., Vitamin A-Mediated Birth Defects: A Narrative Review. *Cureus*, 2023. 15(12): p. e50513.
65. Zhou, J., et al., Maternal Vitamin A deficiency during pregnancy and lactation induced damaged intestinal structure and intestinal flora homeostasis in offspring mice. *Food Sci Nutr*, 2023. 11(6): p. 3422-3432.
66. Cantorna, M.T., L. Snyder, and J. Arora, Vitamin A and vitamin D regulate the microbial complexity, barrier function, and

- the mucosal immune responses to ensure intestinal homeostasis. *Crit Rev Biochem Mol Biol*, 2019. 54(2): p. 184-192.
67. Wang, J., et al., Contemporary Perspectives on the Role of Vitamin D in Enhancing Gut Health and Its Implications for Preventing and Managing Intestinal Diseases. *Nutrients*, 2024. 16(14).
68. Aggeletopoulou, I., et al., Exploring the Role of Vitamin D and the Vitamin D Receptor in the Composition of the Gut Microbiota. *Front Biosci (Landmark Ed)*, 2023. 28(6): p. 116.
69. Jalili, M., et al., Soy isoflavones and cholecalciferol reduce inflammation, and gut permeability, without any effect on antioxidant capacity in irritable bowel syndrome: A randomized clinical trial. *Clin Nutr ESPEN*, 2019. 34: p. 50-54.
70. Efthymakis, K. and M. Neri, The role of Zinc L-Carnosine in the prevention and treatment of gastrointestinal mucosal disease in humans: a review. *Clin Res Hepatol Gastroenterol*, 2022. 46(7): p. 101954.
71. Matar, A., et al., Intestinal Barrier Impairment, Preservation, and Repair: An Update. *Nutrients*, 2024. 16(20).
72. Li, S., et al., Ant may well destroy a whole dam: glycans of colonic mucus barrier disintegrated by gut bacteria. *Microbiol Res*, 2024. 281: p. 127599.
73. Barroso, A., et al., The aryl hydrocarbon receptor and the gut-brain axis. *Cell Mol Immunol*, 2021. 18(2): p. 259-268.
74. Lima, C., et al., Pesticides and Their Impairing Effects on Epithelial Barrier Integrity, Dysbiosis, Disruption of the AhR Signaling Pathway and Development of Immune-Mediated Inflammatory Diseases. *Int J Mol Sci*, 2022. 23(20).
75. Vasiluk, L., L.J. Pinto, and M.M. Moore, Oral bioavailability of glyphosate: studies using two intestinal cell lines. *Environ Toxicol Chem*, 2005. 24(1): p. 153-60.
76. Ignacio, A.D.C., et al., Effects of glyphosate exposure on intestinal microbiota, metabolism and microstructure: a systematic review. *Food Funct*, 2024. 15(15): p. 7757-7781.
77. Ding, W., et al., Negative impacts of microcystin-LR and glyphosate on zebrafish intestine: Linked with gut microbiota and microRNAs? *Environ Pollut*, 2021. 286: p. 117685.
78. Xiang, X., et al., Glutathione Protects against Paraquat-Induced Oxidative Stress by Regulating Intestinal Barrier, Antioxidant Capacity, and CAR Signaling Pathway in Weaned Piglets. *Nutrients*, 2022. 15(1).
79. Chen, Y., et al., Pterostilbene Confers Protection against Diquat-Induced Intestinal Damage with Potential Regulation of Redox Status and Ferroptosis in Broiler Chickens. *Oxid Med Cell Longev*, 2023. 2023: p. 8258354.
80. Hao, L., et al., *Pediococcus pentosaceus* ZJUA-F-4 relieves oxidative stress and restores the gut microbiota in diquat-induced intestinal injury. *Appl Microbiol Biotechnol*, 2021. 105(4): p. 1657-1668.
81. Cao, S., et al., Resveratrol improves intestinal barrier function, alleviates mitochondrial dysfunction and induces mitophagy in diquat challenged piglets(1). *Food Funct*, 2019. 10(1): p. 344-354.
82. Chen, L., et al., Dysregulation of Intestinal Health by Environmental Pollutants: Involvement of the Estrogen Receptor and Aryl Hydrocarbon Receptor. *Environ Sci Technol*, 2018. 52(4): p. 2323-2330.
83. Yan, X.X., et al., [Changes of intestinal mucosal barrier function and effects of early enteral nutrition in patients with severe organophosphorus poisoning]. *Zhonghua Yi Xue Za Zhi*, 2019. 99(6): p. 442-446.
84. Requile, M., et al., Use of a combination of in vitro models to investigate the impact of chlorpyrifos and inulin on the intestinal microbiota and the permeability of the intestinal mucosa. *Environ Sci Pollut Res Int*, 2018. 25(23): p. 22529-22540.
85. Joly Condette, C., et al., Use of molecular typing to investigate bacterial translocation from the intestinal tract of chlorpyrifos-exposed rats. *Gut Pathog*, 2016. 8: p. 50.
86. Joly Condette, C., et al., Increased gut permeability and bacterial translocation after chronic chlorpyrifos exposure in rats. *PLoS One*, 2014. 9(7): p. e102217.
87. Miao, Z., et al., Melatonin ameliorates imidacloprid-induced

- intestinal injury by negatively regulating the PGN/P38MAPK pathway in the common carp (*Cyprinus carpio*). *Fish Shellfish Immunol*, 2022. 131: p. 1063-1074.
88. Zhao, G.P., et al., Imidacloprid increases intestinal permeability by disrupting tight junctions. *Ecotoxicol Environ Saf*, 2021. 222: p. 112476.
89. Feng, L., et al., Bisphenol A increases intestinal permeability through disrupting intestinal barrier function in mice. *Environ Pollut*, 2019. 254(Pt A): p. 112960.
90. Wang, K., et al., Environmental contaminant BPA causes intestinal damage by disrupting cellular repair and injury homeostasis in vivo and in vitro. *Biomed Pharmacother*, 2021. 137: p. 111270.
91. Feng, D., et al., Bisphenol A exposure induces gut microbiota dysbiosis and consequent activation of gut-liver axis leading to hepatic steatosis in CD-1 mice. *Environ Pollut*, 2020. 265(Pt A): p. 114880.
92. Ma, N., et al., Bisphenol P exposure in C57BL/6 mice caused gut microbiota dysbiosis and induced intestinal barrier disruption via LPS/TLR4/NF-kappaB signaling pathway. *Environ Int*, 2023. 175: p. 107949.
93. Chen, S., et al., Reduced dietary Ca, Cu, Zn, Mn, and Mg bioavailability but increased Fe bioavailability with polyethylene microplastic ingestion in a mouse model: Changes in intestinal permeability and gut metabolites. *Sci Total Environ*, 2023. 885: p. 163853.
94. Luan, J., et al., Systemic toxicity of biodegradable polyglycolic acid microplastics on the gut-liver-brain axis in zebrafish. *Sci Total Environ*, 2024. 954: p. 176898.
95. Teng, M., et al., Polystyrene Nanoplastics Toxicity to Zebrafish: Dysregulation of the Brain-Intestine-Microbiota Axis. *ACS Nano*, 2022. 16(5): p. 8190-8204.
96. Zhou, Y., et al., Low particle concentrations of nanoplastics impair the gut health of medaka. *Aquat Toxicol*, 2023. 256: p. 106422.
97. Wu, Y., et al., Combined Effects of Micro- and Nanoplastics at the Predicted Environmental Concentration on Functional State of Intestinal Barrier in *Caenorhabditis elegans*. *Toxics*, 2023. 11(8).
98. Qu, M., et al., Exposure to epoxy-modified nanoplastics in the range of $\mu\text{g/L}$ causes dysregulated intestinal permeability, reproductive capacity, and mitochondrial homeostasis by affecting antioxidant system in *Caenorhabditis elegans*. *Aquat Toxicol*, 2023. 264: p. 106710.
99. Zeng, G., et al., Polystyrene microplastic-induced oxidative stress triggers intestinal barrier dysfunction via the NF-kappaB/NLRP3/IL-1beta/MCLK pathway. *Environ Pollut*, 2024. 345: p. 123473.
100. Ogulur, I., et al., Gut epithelial barrier damage caused by dishwasher detergents and rinse aids. *J Allergy Clin Immunol*, 2023. 151(2): p. 469-484.
101. Tanemoto, R., et al., Chronic skin damage induces small intestinal damage via IL-13-induced apoptosis. *Clin Exp Immunol*, 2024. 217(3): p. 240-252.
102. Dronen, E.K., et al., Suspected gut barrier disruptors and development of food allergy: Adjuvant effects and early immune responses. *Front Allergy*, 2022. 3: p. 1029125.
103. Otani, S., et al., Overexpression of BCL-2 in the Intestinal Epithelium Prevents Sepsis-Induced Gut Barrier Dysfunction via Altering Tight Junction Protein Expression. *Shock*, 2020. 54(3): p. 330-336.
104. Zhao, Y., et al., Lipopolysaccharides (LPSs) as Potent Neurotoxic Glycolipids in Alzheimer's Disease (AD). *Int J Mol Sci*, 2022. 23(20).
105. Paradis, T., et al., Tight Junctions as a Key for Pathogens Invasion in Intestinal Epithelial Cells. *Int J Mol Sci*, 2021. 22(5).
106. Lai, Y.H., et al., Peroxisome proliferator-activated receptor-gamma as the gatekeeper of tight junction in *Clostridioides difficile* infection. *Front Microbiol*, 2022. 13: p. 986457.
107. Barbara, G., et al., Inflammatory and Microbiota-Related Regulation of the Intestinal Epithelial Barrier. *Front Nutr*, 2021. 8: p. 718356.
108. Panpetch, W., S. Tumwasorn, and A. Leelahavanichkul, Presence of *Pseudomonas aeruginosa* in feces exacerbate leaky gut in mice with low dose dextran sulfate solution, impacts of specific bacteria. *PLoS One*, 2024. 19(11): p. e0309106.

109. Park, A.M. and I. Tsunoda, Helicobacter pylori infection in the stomach induces neuroinflammation: the potential roles of bacterial outer membrane vesicles in an animal model of Alzheimer's disease. *Inflamm Regen*, 2022. 42(1): p. 39.
110. Piovani, D., et al., Environmental Risk Factors for Inflammatory Bowel Diseases: An Umbrella Review of Meta-analyses. *Gastroenterology*, 2019. 157(3): p. 647-659 e4.
111. Saxena, A., F. Lopes, and D.M. McKay, Reduced intestinal epithelial mitochondrial function enhances in vitro interleukin-8 production in response to commensal Escherichia coli. *Inflamm Res*, 2018. 67(10): p. 829-837.
112. Klimczak, S., et al., The Influence of the Protozoan Giardia lamblia on the Modulation of the Immune System and Alterations in Host Glucose and Lipid Metabolism. *Int J Mol Sci*, 2024. 25(16).
113. Arguello-Garcia, R., J.C. Carrero, and M.G. Ortega-Pierres, Extracellular Cysteine Proteases of Key Intestinal Protozoan Pathogens-Factors Linked to Virulence and Pathogenicity. *Int J Mol Sci*, 2023. 24(16).
114. Allain, T., E. Fekete, and A.G. Buret, Giardia Cysteine Proteases: The Teeth behind the Smile. *Trends Parasitol*, 2019. 35(8): p. 636-648.
115. Flood, T.R., et al., The effect of sex, menstrual cycle phase and oral contraceptive use on intestinal permeability and ex vivo monocyte TNFalpha release following treatment with lipopolysaccharide and hyperthermia. *Cytokine*, 2022. 158: p. 155991.
116. Ungaro, R., et al., Antibiotics associated with increased risk of new-onset Crohn's disease but not ulcerative colitis: a meta-analysis. *Am J Gastroenterol*, 2014. 109(11): p. 1728-38.
117. Oligschlaeger, Y., et al., Inflammatory Bowel Disease: A Stressed "Gut/Feeling". *Cells*, 2019. 8(7).
118. Ortizo, R., et al., Exposure to oral contraceptives increases the risk for development of inflammatory bowel disease: a meta-analysis of case-controlled and cohort studies. *Eur J Gastroenterol Hepatol*, 2017. 29(9): p. 1064-1070.
119. Snipe, R.M.J. and R.J.S. Costa, Does biological sex impact intestinal epithelial injury, small intestine permeability, gastrointestinal symptoms and systemic cytokine profile in response to exertional-heat stress? *J Sports Sci*, 2018. 36(24): p. 2827-2835.
120. Liang, L., C. Saunders, and N. Sanossian, Food, gut barrier dysfunction, and related diseases: A new target for future individualized disease prevention and management. *Food Sci Nutr*, 2023. 11(4): p. 1671-1704.
121. Tulstrup, M.V., et al., Antibiotic Treatment Affects Intestinal Permeability and Gut Microbial Composition in Wistar Rats Dependent on Antibiotic Class. *PLoS One*, 2015. 10(12): p. e0144854.
122. Nevado, R., et al., Neomycin and bacitracin reduce the intestinal permeability in mice and increase the expression of some tight-junction proteins. *Rev Esp Enferm Dig*, 2015. 107(11): p. 672-6.
123. Jia, L., et al., Combinatory antibiotic treatment protects against experimental acute pancreatitis by suppressing gut bacterial translocation to pancreas and inhibiting NLRP3 inflammasome pathway. *Innate Immun*, 2020. 26(1): p. 48-61.
124. Wang, H., et al., Intestinal dysbacteriosis contributes to decreased intestinal mucosal barrier function and increased bacterial translocation. *Lett Appl Microbiol*, 2014. 58(4): p. 384-92.
125. Ran, Y., et al., Alteration of Colonic Mucosal Permeability during Antibiotic-Induced Dysbiosis. *Int J Mol Sci*, 2020. 21(17).
126. Evans, S.M. and B.J. Whittle, Interactive roles of superoxide and inducible nitric oxide synthase in rat intestinal injury provoked by non-steroidal anti-inflammatory drugs. *Eur J Pharmacol*, 2001. 429(1-3): p. 287-96.
127. Bjarnason, I. and K. Takeuchi, Intestinal permeability in the pathogenesis of NSAID-induced enteropathy. *J Gastroenterol*, 2009. 44 Suppl 19: p. 23-9.
128. Chopyk, D.M., et al., Acetaminophen Intoxication Rapidly Induces Apoptosis of Intestinal Crypt Stem Cells and Enhances Intestinal Permeability. *Hepatol Commun*, 2019. 3(11): p. 1435-1449.

129. Alabbas, S.Y., et al., Gut inflammation and adaptive immunity amplify acetaminophen toxicity in bowel and liver. *J Gastroenterol Hepatol*, 2023. 38(4): p. 609-618.
130. Huang, J., et al., Fecal microbiota transplantation from sodium alginate-dosed mice and normal mice mitigates intestinal barrier injury and gut dysbiosis induced by antibiotics and cyclophosphamide. *Food Funct*, 2023. 14(12): p. 5690-5701.
131. Nighot, M., et al., Long-Term Use of Proton Pump Inhibitors Disrupts Intestinal Tight Junction Barrier and Exaggerates Experimental Colitis. *J Crohns Colitis*, 2023. 17(4): p. 565-579.
132. Kwak, S.Y., et al., Centella asiatica-Derived Endothelial Paracrine Restores Epithelial Barrier Dysfunction in Radiation-Induced Enteritis. *Cells*, 2022. 11(16).
133. Miousse, I.R., et al., Methionine dietary supplementation potentiates ionizing radiation-induced gastrointestinal syndrome. *Am J Physiol Gastrointest Liver Physiol*, 2020. 318(3): p. G439-G450.
134. Ewing, L.E., et al., Methods for induction and assessment of intestinal permeability in rodent models of radiation injury. *Methods Cell Biol*, 2022. 168: p. 235-247.
135. Carter, S.R., et al., Intestinal barrier disruption as a cause of mortality in combined radiation and burn injury. *Shock*, 2013. 40(4): p. 281-9.
136. Park, H.Y. and J.H. Yu, X-ray radiation-induced intestinal barrier dysfunction in human epithelial Caco-2 cell monolayers. *Ecotoxicol Environ Saf*, 2023. 264: p. 115404.
137. Banerjee, S., et al., C/EBPdelta protects from radiation-induced intestinal injury and sepsis by suppression of inflammatory and nitrosative stress. *Sci Rep*, 2019. 9(1): p. 13953.
138. Sharma, A., et al., Musashi expression in intestinal stem cells attenuates radiation-induced decline in intestinal permeability and survival in *Drosophila*. *Sci Rep*, 2020. 10(1): p. 19080.
139. Zhu, N., et al., Radioprotective Effect of Walnut Oligopeptides Against Gamma Radiation-Induced Splenocyte Apoptosis and Intestinal Injury in Mice. *Molecules*, 2019. 24(8).
140. Bensemmane, L., et al., The stromal vascular fraction mitigates radiation-induced gastrointestinal syndrome in mice. *Stem Cell Res Ther*, 2021. 12(1): p. 309.
141. Hua, Q., et al., Lactaseibacillus casei ATCC334 Ameliorates Radiation-Induced Intestinal Injury in Rats by Targeting Microbes and Metabolites. *Mol Nutr Food Res*, 2023. 67(1): p. e2200337.
142. Jang, H., et al., Pravastatin Attenuates Acute Radiation-Induced Enteropathy and Improves Epithelial Cell Function. *Front Pharmacol*, 2018. 9: p. 1215.
143. Jang, H., et al., Baicalein Mitigates Radiation-Induced Enteritis by Improving Endothelial Dysfunction. *Front Pharmacol*, 2019. 10: p. 892.
144. Shang, Y., et al., Study on the mechanism of mitigating radiation damage by improving the hematopoietic system and intestinal barrier with *Tenebrio molitor* peptides. *Food Funct*, 2024. 15(15): p. 8116-8127.
145. Sun, R., et al., Colonic long-term retention and colonization of probiotics by double-layer chitosan/tannic acid coating and microsphere embedding for treatment of ulcerative colitis and radiation enteritis. *Int J Biol Macromol*, 2024. 280(Pt 1): p. 135757.
146. Garg, S., et al., Gamma-Tocotrienol Protects the Intestine from Radiation Potentially by Accelerating Mesenchymal Immune Cell Recovery. *Antioxidants (Basel)*, 2019. 8(3).
147. Zhao, Z., et al., Arabinoxylan rice bran (MGN-3/Biobran) alleviates radiation-induced intestinal barrier dysfunction of mice in a mitochondrion-dependent manner. *Biomed Pharmacother*, 2020. 124: p. 109855.
148. Lu, L., et al., Microbiome in radiotherapy: an emerging approach to enhance treatment efficacy and reduce tissue injury. *Mol Med*, 2024. 30(1): p. 105.
149. Matthews, M.A., et al., Heparin-binding EGF-like growth factor (HB-EGF) protects the intestines from radiation therapy-induced intestinal injury. *J Pediatr Surg*, 2013. 48(6): p. 1316-22.

