



**LEAKY GUT, SIBO, SIFO & MORE**

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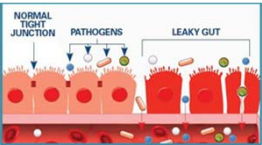
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### WHAT IS LEAKY GUT?

- Ancient Greece: doctors believed that imbalances in the stomach caused certain ailments and conditions
  - As modern medicine and scientific methods developed, this concept was disregarded.
- Intestinal lining covers more than 4,000 sq ft of surface area
- When gut structure & function is intact, the intestinal lining maintains a tight barrier
  - This ensures proper assimilation & elimination
- When structure is compromised, toxins, partially digested food (protein) and microorganisms get inadvertently absorbed into the bloodstream
  - Triggers an inflammatory response and impacts the diversity of our gut microbiome.



1. Mu, Q., Kirby, J., Reilly, C. M., & Luo, X. M. (2017, May 5). Leaky Gut As a Danger Signal for Autoimmune Diseases. *Frontiers in Immunology*.  
2. Odenwald, M. A., & Turner, J. R. (2016, November 16). The intestinal epithelial barrier: a therapeutic target? *Nature Reviews Gastroenterology Hepatology* 14, 9-21 (2017).

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### HOW DO YOU GET LEAKY GUT?

- Genetics may predispose you to be more sensitive to developing leaky gut
  - Modern lifestyles are the main driver of leaky gut
- Diet
  - A poor diet high in inflammatory foods (refined sugars, processed)
- Chronic stress
  - Weakens the immune system and hinders your body's ability to eliminate harmful microbes



1. Mu, Q., Kirby, J., Reilly, C. M., & Luo, X. M. (2017, May 5). Leaky Gut As a Danger Signal for Autoimmune Diseases. *Frontiers in Immunology*.  
2. Odenwald, M. A., & Turner, J. R. (2016, November 16). The intestinal epithelial barrier: a therapeutic target? *Nature Reviews Gastroenterology Hepatology* 14, 9-21 (2017).

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## CLINICAL PRESENTATION

- Digestive issues,
- Headache
- Depression
- Chronic Fatigue
- Hormonal Imbalance
- Joint Pain
- Food Sensitivity
- Memory Loss/Brain Fog
- Nutritional Deficiencies
- Other clinical conditions:
  - Crohn's disease, ulcerative colitis, IBS, celiac disease, acne, type I diabetes, MS, mental illness, obesity, allergies



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1. Mu, Q, Kirby, J, Reilly, C. M., & Luo, X. M. (2017, May 5). Leaky Gut As a Danger Signal for Autoimmune Diseases. *Frontiers*.  
2. Leaky Gut Syndrome – Failure to Maintain the Gut Barrier Can Lead to Disease or Death. *Kemir*. Published January 10, 2020.

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## LEAKY GUT

**Symptoms of Leaky Gut:**

- Diarrhea
- Malnutrition
- Weight loss/ poor absorption of macronutrients and vitamins
- Vitamin deficiency
- Nausea
- Bloating/abdominal pain
- Osteoporosis
- Kidney stones from poor calcium absorption
- Flatulence
- Weakness

**Risk factors for leaky gut:**

- Medical conditions such as Crohn's disease, celiac disease, and IBS
- Structural problems with and around your small intestine
- Abdominal surgery
- Diminished gastric acid production
- Immunodeficiency
- Aging
- Metabolic disorders

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## DIAGNOSTIC TOOLS: WHOLE GENOME SEQUENCING OF GUT MICROBIOME

- State of the art, scientifically validated stool test, using the most advanced and accurate sequencing technology
- Explores some of the many inner functions of the gut microbiome
- Identifies pathogens in your gut as well as keystone species that are crucial to overall health and metabolic functions that rely on the gut microbiome
- Actionable data leading to personalized nutrition, lifestyle, and supplement recommendations tailored to optimize your unique gut microbiome



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## MICROBIAL BLUEPRINT AND DIVERSITY

- Who is taking up real estate in your gut?
- Who are the key players- the "good" guys the "bad"?
- Do you have enough keystone (good guys) species? Are some absent or lacking?  
 Pathogens and other rare species are able to overgrow taking over a particular area of the gut
- Are your commensal ("good") and pathogenic ("bad") organisms in balance or do you have dysbiosis?
- What is your overall species richness (alpha diversity), and how does that compare to the other people living around you and in the United States (beta-diversity)?
- And as a result of your richness and diversity, how resilient is your gut to perturbations (resistome)?

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## STRUCTURE

- Dysbiosis (imbalance of good & bad bacteria) may lead to unwanted bacteria and other pathogens overgrowing, leading to gut barrier dysfunction
- What is gut barrier dysfunction?
  - A leaky gut!
  - Intestinal permeability (IP)
- Causes of IP:
  - Organisms present in higher amounts that produce ammonia, making colon more alkaline and perpetuating the survival of that species causing damage to the lining of the gut
  - Presence of methanogen-producing bacteria that are producing methane which is toxic to the mucosal barrier and cells.
    - Methane also impairs gut motility causing dysfunction that can lead to constipation
  - Hydrogen sulfide-producing organisms are extremely toxic to the cells and lining of the gut causing gut barrier dysfunction

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## FUNCTION

- Lack of microbial diversity and imbalance leads to poor metabolic function:
- Impaired immune response
- Oxidative stress disrupting the integrity of the gut mucosal barrier
- Leaky gut:
  - Low-grade chronic inflammation induced by LPS (lipopolysaccharide) endotoxemia
- Are there enough keystone species present for effective biosynthesis of vitamins, optimal production of SCFAs, neurotransmitters, and other critical substances, as well as proper estrogen recycling



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## PATHOGENESIS OF SIBO

**Abnormalities:**

- Salivary IgA
- Gastric acid
- Duodenal bile
- Abnormal GI motility
- Secretory IgA
- Ileocecal valve

**Factors Associated With SIBO:**

- Female gender
- Old-age
- IBS-D
- Marked bloating & flatulence
- PPI & narcotic intake
- Low hemoglobin



1. Ghoshal UC, Shukla R, Ghoshal U. Small Intestinal Bacterial Overgrowth and Irritable Bowel Syndrome: A Bridge between Functional Organic Dichotomy. *Gut Liver*. 2017;11(1):196-208. doi:10.5009/gnl16119.

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## PREDISPOSING CONDITIONS OF SIBO

- Achlorhydria (surgical, iatrogenic, autoimmune)
- Motor abnormalities
- Scleroderma
- Intestinal pseudo-obstruction
- Diabetic enteropathy
- Vagotomy
- Abnormal communication between colon and small bowel
- Fistulas between colon and small bowel
- Resection of ileocecal valve
- Duodenal or jejunal diverticula

- Partial obstruction of small bowel (stricture, adhesions, tumors)
- Large small Intestine diverticulosis
- Systemic diseases (celiac disease, cirrhosis, pancreatic exocrine insufficiency, non-alcoholic fatty liver disease)
- Alcoholism
- Structural abnormalities
- Systemic and intestinal immune deficiency states
- Surgical loops (Billroth II, entero-entero anastomosis, Roux-en-Y)



1. Bohm M, Swiec RM, Wo JM. Diagnosis and management of small intestinal bacterial overgrowth. *Nutr Clin Pract*. 2013;28(3):289-99  
2. Tursi A, Brandimarte G, Giorgetti G. High prevalence of small intestinal bacterial overgrowth in celiac patients with persistence of gastrointestinal symptoms after gluten withdrawal. *Am J Gastroenterol*. 2003;98(4):839-43

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## SIBO: EXTRINSIC FACTORS ALTERING GUT MICROBIOME

- Proton pump inhibitors
- Antimotility agents
- Fiber
- Prebiotics
- Probiotics
- Antibiotics
- FODMAPs
  - Fructose
  - Lactose
  - Galactans
  - Fructans
  - Sugar alcohols



FODMAPs: acronym for group of highly fermentable foods (fermentables Oligo-, Di-, Monosaccharides and polyols)



1. Chedid V, Dhalla S, Clarke JO, et al. Herbal therapy is equivalent to rifaximin for the treatment of small intestinal bacterial overgrowth. *Glob Adv Health Med*. 2014;3(3):16-24. doi:10.7453/gahmj.2014.019  
2. Bohm M, Swiec RM, Wo JM. Diagnosis and management of small intestinal bacterial overgrowth. *Nutr Clin Pract*. 2013;28(3):289-99

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## SIBO DIAGNOSIS: BREATH TESTING

- Indirect test: can be done in person or at home with a kit
- Measures fermentation: H2 and CH4
- Transit: too fast gives false positive
- Substrate
  - Glucose spec > sens
  - Lactulose sens > spec
- Flat line: consider Hydrogen Sulfide SIBO

1. Rezaie A, Buresi M, Lembo A, et al. Hydrogen and Methane-Based Breath Testing in Gastrointestinal Disorders: The North American Consensus. *Am J Gastroenterol*. 2017;112(5):775-784. doi:10.1038/ajg.2017.46

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## HYDROGEN SULFIDE SMALL INTESTINAL BACTERIAL OVERGROWTH (SIBO)

Criteria for diagnosis:

- Breath test shows flat line (no rise after 100-120 mins):
  - AND have below symptoms
  - Consider adding hydrogen sulfide specific treatment
- Chronic presentation of:
  - Digestive complaints (diarrhea, constipation, bloating, gas, etc)
  - Pain (abdominal/visceral, pancreas & bladder, joint pain)
  - Sensory (photophobia, intolerance to noise, tingling in extremities, numbness)
  - Histamine & salicylate intolerance
  - Feel "toxic" (hydrogen sulfide is a toxic gas that can damage nerves or mitochondria in excess)
  - Sulfur-containing foods and supplements worsen symptoms (Epsom salts, garlic, MSM, berberine sulfate, etc.)
  - Rare: gas smells like sulfur (or "rotten eggs")

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## TREATMENT OPTIONS FOR SIBO

The goal is to treat the underlying cause(s), contain the bacterial overgrowth, and provide nutritional support

- Remove foods that feed the bacteria in your small intestine including sugar, alcohol, and carbohydrates.
- Antibiotic therapy (Weeding)
- Prokinetic agents
  - Ginger
  - Herbal bitters (gentian root, dandelion root and leaf, burdock root)
- Herbs for weeding (berberine, oregano oil, wormwood)
- Spore forming Probiotics (soil based organisms that do not colonize the small intestine or feed the bacteria already growing there)
- Serum Bovine-derived Immunoglobulins (SBIs)
- Digestive enzymes/HCl

1. Cheddi V, Dhalla S, Clarke JO, et al. Herbal therapy is equivalent to rifaximin for the treatment of small intestinal bacterial overgrowth. *Glob Adv Health Med*. 2014;3(3):16-24. doi:10.7453/gahmj.2014.019

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## DIAGNOSIS

- Testing can be done by extracting fluids from the digestive tract with an endoscope
- Highly invasive procedure not practical for clinical practice
- Diagnosis of SIFO based on clinical evidence and empiric treatment



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## TREATMENT FOR SIFO

### Antifungal Rx:

- Standard treatment for SIFO is 3 weeks of antifungal drugs
- Fluconazole is the drug of choice
- Alternative antifungal drugs are itraconazole or posaconazole.
- Nystatin may not be as effective for SIFO because it appears to get broken down by stomach acid and may not reach the small intestine at an effective dose
- Some anti fungals have significant drug interactions



Ruzcio DM. Gut Health Expert Explains SIFO. Dr. Michael Ruzcio, BCDNM, DC. Published January 22, 2021.

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## TREATMENT FOR SIFO

### Natural Treatments:

- Probiotics (saccharomyces boulardii, spore-forming)
- Oregano
- Artemisinin
- Berberine
- Low carb diet

In a study of 181 infants, the probiotic *S. boulardii* was as effective as Nystatin (an antifungal medication) in reducing fungal infection. The infants taking probiotics had fewer side effects than the infants taking Nystatin.



Demirel G, Celik IH, Erdevce O, Saygan S, Dilmen U, Canpolat FE. Prophylactic Saccharomyces boulardii versus nystatin for the prevention of fungal colonization and invasive fungal infection in premature infants. *Eur J Pediatr*. 2013;172(10):1321-1326. doi:10.1007/s00431-013-2041-4

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## RECURRENCE OF SIFO/SIBO

- Some patients have challenging conditions that cause SIFO (and SIBO) to recur
- These patients may have underlying dysmotility
  - Scleroderma
  - Ehlers-Danlos syndrome
  - Gastroparesis
- May have had a colectomy.
- For patients who have recurrence, herbal antimicrobials may be a better choice over prescription medications.



1. Russo DM. Gut Health Expert Explains SIFO. Dr. Michael Russo, BCDNM, DC. Published January 22, 2021.

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## GUT-HORMONE CONNECTION

- Estrobolome, estrogen recycling- how gut microbiome influences this
  - 'Estrobolome,' is the enteric bacterial genes that metabolize estrogen in the microbiome
- Main forms of endogenous estrogens:
  - estradiol (most prominent in women not pregnant & before menopause),
  - estrone (prominent after menopause)
  - estriol (highest during pregnancy)
- Excess of estrogen and the inability to properly recycle it contributes to hormone-driven breast cancer in post menopausal women
- Disequilibrium in the microbiome and estrobolome may contribute to the emergence of disease
- Composition of your estrobolome might affect the risk of developing estrogen receptor-positive breast cancer in postmenopausal women



1. Kiva, M., Pflotz, C. S., Blasser, M. J. & Adams, S. (2016). The Intestinal Microbiome and Estrogen Receptor-Positive Female Breast Cancer. *Journal of the National Cancer Institute*, 108(8), djv029.

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## MODIFIABLE LIFESTYLE FACTORS & PMS, PERIMENOPAUSAL, & POSTMENOPAUSAL SX'S

- Exercise
  - Weight-bearing and strength training exercise; walking
- Diet
  - Decrease sodium- this increases skeletal health
  - Excessive caffeine accelerates bone loss
  - Plant-based calcium sources
  - Adequate vitamin D intake
  - Organic, Non-GMO soy (and other phytoestrogens)
    - Compounds in soy are similar to estradiol (the main estrogen produced by the ovaries)
  - Stress management
  - Sleep
    - Hot flashes, sleep may be disturbed
  - Adequate exercise



1. A Natural Approach to Menopause. Physicians Committee for Responsible Medicine. (n.d.).  
 2. Barrett, J. R. (2006, June). *The science of soy: what do we really know?* Environmental health perspectives. Pien, G. W. (n.d.).  
 3. *How Does Menopause Affect My Sleep?* Johns Hopkins Medicine.

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**SUPPLEMENTS FOR HORMONE BALANCE**

- Maca
  - Plant does not contain estrogen or any other phytohormones
  - Maca stimulates the endocrine system to maintain hormonal balance
  - Plant sterols and pituitary gland enhance adrenal, thyroid, testicular and ovarian function
  - Pre-, peri- & post- menopausal females
- Evening primrose oil
  - Derived from the seeds of the evening primrose plant
  - Helps relieve symptoms of depression, mood swings, breast tenderness, and bloating
  - Also helpful for women with endometriosis
  - May help reduce hot flash severity and frequency

1. Meissner, H. O., Mroziewicz, P., Bobkiewicz-Kozdowska, T., Mociś, A., Kedzia, B., Lowicka, A., Reich-Bilinska, H., Kapczynski, W., & Barzcha, I. (2006). Hormone-Balancing Effect of Pre-Gelatinized Organic Maca (Lepidium peruvianum Chacon). (3) Biochemical and Pharmacodynamic Study on Maca using Clinical Laboratory Model on Ovariectomized Rats. International journal of biomedical science : IJBS, 2(3), 260-272.

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**SUMMARY**

- Microbial diversity, balance, intact intestinal barrier, and optimal functioning of gut microbiome is of paramount importance for health maintenance and prevention of disease.
- Human genome consists of ~23,000 genes, whereas the gut microbiome encodes over 3-5 million genes producing thousands of metabolites that are responsible for over 50% of the metabolic activity in our body.
- The gut microbiomes influence over health and disease has been subject to extensive research, and is involved in maintaining human metabolism, nutrition, physiology, immune function, and mental health.
- SIBO & SIFO are two common and sometimes overlooked conditions that should be considered when addressing leaky gut, and commonly go hand-in-hand with one another

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